

Short applications of very low-magnitude vibrations attenuate expansion of the intervertebral disc during extended bed rest

Nilsson Holguin, MS, Jesse Muir, MS, Clinton Rubin, PhD, Stefan Judex, PhD*

Department of Biomedical Engineering, State University of New York at Stony Brook, Psychology A, 3rd Floor, Stony Brook, NY 11794-2580, USA

Received 16 June 2008; accepted 20 February 2009

Abstract

BACKGROUND CONTEXT: Loss of functional weightbearing during spaceflight or extended bed rest (BR) causes swelling of the lumbar intervertebral discs (IVDs), elongates the spine, and increases the incidence of low back pain (LBP). Effective interventions for the negative effects of unloading are critical but not yet available.

PURPOSE: To test the hypothesis that high-frequency, low-magnitude mechanical signals (LMMS) can attenuate the detrimental morphologic changes in the lumbar IVDs.

STUDY DESIGN/SETTING: Volunteers were subjected to 90d of BR and 7d of reambulation. While retaining this supine position, 18 random subjects received LMMS (30 Hz) for 10 min/d, at peak-to-peak acceleration magnitudes of either 0.3 g (n=12) or 0.5 g (n=6). The remaining subjects served as controls (CTRs).

PATIENT SAMPLE: Eighteen males and 11 female (33±7 y) healthy subjects of astronaut age (35±7 y, 18 males, 11 females) and without a history of back pain participated in this study.

OUTCOME MEASURES: A combination of magnetic resonance imaging and computed tomography scans of the lumbar spine of all subjects were taken at baseline, 60d, 90d, and 7d post-BR. Back pain was self-reported.

METHODS: IVD morphology, spine length, and back pain were compared between CTR and LMMS subjects.

RESULTS: Compared with untreated CTRs, LMMS attenuated mean IVD swelling by 41% (p<.05) at 60d and 30% (p<.05) at 90d. After 7 days of reambulation, disc volume of the CTR group was still 8% (p<.01) greater than at baseline, whereas that for the LMMS group returned the disc volume to baseline levels. In contrast to BR alone, LMMS also retained disc convexity at all time points and reduced the incidence of LBP by 46% (p<.05).

CONCLUSIONS: These data indicate that short daily bouts of LMMS can mitigate the detrimental changes in disc morphology, which arise during nonweightbearing, and provides preliminary support for a novel means of addressing spinal deterioration both on earth and in space. © 2009 Elsevier Inc. All rights reserved.

Keywords:

Intervertebral disc; Bed rest; Swelling; Vibrations; High-frequency mechanical stimuli; Biomechanical countermeasure

Introduction

The loss of functional weightbearing encountered during bed rest (BR) or spaceflight initiates catabolic changes throughout the musculoskeletal system. These periods of

reduced loading lead to increased incidence of low back pain (LBP) as associated with abnormal spinal lengthening [1], atrophy of the spinal musculature [2], increased intervertebral disc (IVD) height and area [1,4], and altered IVD

Institutional Review Board Approval: This study was reviewed and approved by the Committee on Research in Human Subjects of Stony Brook University, the University of Texas Medical Branch at Galveston, and NASA's Johnson Space Center.

FDA device/drug status: not approved; assessed as no significant risk.

Author disclosures: CR (financial relationship, Stockholder and consultant for Juvent Inc.).

* Corresponding author. Department of Biomedical Engineering, Psychology A, 3rd Floor, State University of New York at Stony Brook, Stony Brook, NY 11794-2580, USA. Tel.: (631) 632-1549; fax: (631) 632-8577. E-mail address: stefan.judex@sunysb.edu (S. Judex)

composition [3]. Even restoration of full function may not remedy LBP. More than 50% of astronauts complain of LBP during space missions as well on returning to earth [1]. On earth, LBP is an epidemic with more than 80% of the adult US population experiencing a severe episode during their lifetime [5]. As remedies are mostly palliative once a person experiences LBP on earth or in space from a morphologically altered disc, interventions that can prevent or attenuate long-term morphological IVD changes are critical.

The role of weightbearing in the retention of IVD form and function is not entirely clear. Because of its lack of vascular supply, loading, and load-induced fluid flow are certainly critical to the exchange of nutrients and waste. The extent by which the IVD will alter its morphology on removal of ground reaction forces and muscle forces is evident even over a 24-h diurnal cycle during which the spine can elongate 2 cm [6]. Spaceflight exacerbates crew member height change by as much as 6 cm [1]. Although factors unrelated to the IVD also are certain to play a role in LBP, IVD degeneration and expansion are considered primary etiologic factors in this debilitating disorder [3,4]. Indeed, IVD expansion alone can exacerbate LBP through processes, such as increased strain of neighboring facet joint capsules [7], fracture of innervated vertebral end plates, or stimulation of nociceptors in the posterior annulus fibrosus arising from radial fissures or protrusions.

Currently, no prophylaxes or treatments for IVD pathology exacerbated by extended periods of nonweightbearing are available. Walking exercises with and without loaded backpacks showed that the application of even large mechanical loads during phases of unloading do not return IVD volume to normal levels [8–10]. In a previous study, daily running routines on a lower body negative pressure treadmill partially negated altered disc morphology during spine deconditioning over a 28d unloading period but the daily 45 minutes protocol failed to reduce expansion of the lower lumbar IVDs [11].

