

Postural Reflexes, Balance Control, and Functional Mobility with Long-Duration Head-Down Bed Rest

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Introduction: Spaceflight has functionally significant effects on sensorimotor behavior, but it is difficult to separate the effects of ascending somatosensory changes caused by postural muscle and plantar surface unloading from descending visual-vestibular neural changes. To differentiate somatosensory changes from graviceptor changes in post-spaceflight sensorimotor behavior, bed rest may serve as an exclusionary analog to spaceflight. **Methods:** Four separate tests were used to measure changes in sensorimotor performance: 1) the monosynaptic stretch reflex (MSR); 2) the functional stretch reflex (FSR); 3) balance control parameters associated with computerized dynamic posturography (CDP); and 4) a functional mobility test (FMT). **Results:** A mixed model regression analysis showed significant increases in median MSR start and peak latencies, while the median FSR latency showed no significant increase. Median MSR peak magnitude showed a significant increase during the middle bed rest period (19–60 d). There were no significant effects of bed rest on balance control, but some indication that dynamic head movements may affect posture after bed rest. Time to complete the course for the FMT increased significantly with bed rest. **Discussion:** The four primary tests indicate that long-duration head-down bed rest, through unloading and modification of the body's support surface, serves as an exclusionary analog for sensorimotor responses to spaceflight. Furthermore, the data suggest that procedures designed to alleviate modifications to the sensory substrate serving the soles of the feet may provide a countermeasure to help maintain support afferentation of the postural muscles.

Keywords: spaceflight, stretch reflex, functional reflex, exclusionary hypothesis, microgravity, flight analog, posturography, sensorimotor.

SPACEFLIGHT HAS functionally significant effects on the sensorimotor system. Research from previous studies has shown that spatial orientation, balance control, locomotion, eye-hand coordination, and gaze stabilization are transiently compromised in humans during spaceflight and after return to Earth (29). Unfortunately, a complete investigation of these complex responses to spaceflight is seldom possible with in-flight protocols due to resource constraints. Furthermore, modifications within the vestibulospinal system in response to spaceflight cannot be separated from changes in the somatosensory-spinal system driven by limb unloading, or by associated cardiovascular changes. Whether modulation of the major postural muscles by changes in proprioceptive feedback from the legs and feet (bottom-up) would determine the influence of vestibulo-spinal (or top-down) input on the premotoneurons is unknown (6,16). In part, this paper is one of a series of papers on

NASA's Flight Analog Project, which is designed to lay the groundwork for a standard bed rest protocol that will allow testing of various physiological systems without the expenses associated with spaceflight.

A solution to the limitations imposed on spaceflight investigations associated with sensorimotor adaptation is to supplement spaceflight with ground-based experimental techniques that would allow simulation of select variables that are found in spaceflight and are believed to have an effect on the somatosensory-spinal system. In this context, a bed rest model can serve as an exclusionary analog, allowing differentiation of changes that are unique to induced fluid shifts and muscle unloading from those that are mediated primarily through the vestibulo-spinal system.

We conducted three related sensorimotor studies including investigations of: 1) the sensorimotor system (SMS) that was designed to specifically evaluate the monosynaptic stretch reflex (MSR) and the functional stretch reflex (FSR); 2) balance control using computerized dynamic posture (CDP) measurements; and 3) performance associated with activities of daily living (i.e., obstacle avoidance), identified as a functional mobility test (FMT). We hypothesized that long-duration, head-down bed rest would modify the basic sensorimotor reflex components necessary for complex motor behavior, including upright stance and effective goal-directed movement.

METHODS

Study methods are as described by Meck et al. (23). Bed rest and test protocols were reviewed and approved by the Johnson Space Center Committee for the Protection of Human Subjects, the UTMB Institutional Review Board, and UTMB General Clinical Research Center Science Advisory Committee. Subjects received verbal

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and written explanations of the bed rest and test protocols prior to providing written informed consent.

Subjects

Overall, 12 of 13 subjects were shared among the 3 experiments (SMS, CDP, and FMT). Of these subjects, 12 were shared between SMS and FMT, and 8 were shared among all 3 tests. One subject was dropped from the analysis for noncompliance with all three experimental protocols.

SMS

Data from three pre-bed rest test sessions were obtained for the SMS portion of the investigation, and measurements were made during bed rest just prior to reambulation of the subjects on bed rest days BR59, BR60, or BR90 (depending on the subject) and post-bed rest on BR+0, BR+3, and BR+5/7. For those subjects who were evacuated due to Hurricane Rita, measurements were obtained during bed rest on days BR42, BR44, or BR49 for three of the subjects and once just after reambulation for the fourth subject.

CDP

Valid balance control data were collected for only eight subjects due to foot soreness (three subjects) or noncompliance (two subjects). These data were obtained twice prior to bed rest, on BR+0, and on 2-4 additional recovery days, up to BR+12. In addition data were collected on approximately day BR61 during the 90-d studies. Data were collected on days BR42, BR44, or BR49 for the evacuated subjects.

FMT

FMT data were collected twice prior to bed rest, and on BR+0. Data were also collected on approximately day BR+61 during the 90-d studies, and on days BR42, BR44, or BR49 for the evacuated subjects (23).

Apparatus

SMS apparatus: Data for the first seven subjects were collected using a Cybex NORM system (CSMI, Stoughton, MA) configured for left ankle dorsiflexion/plantarflexion with the subject in the prone position. For the MSR trials the dynamometer was set to essentially freewheel ($500^\circ \cdot \text{s}^{-1}$ velocity limit in each direction). For trials looking at the combined MSR and FSR, the dynamometer was set at the velocity limit of $500^\circ \cdot \text{s}^{-1}$ in the dorsiflexion direction and $15^\circ \cdot \text{s}^{-1}$ in the plantarflexion direction. An aluminum bar was attached to the foot restraint to provide leverage when struck with a force hammer (Model 9724A50000, Kistler Instruments, Winterthur, Switzerland) to elicit reflexes. For subjects 8–13, the data were collected using a device developed specifically for rotating the foot around the ankle joint. As with the Cybex, the device was configured for left ankle dorsiflexion/plantarflexion in the prone position. The device consists of a NeuroKinetics Inc. (Pittsburgh,

PA) 80 ft-lb DC servomotor controlled via position feedback. The footplate was under computer control for all trials. For conditions eliciting the MSR, the motor provided a step input in the dorsiflexion direction and then returned to the starting position. For trials combining the MSR and FSR, the motor provided a step input in the dorsiflexion direction and then held this position for 3 s before returning to the starting position.

