J Musculoskelet Neuronal Interact 2014; 14(3):359-366

Hylonome

Original Article

Effects of five days of bed rest with and without exercise countermeasure on postural stability and gait

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Abstract

Objectives: We tested whether intermittent standing or a combination of heel raising, squatting and hopping exercises was sufficient to prevent alteration in balance and gait following a 5-day bed rest. **Methods:** This cross-over design study was performed with 10 male subjects during 6° head down tilt: (a) with no countermeasure; (b) while standing 25 min per day; (c) during locomotion-like activities 25 min per day. Gait was evaluated by grading subjects' performance during various locomotion tasks. Equilibrium scores were derived from peak-to-peak anterior-posterior sway while standing on a foam pad with the eyes open or closed or while making pitch head movements. **Results:** When no countermeasure was used, head movements led to decreased postural stability and increased incidence of falls immediately after bed rest compared to before. When upright standing or locomotion-like exercises were used, postural stability and the incidence of falls were not significantly different after the bed rest from the baseline. **Conclusion:** These results indicate that daily 25-min of standing or locomotion-like exercise proves useful against postural instability following a 5-day bed rest. The efficacy of these countermeasures on locomotion could not be evaluated, however, because gait was not found to be altered after a 5-day bed rest.

Keywords: Posturography, Balance, Gait, Bed Rest, Centrifugation, Artificial Gravity

Introduction

The deconditioning of physiological function in human subjects during prolonged bed rest has been proposed as an analog to space flight[1]. Indeed, countermeasures that minimize physiological deconditioning during bed rest, such as cycle ergometer exercise or compression garments, have proven to be useful with astronauts during space flight[2]. However, until recently, these countermeasures have addressed the various physiological systems in a piece-meal fashion (e.g. cardiovascular system for exercise; musculoskeletal system for compression garments; etc.). On the other hand, artificial gravity generated by short-radius centrifugation has been proposed as a more general, multi-purpose countermeasure against sensory-motor, cardiovascular, and musculoskeletal deconditioning due to prolonged exposure to weightlessness[3-5].

In a pioneering study, Vernikos et al.[6] demonstrated that intermittent (real) gravity loading can effectively reduce the deconditioning associated with prolonged bed rest in healthy human males. She showed that intermittent standing or controlled walking during otherwise continuous bed rest prevented post-bed rest orthostatic intolerance and attenuated decrements in peak oxygen uptake, plasma volume, and urinary Ca^{++} excretion. Other studies found that intermittent centrifugation supplemented or not with concurrent aerobic exercise during bed rest could completely protect respiratory and cardiovascular responses to upright exercise, improve G-tolerance, suppress plasma volume loss, prevent fluid volume shifts, and reduce the elevated heart rate, muscle sympathetic nerve activity, and exaggerated responses to head-up tilt after bed rest[7-11].

More recently, a study showed that human subjects centrifuged daily for one hour during a 21-day bed rest exhibited less physiological deconditioning than control subjects experiencing the same deconditioning stimulus without centrifuga-

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The authors have no conflict of interest.

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Edited by: F. Rauch
Accepted 28 July 2014

tion. Beneficial effects were seen on muscle strength, volume, homeostasis, and cardiovascular performance[12-16]. However, sensory-motor performance, including reflex function, spatial orientation, and balance control performance were unaffected by daily exposures to centrifugation[17-18], as were psychological and physiological stress, immune function, and cognitive performance[19-20].

In 2005 the European Space Agency (ESA) commissioned a multi-disciplinary Topical Team to advise the agency on artificial gravity research. The outcome of which was a book[21] and a detailed set of recommendations for undertaking a program of ground-based research into the feasibility of using intermittent gravity loading plus supplemental exercise as a multi-system countermeasure. The first step of this program was very short-duration (5 days) bed rest studies to establish the effective ranges of intermittent gravity loading on sensory-motor, cardiovascular, and musculoskeletal systems, using either real gravity such as Vernikos et al.[6] or short-radius centrifugation. These studies used a crossover design that required all subjects to experience each test condition. Thus, multiple campaigns were required, with each subject spending one week in the facility (under a different experimental condition) during each campaign and recovering for at least four weeks between campaigns. The full set of ESA standard bed rest dependent measures were collected on each subject before and after each campaign. As the 5-day campaigns are very short relative to the deconditioning time constants of some of the physiological systems (e.g., bone demineralization, muscle atrophy), a few longer duration campaigns (14-21 days) will be scheduled later in the program to validate the effects predicted in these systems and to develop optimal intermittent artificial gravity prescriptions.

The results reported here concern the effects of intermittent standing or a combination of heel raises, squats and hopping exercises during very short-duration (5-day) bed rest on sensory-motor performance. We focused on posture and gait because these responses have been extensively studied in astronauts returning from space flight and changes have been observed after only 5 days in weightlessness[22-24]. Indeed, these functions are critical in case the crew needs to egress the vehicle in an emergency after landing.