Because fluid motion and displacement are related to the frequency of the applied mechanical signal [12,13], it is possible that increasing the loading frequency may increase the ability of the countermeasure to exude fluid from the disc and therefore attenuate IVD expansion [14]. Higher-frequency mechanical signals can be transmitted into the musculoskeleton via whole body vibrations. Although vibrations may improve neuromuscular function [15], reinforce lumbar proprioception [16], and potentially pose a treatment for LBP [17], they need to be approached with caution as they can cause the back pain they are intended to prevent [18]. Safety concerns for the musculoskeletal system arise when whole body vibrations exceed accelerations of 1 g [19], while the International Organization for Standardization has identified no evidence of acute or chronic complications of 20–90 Hz vibrations when exposure falls below 0.56 g (often termed low-magnitude vibrations). In the current study, controls (CTRs) subjected to 90 days of restricted BR were compared with those confined to BR but also subjected to short bouts (10 min/d) of

EVIDENCE & METHODS

Context

Morphological changes within intervertebral discs and associated low back pain are concerns during spaceflight and extended bed rest. Interventions aimed at preventing both are now being explored.

Contribution

This randomized trial examined healthy volunteers of astronaut age with no history of serious low back pain problems. Control subjects were exposed to 90 days of best rest, whereas experimental subjects were additionally exposed to very low-magnitude vibration for 10 minutes a day. Those exposed to this vibration intervention demonstrated smaller changes in disc morphology and reported less low back pain than those without such exposure.

Implications

The findings are interesting and address an important problem. However, some methodological issues are of concern. The method of randomization is unclear. Subjects and the physician/assessor were not blinded to the treatment type. Only one physician/assessor was involved. Thus, reliability cannot be ascertained and bias is difficult to exclude. The magnitude of the reported effect is small and the clinical and functional significance is unclear. Finally, optimal dosing, if indeed the observed effect is real and clinically important, remains to be determined. Nonetheless, this is an important small step in the giant leap to safer space travel.

—The Editors

high-frequency (30 Hz), low-magnitude (0.3–0.5 g) vibrations to evaluate the potential of these signals to slow IVD expansion during nonweightbearing and a subsequent 7d recovery period.

Methods

Experimental design

This study was reviewed and approved by the Committee on Research in Human Subjects of Stony Brook University, the University of Texas Medical Branch at Galveston, and NASA's Johnson Space Center. Healthy human subjects of astronaut age (35 ± 7 y, 18 males, 11 females) and without a history of back pain were randomly assigned to a CTR ($n=11$) or a low-magnitude mechanical signal

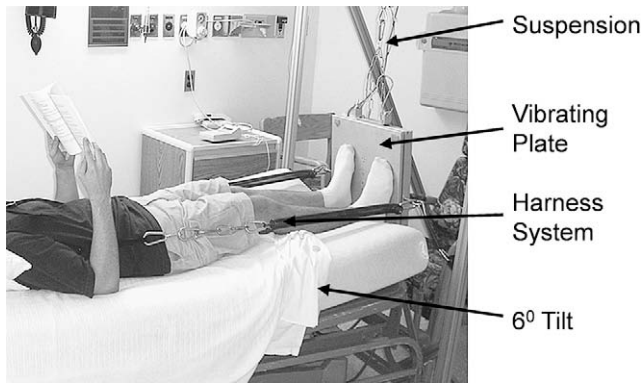


Fig. 1. Six-degree head-down tilt position that was retained by bed rest subjects for 90d, and low-magnitude mechanical signal (LMMS) configuration that was used to apply LMMS to the spine and lower appendicular skeleton. All subjects retained a “relaxed stance” position during the exposure period. The length of the elastic cords which coupled the body harness to the vertically suspended vibrating plate were adjusted to subject each individual to a force that was equal to 60% of his/her baseline body mass. The intervention was gentle enough to simultaneously pursue other activities such as reading.

(LMMS) intervention ($n=18$) group. All subjects underwent continuous 6° head-down BR for 90d followed by a 7d reambulation period.

During BR, the subjects were completely restricted to the supine position throughout the protocol but allowed to raise themselves on one elbow to eat for 30 minutes. Caloric intake was based on baseline body weight. Subjects were restricted from consuming caffeine, nicotine, alcohol, and pharmaceuticals with the exception of acetaminophen for headaches or joint pain. Each room was equipped with a closed-circuit camera to monitor compliance.

While maintaining a supine position, LMMS subjects were exposed to short durations (10 min/d) of LMMS that were applied as sinusoidal high-frequency vibrations at a frequency of 30 Hz and a constant peak-to-peak acceleration magnitude of either 0.3 g ($n=12$) or 0.5 g ($n=6$) where 1 g = acceleration due to gravity on Earth. The vibrations were introduced into the axial skeleton through the plantar surface of the feet by means of an upper-body harness that was coupled to the vibrating plate through linear springs, adjusted to a pretension that amounted to 60% of the subject’s body mass. Subjects receiving LMMS loading were instructed to keep their knees straight during the exposure period but were not required to lock their knees as this may cause discomfort (Fig. 1).

The chosen level of prestress approximated the physiologic load on the lumbar spine during weightbearing in the upright position [20,21] and was required both for transmitting the vibratory signal from the vibrating plate to the lumbar region of the spine [22] and for facilitating dynamic deformations in the IVD [23]. Although it is conceivable, yet unlikely [9], that the static loading component by itself, estimated to temporarily deform the lumbar spine by approximately 1 to 2 mm [24], could provide a treatment

effect, cost restrictions did not allow the inclusion of a statically loaded (sham) group. Stresses induced in the IVD by the daily donning or removing the harness were considered negligible compared with those generated by the subjects’ total daily activities.

