Low-magnitude whole body vibration with resistive exercise as a countermeasure against cardiovascular deconditioning after 60 days of head-down bed rest

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1UMR CNRS 6214–INSERM 771, Faculté de Médecine d’Angers, Angers, France; 2State Key Laboratory of Space Medicine Fundamentals and Application, China Astronaut Research and Training Center, Beijing, China; 3EA3842, Homéostasie Cellulaire et Pathologies, Faculté de Pharmacie, Limoges, France; 4Centre Hospitalier Universitaire Trousseau, Tours, France; 5Centre National d’Etudes Spatiales, Paris, France; and 6Televasc, Centre Hospitalier Universitaire d’Angers, Angers, France

Submitted 4 May 2011; accepted in final form 31 August 2011

Coupé M, Yuan M, Demiot C, Bai YQ, Jiang SZ, Li YZ, Arbeille P, Gauquelin-Koch G, Levrard T, Custaud MA, Li YH. Low-magnitude whole body vibration with resistive exercise as a countermeasure against cardiovascular deconditioning after 60 days of head-down bed rest. Am J Physiol Regul Integr Comp Physiol 301: R1748–R1754, 2011. First published September 7, 2011; doi:10.1152/ajpregu.00234.2011.—Whole body vibration with resistive exercise is a promising countermeasure against some weightlessness-induced dysfunctions. Our objective was to study whether the combination of low-magnitude whole body vibration with a resistive exercise can prevent the cardiovascular deconditioning induced by a nonstrict 60-day head-down bed rest (Earth Star International Bed Rest Experiment Project). Fourteen healthy men participated in this study. We recorded electrocardiograms and blood pressure waves by means of a noninvasive beat-by-beat measurement system (Cardiospace, integrated by Centre National d’Études Spatiales and Astronaut Center of China) during an orthostatic test (20 min of 75-degree head-up tilt test) before and immediately after bed rest. We estimated heart rate, blood pressure, cardiac output, stroke volume, total peripheral resistance, baroreflex sensitivity, and heart rate variability. Low-magnitude whole body vibration with resistive exercise prevented an increase of the sympathetic index (reflecting the sympathovagal balance of cardiac autonomic control) and limited the decrease of the spontaneous baroreflex sensitivity induced by 60 days of head-down bed rest. However, this countermeasure had very little effect on cardiac hemodynamics and did not improve the orthostatic tolerance. This combined countermeasure did not efficiently prevent orthostatic intolerance but prevents changes in the autonomic nervous system associated with cardiovascular deconditioning. The underlying mechanisms remain hypothetical but might involve cutaneous and muscular mechanoreceptors.

autonomic nervous system; cardiovascular deconditioning; baroreflex; hemodynamic; head-up tilt test

DAILY GRAVITATIONAL STRESS is necessary to maintain the cardiovascular system in a healthy state. Orthostatic challenge induces cardiac, hormonal, autonomic, macrocirculatory, and microcirculatory responses. A chronic decrease in the gravitational stress (i.e., bed rest or a weightlessness environment) impairs the cardiovascular system with a deconditioning syndrome leading to orthostatic intolerance (9). Several countermeasures were developed and tested against this orthostatic intolerance. Although aerobic exercise (24) and lower-body negative pressure (23) appear to be beneficial against orthostatic intolerance (however, not fully prevented), resistive exercise alone showed only slight effects or even no effects (3). Whole body vibration has been proposed as a countermeasure to prevent muscle and bone deconditioning induced by bed rest and an environment of weightlessness (2). A recent study (41) compared the effects of whole body vibration associated with resistive exercise versus resistive exercise alone on the vascular changes induced by 60-day bed rest. In that study, the combined countermeasure prevented superficial femoral artery diameter and flow-mediated dilation changes induced by bed rest, whereas resistive exercise alone was insufficient to prevent those macrocirculatory changes.

In the present study, we hypothesized that a daily countermeasure of whole body vibration associated with resistive exercise during 60 days of head-down tilt bed rest (HDT) would prevent orthostatic intolerance and autonomic nervous system changes associated with cardiovascular deconditioning in healthy young men.

MATERIALS AND METHODS

Subjects

A total of 14 healthy, nonathletic, Asian men with a mean ± SE age of 30.5 ± 1.2 yr, body wt of 95.6 ± 8.0 kg, and height of 169 ± 1 cm were included in HDT experiments over 60 days. The subjects had no history of cardiovascular or any major disease and used no medication before the experiment. Volunteers were randomly assigned into the control group without countermeasure (n = 7) or the group with whole body vibration associated to a resistive exercise (n = 7). All procedures and risks associated with these experiments were explained to the men, and written consent was obtained from each participant. The experimental protocol conformed to the Helsinki declaration and was approved by the ethical committee of the China Astronaut Research and Training Center scientific board.