Electromyographic (EMG) data were collected using a Bagnoli-8 EMG amplifier system (Delsys Inc., Boston, MA). Supplementary data (hammer force, dynamometer torque, velocity, and position) were also collected simultaneously. All data were digitized via a 16-bit data acquisition card (Model DAQCard-6036E for subjects 1–7 and Model PCI-6229 for subjects 8–13, National Instruments, Austin, TX) and were sampled at 4000 Hz.

CDP apparatus: A modified commercial CDP system (Equitest, NeuroCom International, Clackamas, OR) was used to evaluate balance control. Subjects stood upon the CDP system force plate, which was used to monitor the ground reaction forces exerted by their feet (24). The first three subjects had post-bed rest foot tenderness that interfered with their ability to comply with the test protocol. Thereafter, the protocol was modified so that the remaining subjects stood on thin Pudgee foam (polyurethane open-cell gel-foam, Dynamic Systems, Inc., Leicester, CA) pads (0.95 cm thick, $480 \text{ kg} \cdot \text{m}^{-3}$ density) to alleviate the foot soreness without compromising balance control performance. Audio communications were provided to the subject via headphones, which also delivered a low-amplitude broadband auditory noise to mask any extraneous auditory cues and provided a cadence to synchronize head movements on select trials. Infrared markers placed on the headset frame were used to quantify head position using an OptoTrak System (Model 3020, Northern Digital Inc, Ontario, Canada). A safety harness and spotter were used to support the subject in the event of loss of balance.

FMT apparatus: The FMT was an obstacle course set up on a base of 10-cm thick medium-density foam (Sunmate Foam, Dynamic Systems, Inc., Leicester, NC). The foam base introduced a proprioceptive challenge into the otherwise normal walking task. The 6.0 m \times 4.0 m course consisted of five vertical foam pylons arranged in a slalom fashion, a 46-cm foam hurdle, a “portal,” and a “gate” (Fig. 1). The portal obstacle was comprised of two successive 31-cm foam hurdles with a horizontal foam bar suspended between them. The horizontal foam bar was adjusted to the height of each subject’s shoulders. The portal required subjects to step over hurdles while bending at the waist to duck under the horizontal foam bar. The gate obstacle was comprised of two vertical foam pylons adjusted to each subject’s shoulder width, requiring the subject to ‘squeeze’ through the pylons without touching them.

Procedures

SMS procedures: Subjects lay prone on the apparatus with their left foot strapped to a foot restraint that

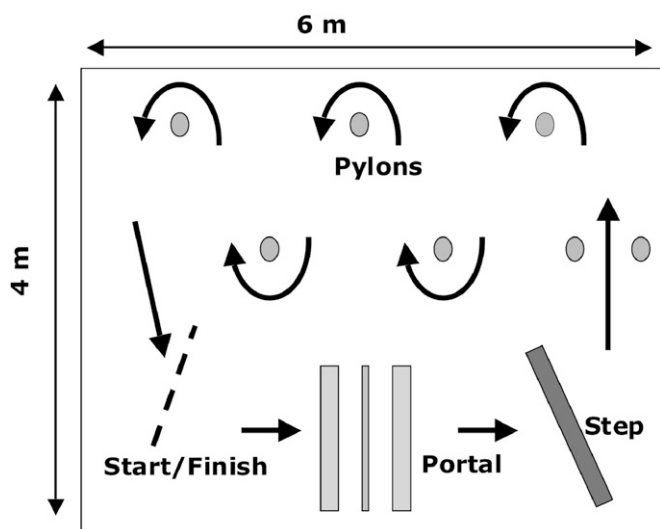


Fig. 1. The Functional Mobility Test performance course.

allowed rotation of the center of the ankle joint about the center of either the dynamometer (Cybex) or motor shaft (NeuroKinetics) on the servo-controlled system. Active EMG electrodes were placed on the triceps surae and anterior tibialis of the left leg with the reference electrode placed on the lateral malleolus. A surgical marker was used to mark the location of each electrode site to maintain the same placement for each test session.

For both the MSR and the FSR trials, the subject's foot was dorsiflexed 5° with respect to the foot's normally relaxed position. The reflexes were elicited by either striking a bar extended from the footplate with a force hammer, or moving the foot with the servomotor, causing the foot to rapidly dorsiflex. For the MSR, the subject was instructed to, "Stay relaxed, do not respond to the stimulus." For the FSR, a time optimal procedure was used and the instruction was, "As soon as you feel the stimulus, plantarflex your foot as quickly and as forceful as possible." For both cases, the time between stimuli were randomized with intervals no shorter than 5 s. During each test session, a minimum of 20 MSR and 6 FSR trials were collected with tendon stretch amplitudes ranging from 1 to 10° in magnitude.

CDP procedures: The six standard CDP sensory organization test (SOT) conditions allow for examination of the somatosensory contributions to postural sway by comparing fixed support surface conditions (SOT 1–3) with sway-referenced support surface conditions (SOT 4–6). They also allow for examination of visual contributions to postural sway by comparing eyes-open (SOT 1&4), eyes-closed (SOT 2&5), and sway-referenced vision (SOT 3&6) conditions. During sway-referenced trials, the orientation of the support surface and/or visual surround is servo-controlled to tilt in direct proportion to the subject's body tilt in the sagittal plane. The role of vestibular contributions is usually inferred from performance on SOT 5&6, since somatosensory and visual cues are experimentally altered during those conditions. Since we did not anticipate any effects of bed rest on vestibular function, we considered these conditions to

be redundant and chose not to use SOT 6. Thus, during each test session, subjects performed SOT 1–5. However, to increase the sensitivity of the test paradigm in eliciting subtle changes in balance control performance, subjects 8–13 also performed head tilt posturography: additional SOT 2 and SOT 5 trials were performed with static and dynamic head tilts.