Subjects received spinal magnetic resonance imaging (MRI) scans ($n=7$ for CTR; $n=17$ for LMMS) at 0d, 60d, 90d, and 7d after completion of BR. The 0d MRI scan of one LMMS subject was not available and all MRI data from this subject were excluded from the analysis. Computed tomography (CT) scans of the lumbar spine ($n=11$ for CTR; $n=18$ for LMMS), were taken at 0d and 90d of BR. The imaging procedures were the only occasions during the 90d of restricted BR when subjects briefly interrupted their supine positions. Physiologic systems other than the spine were also assessed during the protocol but the low-level mechanical signal was the only treatment to which the individuals were subjected. It was not possible to administer a standardized instrument for measuring pain

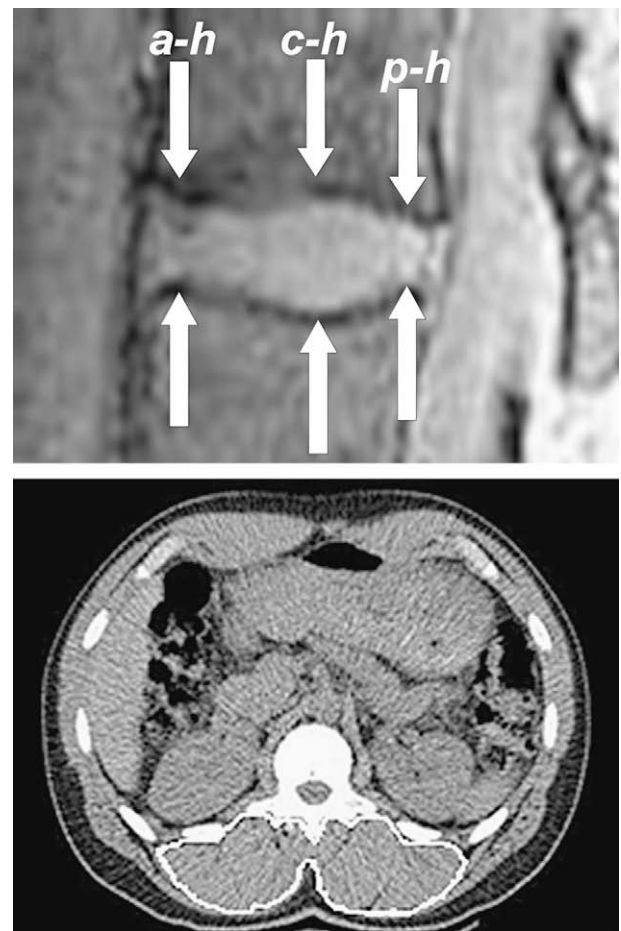


Fig. 2. (Top) Magnetic resonance imaging of an intervertebral disc (IVD) used to measure IVD volume and disc convexity (DC). Anterior height (a-h), posterior height (p-h), and center height (c-h) were used to calculate DC. (Bottom) Computed tomography image with contour of the intrinsic back muscle in white (spinalis, splenius, semispinalis, iliocostalis, longissimus, multifidus, rotators, interspinous, and intertransverse).

but symptom complaint logs were available for 29 subjects (n=11 for CTR; n=18 for LMMS).

MRI and CT

Spinal MRI scans were taken with a 1.5 T MRI scanner (Signa, GE Medical Systems, Milwaukee, WI, USA) between L1 and S1 at two different settings to measure IVD and lumbar nucleus pulposus (NP) volume, and IVD shape (convexity) (Fig. 2). A sagittal gradient lumbar spine scan was used to obtain 3 mm slices with a 10% distance factor. To obtain IVD morphology, repetition time was set at 35 ms and echo time at 7 ms with a field of view of 240 mm and an acquisition matrix of 256×256. For imaging of the NP, the sequence parameters were altered to the following: repetitive time=3850 ms, echo time=105 ms, field of view=240 mm, and acquisition matrix=256×192. The convexity of each IVD slice was determined by the ratio of the greatest center height between vertebrae to the average of the smallest anterior and posterior disc height [25]. The convexity value of any given IVD resulted from the average of the slice convexity values. Spinal length across the lumbar IVDs was measured by drawing a vertical line from the antero-inferior corner of the T12 vertebral body to the anterosuperior corner of the S1 vertebral body [11].

CT scans (Light Speed QX/i, GE Medical Systems, Milwaukee, WI, USA) of T12 to L3 vertebrae measured the erector spinae and transversospinal back muscle (80 kV; 140 mA; 480 mm axial field of view; 512×512 acquisition matrix; slice thickness of 2.5 mm with a 20% distance factor). Cross-sectional area of the erector spinae including transversospinal muscles were determined directly from the CT images. For both MRI and CT measurements, a single operator (NH) determined the tissue volume by multiplying the cross-sectional area with slice thickness, taking the distance factor into account. Temporal volumetric changes were calculated at 60d, 90d, or 90+7d with 0d as referent.

Statistics

Differences in normally distributed variables between the LMMS and CTR group were assessed with two-tailed *t*-tests—paired tests for within subject comparisons and unpaired tests for comparisons across groups. Nonparametric data were compared with Mann-Whitney and Wilcoxon tests, respectively. Unpaired tests were also used to compare the outcome variables between the 0.3 g and 0.5 g LMMS groups to test whether the two different levels of acceleration produced a differential response. In the absence of significant differences, subjects from the two groups were pooled to increase statistical power. Pearson’s *R*² values were computed to identify associations between selected variables. Two-way analysis of variance tested for the interdependence between LMMS and the specific time point or disc level. Chi-squared tests were used to compare LBP incidence. Data