Study Design

The protocol Earth Star International Bed Rest Experiment Project took place in the Astronaut Center of China, Beijing, China and lasted for 99 days. The subjects arrived 15 days before the HDT for
ambulatory baseline data collection (BDC-15 to BDC-1) and left after 24 recovery days (R+1 to R+24). The −6-degree nonstrict HDT lasted for 60 days. The subjects were allowed to have a daily 10-min stand for hygienic requirements. Coffee, tea, and nicotine substances were prohibited during the course of the experiment. An orthostatic test was performed at BDC-4 and HDT+60. During the entire experiment, the subjects followed the same diet with a daily caloric intake of 2,400–2,900 kcal and water intake ad libitum. The specific composition of the nutrients during this protocol was not a priori strictly controlled. The photoperiod was a 16:8-h of light-dark cycle.

Countermeasure: Whole Body Vibration Plus Resistive Exercise

Subjects in the countermeasure group were exposed to one daily session of resistive vibration exercise for 24 min according to the training protocol during the whole HDT, i.e., each session consisted of five stretches with vibration: 4 min vibration and 1 min rest. Exercise was performed on a specific vibration system, which was developed for application under bed rest condition by The Chinese University of Hong Kong. A recent consortium gave recommendation for descrip-

Fig. 1. A subject during a session of whole body vibration+resistive exercise.

tion of whole body vibration intervention (37). Our system consisted of a vibration platform, which was vertically suspended on a trolley. Subjects remained in −6-degree HDT position with their feet resting on the vibration platform and with supporting belts attached to shoulders and hips (Fig. 1). During this countermeasure, the vibration frequency was 30 Hz, resistive load was 1.5 times of the body weight of each subject, the peak acceleration was 0.3 g and the vibration amplitude was < 0.1 mm. This resistive effort against a harness could be considered as a low-level resistance training. A well-trained exercise staff supervised all the training sessions.

To check this low amplitude of vibration, a uniaxial accelerometer placed on the center of vibration platform was used, which was connected to a cathode-ray oscillograph. For the vibration frequency, 30 Hz has been chosen as a good compromise (36) for combined countermeasure acting on different systems such as bones (21) or skin vascular flow (32). The frequency of 30 Hz is also close to the frequency (19–25 Hz) efficient on muscles functions (5).

General Data

During this study, subjects were continuously observed by video monitoring. Measurements of weight were done at BDC-7, HDT+20, HDT+41, and HDT+60. Blood pressure was also measured regularly in the morning using a sphygmomanometer during bed rest.

Orthostatic Test and Head-Up Tilt Test

Each subject participated in an orthostatic test at BDC-4 and HDT+60 (first rising after the end of HDT). The test was performed in the morning 1 h or more after the breakfast. After 20 min in the horizontal position (10 min for instrumenta-

tion and 10 min for data acquisition under basal conditions), the subjects were tilted from 0 to 75 degrees for 20 min followed by a recovery period of 10 min in the horizontal position. During this orthostatic test, heart rate (HR) as well as systolic and diastolic blood pressure (SBP and DBP) were recorded with the Cardiospace (Astronaut Center of China/Centre National d’Etudes Spatiales system) which provides a noninvasive beat-by-beat measurement and includes a finger photoplethysmography and a three-lead electrocardiogram (Cardiopres). Cardiac output, stroke volume, and total peripheral resistance were estimated by an analysis of blood pressure waveform (Windkessel model; 10). This model takes into account different parameters, such as weight, height, age, and sex (29).

Analysis of Orthostatic (In)Tolerance

Because the occurrence of syncope in orthostatic tests is not a reproducible parameter, we also analyzed the type of response to the orthostatic test. The different responses were organized in two ways: finisher/nonfinisher and normal/abnormal.

Finisher/nonfinisher were determined during the test. Finishers (Fig. 2, A and B) accomplished the 20-min test, whereas nonfinishers stopped earlier (Fig. 2, C and D) because of signs of presyncope (feeling of faintness, paleness, dizziness, and/or sweating).

Normal/abnormal responses were determined a posteriori by analyzing heart rate and blood pressure changes. The response was considered abnormal if it was a vaso-vagal type (defined as a normal initial response but with the occurrence of hypotension and bradycardia Fig. 2 D) or if it was of postural orthostatic tachycardia syndrome type (POTS) characterized by an increase in HR of > 30 beats/min or < 10 beats/min within the first 5 min of the orthostatic test (30) (Fig. 2, B and C). Otherwise, the response was considered as normal. Analysis of each tilt test was not blinded but was performed by three specialists together.

To estimate the response to the tilt test, we selected 5 min of stable recording under basal conditions and the last 5 min of the head-up tilt test. We calculated the variations of the cardiovascular parameters during these two periods to determine the variation, which was defined as Δ = meanend − meanbasal.