Subjects stood on the CDP platform, their ankle joints were aligned with the rotational axis of the support surface (and visual surround), and the safety harness was attached. For all tests, subjects were instructed to maintain natural upright posture with arms folded across the chest. Each 20-s standard SOT trial was performed with normal, absent, or sway-referenced visual conditions and a fixed or sway-referenced support surface. During the sway-referenced conditions, the foot support surface and/or visual surround was dynamically rotated (about an axis through the ankle joints) in the sagittal plane in direct proportion to the subject's estimated instantaneous center-of-mass (COM) sway angle. During each test session a maximum of three repetitions were performed for each of the five SOT conditions.

All head tilt posturography trials were performed with eyes closed. Prior to each static head tilt trial, subjects actively pitched their heads back (from vertical) by approximately 20° and attempted to maintain that head position throughout the trial. Prior to each dynamic head tilt trial, subjects began to perform continuous $\pm 20^\circ$ sinusoidal pitch plane head oscillations, paced by a 0.33-Hz audible tone, and attempted to maintain one complete head oscillation cycle every 3 s throughout the trial. During each test session, subjects performed a maximum of three trials for each head tilt condition with fixed support (SOT 2) and with sway-referenced support (SOT 5) conditions.

FMT procedures: Subjects walked in bare feet or socks at a preferred pace through the course, beginning and ending each trial at a start/finish line marked on the foam floor. They were instructed to complete the course as quickly as possible without running and without touching any of the obstacles. This task was performed three times in the clockwise direction and three times in the counterclockwise direction in a randomized order for a total of six trials during any given session. The dependent measure for each trial was time to complete the course (TCC), measured in seconds. Subjects wore a safety harness for all sessions. For post-bed rest sessions, two spotters accompanied subjects around the course to support them in case of a loss of balance.

Data Analysis

SMS data analysis: The data were processed using scripts developed in Matlab (Version 7, The Mathworks, Natick, MA) software and reduced into four stretch-reflex features (MSR start latency, peak latency, peak magnitude, and FSR latency). Data for each of these features were retained for a particular test type (MSR or FSR) for further analysis. Fig. 2A illustrates the three MSR features, while Fig. 2B shows the FSR latency feature. All

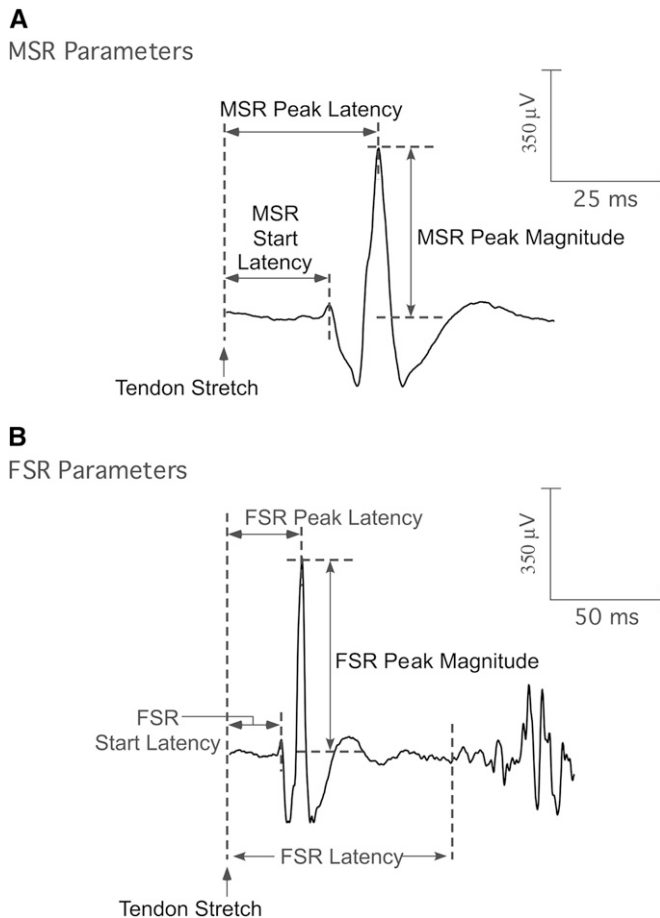


Fig. 2. A) Representative MSR response with the points used to calculate start latency, peak latency and peak amplitude. B) FSR latency calculation.

four features were measured repeatedly over multiple trials (usually 9 or 10) during 6–11 sessions per subject, each session taking place on a different day. Although about 20 MSR trials and 6 FSR trials were originally collected, only the tendon stretches that were 8° or more were included in the analysis since there were no differences in the tendon reflex features in stretches 8° and higher. To prevent outliers from unduly influencing subsequent analysis, the data were then collapsed to the median within a session for each subject and then transformed logarithmically for the next analysis phase.

For each feature, log transformed medians were fit to Gaussian linear regression models with random effects and interactions (9) with bed rest to explain intersubject variability. From the fitted models, we tested for significant effects of short (18 d or less), medium (19–60 d), or long (61–90 d) duration on mean log latency or log amplitude. In addition, we calculated interval estimates for the probability that a randomly selected subject would experience at least a given percent increase in each type of latency or magnitude relative to his/her mean pre-bed rest level, after a short, medium, or long period of bed rest. In fitting the models, data were augmented with similar SMS features obtained prior to bed rest for two additional NASA studies so that more reliable estimates of within and between-subject variation could be

obtained. These additional studies were designed to test countermeasures during bed rest; however, data prior to bed rest was gathered using a protocol similar to that used in subjects 1–3 and 8–11, and could thus be incorporated into this analysis without bias. There were not enough post-bed rest measurements to estimate an exponential recovery model, but we used the above technique to obtain 90% confidence limits for the percent change between the population median at BR+0, BR+3, BR+5, and BR+7 d post-bed rest, and the pre-bed rest median for each SMS feature.

CDP data analysis: COM sway angles were estimated from instantaneous anterior-posterior center-of-force positions computed from the normal force transducers mounted within the Equitest force plates (25). The peak-to-peak COM sway angle, θ , from each 20-s trial was used to compute an equilibrium score (EQ) from: $EQ = 100 \times [1 - (\theta/12.5)]$, where 12.5° is the maximum theoretical stable peak-to-peak sway in the sagittal plane. For $\theta \geq 12.5^\circ$, the trial was scored as a fall and the EQ was set to zero.