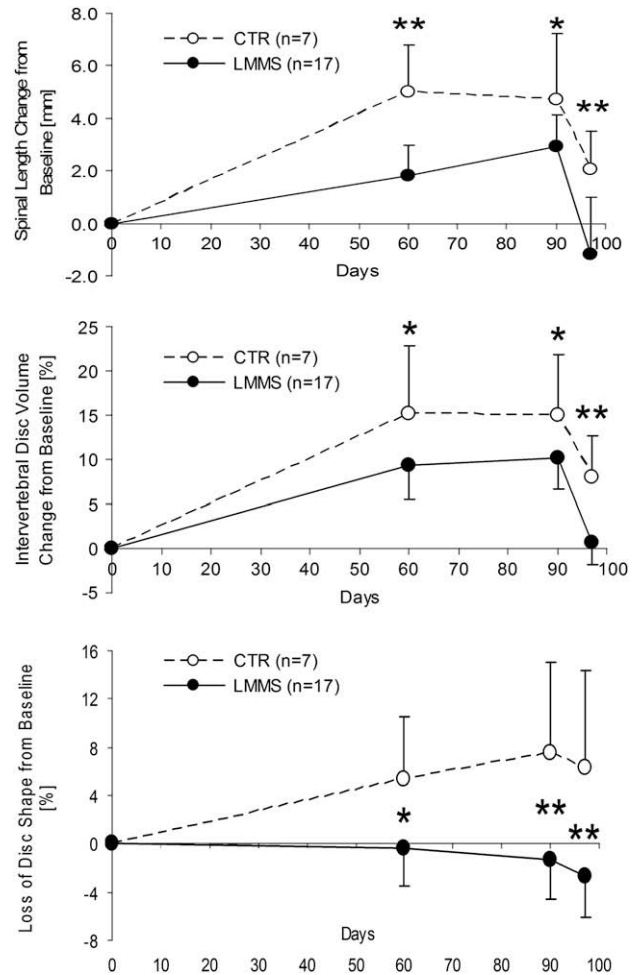


Fig. 3. Changes in spine morphology in control (CTR) and vibrated low-magnitude mechanical signal (LMMS) subjects over the 97d experimental protocol (mean±standard deviation). Each intervertebral disc (IVD) data point represents an average of the five lumbar discs. (Top) Changes in spinal length compared with baseline. (Middle) Changes in IVD volume compared with baseline. (Bottom) Changes in IVD convexity compared with baseline. **p*<.05, ***p*<.01 for comparisons between CTR and LMMS.

were expressed as mean±standard deviation. Statistical significance was considered at *p*<.05.

Results

At baseline, there was no difference in age, body mass, or height between CTR (35±8 y, 74±1 kg, 171±1 cm) and LMMS (35±7 y, 75±9 kg, 172±7 cm) subjects. Coefficients of variation for the individual measurements were 0.6% for spinal length, 1.8% for IVD volume, 2.4% for NP volume, 5.0% for IVD convexity, and 1.5% for muscle volume. None of the subjects experienced any complications such as deep vein thrombosis or sequelae. Because there were no significant differences in any variable

Table

Mean (\pm standard deviation) spinal length, NP volume, IVD volume, and DC of lumbar discs from CTR (n = 7) and vibrated LMMS (n = 17) subjects as measured by MRI

BR(d)	L1–L2	L2–L3	L3–L4	L4–L5	L5–S1	Spine length (mm)
0						
NP (cm ³)						
CTR	5.0 \pm 1.4	6.5 \pm 2.0	8.1 \pm 2.7	10.3 \pm 4.3	8.0 \pm 3.2	
LMMS	4.9 \pm 1.8	6.2 \pm 2.4	7.2 \pm 2.3	8.3 \pm 2.5	7.1 \pm 1.9	
IVD (cm ³)						
CTR	9.9 \pm 2.6	13.0 \pm 3.6	16.3 \pm 4.2	17.3 \pm 5.3	13.7 \pm 4.9	169.7 \pm 9.1
LMMS	10.5 \pm 2.8	13.4 \pm 3.5	15.5 \pm 3.5	15.5 \pm 3.1	12.2 \pm 3.7	162.8 \pm 6.3
DC (10 ⁻¹)						
CTR	12.3 \pm 1.6	12.6 \pm 1.7	11.9 \pm 0.5	11.6 \pm 0.8	12.2 \pm 1.5	
LMMS	13.2 \pm 1.3	12.9 \pm 0.9	12.1 \pm 0.9	11.8 \pm 0.6	10.4 \pm 1.0	
60						
NP (cm ³)						
CTR	5.5 \pm 1.7*	7.4 \pm 2.5**	9.3 \pm 3.0***	11.2 \pm 4.7*	9.1 \pm 4.0*	
LMMS	5.6 \pm 2.0***	7.4 \pm 2.8***	8.6 \pm 2.7***†	9.7 \pm 2.7***	7.5 \pm 1.8	
IVD (cm ³)						
CTR	11.1 \pm 2.7***	14.7 \pm 4.1**	19.1 \pm 4.6**	20.2 \pm 5.1**	16.0 \pm 4.9**	174.7 \pm 8.4*
LMMS	11.6 \pm 3.1***	14.7 \pm 4.1***	16.8 \pm 4.0***†	17.3 \pm 4.0***	14.1 \pm 3.4***†	164.1 \pm 6.6***††
DC (10 ⁻¹)						
CTR	11.8 \pm 1.2	11.3 \pm 1.0*	11.3 \pm 0.7*	10.9 \pm 0.8	11.2 \pm 1.7*	
LMMS	12.7 \pm 0.8	12.5 \pm 0.6†	12.1 \pm 0.6	11.9 \pm 0.6†	10.6 \pm 1.0*††	
90						
NP (cm ³)						
CTR	5.4 \pm 1.6**	7.3 \pm 2.4**	9.7 \pm 3.0**	11.3 \pm 3.6	9.1 \pm 3.5**	
LMMS	5.5 \pm 1.8***	7.1 \pm 2.5***	8.3 \pm 2.5***	9.4 \pm 2.6***	7.2 \pm 1.8	
IVD (cm ³)						
CTR	10.9 \pm 2.5***	14.9 \pm 4.0***	18.4 \pm 4.2***	19.7 \pm 4.8***	15.9 \pm 4.6***	174.4 \pm 7.9*
LMMS	11.6 \pm 3.0***	15.1 \pm 4.2***	17.0 \pm 4.1***	17.0 \pm 3.5***†	13.9 \pm 2.8***	165.7 \pm 6.3***††
DC (10 ⁻¹)						
CTR	10.9 \pm 1.0	11.4 \pm 1.1*	11.1 \pm 0.8	10.7 \pm 0.9	10.9 \pm 1.5*	
LMMS	12.6 \pm 0.5	12.6 \pm 0.7†	12.2 \pm 0.5†	11.7 \pm 0.5††	10.6 \pm 1.0*††	
90+7						
NP (cm ³)						
CTR	5.2 \pm 1.3*	7.0 \pm 2.2*	9.0 \pm 2.9**	10.6 \pm 3.6	8.4 \pm 3.6	
LMMS	4.7 \pm 1.6	6.2 \pm 2.3	7.2 \pm 2.1	8.5 \pm 2.4*	6.6 \pm 1.8*	
IVD (cm ³)						
CTR	10.6 \pm 2.6**	14.2 \pm 4.0*	17.4 \pm 4.4**	18.5 \pm 4.7*	14.5 \pm 4.7	171.8 \pm 9.2*
LMMS	10.7 \pm 2.9	13.4 \pm 3.8†	15.2 \pm 3.5†	15.3 \pm 3.2†	12.6 \pm 2.8	161.7 \pm 6.3***††
DC (10 ⁻¹)						
CTR	11.5 \pm 1.3	11.4 \pm 1.4	10.8 \pm 0.9	10.8 \pm 0.8	11.2 \pm 2.1*	
LMMS	13.5 \pm 1.0	12.8 \pm 0.7	12.2 \pm 0.6	11.9 \pm 0.8	10.5 \pm 0.8*	