Bed rest does not alter the otolith input in the same manner as space flight because gravity continues to exert a vertical force on the utricles in supine subjects during bed rest whereas this static stimulation is absent in weightlessness. However, bed rest does mimic aspects of the restricted visual environment of spacecraft and the reduced stimulation of proprioceptive reflexes of the lower limbs. Ground-based studies have shown that somatosensory loss increases vestibulospinal sensitivity[25] and alters head movement control during locomotion[26]. There is also ample evidence of interactions between the vestibular system and cardiovascular control[27]. We therefore predicted that decrements in postural stability following bed rest would reflect altered proprioceptive function, and might also be affected by orthostatic deconditioning.

Material and methods

General design

The present study was part of a series of bed rest studies organized by ESA, starting with a short-duration bed rest in preparation for more long-duration studies. Details of the experiment design have been presented elsewhere[28]. In short, a total of three bed rest campaigns were scheduled. Each campaign consisted of 5 days of baseline data collection (BDC-5 through BDC-1), 5 days of bed rest in 6° head down tilt (HDT1 through HDT5), and 6 days of recovery (R+0 through R+5). Each subject randomly performed bed rest only (CON), bed rest with 25 min of daily upright standing (STA), or bed rest with 25 min of daily locomotion replacement training (LRT). In bed, the subjects maintained the 6° HDT for 24 h/day (except for 25 min in the LRT and STA interventions).

Subjects

Ten healthy male subjects (mean±SEM age: 29.4±5.9 years, height: 178.8±3.7 cm; weight: 77.7±4.1 kg) were used in this study. All participants received a comprehensive clinical assessment and gave their informed consent prior to the beginning this study. The study design was approved by the Ethics Committee of the Northern Rhine medical association in Düsseldorf, Germany and was organized by the DLR Institute of Aerospace Medicine and sponsored by ESA.

Interventions and control condition

Locomotion replacement training (LRT). Subjects executed the upright 25-min LRT session daily during the HDT phase, which consisted of a combination of heel raises, squats and hopping exercises in the upright position (see Mulder et al., 2014 for details). A Smith Machine with fixed rails (PTS-1000 Dual Action Smith™ Cage, Hoist Fitness Systems, San Diego, USA) was used to guide the heel raise and squat exercises. Squats and heel raises were performed against body weight plus the additional weight of the barbell (15 kg). The heel raises were performed with straight knees and without ankle dorsiflexion. The shallow squats were performed continuously for 3 minutes. The reactive jumps and the cross-hopping (left-right-left-right etc.) exercises were performed without Smith Machine. The reactive jumps were performed with the ball of the foot (heels not touching the ground) at about 3 repetitions per second separated by 15 s of rest after 6 jumps. Cross hopping was performed continuously for 3 min at about 1.3 repetitions per second. The exercises had the same duration throughout the study, except for the duration of static squat that increased from 45 s at HDT1 to 70 s at HDT5[28].

Standing intervention (STA). Each subject stood upright for 25 min, directly next to the bed. Both feet were in contact with the floor during the entire standing phase and any type of physical activity (e.g. heel raise, squatting or walking) was prohibited.

Control condition (CON). Subjects in the CON group remained in HDT 24 h/day for 5 days and refrained from any type of physical exercise and/or upright posture during the bed rest phase.

Posturography

This test utilized dynamic posturography to quantitatively assess both sensory and motor components of postural control[29]. The subjects with their hands across the waist stood with the feet together, while looking straight ahead, for 30 s on a foam pad that rested on a force platform. The foam pad was made of a 12-cm thick medium-density foam (Sunmate, Dynamic Systems Inc., Leicester NC, USA). Standing on foam alters somatosensory inputs, and is a useful option for testing balance control when more expensive dynamic posturography testing equipment (e.g. EquiTest) is not available[30].

There is evidence that the diagnostic assessment of postural instability is more pronounced during unstable support conditions requiring active head movements. For this reason, in some trials, subjects were oscillating their head in pitch (frequency 0.33 Hz; amplitude ±20°) in phase with a sinusoidally varying auditory tone. These dynamic head tilts stimulate the vestibular system, which renders the maintenance of upright posture more challenging. This method improves the diagnostic sensitivity of posturography, as shown in healthy subjects and astronauts returning from space flight[31-32].

Consequently, three conditions were used to objectively evaluate the subject's ability to make effective use of (or suppress inappropriate) visual, vestibular, and proprioceptive information for balance control: (a) eyes open with the head erect (EO); (b) eyes closed with the head erect (EC); and (c) eyes closed with dynamic head tilts (ECDHT). Each condition was performed three times. The order of conditions was randomized. Between trials, subjects could rest and sit on a chair. Duration of the test was 15 minutes.

Center-of-mass sway angles were estimated from instantaneous anterior-posterior (AP) and medial-lateral center-of-force positions, which were computed from force transducers mounted within the force platform (Leonardo Mechanograph, Novotec Medical GmbH, Pforzheim, Germany). The AP peak-to-peak sway angle, Θ (in degrees), was used to compute the equilibrium score (EQ): $EQ=100 \times (1-(\Theta/12.5))$ where 12.5° is the maximum theoretical peak-to-peak sway in the sagittal plane. For $\Theta=12.5°$, which is scored as a fall, the EQ score is zero[33].