Since balance control was expected to be unaffected by bed rest, our initial analyses were limited to a comparison between pre- and the first post-bed rest test session. Statistical analysis of EQ scores is confounded by a non-normal distribution of EQ scores in normative populations as well as by “falls” which are singular, discrete events that cannot be considered part of a continuous EQ distribution. We have previously developed a mixed discrete-continuous beta distribution model (11) that was used in this study to characterize the population performance. Beta distributions were fit to EQ scores for pre- and post-bed rest test sessions. From the estimated beta parameters, we obtained point estimates of the following: 1) the ratio of medians (post/pre); 2) the ratio of fifth percentiles (post/pre); and 3) the probability of a post-bed rest EQ score being less than the fifth percentile of the pre-bed rest EQ distribution. Using the delta method (12) applied to these estimates and their covariance matrices, we then obtained approximate standard errors and 90% confidence limits for 1, 2, and 3.

FMT data analysis: The FMT was used to quantify changes in subjects’ locomotor control following the bed rest period. Two discrete pre-bed rest sessions and one post-bed rest session were evaluated. Each subject’s “normal” (pre) response was determined by calculating the average TCC measurement across the 12 pre-bed rest trials spanning the 2 discrete pre-bed rest sessions (6 trials per session). A similar procedure was adopted to quantify each subject’s performance on the first day after bed rest (post), by calculating the average TCC measurement across the six trials performed during this test session.

With regard to locomotion, studies have shown that body loading is of particular importance as a somatosensory input because it is essential for modulation of motor control during locomotion (8), particularly with regard to shaping motor output patterns during stepping (10,14), for controlling balance and posture during locomotion, and the termination of locomotion (8,14,27).

In order to assess the impact of applying pressure to the soles of the feet through “foot massages” during bed rest, a paired *t*-test was performed across all the subjects’ average pre- and post-measurements in the two groups. Further, the percentage change in the TCC of the mean post-bed rest performance relative to their corresponding pre-bed rest performances were also calculated for each subject. These average percentage changes in TCC for the group of subjects 1–3 (no foot massage) were then compared with those calculated across subjects 4–13 (with foot massage) using a student’s *t*-test. FMT data were analyzed at a significance level of 0.05 using a standard statistical software package (SPSS v. 10.0, Chicago, IL). CDP and SMS data were analyzed using Stata statistical software (1)

RESULTS

SMS Results

A short descriptive summary of the four stretch-reflex features is shown in **Table I**. The effect of even a week or two of bed rest, estimated from the mixed model regression analysis, showed that the population median start and peak latencies were increased by about 4.2% and 3.7%, respectively. Both of these increases were more than could be attributed to chance variation; *P* = 0.019 (start latency) and *P* < 0.001 (peak latency). However, there was no significant further increase in either latency as stays in bed increased to 90 d. On the other hand, median peak magnitude did not noticeably increase at the start of bed rest (0–18 d), but was estimated to increase by about 47% (*P* = 0.003) during the middle bed rest period (19–60 d). Peak magnitude measurements were much more variable than the start and peak latencies, thus there were too few subjects and measurements available to evaluate the possibility of a substantial increase during early or late bed rest. No significant change was observed during any bed rest period for FSR latency. **Fig. 3A and B** show the respective estimated probabilities of a particular subject increasing his/her start and peak latency (with respect to a pre-bed rest average over three sessions) by a given percentage (abscissa) during bed rest, with 95% confidence limits. Note that these calculations are for change in a specific subject’s median response, not the change in the population me-

dian. In general, percent changes for individuals can be much larger than percent changes in population medians. Finally, **Fig. 3C** shows the probability of a given percent increase in peak magnitude during the middle period of bed rest. Note that this measure may very well change by a factor of 2 or more relative to a pre-bed rest average.

Fig. 4 shows point estimates and 95% confidence intervals (CI) for the percent difference between the population median of each stretch reflex feature after bed rest and the corresponding pre-bed rest median. These plots show that start latency was back to normal by the third day after bed rest, while peak latency and peak magnitude appeared to take somewhat longer to recover—perhaps 4 or 5 d. We did not see any significant change in FSR latency during any part of the bed rest period, so it is not surprising that there was no discernable trend of this feature during the recovery period.

CDP Results

Data were analyzed from 8 of the 13 subjects participating in the CDP testing. In addition to the subject excluded from all sensory-motor analyses for noncompliance, one subject was excluded from CDP analyses due to nausea upon reambulation, and subjects 1–3 were excluded from CDP analyses because post-bed rest foot (plantar surface) soreness interfered with their abilities to comply with the test performance requirements (standing as still as possible). To reduce any variance associated with bed rest duration, we selected the post-bed rest data points closest in time for analysis. Nevertheless, the bed rest durations included in the analyses ranged from 42 to 63 d.

All eight subjects completed SOT 1–5 before bed rest, and their scores were all within normal ranges for these standard tests (24). On the day of reambulation following 42–63 d of bed rest, the ratios of pre-/post-bed rest EQ scores indicated a small decrement in each of the standard SOT (range = 0.945 to 0.990); however, the 90% CI encompassed a ratio of 1.00 (no change) in all but SOT 4, where the CI ranged from 0.904–0.985. Similarly, the probability that a post-bed rest EQ score would fall below the pre-bed rest fifth percentile EQ score only appeared to be increased in SOT 4 and 5 to 0.176

TABLE I. MINIMUMS, MAXIMUMS, AND MEDIANS FOR THE FOUR STRETCH REFLEX PARAMETERS.

Feature	Type	Bed Rest Period	No. of Subjects	No. of Trials	No. of Sessions	Min	Median	Max
Start Latency	MSR	pre	35	4121	105	32.5	54.5	95
		in	12	1462	49	31.3	51.5	72.3
		post	9	673	24	31.5	44.5	62.8
Peak Latency	MSR	pre	35	4041	105	44.8	66.3	86.3
		in	12	1454	49	44.8	64.8	99.5
		post	9	672	24	46.3	56.8	73.8
FSR Latency	FSR	pre	34	985	102	78	152.8	378.5
		in	12	453	49	98.3	172.7	353.5
		post	9	228	24	105.6	173.2	399.9
Peak Magnitude	MSR	pre	35	983	105	8.3	346.1	2166.3
		in	12	476	49	48.2	461.9	3085.5
		post	9	238	24	6.4	465.4	2442.8

MSR = monosynaptic stretch reflex; FSR = functional stretch reflex.