BR, bed rest; CTR, control; LMMS, low-magnitude mechanical signals; NP, nucleus pulposus; IVD, intervertebral disc volume; DC, disc convexity; MRI, magnetic resonance imaging. *p<.05, **p<.01, ***p<.001 compared with baseline; †p<.05, ††p<.01, †††p<.001 LMMS swelling from baseline compared with CTR swelling from baseline.

between the 0.3 g and the 0.5 g LMMS groups, all LMMS data presented below reflect the pool of the two acceleration groups.

Spinal length

At baseline, spinal length between CTR (169.7 \pm 9.1 mm) and LMMS (162.8 \pm 6.3 mm) subjects was similar. Compared with baseline, the length of CTR spines was increased by 5.0 mm (p<.05) at 60d, by 4.7 mm (p<.05) at 90d, and by 2.1 mm (p<.05) after 1 week of reambulation (Fig. 3). Although LMMS spinal length also significantly increased during the 90d BR protocol, this increase was significantly less than in CTR subjects at 60d (3.2 mm, p=.001) and 90d (1.8 mm, p=.05). In contrast to CTR subjects, spinal length

of LMMS subjects returned to baseline levels on 7d of reambulation.

IVD and NP volume

MRI measurements indicated that BR in CTR subjects increased IVD volume (averaged between L1 and S1) by 16% (p<.001) over 60d and by 15% (p<.001) over 90d (Table). Importantly, even 7 days after completion of the BR trial, CTR subjects still showed 8% greater (p<.001) IVD volumes relative to baseline (averaged between L1 and S1). LMMS attenuated IVD expansion during BR to 9% (p<.001) after 60d, and 10% (p<.001) after 90d, thus providing a relative net benefit of 41% at 60d (p<.05) and 30% at 90d (p<.05) (Fig. 3). In LMMS

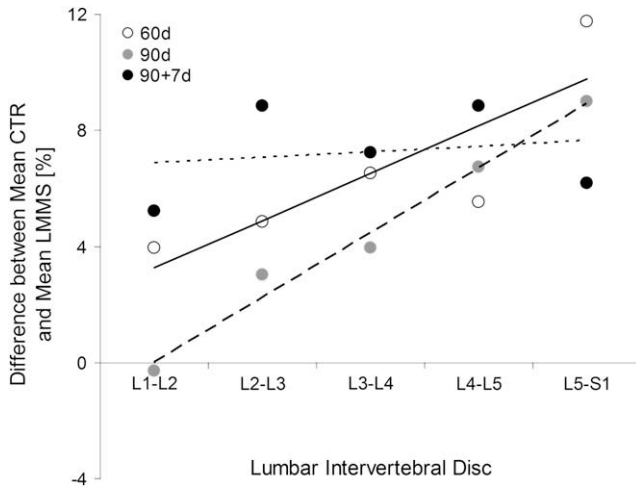


Fig. 4. Net benefit of low-magnitude mechanical signals (LMMS) for each of the five lumbar intervertebral discs (IVDs). Each data point presents the difference in the mean change of a given lumbar IVD between control (CTR) and LMMS subjects at 60d (open circles) and 90d (gray circles) of bed rest and after 7d of reambulation (solid circles). Larger values indicate a greater effect of the intervention. Thus, at both 60d and 90d, vibrations provided a greater effect to more caudal IVDs. In contrast, the effect of vibrations on changes during reambulation was more uniformly distributed across the spine.