Dynamic Gait Index

The Dynamic Gait Index (DGI) was developed as a clinical tool to assess gait, balance and fall risk[34]. It evaluates not only usual steady state walking, but also walking during more challenging tasks. Eight functional walking tests are performed by the subject: (1) walk a distance of 6 m on a level surface at normal pace; (2) walk the same distance while changing gait speed at instructor's command; (3) walk 6 m at normal pace while looking to the right or to the left upon instructor's command; (4) walk 6 m at normal pace while looking up or down; (5) walk at normal pace, then turn as quickly as possible to face the opposite direction and stop; (6) walk at normal pace and step over an obstacle (shoebox); (7) walk at normal pace and step around the right side of a cone placed at 3 m, and around the left side of a cone placed at 6 m; and (8) walk up stairs, using the railing if necessary, and when arrived at the top, turn around and walk down. Duration of the test is 30 minutes.

Each of these 8 tasks was performed once, in random order. Performance of each task was rated by a trained observer on a scale of 0 to 3 (where 3 indicated the best score), based on the following criteria:

- 3 (normal): successful execution of task with no assistance, no evidence for imbalance, normal and smooth gait pattern.
- 2 (mild impairment): slow execution speed, may require verbal cueing, mild gait deviations, no signs of imbalance.
- 1 (moderate impairment): very slow execution speed, abnormal gait pattern, evidence for imbalance, must use rail, staggers but recovers before continuing the task.
- 0 (severe impairment): cannot safely complete the task, severe gait deviations or imbalance, unable to clear obstacles, subject stops and reaches for wall or requires physical assistance.

The Dynamic Gait Index (DGI) was obtained by summing scores for all 8 tasks. Twenty-four is the maximum individual DGI possible. Based on previous studies in older adults, DGI ranging from 22-24 are indicators of safe ambulators, whereas scores of 19 or less have been related to increased incidence of falls[34].

Data analysis

Both posturography and DGI tests were repeated by the same subjects two days before bed rest (BDC-2), then on the last day of bed rest (R+0), i.e., approximately 20 min after the subjects first stood upright during a 5-30-min orthostatic tolerance test, and then three days later (R+3). EQ and DGI scores were compared across days (BDC-2, R+0, R+3) and bed rest countermeasures conditions (CON, STA, LRT).

All statistical analyses were performed using SPSS (V20, IBM Corp, Armonk NY, USA). Since EQ scores cannot be treated as continuous, normally distributed data when falls are present[35], posture data were analyzed using the non-parametric repeated measures Friedman test. DGI scores were analyzed using the same procedure. When Friedman tests were significant, follow-up (post hoc) analyses between paired data were achieved using the Wilcoxon Signed Ranked test. Statistical significance was accepted at $P<0.05$ before appropriate Bonferroni correction was applied.

Results

To determine whether there were any effects of adaption/learning/familiarization to the test paradigm, we evaluated the temporal stability of the data for all BDC and R+3 data sessions across the three bed rest campaigns. Our null hypotheses were that: (a) no differences would be observed in BDC scores from campaign to campaign; and (b) recovery would always be complete by R+3, so that no differences would be observed between BDC and R+3 scores in any campaign.

All 30 EQ Scores (3 trials x 10 subjects) for each of the three posture conditions (EO, EC, and ECDHT) conducted at the BDC and R+3 test sessions for each of the three campaigns

	Campaign 1		Campaign 2		Campaign 3	
	BDC-2	**R+3**	**BDC-2**	**R+3**	**BDC-2**	**R+3**
EO	88.0*±1.6	90.4±1.6	90.4±1.6	90.4±1.6	89.2±2.0	91.2±1.6
EC	76.0*±4.0	79.6±2.8	80.0±2.8	80.0±4.0	79.2±3.2	80.0±3.6
ECDHT	43.6*±24.0	64.8±5.6	61.6±6.8	62.4±6.0	55.2#±11.6	65.2±8.0

Table 1. Median equilibrium scores (± median average deviation) in the three posture conditions (EO: eyes open; EC: eyes closed; ECDHT: eyes closed during dynamic head tilt) for the BDC and R+3 sessions of each bed rest campaign. *$P<0.05$ with respect to all other sessions; #$P<0.05$ with respect to preceding and succeeding sessions.