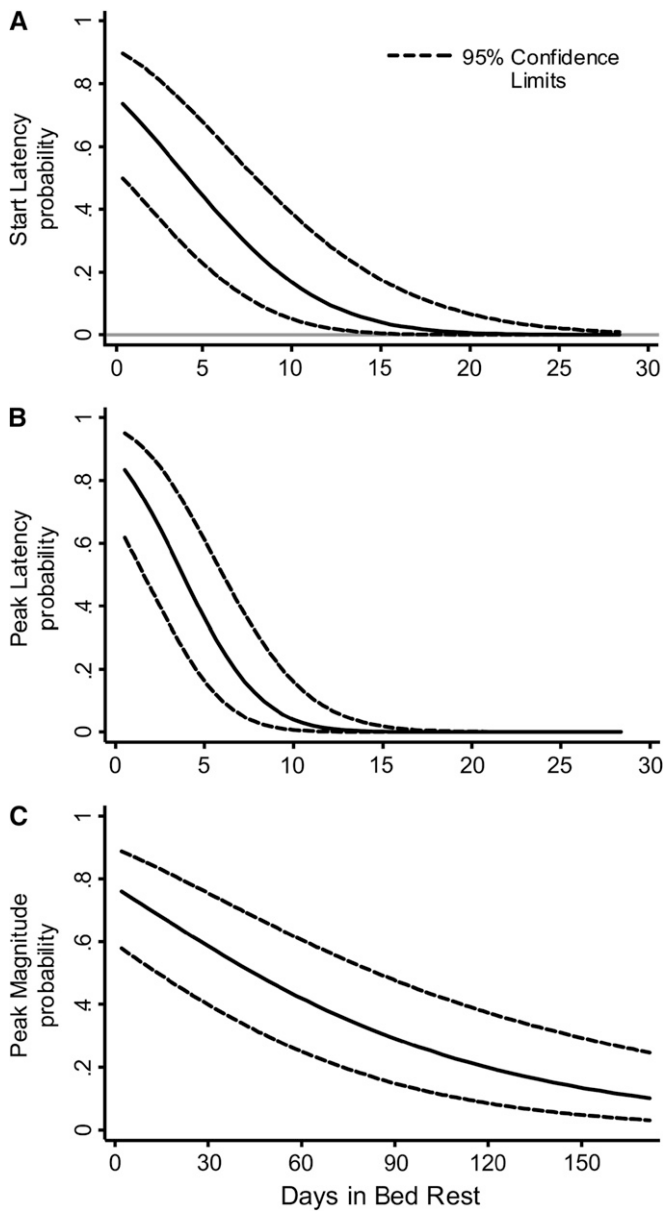


Fig. 3. Effect of 5 d of bed rest on start latency showing the estimated probability that a subject will increase MSR: A) start latency, B) peak latency, and C) peak amplitude by a certain percent with 95% confidence limits indicated by the dashed lines.

(CI: 0.062–0.407) and 0.209 (CI: 0.062–0.514), respectively, but the lower limit of the broad CI were only slightly above the pre-bed rest level of 0.050.

Five of the eight subjects also completed head-tilt posturography tests before and after bed rest. The small *N* precluded similar statistical analyses of the data from these tests, but qualitatively, performance on head tilt tests appeared to be somewhat more challenging after bed rest than it was on the static tests.

FMT Results

Fig. 5 shows the pre- and post-bed rest average (\pm 1 SEM) of the TCC (s) performance from subjects 1–3, who did not receive foot massage, compared to subjects 4–13, who did receive additional foot massage. Subjects in

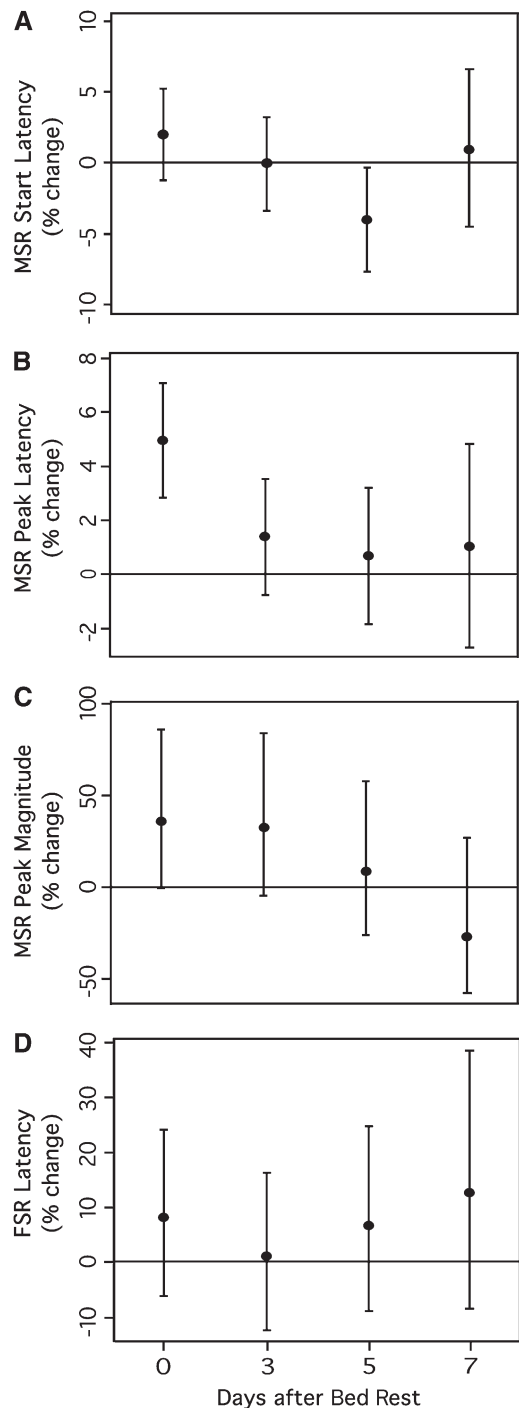


Fig. 4. Percent difference between population median of pre-bed rest: A) MSR start latency, B) MSR peak latency, C) MSR peak amplitude, and D) FSR latency, and the post-bed rest days. Error bars show the 95% confidence limits.

both groups showed a significant increase in their TCC response times after 60 d of bed rest ($P < 0.05$) in comparison to their pre-bed rest performance. Subjects 1–3 showed a 94% increase in TCC while subjects 4–13 showed a 27% increase in TCC. Further, comparison between the pre- to post-bed rest percentage change of the TCC (s) performance across subjects in the two groups show that subjects 1–3, who were not given additional foot massages during bed rest, had significantly ($P <$