subjects, 7d of reambulation, without LMMS treatment, returned IVD volumes to baseline ($p=.33$), a response that was significantly different from CTR subjects ($p<.001$). There was no significant ($p=.59$) interaction between LMMS and the specific time point, indicating that the efficacy of LMMS was not specific to either the 60d, 90d, or 90+7d time point. Even though the interaction between LMMS and the specific disc level did not reach significance ($p=.143$) for the 60d and 90d time points, correlations between disc level and the net benefit of LMMS showed that the largest benefit of vibrations tended to be in the caudal lumbar IVDs with smaller benefits in the cranial lumbar IVDs (Fig. 4). In contrast, reambulation showed an equal benefit to all IVDs. There was no difference in expansion of the NP observed between CTR and LMMS subjects at any given time point or disc level (Table).

Disc convexity

In CTR subjects, 90d of continuous BR caused a loss in IVD convexity, a measure of spinal health, amounting to 5% ($p<.05$) after 60d, 8% ($p<.05$) after 90d, and 6% ($p<.05$) after 90+7d of BR (Fig. 3). Disc convexity (DC) loss of LMMS subjects was unchanged at 60d (0%, $p=.48$), 90d (−1%, $p=.60$) and 90+7d of BR (−3%, $p=.07$). LMMS convexity values were 6% (60d, $p<.05$), 9% (90d, $p<.01$), and 9% (90+7d, $p<.01$) greater than CTR values (Fig. 2). A linear regression of the change in shape of the IVD with the swelling of the IVD showed an inverse relationship at 60d ($R^2=0.29$, $p<.05$), 90d ($R^2=0.32$, $p<.01$), and 90+7d ($R^2=0.54$, $p<.001$).

Muscle atrophy

Similar to the IVD, intrinsic back muscle volume decreased 7.3% ($408\pm 155\text{ cm}^3$ vs. $380\pm 147\text{ cm}^3$, $p<.001$) over the 90d of BR in the CTR subjects. Muscle atrophy in subjects treated with vibrations was 6.6% ($429\pm 102\text{ cm}^3$ vs. $400\pm 99\text{ cm}^3$, $p<.001$), a nonsignificant 9.0% smaller loss than in untreated subjects. For this analysis, one subject in the LMMS group was excluded because the magnitude of muscle atrophy was more than 3SD (14.2%) greater than the group average. Across CTR and LMMS subjects, disc expansion was negatively correlated with muscle atrophy ($R^2=0.50$, $p<.001$).

Low back pain

Independent of treatment, more than half of the subjects (59%) experienced LBP at some point during the study, primarily during the first week of BR and during reambulation. During the first week of BR, 5 of the 11 CTR subjects experienced LBP. During reambulation, the incidence of LBP increased to 6/11. Across both time points, 9/11 of the CTR group experienced LBP. The incidence of LBP in LMMS subjects was 51% ($p=.19$) and 29% ($p=.41$) less than in CTR during the first week of BR and during reambulation, respectively. Across both time points, 46% fewer LMMS subjects experienced LBP than CTR subjects ($p<.05$).

LBP was associated with IVD expansion, NP-to-IVD volume ratio change, and muscle atrophy. Across CTR and LMMS groups, subjects who experienced LBP during the first week showed a 14.4% increase in mean IVD volume over the 90d BR period, whereas those subjects without LBP only had a 8.1% increase ($p<.05$). Similarly, subjects who experienced LBP during the week of reambulation had a smaller NP-to-IVD volume ratio than subjects without LBP (−6.5% vs. 0.6%, $p<.05$). Subjects with LBP were also afflicted with greater muscle atrophy (−5.9% vs. −7.8%, $p=.05$).

Discussion

Deconditioning because of nonweightbearing typically results in elongation of the spine and a volumetric increase in the size of the IVD [1,4], outcomes that can directly promote LBP [1]. Here, we show that short daily exposure to low-magnitude vibratory stimuli, given to volunteers subject to 90d of restricted BR will attenuate deleterious changes in IVD morphology, particularly in the most caudal IVDs, and serve to retain the convexity of the disc, a key indication of disc health. The potential benefit of these LMMS was not confined to the BR period per se, but extended into the immediate reambulation period. As the magnitude of the mechanical signal is so small and the treatment period so brief, these data point toward a unique means of mitigating the detrimental changes in IVD morphology which typically parallels deconditioning of the spinal tissues.

A limitation of this study includes the lack of controlling for the static force component of the harness-elastic cord system during the application of the LMMS. Although the addition of a third group of individuals subjected for 10 min/d to a static force equal to 60% of their body weight was not possible because of cost restrictions, there is strong evidence that bouts of static spinal compression do not mitigate the increase in lumbar IVD height during unloading [8,9,26]. Consistent with these results, static compression hinders, rather than enhances, fluid movement in viscoelastic collagen tissues [27] because the low hydraulic permeability forces the incompressible fluid in the tissue to support most of the applied load [28]. During creep, the interstitial fluid supports ~90% of the applied stress for ~7 minutes [28]. Thus, it is unlikely that a static load applied for 10 min/d to the spine of BR subjects would have been able to reduce the swelling as its primary effect would have been the pressurization of interstitial fluid. Further, even large *dynamic* mechanical signals have to be applied for a considerable duration to be effective. For instance, a short exercise protocol failed to alter IVD expansion caused by BR [9]. Walking with a backpack loaded at 40% of body mass required 4 hours of physical activity before IVD volumes returned to baseline levels [8] and 7 hours of continuous standing and sitting were necessary to note differences in IVD morphology from 6 hours of BR [29]. Nevertheless, while no long-term BR study has ever shown a mitigating effect of applying bouts of static compression on spine length or IVD morphology, the possibility that the static force component affected our results has to be considered.