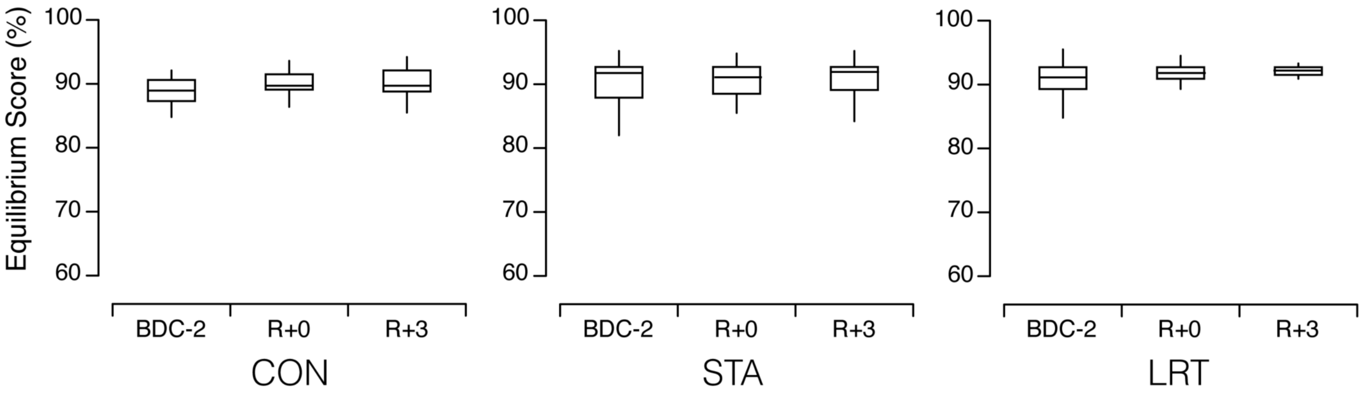

Figure 1. Equilibrium scores for 10 subjects trying to stand upright for 30 s on a 12-cm thick foam pad with the eyes open. Measurements were made two days before (BDC-2), and then immediately (R+0) and three days (R+3) after 5-day bed rests with no countermeasure (CON), standing 25 min per day (STA), and locomotion replacement training (LRT) 25 min per day.

were analyzed. Median values for each of the six sessions are presented in Table 1. These data are presented in the temporal order they were collected, so, owing to the randomization process, interventions (CON, STA, LRT) varied approximately equally among subjects between each of the three BDC and R+3 sessions.

Scores during the BDC session of the first campaign were lower than the other campaigns presumably because of the novelty of the testing paradigms. Had a familiarization session been provided prior to this first BDC, the scores on that session would likely have been similar to the scores in all of the remaining sessions.

The repeated-measures Friedman test on EQ scores from the EO, EC, and ECDHT conditions indicated a significant ($P=0.04$, $P=0.004$, and $P<0.001$, respectively) overall effect, i.e., all sessions were not the same. Removing the first session from consideration and repeating the Friedman test on the five remaining sessions resulted in a non-significant overall effect for the EO ($P=0.241$) and EC ($P=0.04$) conditions, suggesting that the first session was different from the others.

For the EQ scores from the ECDHT condition, removing the first session from consideration and repeating the Friedman test on the five remaining sessions still resulted in a significant ($P<0.001$) overall effect. Follow-up Wilcoxon tests showed a significant decrease in EQ scores from R+3 of campaign 2 to BDC of campaign 3 ($P=0.002$) (see also Table 1), and a significant increase from BDC of campaign 3 to R+3 of campaign 3 ($P<0.001$). These results suggest that the long delay between the second and the third campaign may have affected the performance of our subjects during BDC of campaign 3.

Because of the above observations, the effects of the interventions during bed rest were investigated using data where the results of the first condition for each subject were removed. For example, subject A received the LRT intervention first, so for subject A the first LRT data were removed from his data set. Similarly subject B received the STA intervention first, so the first STA data were removed, and so on.

When subjects were standing upright with no head movements, no significant differences in the EQ scores were observed between before and after bed rest (R+0 or R+3), neither with the eyes open (Figure 1) nor with the eyes closed (Figure 2).

However, a decrease in postural stability was observed when subjects had the eyes closed while pitching their head back and forth (Figure 3). When no countermeasures were used during bed rest (CON), the EQ score significantly decreased (Wilcoxon, $P=0.003$) immediately after the bed rest