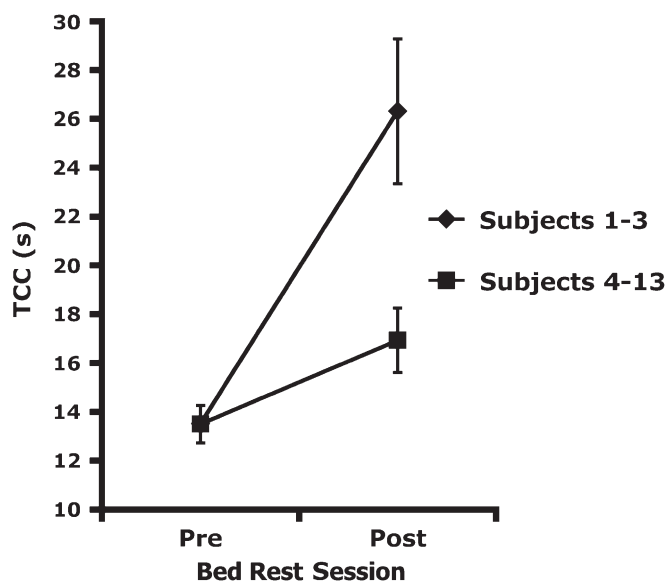


Fig. 5. Average (± 1 SEM) of the time to complete the FMT course across all subjects pre- and post-60 d of bed rest.

0.05) larger average percent changes in TCC after bed rest compared to subjects 4–13, who did receive foot massage.

DISCUSSION

The results of the current investigations offer support that head-down bed rest can serve as a useful exclusionary analog that is helpful in distinguishing the effects of spaceflight on the sensorimotor system from those adaptative responses that occur alone in response to muscle unloading. The second concept for discussion concerns the underlying differences in responses that were observed between subjects who did and subjects who did not receive foot massage during bed rest. While there was not a reason to believe that the sensorimotor responses across groups would be different, the results for all the sensorimotor investigations (reflex, posture, and mobility) suggest that there was a difference in the way the subjects responded with or without the foot massage. A plausible explanation is that the first three subjects tested in each of the sensorimotor investigations simply had sore feet and could not complete the posture tests. They had similar complaints during the tilt tests, described in Platts et al. (28) within this issue. However, other explanations are possible.

Stretch Reflex and FSR Function in Response to Bed Rest and Spaceflight

The stretch reflex and FSR are primary components involved in the maintenance of postural stability and locomotion. The typical latency of a stretch reflex recorded from the triceps surae is approximately 40 ms, while the same muscle complex shows that the earliest detectable contraction in response to an imposed sway of the standing subject occurs with a latency of about 120 ms. It is reasoned that a response with this latency must be supraspinal rather than segmental like the stretch or

T-reflex. This conclusion was confirmed by the absence of this long latency reflex, identified as the FSR, in patients with spinal transections or post central lesions (4). Evidence that the FSR is critical to postural performance and locomotion was first described by Gurfinkel and his colleagues (13) when they did not find evidence of a long latency reflex with ankle rotation in a standing subject, but did evoke a long latency reflex when the body swayed about the ankle joint. The conclusion was that the FSR activation requires additional sensory input to inform the major postural muscles that sway is present.

In 1975, two short bed rest studies (14 and 28 d, respectively) in which the subjects remained horizontal, were conducted by NASA at the Johnson Space Center to address some of the changes observed during the Skylab spaceflights (15). As a part of these studies both postural performance and motor responses were obtained before and after bed rest. The postural testing was a follow-on to the marked ataxia that was documented following spaceflight (15), and the sensorimotor testing (Achilles tendon stretch reflex and the Hoffmann reflex) was done to complement the observation that the stretch reflex was potentiated following spaceflight (2,15). While the results of these two bed rest studies did not show changes in postural stability, there was a transient hyperreflexia observed in both the stretch and Hoffmann reflexes (H-reflex) recorded immediately following bed rest.

There is now considerable evidence to suggest that spaceflight has a rather significant effect on motor behavior. Building on the Skylab observation of a post-flight potentiation of the stretch reflex (2), a number of experiments, both in flight and postflight, have been conducted. Four such tests were performed during the first Spacelab (SL-1) spaceflight aboard the Space Shuttle. The H-reflex showed a gradual decline in flight followed by an increase immediately postflight, with a return to preflight levels over a number of days. In a related experiment (32), otolith-spinal reflexes were elicited by sudden, unexpected falls. EMG activity recorded early in flight from the triceps surae during the fall declined in amplitude as the spaceflight progressed, and returned to normal by 3.5 h after landing. In a third experiment (32), soleus muscle potentials in response to a sudden unexpected linear translational platform movement imposed on a standing subject showed that muscle response latency was greater immediately postflight (comparable to what we have observed in the present study). In the fourth experiment, the postflight posture platform test (32), the crewmember’s erect posture was tested by pitching the platform base about the ankle joint. The EMG activity from the tibialis anterior and gastrocnemium muscles showed that the early reflex activity did not change as a function of spaceflight. However, EMG activity which occurred later than 500 ms showed higher magnitudes than those recorded preflight, suggesting that there is perhaps a secondary central reflex that can be used to help maintain posture. The results from the current series of bed rest studies suggest that the previous spaceflight sensorimotor studies

may have been impacted by more than microgravity effects on the vestibular system. Muscle unloading clearly plays a significant role in the changes observed in both spaceflight and bed rest.

Postural Responses Following Bed Rest and Spaceflight

Spaceflight crews typically exhibit performance decrements immediately after spaceflight in all of the standard CDP sensory organization tests. The greatest functional deficits are observed in SOT 5 and 6, which are most sensitive to altered vestibular information processing (26). Recent testing of long-duration crews demonstrated that head tilt posturography is more sensitive than the standard CDP protocol in this population, registering performance decrements well after performance on the standard SOT has recovered (17). To our knowledge, CDP has not previously been used to assess modifications in postural stability following long-duration bed rest. In the current study, we observed no significant decrements in performance on a standard battery of CDP sensory organization tests, suggesting that either no functionally significant change occurred or that the standard battery was insensitive to those changes that did occur. However, we were able to make qualitative observations of performance decrements in the limited number of subjects who performed the more sensitive head tilt posturography tests. This suggests that there might be some measurable decrements in balance control performance associated with bed rest, but more data will be required for validation. If true, it is possible that these decrements could result from a change in the central estimation of the gravitational orientation reference (see above) owing to either an altered canal-otolith relationship driven by prolonged tilt of the utricular macula with respect to the gravity vector or, more likely given our FSR results, to a modulation of the proprioceptive-spinal reflex response from the central nervous system that is in conflict with ascending input from the major postural muscles.