Expansion of the IVD during 1d of BR can exceed 10% of its original volume [10]. Compared with overnight expansion, lumbar IVDs of CTR subjects in our study showed 54% greater expansion at 60d and 43% increase at 90d. Interestingly, the reduction in swelling measured in LMMS subjects at 60d and 90d of BR led to values that were similar to those observed during 1d BR [10], suggesting that the high-frequency mechanical signal worked to prevent the compound increase in IVD volume exacerbated by BR which extends beyond a single day. Whether optimizing the frequency, amplitude, and duration of the vibration intervention can retain IVD morphology at baseline levels, or whether the nature of the mechanical signal is only capable of preventing the additional increase, remains to be determined.

Treadmill running under negative body pressure [11] and exercise with high-frequency, high-amplitude vibrations [14] reduced IVD height extension, *albeit* at force levels and intervention durations significantly greater than those used in this study, demonstrating that the ability of a mechanical signal to prevent expansion of the IVD is not necessarily dependent on the signal being large in either magnitude or duration. However, peak accelerations in the musculoskeletal tissue are magnified with vibration amplitudes above 0.5 mm [30], an order of magnitude larger than used here (approximately 83 μ m at 0.3 g and 138 μ m at 0.5 g). The transmissibility of the specific signal used in this study to the hip and spine is 70% to 80% of the

magnitude observed from standing on the plate [22]. Although the residual IVD swellings on completion of the 28d of BR negative pressure protocol were not measured [11], data from our 90d of BR study indicate that even 7 days of reambulation failed to return IVD morphology to normal levels in CTR subjects. The persistent expansion suggests the presence of a degraded matrix [3] and is consistent with LBP reported by astronauts on return from spaceflight [1]. Taking this one step further, the absence of residual IVD expansion in LMMS subjects suggests that the low-level mechanical signal more effectively preserved spinal health and, perhaps, has the potential to reduce the incidence of back pain at later time points in life.

IVD shape, as measured by its convexity, was significantly altered during BR in CTR subjects, but was retained over baseline levels in LMMS subjects. Importantly, alterations in IVD convexity has previously been linked to IVD degeneration and aging [25]. Degenerated IVDs tend to have lower swelling pressures than normal discs, and the pressure distribution in degenerated discs becomes directional and nonisotropic, causing the disc to assume a less convex shape [31]. The data reported here suggest that even though volumetric changes were not entirely prevented with the mechanical-based countermeasure over the course of 90d of BR, the retention of DC was not only related to the amount of swelling but supports the hypothesis that degenerative changes of the extracellular matrix were inhibited by these low-level signals.

In summary, the application of short, daily sessions of high-frequency, LMMS mitigated the deleterious expansion of IVDs which normally parallels long-term BR. In addition, the shape of the disc (IVD convexity), an indicator of IVD degradation and quality, was preserved. The lower incidence of LBP in vibrated subjects is supportive of the putative link between swelling and back pain, and thus any measure to reduce changes in morphology may well lead to an effective countermeasure to LBP. The mechanisms by which these very small mechanical stimuli were able to retain disc morphology are not known but may be related to both a physical (eg, the ability of higher frequency stimuli to displace fluids [12]), and biologic mechanism (eg, the ability of cells, or their stem cell precursors, to respond to vibrations [32]). Regardless of the underlying mechanisms, results from this study suggest that in addition to their anabolic effects in muscle and bone [33] this extremely low-magnitude mechanical intervention may someday serve as a nonpharmacologic means of preserving spinal health, and reducing the disc degeneration that normally parallels nonweightbearing.

Acknowledgments

We would like to thank Dr Janice Meck, Sherlene Dryer, Robert Pietrzyk, and the entire NASA JSC and UTMB bed rest team for their invaluable contributions. Technical

assistance with the MRI and CT measurements by Dr. Mark Wagshul, Dr. Harlan Evans, and Dennis Dornfest was greatly appreciated. We are also grateful for the financial support from NSBRI (BL00802) and NASA (NNJ04HI06G), and the NASA Flight Analogs/Bed Rest Research Project.

