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RESEARCH ARTICLE

Intermittent short-arm centrifugation is a partially effective countermeasure against upright balance deterioration following 60-day head-down tilt bed rest

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Abstract

This study investigated whether artificial gravity (AG), induced by short-radius centrifugation, mitigated deterioration in standing balance and anticipatory postural adjustments (APAs) of trunk muscles following 60-day head-down tilt bed rest. Twenty-four participants were allocated to one of three groups: control group (n = 8); 30-min continuous AG daily (n = 8); and intermittent 6 × 5 min AG daily (n = 8). Before and immediately after bed rest, standing balance was assessed in four conditions: eyes open and closed on both stable and foam surfaces. Measures including sway path, root mean square, and peak sway velocity, sway area, sway frequency power, and sway density curve were extracted from the center of pressure displacement. APAs were assessed during rapid arm movements using intramuscular or surface electromyography electrodes of the rectus abdominis; obliquus externus and internus abdominis; transversus abdominis; erector spinae at L1, L2, L3, and L4 vertebral levels; and deep lumbar multifidus muscles. The relative latency between the EMG onset of the deltoid and each of the trunk muscles was calculated. All three groups had poorer balance performance in most of the parameters (all $P < 0.05$) and delayed APAs of the trunk muscles following bed rest (all $P < 0.05$). Sway path and sway velocity were deteriorated, and sway frequency power was less in those who received intermittent AG than in the control group (all $P < 0.05$), particularly in conditions with reduced proprioceptive feedback. These data highlight the potential of intermittent AG to mitigate deterioration of some aspects of postural control induced by gravitational unloading, but no protective effects on trunk muscle responses were observed.

NEW & NOTEWORTHY This study presents novel insights into the effect of artificial gravity (AG) on the deterioration of standing balance and anticipatory postural adjustments (APAs) of trunk muscles induced by 60-day strict head-down bed rest. The results indicated severe balance dysfunction and delayed APAs during rapid arm movement. AG partially mitigated the deterioration in standing balance and may thus be considered as a potential countermeasure for future planetary surface explorations. Optimization of AG protocols might enhance effects.

anticipatory postural adjustments; artificial gravity; intramuscular EMG; postural control; sway

INTRODUCTION

Exposure to spaceflight has numerous adverse effects on body tissues and nervous system (1). Effective means to mitigate these effects are essential to consider, particularly given plans for extended periods in microgravity and hypogravity during operations on the Moon and Mars (2), but affects and impact of potential mitigation strategies are

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difficult to replicate on Earth. To simulate the effects of spaceflight, head-down tilt (HDT) bed rest and "dry" water immersion are referred to as ground-based analogs, providing "vertical unloading," as they remove the influence impact of gravitational forces on the head-to-feet axis of the body (3). Reduction of both sensory inputs and skeletal muscle activation induced by vertical unloading has been implicated in development of impaired standing balance and altered anticipatory postural adjustments (APAs) of paraspinal muscles, as has been shown after exposure to microgravity (4–6). These effects may collectively endanger the musculoskeletal system as a consequence of increased risk of falls and increased risk for lumbar intervertebral disk herniation after spaceflight (7).

Standing balance is intimately related to the control of the trunk muscles. The trunk is the body segment with the largest mass, and its elevated position relative to the base of support results in a high moment of inertia (8, 9). Maintenance of both standing balance and health of spinal tissues, including the intervertebral disk, depends on spinal and supraspinal motor networks to anticipate or respond to threatening events by coordination of suitable muscle responses (10, 11). This depends on accurate sensory inputs from proprioceptive, visual and vestibular systems (12, 13) regarding the position of the body and segments. Changes in the quality of this information after unloading would have potential negative impacts on balance, which would be compounded by its impact on the quality of trunk control.

Postural body sway in standing is generally assessed with force plates to quantify the motion of the center of pressure (CoP). Multiple variables can be extracted from this measure (14), and studies have reported impaired standing balance after spaceflight (5, 6, 15) and after 60-day HDT bed rest (16–18). Detailed analysis of the global postural parameters, which estimate the overall "size" of the sway pattern, and structural postural parameters, which attempt to decompose the sway pattern into elements and then examine their interaction, is lacking after HDT bed rest and spaceflight. Importantly, poor standing balance has been associated with compromised contribution of the trunk muscles to balance, as identified in individuals with low back pain (19, 20). This might be secondary to impaired sensory input, which has been associated with higher risks of intervertebral disk herniation (21) and poor spinal sagittal alignment (22). There is some evidence that countermeasures can mitigate the effects of HDT bed rest on balance, such as low-intensity vibration (16) and high-load jump exercise (17), but it is unclear whether this is related to improved trunk control.

Multiple methods are available to quantify the quality of control of the trunk. Investigation of anticipatory mechanisms for spine control has involved the assessment of the timing of trunk muscle activation as part of APAs associated with rapid arm movements (11, 23). This method assesses the capacity of the central nervous system to activate trunk muscles in advance of predictable postural disturbances (10, 24). The rapid arm movement task also provides information regarding the control of the superficial and deep trunk muscles in healthy individuals (11, 23), and it was demonstrated that delayed muscle activation of specific paraspinal muscles, such as deep lumbar multifidus (LM) and transversus abdominis (TrA), is more pronounced in individuals with chronic low back pain (11, 25). Although 14-day (26), but not 21-day (27), HDT bed rest has been shown to induce faster muscle onsets of superficial trunk muscles during arm movements, a more comprehensive analysis including the responses of the deeper trunk muscles is not available. This knowledge is important as it could potentially inform the development and optimization of countermeasures to prevent back pain, spinal injury, and increased risk of falls after prolonged exposure to vertical unloading. Furthermore, whether countermeasures can mitigate these adaptations is also unknown.

Artificial gravity (AG), achieved by short-radius centrifugation, seems to provide some protective effects against the physiological deconditioning associated with prolonged gravitational unloading (28). Consequently, the international space agencies consider it as a possible countermeasure during future deep space explorations (29). By creating a head-to-feet force along the body axis while in a supine position, AG has been shown to mitigate some cardiovascular, musculoskeletal, and neurovestibular adaptations induced by 5- and 21-day HDT bed rest by stimulating the sensory, vestibular, cardiovascular, and neuroendocrine systems (30–32). More specifically, AG has been shown to improve orthostatic tolerance, increase aerobic exercise capacity, and attenuate plasma volume loss, particularly when AG was administered in an intermittent protocol (32). In addition to the protective cardiovascular effects, both intermittent and continuous AG have been shown to partially preserve vertical jump performance (33) and attenuate impaired neuromuscular and sensorimotor coordination (31). However, those 5- and 21-day HDT bed rest studies were too short to thoroughly examine intermittent and continuous AG efficacy. Furthermore, whether daily intermittent and continuous AG can also alleviate the deterioration in standing balance and lumbopelvic APAs to sudden predictable postural perturbations has not been investigated following 60-day HDT bed rest.

This project investigated how exposure to 60-day HDT bed rest altered global and structural postural parameters in several standing balance tasks. Moreover, the present study investigated whether 60-day HDT bed rest modified the timing of onset of the deep trunk muscles during rapid arm movements (i.e., standardized and predictable postural disturbances). It was hypothesized that daily exposure to AG, either in a single long or multiple intermittent bouts, would mitigate the deterioration of standing balance quality and delayed APAs of the trunk muscles provoked by 60-day gravitational unloading through HDT bed rest.