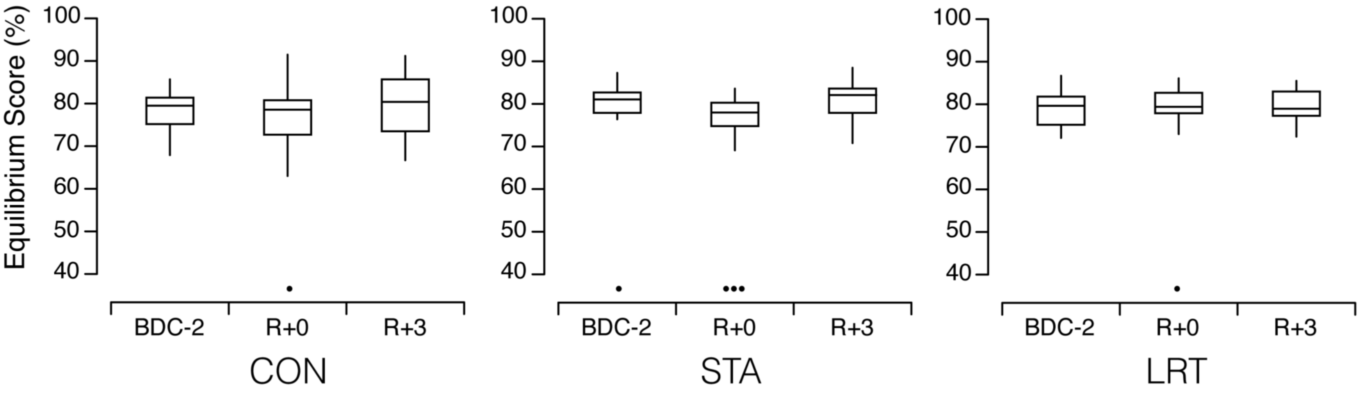

Figure 2. Equilibrium scores with the eyes closed for the three interventions (CON, STA, LRT) before and after bed rest. The black dots represent the number of falls in each condition.

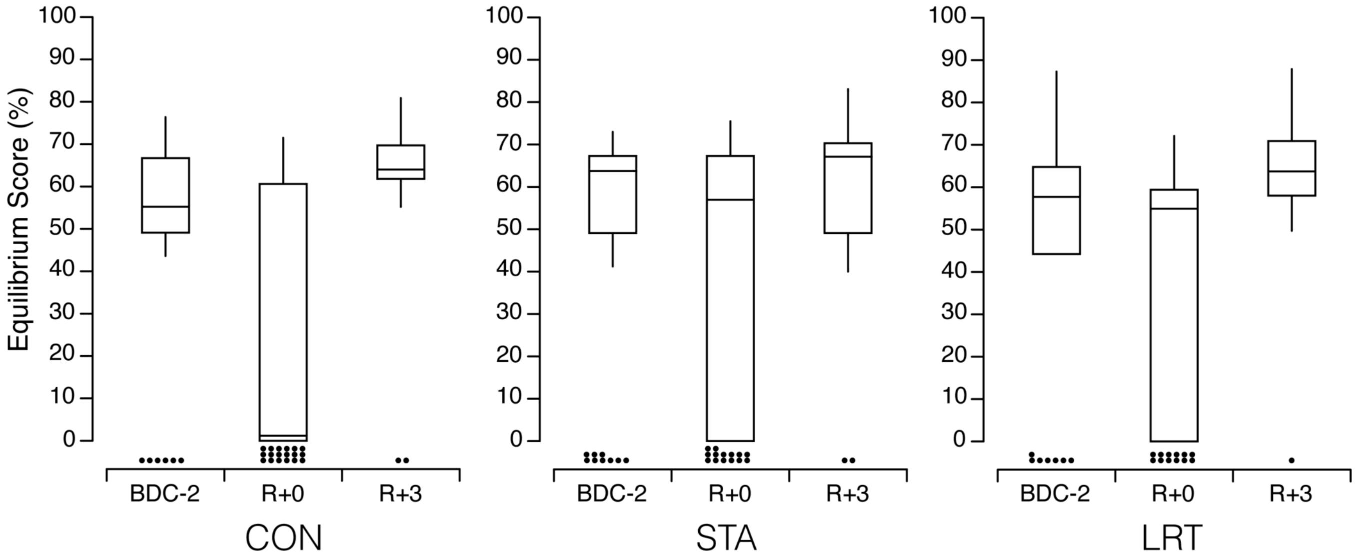

Figure 3. Equilibrium scores with the eyes closed while making dynamic head tilts for the three interventions (CON, STA, LRT) before and after bed rest. The black dots represent the number of falls in each condition.

(R+0) relative to before (BDC-2). This decrease was still statistically significant after applying Bonferroni adjustment (*P*<0.017). Also, the number of falls increased from 6 to 18 after the bed rest.

By comparison, when STA and LRT were used, there was no significant change in EQ score between R+0 and BDC (Freidman, *P*=0.069 for STA; Wilcoxon, *P*=0.234 for LRT). The incidence of falls after STA and LRT still increased on R+0 relative to BDC. Three days after the bed rest, EQ scores were significantly larger than on R+0 (Wilcoxon, *P*=0.002 for LRT), but not significantly different from BDC.

Most subjects got nearly perfect DGI scores (24/24) when tests were performed two days before and three days after bed rest. Immediately after bed rest though, DGI scores were lower by one point in half of the subjects (Figure 4). This occurred for the tasks where they were instructed to look sideways or up or down when walking on a level surface, or when they walked up and down the stairs. However, this difference was not statistically significant. In addition, there was no significantly difference in the DGI before and after the bed rest between CON, STA, and LRT.