References

- [1] Wing PC, Tsang IK, Susak L, et al. Back pain and spinal changes in microgravity. *Orthop Clin North Am* 1991;22:255–62.
- [2] LeBlanc A, Rowe R, Schneider V, et al. Regional muscle loss after short duration spaceflight. *Aviat Space Environ Med* 1995;66:1151–4.
- [3] Sinha RK, Shah SA, Hume EL, Tuan RS. The effect of a 5-day space flight on the immature rat spine. *Spine J* 2002;2:239–43.
- [4] LeBlanc AD, Evans HJ, Schneider VS, Wendt RE 3rd, Hedrick TD. Changes in intervertebral disc cross-sectional area with bed rest and space flight. *Spine* 1994;19:812–7.
- [5] Hicks GS, Duddleston DN, Russell LD, et al. Low back pain. *Am J Med Sci* 2002;324:207–11.
- [6] Tyrrell AR, Reilly T, Troup JD. Circadian variation in stature and the effects of spinal loading. *Spine* 1985;10:161–4.
- [7] Ianuzzi A, Little JS, Chiu JB, et al. Human lumbar facet joint capsule strains: I. During physiological motions. *Spine J* 2004;4:141–52.
- [8] Hutton WC, Malko JA, Fajman WA. Lumbar disc volume measured by MRI: effects of bed rest, horizontal exercise, and vertical loading. *Aviat Space Environ Med* 2003;74:73–8.
- [9] Malko JA, Hutton WC, Fajman WA. An in vivo magnetic resonance imaging study of changes in the volume (and fluid content) of the lumbar intervertebral discs during a simulated diurnal load cycle. *Spine* 1999;24:1015–22.
- [10] Malko JA, Hutton WC, Fajman WA. An in vivo MRI study of the changes in volume (and fluid content) of the lumbar intervertebral disc after overnight bed rest and during an 8-hour walking protocol. *J Spinal Disord Tech* 2002;15:157–63.
- [11] Cao P, Kimura S, Macias BR, et al. Exercise within lower body negative pressure partially counteracts lumbar spine deconditioning associated with 28-day bed rest. *J Appl Physiol* 2005;99:39–44.
- [12] Cheung JT, Zhang M, Chow DH. Biomechanical responses of the intervertebral joints to static and vibrational loading: a finite element study. *Clin Biomech (Bristol, Avon)* 2003;18:790–9.
- [13] Qin YX, Kaplan T, Saldanha A, Rubin C. Fluid pressure gradients, arising from oscillations in intramedullary pressure, is correlated with the formation of bone and inhibition of intracortical porosity. *J Biomech* 2003;36:1427–37.
- [14] Belavy DL, Hides JA, Wilson SJ, et al. Resistive simulated weight-bearing exercise with whole body vibration reduces lumbar spine deconditioning in bed-rest. *Spine* 2008;33:E121–31.
- [15] Torvinen S, Kannus P, Sievanen H, et al. Effect of four-month vertical whole body vibration on performance and balance. *Med Sci Sports Exerc* 2002;34:1523–8.
- [16] Fontana TL, Richardson CA, Stanton WR. The effect of weight-bearing exercise with low frequency, whole body vibration on lumbosacral proprioception: a pilot study on normal subjects. *Aust J Physiother* 2005;51:259–63.
- [17] Rittweger J, Just K, Kautzsch K, Reeg P, Felsenberg D. Treatment of chronic lower back pain with lumbar extension and whole-body vibration exercise: a randomized controlled trial. *Spine* 2002;27:1829–34.
- [18] Smith SD. Seat vibration in military propeller aircraft: characterization, exposure assessment, and mitigation. *Aviat Space Environ Med* 2006;77:32–40.
- [19] Abercromby AF, Amonette WE, Layne CS, et al. Vibration exposure and biodynamic responses during whole-body vibration training. *Med Sci Sports Exerc* 2007;39:1794–800.
- [20] Nachemson A. The load on lumbar disks in different positions of the body. *Clin Orthop Relat Res* 1966;45:107–22.
- [21] Lee SU, Hargens AR, Fredericson M, Lang PK. Lumbar spine disc heights and curvature: upright posture vs. supine compression harness. *Aviat Space Environ Med* 2003;74:512–6.
- [22] Rubin C, Pope M, Fritton JC, et al. Transmissibility of 15-hertz to 35-hertz vibrations to the human hip and lumbar spine: determining the physiologic feasibility of delivering low-level anabolic mechanical stimuli to skeletal regions at greatest risk of fracture because of osteoporosis. *Spine* 2003;28:2621–7.
- [23] Garman R, Gaudette G, Donahue LR, Rubin C, Judex S. Low-level accelerations applied in the absence of weight bearing can enhance trabecular bone formation. *J Orthop Res* 2007;25:732–40.
- [24] Macias BR, Cao P, Watenpaugh DE, Hargens AR. LBNP treadmill exercise maintains spine function and muscle strength in identical twins during 28-day simulated microgravity. *J Appl Physiol* 2007;102:2274–8.
- [25] Pfirrmann CW, Metzdorf A, Elfering A, Hodler J, Boos N. Effect of aging and degeneration on disc volume and shape: a quantitative study in asymptomatic volunteers. *J Orthop Res* 2006;24:1086–94.
- [26] Kimura S, Steinbach GC, Watenpaugh DE, Hargens AR. Lumbar spine disc height and curvature responses to an axial load generated by a compression device compatible with magnetic resonance imaging. *Spine* 2001;26:2596–600.
- [27] Mow VC, Ateshian GA, Spilker RL. Biomechanics of diarthrodial joints: a review of twenty years of progress. *J Biomech Eng* 1993;115(4B):460–7.
- [28] Soltz MA, Ateshian GA. Experimental verification and theoretical prediction of cartilage interstitial fluid pressurization at an impermeable contact interface in confined compression. *J Biomech* 1998;31:927–34.
- [29] Botsford DJ, Esses SI, Ogilvie-Harris DJ. In vivo diurnal variation in intervertebral disc volume and morphology. *Spine* 1994;19:935–40.
- [30] Kiiski J, Heinonen A, Jarvinen T, Kannus P, Sievanen H. Transmission of vertical whole body vibration to the human body. *J Bone Miner Res* 2008;23:1318–25.
- [31] Cassinelli EH, Hall RA, Kang JD. Biochemistry of intervertebral disc degeneration and the potential for gene therapy applications. *Spine J* 2001;1:205–14.
- [32] Rubin CT, Capilla E, Luu YK, et al. Adipogenesis is inhibited by brief, daily exposure to high-frequency, extremely low-magnitude mechanical signals. *Proc Natl Acad Sci U S A* 2007;104:17879–84.
- [33] Xie L, Rubin C, Judex S. Enhancement of the adolescent murine musculoskeletal system using low-level mechanical vibrations. *J Appl Physiol* 2008;104:1056–62.