METHODS

Participants

Participants from two cohorts (n = 12 each) were assessed. The study was performed at the ":envihab" facility (33) in Cologne (Germany), as part of a series of studies organized by the European Space Agency (ESA) and National Aeronautics and Space Administration (NASA). Data were collected from the first cohort between March to June 2019, and the second from September to December 2019. Participants arrived at the facility for the baseline data collection (BDC) for 14 days before 60-day strict 6° HDT bed

rest and remained in the facility for 13 days after the 60 days of HDT bed rest for the reconditioning period. The 24 participants were randomly allocated to 3 groups of 8 participants: *1*) CTRL: control group that was not exposed to centrifugation; *2*) cAG: group that underwent 30-min continuous centrifugation/day; and *3*) iAG: group that underwent six sets of 5-min centrifugation/day, separated by 5 min. The gender, age, height, and weight of the three groups were comparable (CTRL: 2 females, 34 ± 8 yr, 177 ± 7 cm, and 79 ± 13 kg; cAG: 3 females, 32 ± 10 yr, 173 ± 8 cm, and 72 ± 10 kg; and iAG: 3 females, 34 ± 11 yr, 174 ± 11 cm, and 71 ± 5 kg).

During the period of bed rest, all activities were performed in a supine position, and wearable motion sensors monitored the participants to confirm adherence with the study requirements. Diet, caloric intake, and food portions were individually set. Further details of the study protocol, inclusion, and exclusion criteria are presented elsewhere (34). The Ethics Committee of the Northern Rhine Medical Association approved this study (Düsseldorf, Germany, Application No. 2018143), and participants provided written informed consent to participate in the study. The study was registered at the German Clinical Trial Register (DRKS) under No. DKRS00015677.

Data Collection

Data were collected over two identical sessions on 2 different days. The first data collection was conducted 4 days before starting HDT bed rest (BDC-4) and the second session at R + 0 (the 1st day standing at the end of 60-day HDT bed rest).

EMG Recordings

Bipolar intramuscular fine-wire electromyography (iEMG) electrodes were prepared using two Teflon-coated 75-μm stainless steel wires, with 1-mm insulation removed from the ends, inserted into a hypodermic needle (22 G × 5.08 cm) and bent back to form hooks at 2- and 3-mm lengths. At the beginning of each experimental session, 10 min before iEMG placement, a subcutaneous injection of 1 mL of lidocaine (1%) was administered to reduce skin discomfort. Electrodes were inserted on the right side with ultrasound guidance (Logiq E BT12, General Electric, Duluth, MN) using a linear transducer (12 L-RS, General Electric, Duluth, MN). In the original selected ESA project (ESA-HSO-U-LE-0629), seven iEMG electrodes were planned for insertion into the obliquus externus (OE) and internus (OI) abdominis, TrA, longissimus thoracis, iliocostalis lumborum, quadratus lumborum, and deep LM muscles with the same configuration used previously (35). However, at BDC-4, 3 of 12 participants in the first cohort reported pain during the needle insertions in the trunk muscles, and the study team decided to exclude iEMG measurements from R + 0 on these 12 participants. In the second cohort, a different EMG configuration was selected, which included only two iEMG (deep LM and TrA) electrodes with the other iEMG electrodes replaced by seven surface EMG (sEMG) electrodes. In the second cohort, no participant complained about pain during the needle insertion, neither at BDC-4 nor at R + 0.

With ultrasound guidance, for deep LM muscle, the needle was inserted ~4 cm lateral to the L4 spinous process until the needle reached the most medial location of the lamina of the L4 vertebra (23). For TrA, the needle was inserted midway between the anterior superior iliac spine and the rib cage into the muscle belly (11). After insertion, the hypodermic needles were removed, leaving only the wires in situ. The free ends of the wires were connected to a wireless spring contact sensor (Trigno, Delsys, Boston, MA). The sEMG electrodes (DELSYS Trigno wireless sensors) were placed over the rectus abdominis (RA; 3 cm lateral to the umbilicus), OE (midway between the anterior superior iliac spine and the distal border of the rib cage), and OI (midway between anterior superior iliac spine and the symphysis pubis) and over the lumbar erector spinae at the vertebral levels L1 (ES_{L1}; 3 cm lateral to L1 spinous process), L2 (ES_{L2}; 5 cm lateral to L2 spinous process), L3 (ES_{L3}; 7 cm lateral L3 spinous process), and L4 (ES_{L4}; 3 cm lateral to L4 spinous process). sEMG electrodes were placed over the middle of the muscle bellies of the anterior (AD) and posterior (PD) deltoid muscles following the SENIAM guidelines for surface EMG (36). Electromyography signals were transmitted telemetrically to a data receiver (Trigno Digital Base Station, Delsys, Boston, MA). Signals were amplified (×100) and sampled at 2,000 samples per second.

Standing Balance: Task and Postural Parameters

Participants stood barefoot on a force platform (AMTI Biomechanics Force Platform model OR6-7, Advanced Mechanical Technology, Watertown, MA) with their arms by their sides, and their feet positioned shoulder-width apart and externally rotated ~20°. Participants maintained quiet stance for 70-s recordings in four conditions: Standing Eyes Open, Standing Eyes Closed, Standing Eyes Open on Foam (6-cm thick dense foam to create an unstable standing surface), and Standing Eyes Closed on Foam (37, 38) (Fig. 1). During the tests with eyes open, participants were asked to focus on a visual target placed at a 2-m distance in front of them at eye level. The room was illuminated with diffuse light, and the background noise was low.

The forces (Fx, Fy, and Fz) and moments (Mx, My, and Mz) were recorded with strain gauges attached to load cells at the four corners of the platform. Signals were sampled at 2,000 Hz and digitized using AMTI minicamp MSA-6 amplifiers (Advanced Mechanical Technology, Watertown, MA). CoPx (frontal plane: mediolateral) was calculated by dividing My by Fz and CoPy (sagittal plane: anteroposterior) by dividing Mx by Fz. CoP data were low-pass filtered at 12.5 Hz (Butterworth filter, 2nd order) (39). The time window from 5 to 65 s of the trial was used for the analysis to avoid disturbance from delayed stabilization of the recording equipment after the initiation of the recording. Global posturographic parameters, which estimate the overall "size" of the sway pattern, were extracted in the time and frequency domain (14). The underlying basis for this analysis is that a posturogram represents stochastic processes that express the "noise" in the posture control system (14). The following outcomes were extracted:

1) Total sway path (cm): cumulative sum of the displacement between consecutive samples for CoPx and CoPy (14, 40);