Functional Mobility Following Bed Rest and Spaceflight

The FMT was developed to quantify an individual's functional performance. In a recent comparison of common balance tests, the FMT, as used in this bed rest analog, correctly classified 88% of clinical patients with vestibular and balance disorders, outperforming the success rates of the more standard testing counterparts: Dynamic Gait Index, Time Up and Go, and the Berg Balance Scale (5). FMT data, used in conjunction with complementary test data, may highlight cases in which a subject's central nervous system has reorganized its subcomponents to compensate for sensorimotor deficits. Hence, FMT data is most revealing when combined with other metrics of recovery of the sensorimotor system.

Although all subjects received body massages in the current study, there appeared to be a marked difference in the subjects who did and did not receive a daily foot massage to ameliorate the tenderness of the soles of the

feet as a planned countermeasure. It is unfortunate, given the current experimental design, that we cannot separate the importance of the foot soreness on our results versus underlying changes in proprioceptive function. The subjects who had sore feet (subjects who did not receive foot massage) performed much worse after bed rest (94% increase in time) compared to those who did not have sore feet (subjects who did receive foot massage, 27% increase in time). In comparison, data from subjects who have been in space for 180 d have shown a 50% change in their TCC on the same task. The difference between the spaceflight and bed rest results reflects the fact that bed rest mimics only sensory changes associated with axial body unloading without the concomitant adaptive changes in the vestibular system that is typical from spaceflight.

Sensorimotor Response Difference Across Bed Rest Studies

The data are complicated by two factors. First, all subjects were not in head-down tilt for the same duration. The first three subjects were in bed rest for 60 d. Four subjects were evacuated due to Hurricane Rita. The rest were in bed rest for 90 d. However, 60-d data were obtained from those subjects, making fairly consistent data collection near 42 and 60 d. Second, although daily body massages were given to all bed rest subjects, they were augmented after the first three subjects with a daily foot massage to ameliorate the tenderness of the soles of the feet. This additional foot massage, given to subjects 4–13, has played an important role in the interpretation of study results, and may be a driving factor in providing a potential countermeasure associated with sensorimotor function.

The evidence that foot massage may serve as an effective countermeasure to limb unloading in head-down bed rest comes from the differences in FSR latency observed across groups. There were delays in FSR latency for the first three subjects while the remaining subjects showed less of a delay around day 60. One subject, in fact, had a shorter response time on day 60 compared to pre-bed rest. When bed rest was completed, two of the first three subjects showed delays even 7 d post-bed rest while the other subjects returned to baseline very quickly. For the stretch reflex, the first three subjects all showed an increased latency while the majority of the remaining subjects had either a decreased latency or no change compared to their baseline.

The potential of massage as a countermeasure has been supported by other investigations. In a recent study assessing the effects of changes in somesthetic plantar information on upright quiet stance in healthy subjects, application of a rotary plantar massage under the feet for 10 min resulted in reduced sway measurements along the medial-lateral plane during quiet standing (3). More importantly, these data suggest foot massages do help the postural control system during quiet upright stance. Kozlovskaya et al. (18–20) have reported that, upon analyzing the countermeasures used by the crewmembers of different spaceflight durations, the postural

control changes were reduced when there was an increase in the support loads in spaceflight. This was further corroborated by the results from Layne et al. (21), which showed an increase in the support surface reaction force and an increase in the magnitude and duration of the activation of flexor and extensor muscles during an arm raise task in microgravity. Also, other experiments by Roll et al. (30,31) in microgravity report that the “lift illusion” in response to ankle muscle vibration gave way almost instantaneously to an illusion of anteroposterior body tilt (the same as in 1 G) as soon as braces were used to replicate the missing axial ground pressure forces. These studies point to the importance of support unloading in the genesis of ataxia upon return to the 1-G Earth environment as a result of exposure to microgravity (18–20). However, since there were only three subjects who did not receive foot massages in comparison to the larger group of subjects that did in the subsequent studies, a larger group will be required to validate the results reported on the changes in sensorimotor performance parameters after head-down bed rest.

Conclusions

The results of the sensorimotor studies conducted as a part of long-duration head-down bed rest support the concept that unloading through bed rest can serve as an exclusionary analog to spaceflight. This observation is important because it suggests that bed rest is an appropriate paradigm that will allow investigators to differentiate between the bottom-up modifications in posture and locomotion due to unloading and the top-down changes associated with visual-vestibular adaptation to spaceflight. There is a good deal of evidence that supports this view. For example, it is possible to hypothesize that body loading is a fundamental parameter that modulates motor output during upright stance and locomotion (7). Loading, as an independent sensory input, is essential for controlling the generation of stepping patterns, balance, posture during locomotion, and the termination of locomotion (8,14,22,27). With spaceflight alone, it is not possible to separate the modification in load due to microgravity and the adaptive changes to the visual-vestibular system that are believed to be necessary for improved performance in a weightless environment. Coupled with the results from the current study, bed rest or another analog (dry immersion), may be a mandatory control to differentiate unloading from the overall effects of spaceflight. Furthermore, given the effect of foot massage in this study, it may be useful to implement a similar procedure during flight as a way of addressing the bottom up component as a potential flight countermeasure.