Discussion

Our results showed that the standard Romberg conditions with the eyes open or closed were the least sensitive to bed rest. By contrast, pitching the head back and forth while standing with the eyes closed increased postural instability and the inci-

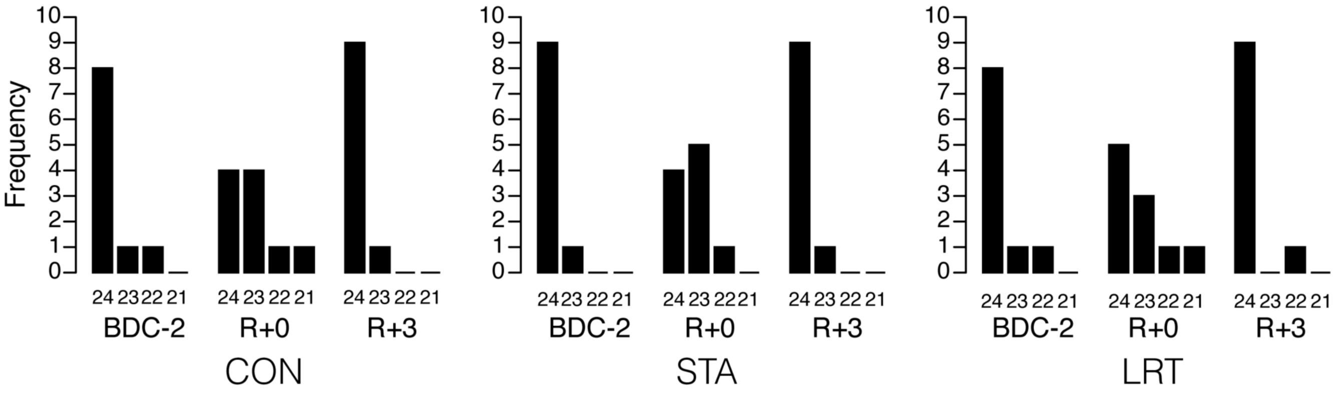

Figure 4. Frequency of Dynamic Gait Index scores obtained in 10 subjects two days before (BDC-2), and then immediately (R+0) and three days (R+3) after 5-day bed rests with no countermeasure (CON), standing 25 min per day (STA), and locomotion replacement training (LRT) 25 min per day. None of the subjects scored 20 or lower.

dence of falls after five days of bed rest. When subjects stood upright by their bed, or executed a combination of heel raises, squats, and hopping exercises for 25 min each day, the postural instability and the number of falls decreased after the bed rest.

Astronauts typically exhibit performance decrements in postural control immediately after space flight when exposed to sensory organization tests. As in our study, the greatest functional deficits are observed when visual and proprioceptive inputs are sway-referenced, which leaves vestibular information as the only contributing input for balance control[36]. Recent testing of 117 crewmembers after Shuttle flights lasting 4-17 days, and of 64 crewmembers following long-duration missions lasting 48-380 days demonstrated that balance performance decrement during dynamic head tilts was present well after performance on the standard sensory organization tests (i.e. with no dynamic head tilts) had recovered[32,37].

No significant decrements in performance on a standard battery of sensory organization tests, i.e. with the head erect, was observed after 42-63 days of bed rest[38], suggesting that either no functionally significant change occurred or that the standard battery was insensitive to the changes that did occur. Ocular counter-rolling and subjective visual vertical assessed during 90° whole body roll tilt to the left and right were also unaffected by 21 days of bed rest[18,39]. Our result that postural instability increases during dynamic head tilts after bed rest of only 5 days indicates that there are some measurable decrements in balance control performance associated with bed rest.

One interpretation for the increased postural instability following bed rest is an error in the central estimation of the gravitational orientation reference, perhaps due to an altered canal-otolith relationship driven by prolonged tilt of the utricular macula with respect to the gravity vector. Another possibility is that the postural performance decrements seen in our control condition are due 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[40].

Astronauts also have difficulty walking after returning from space flight due to alterations in multiple systems responsible for the control of locomotion including disruptions in leg muscle activations patterns, head-trunk coordination, and spatial orientation[41]. Functional mobility testing after long-duration space flight using an obstacle course has shown that performance impairment lasts for two weeks after landing, which is similar to the deficits in postural equilibrium control after long-duration space flight[24]. Following space flight, astronauts also experience changes in otolith-spinal reflex function[40,42,43]. These reflex mechanisms are essential for many pre-programmed motor responses such as those required to stabilize posture after a voluntary jump down from a platform, and therefore astronauts experience disruption in their ability to maintain postural equilibrium when performing these tasks[44].

The Dynamic Gait Index scores in our study were not significantly different after bed rest from before, with or without exercise countermeasures. In comparison, astronauts following 6-month space missions on board the ISS have shown a 50% change in their time to complete an obstacle course that share similar tasks as in our study[24]. The difference between the space flight and bed rest results could therefore reflect 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 space flight[38].