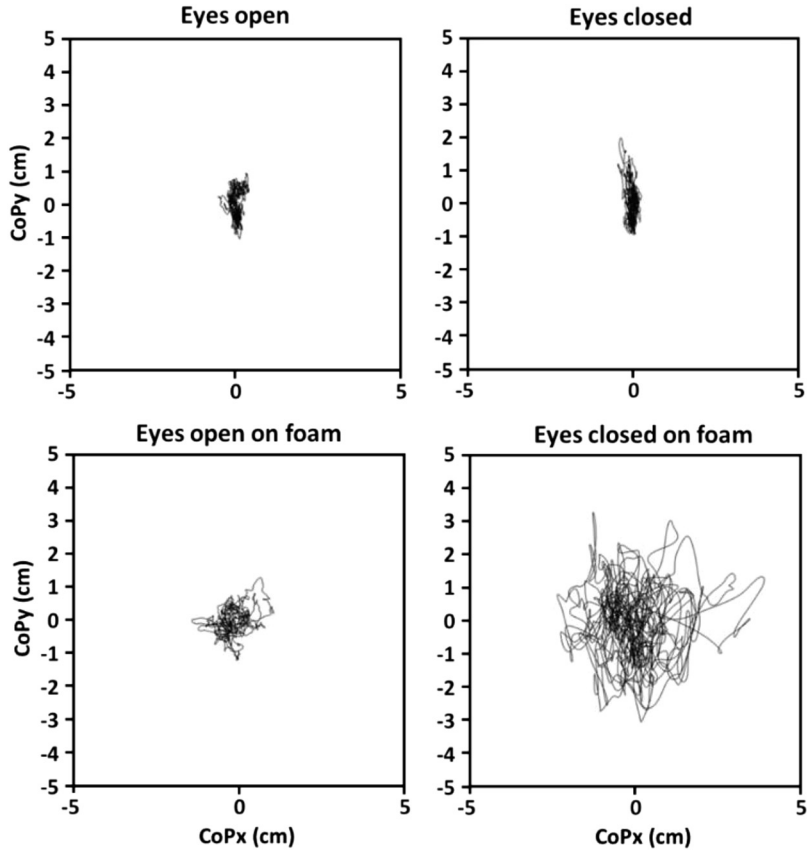

Figure 1. Planar trajectory of the CoP for 60 s from 1 representative participant during upright balance with eyes open, eyes closed, eyes open on a foam and eyes closed on a foam. CoP, center of pressure; *x*, mediolateral plane; *y*, anteroposterior plane.

2) Peak sway velocity (cm/s): calculated from the instantaneous CoP velocity, which was estimated as the derivative of the CoP displacement time-series in the *x*- and *y*-directions (41).

3) Root mean square (RMS) sway velocity (cm/s): RMS sway velocity in the CoPx and CoPy directions were calculated from the instantaneous CoP (41).

4) Area (cm^2): Sway area depends on the distance from the mean CoP and the distance travelled by the CoP and can be conceptualized as proportional to the product of mean distance and mean velocity (40, 42); and

5) Sway frequency power (Hz): fast Fourier transform was applied to time-series data of CoPx and CoPy to calculate the power spectrum and the frequency, below which 95% of the spectral content is found, was identified (40).

Structural posturographic parameters, which attempt to decompose the sway pattern into elements and then examine their interaction, were extracted from sway density plots (14). The underlying basis of this analysis is that feed-forward control of the ankle extensor muscles is a crucial mechanism in the anteroposterior postural stabilization process (43). Therefore, the balance control process can be divided into a sequence of anticipatory motor commands (14). The sway density curve (SDC) was computed by counting the number of consecutive samples of the trajectory of the CoP falling inside a circle with a radius of 2.5 mm (14, 44). The sample count was divided by sampling rate, yielding a time dimension in seconds, and the SDC was low-pass filtered at 2.5 Hz using a fourth order Butterworth filter (44). Each SDC data point represents the time spent inside the circle centered at the corresponding CoP position. The peaks in the SDC were identified, representing periods of relatively stable CoP displacement, i.e., high CoP density. Then, the mean duration of the peaks (SDC duration), the mean time interval between consecutive peaks (SDC interval), and the mean distance between consecutive peaks (SDC distance) were extracted for the statistical analysis (14).

Rapid Arm Movement: Task and Analysis

Participants stood in a relaxed position with their feet shoulder-width apart and their arms by their sides to perform the rapid unilateral arm movement task (RAMT) in response to a light signal. They were instructed to react as quickly as possible to flex (green light) or extend (red light) their left shoulder to ~15/30° as quickly as possible (11). The small-amplitude shoulder movement was used to minimize potential for movement artifacts caused by trunk rotation. At least ten repetitions were completed in each direction, as this number of trials has been shown to provide reliable data (45).

EMG data were digitally band-pass filtered using a fourth-order Butterworth filter (iEMG: 50-1,000 Hz; sEMG: 20–500 Hz). For each arm movement, the times of EMG onset were detected using the approximated generalized likelihood ratio method (46). This algorithm uses statistically optimal decisions to detect changes in EMG amplitude. The automatically detected times of change in amplitude were then visually inspected to avoid spurious "onset candidates" not related to the arm movement, e.g., ECG bursts or other

movement artifacts (47). Both visual determination and approximated generalized likelihood ratio method of EMG onset has been found to be highly repeatable between days during RAMT using a combination of sEMG and iEMG (48, 49). The relative latency between the EMG onset of each of the trunk muscles and that of the deltoid (arm flexion: AD; extension: PD) was calculated and used for analysis. Reaction time was calculated as the latency between the light signal and the onset of AD EMG.

Short-Arm Centrifugation

AG exposures were performed in the supine position (6° head-down tilt) in a 3.0-m short-arm human centrifuge (50). During the 60-day HDT bed rest, participants were transferred on a 6° HDT gurney to the centrifuge facility. The speed of rotation and the positioning of the participants were adjusted so that they were exposed to 1 G at the center of mass of the body. Participants rested with their feet on a footplate and could perform small antiorthostatic maneuvers, such as heel raises and shallow knee bends, to avoid calf pain and maintain circulation while spinning but were otherwise instructed to remain still.

Statistics

Statistical analysis was undertaken using the Statistical Package for Social Sciences (SPSS; Version 25, IBM, Chicago, IL). All data are presented as means ± SD. Statistical significance was set to maintain two-sided 5% level (using multiplicity adjustment where appropriate) for comparisons. All parameters were assessed for normality using visual inspection (histograms and Q-Q plots) for extreme violations. Separate two-way mixed-model repeated-measures ANOVA was used to compare each outcome measure between Groups (CTRL vs. cAG vs. iAG; between-group factor) and Time (BDC-4 vs. R + 0; within-subject factor). Standing balance outcomes were Total sway path CoPx, Total sway path CoPy, Peak sway velocity CoPx, Peak sway velocity CoPy, RMS sway velocity CoPx, RMS sway velocity CoPy, Area, Sway frequency power CoPx, Sway frequency power CoPy, SDC duration, SDC interval, and SDC distance; and RAMT data were relative latency of RA, OE, OI, TrA, ES_{L1}, ES_{L2}, ES_{L3}, ES_{L4}, and deep LM and reaction time. An interaction effect between Group and Time was included in the models. Where appropriate, post hoc analyses were performed using Bonferroni corrected multiple pairwise comparisons, and corresponding adjusted 95% confidence interval (CIs), and *P* values were generated and reported in RESULTS. Effect sizes (partial eta-squared $\eta^2_{partial}$) were calculated. Partial eta-squared reflects the proportion of variance in each effect or interaction and the error that is accounted for by that effect (51).