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REFERENCES

1. Stata statistical software, 9 ed. College Station: Stat Corp, L.P.; 2005.
2. Baker JT, Nicogossian AE, Hoffler GW, Johnson RL, Hordinsky JR. Changes in the Achilles-tendon reflexes following Skylab missions. Biomedical results from Skylab. Washington, DC: U.S. Government Printing Office; 1977. Report No.: NASA SP-377.
3. Bernard-Demanze L, Burdet C, Berger L, Rougier P. Recalibration of somesthetic plantar information in the control of undisturbed upright stance maintenance. *J Integr Neurosci* 2004; 3:433–51.
4. Chan CW, Jones GM, Kearney RE, Watt DG. The 'late' electromyographic response to limb displacement in man. I. Evidence for supraspinal contribution. *Electroencephalogr Clin Neurophysiol* 1979; 46:173–81.
5. Cohen HS, Kimball KT, Bloomberg JJ, Mulavara AP. Usefulness of current standardized balance tests for determining if balance-impaired individuals differ from normals. The Seventh Symposium on the Role of the Vestibular Organs in Space Exploration; June 7-9, 2006; Noordwijk, the Netherlands. Paris, France: ESA; 2006.
6. Dietz V, Baaken B, Colombo G. Proprioceptive input overrides vestibulo-spinal drive during human locomotion. *Neuroreport* 2001; 12:2743–6.
7. Dietz V, Duysens J. Significance of load receptor input during locomotion: a review. *Gait Posture* 2000; 11:102–10.
8. Dietz V, Muller R, Colombo G. Locomotor activity in spinal man: significance of afferent input from joint and load receptors. *Brain* 2002; 125(Pt. 12):2626–34.
9. Diggle P, Liang KY, Zeger SL. Analysis of longitudinal data, 1st ed. New York: Oxford University Press; 1995.
10. Duysens J, Clarac F, Cruse H. Load-regulating mechanisms in gait and posture: comparative aspects. *Physiol Rev* 2000; 80:83–133.
11. Feiveson AH, Metter EJ, Paloski WH. A statistical model for interpreting computerized dynamic posturography data. *IEEE Trans Biomed Eng* 2002; 49:300–9.
12. Green WH. Economic analysis, 4th ed. Upper Saddle River: Prentice Hall; 2000.
13. Gurfinkel VS, Lipshits MI, Popov KE. [Is the stretch reflex a basic mechanism in the system of regulation of human vertical posture?]. *Biofizika* 1974; 19:744–8.
14. Harkema SJ, Hurley SL, Patel UK, Requejo PS, Dobkin BH, Edgerton VR. Human lumbosacral spinal cord interprets loading during stepping. *J Neurophysiol* 1997; 77:797–811.
15. Homick JL, Reschke MF, Moore MJ, Anderson DJ. Vestibular system evaluation. In: Johnson PC, Mitchell C, eds. Report of 28-day bedrest simulation of Skylab, Vol. II. Washington, DC: NASA; 1976:11-135. Report No.: NASA SP NAS 9-14578.
16. Horak FB, Earhart GM, Dietz V. Postural responses to combinations of head and body displacements: vestibular-somatosensory interactions. *Exp Brain Res* 2001; 141:410–4.
17. Hwang EY, Paloski WH. Head tilt posturography to enhance balance control assessment for astronauts: a case study. Seventh Symposium on the Role of the Vestibular Organs in Space Exploration; June 7-9, 2006; Noordwijk, The Netherlands. Paris, France: ESA; 2006:32–3.
18. Kozlovskaya I, Dmitrieva I, Grigorieva LS, Kirenskaya A, Kreydich Y. Gravitational mechanisms in the motor system. Studies in real and simulated weightlessness. In: Gurfinkel VS, Ioffe ME, Massion J, eds. Stance and motion. New York: Plenum; 1988:37–48.

19. Kozlovskaya IB, Aslanova IF, Grigorieva LS, Kreidich Yu V. Experimental analysis of motor effects of weightlessness. *Physiologist* 1982; 25:S49–52.
20. Kozlovskaya IB, Kreidich YV, Rakhmanov AS. Mechanisms of the effects of weightlessness on the motor system of man. *Physiologist* 1981; 24:559–64.
21. Layne CS, Lange GW, Pruett CJ, McDonald PV, Merkle LA, Mulavara AP, et al. Adaptation of neuromuscular activation patterns during treadmill walking after long-duration space flight. *Acta Astronaut* 1998; 43:107–19.
22. Maegele M, Muller S, Wernig A, Edgerton VR, Harkema SJ. Recruitment of spinal motor pools during voluntary movements versus stepping after human spinal cord injury. *J Neurotrauma* 2002; 19:1217–29.
23. Meck JV, Dreyer SA, Warren LE. Long-duration head-down bed rest: project overview, vital signs, and fluid balance. *Aviat Space Environ Med* 2009; 80(5, Suppl.):A1–8.
24. NeuroCom International I. EquiTest system operations manual, version 7.04. Clackamas, OR: NeuroCom International; 2000 August. Report No.: EQTN D-1.
25. Paloski WH, Black FO, Reschke MF, Calkins DS, Shupert C. Vestibular ataxia following shuttle flights: effects of microgravity on otolith-mediated sensorimotor control of posture. *Am J Otol* 1993; 14:9–17.
26. Paloski WH, Reschke MF, Black FO, Doxey DD, Harm DL. Recovery of postural equilibrium control following spaceflight. *Ann N Y Acad Sci* 1992; 656:747–54.
27. Perry SD, Santos LC, Patla AE. Contribution of vision and cutaneous sensation to the control of centre of mass (COM) during gait termination. *Brain Res* 2001; 913:27–34.
28. Platts SH, Martin DS, Stenger MB, Perez SA, Ribeiro LC, Summers R, Meck JV. Cardiovascular adaptations to long-duration head-down bed rest. *Aviat Space Environ Med* 2009; 80(5, Suppl.):A29–36.
29. Reschke MF, Kornilova LN, Harm DL, Bloomberg JJ, Paloski WH. Neurosensory and sensory-motor function. In: Leach Huntoon CS, Antipov VV, Grigoriev AI, eds. *Space biology and medicine, volume III: humans in spaceflight, book II*. Reston, VA: AIAA; 1996:135–93.
30. Roll JP, Popov K, Gurfinkel V, Lipshits M, Andre-Deshays C, Gilhodes JC, et al. Sensorimotor and perceptual function of muscle proprioception in microgravity. *J Vestib Res* 1993; 3:259–73.
31. Roll R, Gilhodes JC, Roll JP, Popov K, Charade O, Gurfinkel V. Proprioceptive information processing in weightlessness. *Exp Brain Res* 1998; 122:393–402.
32. Young LR, Oman CM, Watt DG, Money KE, Lichtenberg BK. Spatial orientation in weightlessness and readaptation to earth's gravity. *Science* 1984; 225:205–8.