The gravitational force along the longitudinal body axis exerts a strong influence on the control of posture and locomotion[45,46]. During space flight, it is difficult to distinguish between the direct effects of body unloading due to microgravity and the adaptive changes aimed at optimizing performance in this new environment. The results of our study support the concept proposed by Reschke et al. that "bed rest is an appropriate paradigm for differentiating between the bottom-up modifications in posture and locomotion due to unloading, and the top-down changes associated with visual-vestibular adaptation to space flight" (ref. [38], p. A53). The impairment seen in postural control after bed rest with the eyes closed and during dynamic head tilt might reflect altered proprioceptive function, and might also be affected by orthostatic deconditioning[27]. Postural and gait disturbances have significant implications for performance of operational tasks that require ambulation immediately following landing on a planetary surface including rapid emergency egress from a landing vehicle[36]. Consequently, bed rest could be a useful analog for evaluating potential flight countermeasures to body unloading.

Acknowledgements

The authors are grateful to the subjects for their participation in this experiment, the staff of the DLR Institute of Aerospace Medicine for conducting all the tests, and to Mr. Rahul Goel of the University of Houston for performing the statistical analysis. This study was supported by ESA, DLR, and CNES.

References

1 Pavy-LeTraon A, Heer M, Narici MV, Rittweger J, Vernikos J. From space to earth: Advances in human physiology from 20 years of bed rest studies (1986-2006). Eur J Appl Physiol 2007;101:143-194.

2 Buckey JC, Lane LD, Levine BD, Watenpaugh DE, Wright SJ, Moore WE, Gaffney FA, Blumqvist CG. Orthostatic intolerance after spaceflight. J Appl Physiol 1996;81:7-18.

3 Vil-Viliams IF. Principle approaches to selection of the short-arm centrifuge regimens for extended space flight. Acta Astronaut 1994;33:221-229.

4 Young LR. Artificial gravity considerations for a Mars exploration mission. Ann NY Acad Sci 1999;28:367-378.

5 Clément G, Pavy-Le Traon A. Centrifugation as a countermeasure during actual and simulated microgravity: a review. Eur J Appl Physiol 2004;92:235-248.

6 Vernikos J, Ludwig DA, Ertl AC, Wade CE, Keil L, O'Hara D. Effect of standing or walking on physiological changes induced by head down bed rest: Implications for spaceflight. Aviat Space Environ Med 1996;67:1069-1079.

7 Evans JM, Stenger MB, Moore FB, Hinghoffer-Szalkay H, Rossler A, Patwardhan AR, et al. Centrifuge training increases presyncopal orthostatic tolerance in ambulatory men. Aviat Space Environ Med 2004;75:850-858.

8 Greenleaf JE, Gundo DP, Watenpaugh DE, Mulenburg GM, Marchman N, Looft-Wilson R, et al. Cycle-powered short radius (1.9 m) centrifuge: exercise vs. passive acceleration. J Gravit Physiol 1996;3:61-62.

9 Akima H, Katayama K, Sato K, Ishida K, Masuda K, Takada H, et al. Intensive cycle training with artificial gravity maintains muscle size during bed rest. Aviat Space Environ Med 2005;76:923-929.

10 Iwasaki K, Shiozawa T, Kamiya A, Michikami D, Hirayanagi K, Yajima K, et al. Hypergravity exercise against bed rest induced changes in cardiac autonomic control. Eur J Appl Physiol 2005;94:285-291.

11 Iwase S. Effectiveness of centrifuge-induced artificial gravity with ergometric exercise as a countermeasure during simulated microgravity exposure in humans. Acta Astronaut 2005;57:75-80.

12 Arya M, Paloski WH, Young LR. Centrifugation protocol for the NASA artificial gravity-bed rest pilot study. J Gravit Physiol 2007;14:5-8.

13 Warren LE, Reinertson R, Camacho ME, Paloski WH. Implementation of the NASA artificial gravity bed rest pilot study. J Gravit Physiol 2007;14:1-4.

14 Symons TB, Sheffield-Moore M, Chinkes DL, Ferrando AA, Paddon-Jones D. Artificial gravity maintains skeletal muscle protein synthesis during 21 days of simulated microgravity. J Appl Physiol 2009;107:34-38.

15 Caiozzo VJ, Haddad F, Lee S, Baker M, Paloski WH, Baldwin KM. Artificial gravity as a countermeasure to microgravity: A pilot study examining the effects on knee extensor and plantar flexor muscle groups. J Appl Physiol 2009;107:39-46.

16 Stenger MB, Evans JM, Knapp CF, Lee SMC, Phillips TR, Perez SA, Moore AD, Paloski WH, Platts SH. Artificial gravity training reduces bed rest-induced cardiovascular deconditioning. Eur J Appl Physiol 2012; 112:605-616.

17 Jarchow T, Young LR. Neurovestibular effects of bed rest and centrifugation. J Vestib Res 2010;20:45-51.

18 Moore S, MacDougall HG, Paloski W. Effects of head-down bed rest and artificial gravity on spatial orientation. Exp Brain Res 2010;204:617-622.

19 Mehta SK, Crucian B, Pierson DL, Sams C, Stowe RP. Monitoring immune system function and reactivation of latent viruses in the artificial gravity pilot study. J Gravit Physiol 2007;14:21-25.