RESULTS

Participants and Missing Data

All participants completed the 60-day HDT bed rest successfully. One trial of one participant was excluded from the standing balance data because of excessive noise in the force sensor recording (standing with closed eyes on a foam).

Standing Balance

Table 1 shows a summary of the comparison of balance variables between groups and over time.

Table 1. *Summary of comparison of balance variables between groups and over time*

Measure	Standing Eyes Open	Standing Eyes Closed	Standing Eyes Open on Foam	Standing Eyes Closed on Foam
Total sway path CoPx	All ↑	All ↑	All ↑† CTRL > iAG†	All ↑
Total sway path CoPy	All ↑	CTRL ↑ cAG ↑iAG ↑	All ↑† CTRL > iAG†	CTRL ↑* cAG ↑* iAG NS*
Peak sway velocity CoPx	All ↑	All ↑	All ↑	All ↑
Peak sway velocity CoPy	All ↑	CTRL ↑* cAG NS* iAG NS*	All ↑	CTRL ↑* cAG ↑* iAG NS*
RMS sway velocity CoPx	All ↑	All ↑	All ↑† CTRL > iAG†	All ↑
RMS sway velocity CoPy	All ↑	CTRL ↑ cAG ↑ iAG ↑	All ↑† CTRL > iAG†	CTRL ↑* cAG ↑* iAG NS*
Area	All ↑	All ↑	All ↑	All ↑
Sway frequency power CoPx	All NS	All NS	All ↑	All ↑
Sway frequency power CoPy	CTRL ↑* cAG ↑* iAG NS* CTRL > iAG*	CTRL ↑* cAG NS* iAG NS* CTRL > iAG*	All ↑	All NS
SDC duration	All ↓	All ↓	All ↓	All ↓
SDC interval	All NS	All ↑	All NS	All ↓
SDC distance	All ↑	All ↑	All ↑	All ↑

cAG, continuous artificial gravity; RMS, root mean square; SDC, sway density curve; CoP, center of pressure; *x*, mediolateral plane; *y*, anteroposterior plane. ↑, Greater value at R + 0 (1st day after bed rest) than BDC-4 (4 days before bed rest); NS, no significant difference. *Variables that show that intermittent artificial gravity (iAG) prevented decline. †Variables that show that iAG declined but less than control (CTRL).

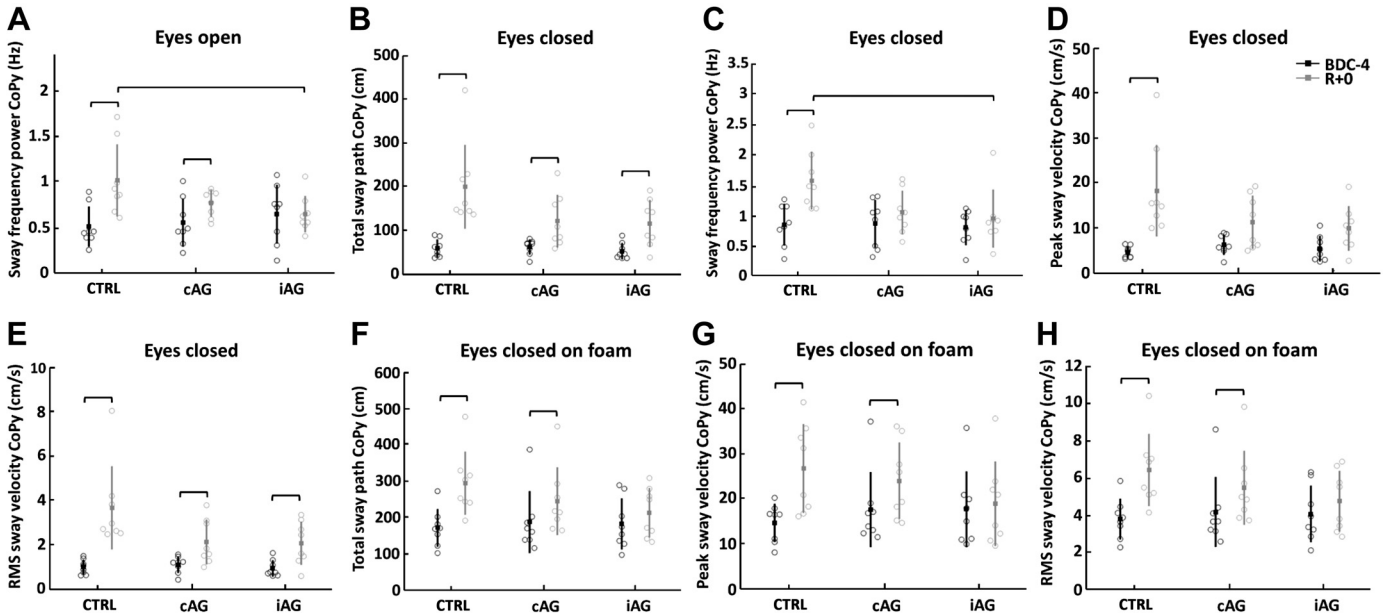

Figure 2. Parameters of upright balance assessed before (BDC-4, in black) and after (R + 0, in gray) HDT bed rest. Only parameters showing a significant Time × Group interaction are shown. Data from individual participants are represented by open circles, whereas the group means ± SD are represented by filled squares with vertical lines. *A*: Sway frequency power CoPy (Hz) during eyes open; *B*: Total sway path CoPy (cm) during eyes closed; *C*: Sway frequency power CoPy (Hz) during eyes closed; *D*: Peak velocity sway CoPy (cm/s) during eyes closed; *E*: RMS velocity sway CoPy during eyes closed; *F*: Total sway path CoPy (cm) during eyes closed on foam; *G*: Peak velocity sway CoPy (cm/s) during standing eyes closed on foam; *H*: RMS velocity sway CoPy during standing eyes closed on foam. HDT, head-down tilt; BDC, 4 days before bed rest; R + 0, 1st day after bed rest; CTRL, control; cAG, continuous artificial gravity; iAG, intermittent artificial gravity; CoP, center of pressure; *y*, anteroposterior plane; RMS, root mean square.

Standing eyes open.

In general, data showed that balance in the condition "Standing Eyes Open" became more unstable at R + 0 than BDC-4. A significant main effect of Time was identified for most parameters: Total sway path CoPx, Total sway path CoPy, Peak sway velocity CoPx, Peak sway velocity CoPy, RMS sway velocity CoPx, RMS sway velocity CoPy, Area, SDC distance, and SDC duration (all: $F_{1,21} > 12$; $P < 0.005$; $\eta^2_{partial} > 0.4$; see Supplemental Table S1 for detail of statistical analysis; all Supplemental materials are available at https://doi.org/10.6084/m9.figshare.14034902). There were no significant main effects of Group for all parameters (all: $F_{2,21} < 3$, $P > 0.05$, $\eta^2_{partial} < 0.25$). A significant Time × Group interaction was found for Sway frequency power CoPy ($F_{2,21}$ = 6.35; P = 0.007, $\eta^2_{partial}$ = 0.38) (Fig. 2*A*). Post hoc analysis revealed that Sway frequency power CoPy was higher at R + 0 than BDC-4 for the CTRL ($P < 0.001$; 95% CI [0.3, 0.7]) and cAG (P = 0.049; 95% CI [0.0, 0.4]) groups, but there was not difference for iAG (P = 1.000; 95% CI [−0.2, 0.2]). Consistent with this observation, Sway frequency power CoPy at R + 0 was higher in CTRL than iAG (P = 0.036; 95% CI [0.0, 0.7]) group.

Standing eyes closed.

Similar to the condition "Standing Eyes Open," a main effect of Time was significant for most parameters: Total sway path CoPx, Peak sway velocity CoPx, RMS sway velocity CoPx, Area, SDC distance, SDC interval, and SDC duration (all: $F_{1,21} > 4$; $P < 0.050$; $\eta^2_{partial} > 0.2$; see Supplemental Table S2). There were no significant main effects of Group for all parameters (all: $F_{2,21} < 3$, $P > 0.05$, $\eta^2_{partial} < 0.25$). A significant Time × Group interaction was found for Total sway path CoPy, Sway frequency power CoPy, Peak sway velocity CoPy, and RMS sway velocity CoPy (all: $F_{2,21} > 5$; $P < 0.050$, $\eta^2_{partial} > 0.25$) (Fig. 2, *B–E*). For the CTRL group, Total sway path CoPy ($P < 0.001$; 95% CI [81.3, 161.1]), Sway frequency power CoPy ($P < 0.001$; 95% CI [0.4, 1.1]), Peak sway velocity CoPy ($P < 0.001$; 95% CI [8.6, 18.9]), and RMS sway velocity CoPy ($P < 0.001$; 95% CI [1.8, 3.6]) were greater at R + 0 than BDC-4. For the cAG group, Total sway path CoPy (P = 0.020; 95% CI [8.6, 88.4]) and RMS sway velocity CoPy (P = 0.027; 95% CI [0.1, 1.9]) were greater at R + 0. For the iAG group, Total sway path CoPy (P = 0.014; 95% CI [11.4, 91.2]) and RMS sway velocity CoPy (P = 0.015; 95% CI [0.2, 2.0]) were greater at R + 0. At R + 0, and the Sway frequency power CoPy was higher for the CTRL than iAG group (P = 0.029; 95% CI [0.1, 1.1]).

Standing eyes open on foam.

A main effect of Time was found for all parameters assessed (all: $F_{1,21} > 5$; $P < 0.050$; $\eta^2_{partial} > 0.2$), except SDC interval (see Supplemental Table S3). There was also a Group effect for the Total sway path CoPx, Total sway path CoPy, RMS sway velocity CoPy, and RMS sway velocity CoPy (all: $F_{2,21} > 5$; $P < 0.050$, $\eta^2_{partial} > 0.3$), which was explained by higher values for the CTRL than iAG group, irrespective of Time (all $P < 0.050$).

Standing eyes closed on foam.

A main effect of Time was found for most parameters: Total sway path CoPx, Area, Sway frequency power CoPx, Peak sway velocity CoPx, RMS sway velocity CoPx, SDC interval, and SDC distance (all: $F_{1,21} > 13$; $P < 0.001$; $\eta^2_{partial} > 0.4$) (see Supplemental Table S4). There were no significant main effects of Group for all parameters (all: $F_{2,21} < 3$, $P > 0.05$,

$\eta^2_{partial} < 0.25$). There was a significant Time × Group interaction for the Total sway path CoPy, Peak sway velocity CoPy, and RMS sway velocity CoPy (all: $F_{2,21} > 4$; $P < 0.050$, $\eta^2_{partial} > 0.3$; Fig. 2, *F–H*). The CTRL group had greater Total sway path CoPy ($P < 0.001$; 95% CI [69.6, 176.9]), Peak sway velocity CoPy ($P < 0.001$; 95% CI [7.8, 21.2]), and RMS sway velocity CoPy ($P < 0.001$; 95% CI [1.4, 3.8]) at R + 0 than BDC-4. For the cAG group, the Total sway path CoPy ($P = 0.036$; 95% CI [4.1, 111.5]), Peak sway velocity CoPy ($P = 0.026$; 95% CI [1.0, 14.4]), and RMS sway velocity CoPy ($P = 0.033$; 95% CI [0.1, 2.5]) were greater at R + 0. The iAG group did not show a significant difference over Time (all: $P > 0.4$).

Rapid Arm Movement Task

Electromyography results for this task are based on 12 individuals (4 per each group) because R + 0 data for the first cohort were missing.

During arm flexion, reaction time at BDC-4 was 209 ± 42 ms, 259 ± 74 ms, and 256 ± 60 ms for the CTRL, cAG, and iAG groups, respectively. This did not differ between groups or from values at R + 0 (210 ± 57 ms, 238 ± 74 ms, and 247 ± 31 ms, respectively; Time: $F_{1,9} = 0.43$, $P = 0.53$, $\eta^2_{partial} = 0.05$; Group: $F_{2,9} = 0.78$, $P = 0.49$, $\eta^2_{partial} = 0.15$; Time × Group interaction: $F_{2,9} = 0.20$, $P = 0.82$, $\eta^2_{partial} = 0.04$). EMG onsets of TrA, ES_{L1}, ES_{L2}, ES_{L3}, and ES_{L4} relative to AD during arm flexion were later at R + 0 than at BDC-4 for all groups (Time: all: $F_{1,9} > 5$, $P < 0.05$, $\eta^2_{partial} > 0.4$; see Supplemental Table S5). There were no significant main effects of Group for all relative onset (all: $F_{2,9} < 3$, $P > 0.1$, $\eta^2_{partial} < 0.35$). There was a significant Time × Group interaction for relative onset of OE EMG ($F_{2,9} = 5.44$, $P = 0.028$, $\eta^2_{partial} = 0.55$). For the CTRL group, the OE EMG onset during arm flexion was later at R + 0 than BDC-4 ($P = 0.010$; 95% CI [23.2, 128.4]) but no difference between time points was identified for the cAG ($P = 0.615$; 95% CI [−40.5, 64.7]) or iAG ($P = 0.200$; 95% CI [−84.7, 20.4]) groups (Fig. 3). At R + 0, the OE EMG onset was not different between iAG and CTRL groups ($P = 0.14$; 95% CI [−184.7, 22.2]) and cAG and CTRL groups ($P = 0.55$; 95% CI [−154.2, 52.8]), and iAG and cAG ($P = 1.00$; 95% CI [−61.2, 88.7]).

During arm extension, reaction time at BDC-4 was 201 ± 46 ms, 252 ± 95 ms, and 223 ± 38 ms for the CTRL, cAG and iAG groups, respectively. Reaction times did not differ between groups or from values at R + 0 (195 ± 53 ms, 228 ± 71 ms, and 254 ± 60 ms, respectively; Time: $F_{1,9} = 0.11$, $P = 0.76$, $\eta^2_{partial} = 0.01$; Group: $F_{2,9} = 0.47$, $P = 0.64$, $\eta^2_{partial} = 0.10$; Time × Group: $F_{2,9} = 2.45$, $P = 0.14$, $\eta^2_{partial} = 0.35$). Onsets of OE, OI, ES_{L1}, ES_{L2}, and ES_{L4} EMG relative to PD during arm extension were later at R + 0 than BDC-4 in all groups (all time: $F_{1,9} > 5$, $P < 0.050$, $\eta^2_{partial} > 0.4$; Fig. 4; see Supplemental Table S6). There were no significant main effects of Group (all: $F_{2,9} < 3$, $P > 0.1$, $\eta^2_{partial} < 0.4$) or Time × Group interaction (all: $F_{2,9} < 3$, $P > 0.1$, $\eta^2_{partial} < 0.4$) for all relative onset.