20 Seaton KA, Slack KJ, Sipes W, Bowie K. Artificial gravity as a multi-system countermeasure: Effects on cognitive function. J Gravit Physiol 2007;14:27-30.

21 Clément G, Bukley A. (eds) Artificial gravity. New York: Springer; 2007.

22 Reschke MF, Bloomberg JJ, Harm DL, Paloski WH, Layne C, McDonald V. Posture, locomotion, spatial orientation, and motion sickness as a function of space flight. Brain Res Rev 1998;28:102-117.

23 Paloski WH, Reschke MF, Black FO, Doxey DD, Harm DL. Recovery of postural equilibrium control following spaceflight. Ann NY Acad Sci 1992;656:747-754.

24 Mulavara AP, Feiveson AH, Fiedler J, Cohen H, Peters BT, Miller C, Brady R, Bloomberg JJ. Locomotor function after long-duration space flight: Effects and motor learning during recovery. Exp Brain Res 2010;202:649-659.

25 Horak F, Hlavacka F. Somatosensory loss increases vestibulospinal sensitivity. J Neurophysiol 2001;86:575-585.

26 Mulavara AP, Ruttley T, Cohen HS, et al. Vestibular-somatosensory convergence in head movement control during locomotion after long-duration space flight. J Vestib Res 2012;22:153-166.

27 Yates BJ, Bronstein AM. The effects of vestibular system lesions on autonomic regulation: observations, mechanisms, and clinical implications. J Vestib Res 2005;

15:119-129.

28 Mulder E, Frings-Meuthen P, von der Wiesche M, Clément G, Linnarsson D, Paloski WH, Wuyts F, Zange J, Rittweger J. Study protocol, implementation, and verification of a short versatile upright exercise regime during 5 days of bed rest. J Musculoskelet Neuronal Interac 2014;14:111-123.

29 Black FO. What can posturography tell us about vestibular function? Ann NY Acad Sci 2001;942:446-464.

30 Black FO, Wall C, Nashner LM. Effects of visual and support surface orientation references upon postural control in vestibular deficit subjects. Acta Otolaryngol 1983; 95:199-210.

31 Paloski WH, Wood SJ, Feiveson AH, Black FO, Hwang EY, Reschke MF. Destabilization of human balance control by static and dynamic head tilts. Gait Posture 2006; 23:315-323.

32 Jain V, Wood SJ, Feiveson AH, Black FO, Paloski W. Diagnostic accuracy of dynamic posturography testing after short-duration spaceflight. Aviat Space Environ Med 2010;81:625-631

33 Nashner LM. Computerized dynamic posturography: Clinical applications. In: Jacobson GP, Newman CW, Kartush JM, editors. Handbook of Balance Function Testing. Chicago, IL: Mosby-Year Book Inc,; 1993. p. 308-334.

34 Shumway-Cook A, Baldwin M, Polissar NL, Gruber W. Predicting the probability for falls in community-dwelling older adults. Physical Therapy 2007;77:812-819.

35 Feiveson AH, Metter EJ and Paloski WH. A statistical model for interpreting computerized dynamic posturography data. IEEE Transactions on Biomedical Engineering 2002;49:300-309.

36 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.

37 Wood SJ, Fiedler J, Taylor LC, Sayenko D, Kozlovskaya I, Black FO, Paloski WH. Comparison of postural recovery after short and long duration spaceflights. Proceedings of 8th Symposium on the Role of Vestibular Organs in Space Exploration, Houston, TX, May 5-9, 2011.

38 Reschke MF, Bloomberg JJ, Paloski WH, Mulavara AP, Feiveson AH, Harm DL. Postural reflexes, balance control, and functional mobility with long-duration head-down bed rest. Aviat Space Environ Med 2009; 80:A45-A54.

39 Young LR, Paloski WH. Short radius intermittent centrifugation as a countermeasure to bed-rest and 0-G deconditioning: IMAG pilot study summary and recommendations for research. J Gravit Physiol 2007; 14:P31-P33.

40 Watt DG, Money KE, Tomi LM. M.I.T./Canadian vestibular experiments on the Spacelab-1 mission: 3. Effects of prolonged weightlessness on a human otolith-spinal reflex. Exp Brain Res 1986;64:308-315.

41 Bloomberg JJ, Mulavara AP. Changes in walking strategies after spaceflight. IEEE Eng Med Biol Mag 2003; 22:58-62.

42 Clément G, Gurfinkel VS, Lestienne F, Lipshits MI, Popov KE. Adaptation of postural control to weightlessness. Exp Brain Res 1984;57:61-72.

43 Reschke MF, Anderson DJ, Homick JL. Vestibulospinal reflexes as a function of microgravity. Science 1984; 225:212-214.

44 Newman DJ, Jackson DK, Bloomberg JJ. Altered astronaut lower limb and mass center kinematics in downward jumping following space flight. Exp Brain Res 1997; 117:30-42.

45 Dietz V, Duysens J. Significance of load receptor input during locomotion: a review. Gait Posture 2000;11:102-110.

46 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.