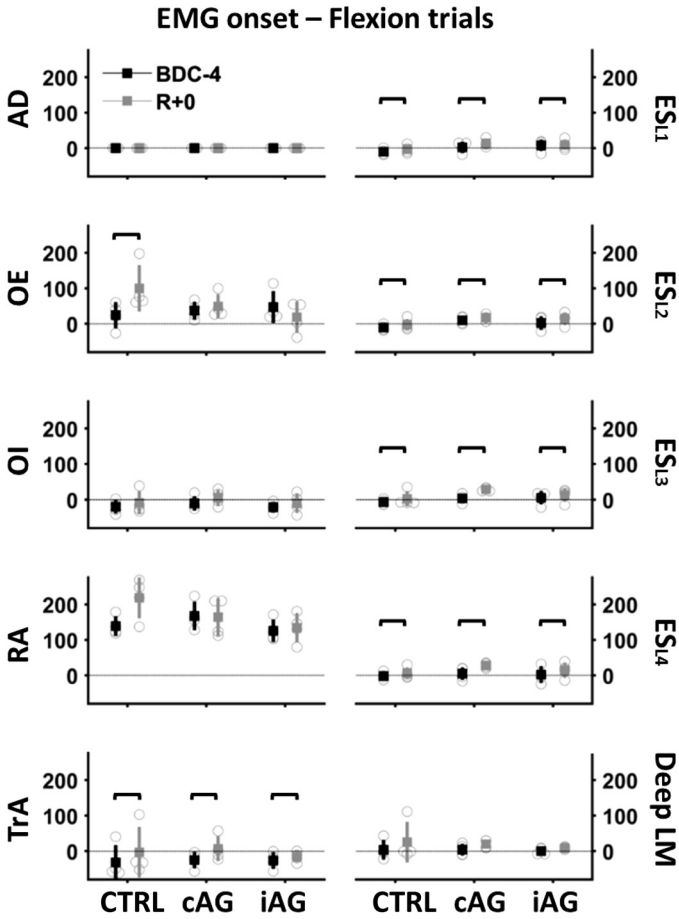

Figure 3. Times of EMG onset of the trunk muscles assessed during rapid shoulder flexion for obliquus externus (OE) and internus (OI) abdominis; rectus abdominis (RA); transversus abdominis (TrA); lumbar erector spinae at vertebral levels L1 (ES_{L1}), L2 (ES_{L2}), L3 (ES_{L3}), and L4 (ES_{L4}); and deep lumbar multifidus (Deep LM). EMG onset times are expressed in milliseconds relative to the onset of the prime mover in each condition: Anterior deltoid (AD) in shoulder flexion trials. Data from individual participants are represented by open circles, whereas the group means ± SD are represented by filled squares with vertical lines. CTRL, control; cAG, continuous artificial gravity; iAG, intermittent artificial gravity

DISCUSSION

This study investigated the effects of daily iAG and cAG, using short-arm centrifugation, on standing balance and timing of trunk muscle activation during rapid arm movement following 60-day of strict 6° HDT bed rest. Based on a variety of parameters of the CoP, the results confirmed that balance control was compromised by vertical gravitational unloading and showed that these effects could be partially mitigated by daily exposure to intermittent but not continuous, AG. By contrast, although vertical gravitational unloading induced a delay in the relative latency of multiple trunk muscles in association with rapid arm movement, there was a minimal, if any, impact of AG on the preservation of this parameter. These results suggest that iAG can partially mitigate the impairments in standing balance, although these protective effects could not be detected in the control/coordination of the superficial and deep lumbar spinal muscles during anticipatory adjustments to quick arm movements.

Standing Balance

Balance performance declines after 60-day HDT bed rest.

In the control group, the present results showed that most of the global postural parameters (area, displacement, velocity,

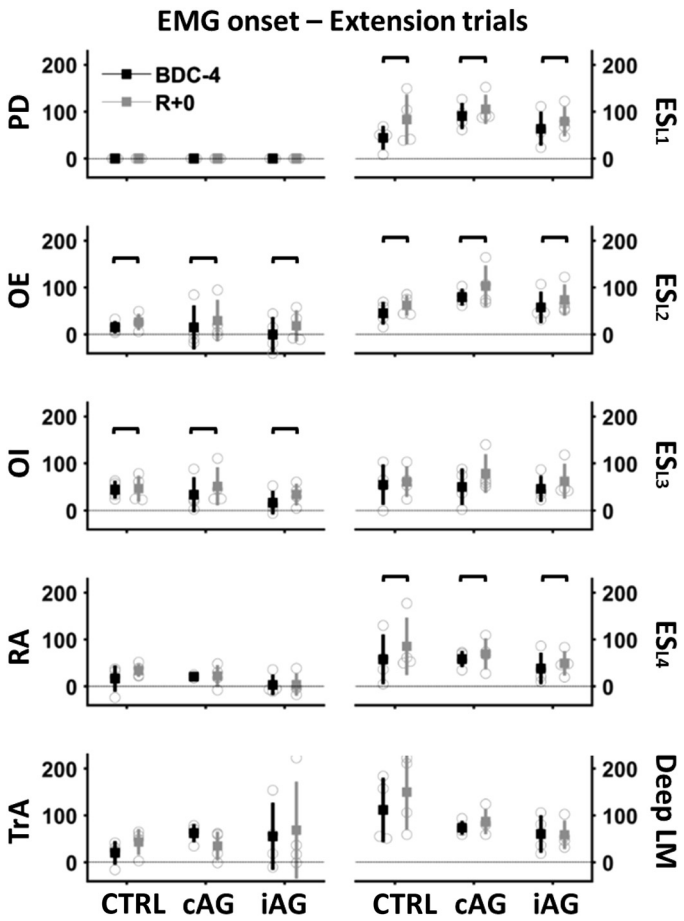

Figure 4. Times of EMG onset of the trunk muscles assessed during rapid shoulder extension for obliquus externus (OE) and internus (OI) abdominis; rectus abdominis (RA); transversus abdominis (TrA); lumbar erector spinae at vertebral levels L1 (ES_{L1}), L2 (ES_{L2}), L3 (ES_{L3}), and L4 (ES_{L4}); and deep lumbar multifidus (Deep LM). EMG onset times are expressed in milliseconds relative to the onset of the prime mover in each condition: Posterior deltoid (PD) in shoulder extension trials. Data from individual participants are represented by open circles, whereas the group means ± SD are represented by filled squares with vertical lines. CTRL, control; cAG, continuous artificial gravity; iAG, intermittent artificial gravity.

and power spectra of the CoP) and structural postural parameters (sway density curve of the CoP) deteriorated after 60-day HDT bed rest in all standing balance tasks. Relative and absolute changes in the area, displacement, and velocity of the CoP showed a similar increase in anteroposterior and mediolateral trajectories. Similar changes have been previously reported during standing eyes open and closed on stable and unstable surfaces after 60-day HDT bed rest (16–18). The present results support and extend previous findings by showing increased anteroposterior sway frequency power following 60-day HDT bed rest, which is a sensitive measure associated with age-related changes in postural balance (40, 52). This increase in anteroposterior sway frequency power was not observed when standing on foam with eyes closed, most likely due to the already high spectral contents observed at BDC-4 on this task (>1 Hz). By contrast, the sway frequency power in the mediolateral plane only increased when standing on unstable surfaces, which corroborates the increase in mediolateral sway observed when participants stood on foam (53). These results collectively indicate that ankle mechanisms, which mainly control anteroposterior displacements (43), and hip/trunk mechanisms, which primarily control mediolateral displacements (54), are similarly affected by 60-day HDT bed rest, except for minor differences in sway frequency power. More pronounced displacements appeared on an unstable surface than a stable surface, likely due to reduced capacity of plantar flexor muscles to generate ankle torque (55), as well as reduced interpretability of peripheral sensory information from ankle joint receptors and the cutaneous pressure receptors of the foot sole (18, 56).

The SDC analysis demonstrated that, after prolonged bed rest, participants spent less time in a stable region (decreased SDC duration) and that a larger distance separated two consecutive local stability regions (increased SDC distance). Although speculative, as SDC parameters reflect the capacity of the postural control system to detect and integrate the sensory inputs and anticipate internal physiological delays to maintain the vertical alignment of the whole body (14, 44), it is possible that participants had to increase their postural oscillations to receive sufficient information about the position of the whole body. Alternatively, this might be explained by reduced muscle stiffness of the so-called "antigravity" muscles (i.e., ankle plantar flexors and hip/trunk extensors), which provide an action that tends to counteract the destabilizing torque caused by gravity.

Taken together, the present analyses suggest that, due to the multifactorial nature of postural control, both global (e.g., sway path and sway area) and structural postural (sway-density curve) parameters are required to properly decode CoP information during standing balance and adequately characterize the postural control dysfunction imposed by prolonged vertical unloading. Detailed analysis of the timing of CoP provided insight into the degradation of peripheral sensory information, as is revealed by the associated SDC parameters.

Intermittent AG prevents decline in some balance variables after 60-day HDT bed rest.

Exposure to intermittent bouts, but not to a single longer bout, provided partial protection against the deleterious effects of reduced prolonged vertical gravitational load in the upright standing balance as measured by some outcomes. The present results indicated that the impact of iAG was stronger in the anteroposterior plane, as demonstrated by smaller changes in CoP displacement, velocity, and frequency sway parameters than identified for the control group. Our observations may partially confirm the results of Kramer et al. (55), which showed moderate preservation of the function of the plantar flexor muscles in the current HDT bed rest by use of the AG protocols. This is congruent with our results for the anteroposterior direction, as the plantarflexor muscles make the primary contribution to balance control in this direction (43). Unlike our data, Kramer et al. (55) did not detect any differences between the two AG protocols, which suggests plantar flexor muscle strength does not fully explain iAG effects. In our study, iAG mitigated the deleterious effects of HDT bed rest on sway displacement, sway velocity, and sway power spectra, particularly in conditions with eyes closed and standing on an unstable surface (see Table 1 for details). The difference

between surface conditions indicates a stronger protective effect of iAG in situations that involve reduced visual and proprioceptive feedback. Hence, it is possible that the repeated periods of acceleration and deceleration, rather than a sustained velocity, had a more beneficial effect on the sensory (proprioceptive) receptors and cutaneous receptors in the foot sole during centrifugation. Alternatively, the stronger protective effect of iAG might also be explained by the repeated periods of acceleration and deceleration of AG in the otolith organ (vestibular system).

In contrast with the current results, a previous study failed to detect a protective effect of iAG after a 5-day (31) HDT bed rest period. However, different balance tasks, bed rest duration, and postural outcomes measures may explain these contrary results. In the current study, to obtain more robust measures of the postural system, we extracted several postural balance outcomes (global and structural postural parameters) over trials of 60-s duration, in contrast to previous studies that assessed a single outcome (peak anteroposterior sway path) over trials of 30 s of duration (31). As postural balance is not a stationary stochastic process, measures made during the first 30 s of a trial differ from the same parameters determined during the second 30 s (37). Moreover, a longer duration of HDT bed rest and AG exposure may also explain the magnitude of deterioration of standing balance observed in the control group and thus greater potential for more substantial protective effects of iAG.

Rapid Arm Movement Task

Activation of trunk muscles in APAs is delayed after 60-day HDT bed rest.

At BDC-4, the trunk muscle onset before, or 50 ms after the onset of deltoid EMG, is consistent with previous studies in healthy individuals, indicating an anticipatory activation of the OI, TrA, ES, and DM muscles in association with shoulder flexion, and activation of the OE and RA muscles in association with rapid shoulder extension (10, 11, 23). Considering electromechanical delay and latency for nerve conduction, even the shortest latency response to feedback from limb movements cannot be initiated earlier than 50 ms after the onset of deltoid EMG (10, 57). After 60-day HDT bed rest, the present results showed that EMG onsets of the TrA and superficial lumbar ES muscles occurred later during shoulder flexion, but were still earlier than 50 ms after the onset of the activation AD muscle. Similarly, activation of the OE muscle was delayed during arm extension after HDT bed rest, but the onset of EMG was earlier than 50 ms after the onset of the PD muscle. Taken together, the present results indicate that trunk APAs were delayed after prolonged body unloading, but APAs associated with limb movements were still present.

Several possible mechanisms might explain the delayed onset of trunk muscles onsets after 60-day HDT bed rest. First, it has been reported previously that skeletal muscle deterioration due to prolonged unloading may interfere with distal motor nerve function (58). Furthermore, in studies of rats exposed to 2 or more wk of microgravity, absence of synaptic vesicles in the motoneuron terminals and degenerative changes in the neuromuscular junction of atrophied antigravity muscles has been reported (59). Regarding the paraspinal muscles, previous studies have observed atrophy of 5–15% in the LM, the lumbar erector spinae and quadratus lumborum at different lumbar levels following 60-day bed rest (60). A complementary explanation of delayed APAs in the current study is that of possible decrease in excitability of the corticomotor output, reducing the motor drive to antigravity muscles. By using transcranial magnetic stimulation, reduced amplitude of motor-evoked potentials has been previously detected in the leg muscles after prolonged bed rest (61). Finally, vestibular influences may be involved in delayed muscle responses observed in the present study. For instance, motoneuron excitability is modified by vestibular inputs to the synapse between the Ia afferent from the muscle spindle and the alpha motoneuron (62). Vertical unloading on the vestibular apparatus has been shown to affect the motoneuron pools of extensor and flexor "antigravity" muscles (4).

Some conflicting findings to those of the current investigation have been reported in previous bed rest studies (26, 27). Faster APAs during bilateral shoulder flexion and delayed reflex responses to sudden loading were observed in superficial trunk muscles in aging adults after 14-day HDT bed rest (26). In contrast, no latency changes and reduced maximal amplitude of APAs during bilateral arm flexion were detected after 21-day HDT bed rest in a young population (27). Several differences between these studies may explain these partially divergent findings. In Šarabon et al. (26, 27), participants held a 1.2-kg accelerometer bar with arms extended down by sides, and they were asked to raise it as fast as possible with extended arms up to the shoulder height. Holding a weight likely produces a tonic activation of the trunk muscles, which may affect the detection of trunk muscle onsets. A previous study showed that tonic activation delayed the onsets of trunk muscles during RAMT (47). A higher background muscle activity before the RAMT is likely to increase the level of descending drive, rendering "additional" muscle activity unnecessary until later (47). Moreover, algorithms to detect EMG onset are sensitive to the level of background activity (more specifically, the signal-to-noise ratio), so that larger activity levels during baseline may result in a later onset detection. In addition, the length of bed rest and participant position (e.g., horizontal versus HDT) may justify these partially differing results.

AG has limited impact on trunk muscle contribution to APAs after 60-day HDT bed rest.

It was hypothesized that daily exposure to AG would mitigate delay of responses of the deep LM and TrA muscles during APAs at the end of 60-day HDT bed rest, most likely by stimulating the mechanoreceptors located in joints, ligaments, tendons, and deep paraspinal muscles, which contribute to lumbar proprioception (63). In contrast, the results indicated that neither iAG nor cAG modified the relative onsets of TrA and deep LM during rapid voluntary arm movement after exposure to 60-day HDT bed rest. It is possible that the short duration of the AG centrifugation protocol used in the current study (30 min/day of 1 G_z) was not sufficient to produce a protective effect via mechanisms such as enhanced trunk proprioceptive input. Alternatively, the application of forces to the spine without muscle contraction may be insufficient to mitigate lumbar spine adaptations. Further studies are needed to investigate whether variants of

the AG protocol used here, including higher G-loads or longer durations of exposure to AG, combined with the application of either dynamic lumbar spine movement or different trunk position that increases tonic activation of the trunk muscles, can mitigate the delay in trunk muscle onsets following prolonged bed rest.

Although earlier activation of the OE muscle is most critical during arm extension movements (64), the present data showed that the OE latency was unchanged in the AG groups during arm flexion, whereas the CTRL group participants demonstrated delayed onsets. The protective effects of AG in OE onset may have been underpinned by muscle tension of the abdomen and the extremities during centrifugation to maintain the blood flow in the carotid arteries (65). Although participants were not explicitly instructed to utilize the Valsalva maneuver (as part of an anti-G straining maneuver), there is a possibility that they spontaneously engaged in respiratory straining maneuvers or abdominal muscle bracing.

Operational Relevance and Recommendations for Future Planetary Surface Explorations

One of the goals of NASA/ESA's Human Research Roadmap is to develop optimal countermeasures to mitigate the deterioration of standing balance and musculoskeletal injuries of astronauts following prolonged exposure to microgravity. Standing balance impairments and poor trunk muscle control would have implications for the performance of operational tasks that would likely require ambulation following landing on a planetary surface and emergency egress from a landing vehicle (66). Thus falls and musculoskeletal injuries are a major concern for space agencies because they may represent one of the causes of functional disability and death during a Lunar or Martian mission.

In the current study, iAG was protective of standing balance measures in the anteroposterior plane after prolonged vertical unloading compared with CTRL, probably due to repeated stimulation of sensory receptors, including the cutaneous receptors of the foot, ankle muscles, and vestibular apparatus. Nevertheless, some deterioration of standing balance was still evident, particularly in the mediolateral direction. Thus daily iAG, as it was applied here, did not eliminate the effect of prolonged unloading. A previous bed rest study has demonstrated a protective effect of daily low-magnitude mechanical vibration on postural balance, as shown by a 73% improvement in anteroposterior CoP displacement when compared with results from untreated controls (16). In the current study, the improvement of the anteroposterior CoP displacement was ~60% in the iAG group when compared with the CTRL group. It may be speculated that the combination of AG and low-frequency vibration countermeasures could provide more robust benefits to postural control, although this hypothesis requires appropriate investigation.

By contrast, AG seemed insufficient to mitigate the delayed APAs of trunk muscles following bed rest. The consequence of the delayed onset of muscle activation implies that control of the spine is reduced after a period of bed rest, and this might compromise spine tissues. Importantly, increases of IVD height due to hyperhydration have been observed following bed rest studies and spaceflights (67, 68), as well as atrophy of the LM (69, 70). Taken together, changes in the intervertebral disk morphology and chemical proprieties, atrophy of the lumbar paraspinal muscles, and delayed onset of the lumbar and abdominal muscles after prolonged gravitation unloading may have clinical consequences. Importantly, passive AG, as applied here, had no protective effect on the present outcome measures of trunk muscle control. However, dynamic movements and active voluntary resisted contraction of trunk muscles combined with other paradigms of AG might produce additional protective effects on the lumbar spine. Finally, monitoring the activity of superficial abdominal muscles during centrifugation may require further investigation to better understand the present findings.

Limitations

An important limitation of all bed rest studies, including this one, is the small sample size due to the physical and social demands put on the participants and the high costs. Related to this, many linked and similar outcomes have been analyzed, given the rare opportunity to measure these factors. The small sample size limited the analytic options to address complexity in the data.

A second limitation relates to the availability of EMG data. First, EMG recordings were not available for analysis for the first cohort of participants. Second, sEMG was used to investigate the activity of most trunk muscles. As trunk muscles are multilayered and have different fiber orientations, the intensity and selectivity of signals recorded using sEMG may be compromised due to cross-talk from adjacent muscles and a low signal-to-noise ratio (71, 72).

Finally, arm acceleration during RAMT was not assessed in the current study. Although it is not possible to be certain that the arm acceleration was identical before and after bed rest, any trial assessed visually as not performed as a quick and sharp response was discarded and repeated until at least ten repetitions were completed in each direction.

Conclusions

Prolonged bed rest led to impairments in balance demonstrated by numerous indices of postural control and delayed onsets of the lumbar and abdominal muscles in a predictable postural perturbation. Intermittent AG alleviated the degree of deterioration of some CoP measures of postural stability in the anteroposterior direction, but these effects did not appear to be related to improved control/coordination of the trunk muscles. These findings suggest that intermittent AG may be considered as a potential countermeasure for future recommendations for planetary surface explorations, but further optimization of AG protocols is warranted to fully preserve postural control in all movement planes.

SUPPLEMENTAL DATA

Supplemental Tables S1–S6 are available at https://doi.org/10.6084/m9.figshare.14034902.

GRANTS

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

E.D.M., J.S., T.W., N.C., S.E.S., P.W.H., J.H., D.D., and A.W. conceived and designed research; E.D.M., R.E., L.H., and K.L. performed experiments; E.D.M. and S.E.S. analyzed data; E.D.M., D.B., and P.W.H. interpreted results of experiments; E.D.M. and S.E.S. prepared figures; E.D.M. drafted manuscript; E.D.M., D.B., J.A.C., J.S., T.W., N.C., S.E.S., P.W.H., J.H., K.L., D.D., A.W., J.M.E., and M.H. edited and revised manuscript; E.D.M., D.B., J.A.C., R.E., L.H., J.S., T.W., N.C., S.E.S., P.W.H., J.H., K.L., D.D., A.W., J.M.E., and M.H. approved final version of manuscript.

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