Power Spectrum Analysis of HR Variability

HR variability is a measure of spontaneous variations in HR. HR variability was analyzed by a spectral analysis method (39, 39a). The power spectral density was estimated using the HR variability software [available at www.televasc.fr (eCAR software v1.1)]. This methodology provides the spectral markers of cardiac sympathetic [low-frequency power (LF): 0.04–0.15 Hz] and vагal [high-frequency power (HF): 0.15–0.4 Hz] modulation of the sinoatrial node activity. LF- and HF-power were determined and normalized by the total power (LF+HF). The LF-to-HF ratio (as sympathetic index), which reflects the sympathovagal balance of HR control, was calculated (15, 35).

Analysis of the Spontaneous Baroreflex Sensitivity

The assessment of baroreflex sensitivity is based on the integrative study of short-term regulation of arterial pressure and heart rate (26). Spontaneous baroreflex sensitivity was calculated using online software [www.televasc.fr (eCAR software v1.1)]. A spontaneous baroreflex sequence was defined as same-direction changes in R-R interval and SBP for at least three beats. A linear regression was applied to each sequence, and the mean slope was taken as the spontaneous baroreflex sensitivity.
Results were expressed as means ± SE. All data, with the exception of orthostatic tolerance, were analyzed by two-way ANOVA for repeated measurements followed by the protected least significant difference Fisher test. The orthostatic tolerance (finishers and nonfinishers as well as the different types of response) were analyzed using a Pearson's χ² test. Statistical significance was set at P < 0.05.

RESULTS

General Data

All subjects completed the 60 days of HDT and the entire protocol without any problem. Body weight did not change significantly after bed rest in the control group (63.1 ± 0.9 kg BDC-7 vs. 64.5 ± 0.7 kg HDT-60) and in the vibration group (62.7 ± 2.1 kg BDC-7 vs. 62.3 ± 2.3 kg HDT-60). Mean blood pressure remained within physiological limits throughout the experiment with a similar evolution in both groups.

Orthostatic Intolerance

The main results regarding orthostatic intolerance are shown in Table 1. During the head-up tilt test, we obtained different responses before and after HDT. Before HDT, all of the subjects completed the test. However, two of the subjects presented a POTS response (1 assigned to the control group, and 1 assigned to the vibration+exercise group).

At the end of HDT, four out of fourteen orthostatic tests were stopped because of intolerance (2 in the control group and 2 in the vibration+exercise group). Nine subjects out of fourteen presented an abnormal response: none vaso-vagal and five POTS in the control group, and two vaso-vagal and two POTS in the vibration+exercise group (Table 1).

Cardiac Sympathetic Neural Control

Whole body vibration and resistive exercise prevented an increase of the sympathetic index observed after HDT in the standing position (Fig. 3, A and B). In accordance with the sympathetic index, HF norm and LF norm are preserved after HDT in standing position in the vibration+exercise group (Table 2). This countermeasure limited the decrease of the spontaneous baroreflex slope in the supine position after HDT (Fig. 3, C and D).

Hemodynamic Parameters

The hemodynamic parameters during the tilt test in the different groups are presented in Fig. 4. When we compared the variations during the tilt test (Δ = mean value end − mean value basal) before and after HDT in each group, we noticed a significant increase of HR variation in the control group (+17 ± 3 vs. +34 ± 5 beats/min, respectively) and in the vibration+exercise group (+19 ± 5 vs. +35 ± 4 beats/min, respectively) (Fig. 4C). There was no significant change in SBP and DBP (Fig. 4, A and B) before vs. after HDT in the two groups. Stroke volume and total peripheral resistance did not change significantly in both groups (Fig. 4, D and F). For cardiac output, despite a more important decrease in the control group compared with the countermeasure group (−0.41 ± 0.10 vs. −1.07 ± 0.25 l/min, respectively), the difference between cardiac output before and after HDT was not significant in the two groups (Fig. 4E).

DISCUSSION

Low magnitude, whole body vibration with resistive exercise prevented an increase in the sympathetic index and limited...
the decrease of the spontaneous baroreflex sensitivity induced by 60 days of HDT. However, this countermeasure had very few effects on cardiac hemodynamics and did not improve orthostatic tolerance.

**Effects of Countermeasure on the Autonomic Nervous System**

Daily whole body vibration and resistive exercise have beneficial effects on the autonomic nervous system. A decrease in the cardiac baroreflex sensitivity is constantly observed after HDT and weightlessness (9, 12, 16, 27). However, the effect of weightlessness on sympathetic activity is more controversial, and during the recovery period the sympathetic system seems to become overactivated.

There is no doubt that aerobic exercise training can decrease basal sympathetic activity; however, resistance training does not seem to change sympathetic tone (18). The precise physiological mechanisms responsible for the cardiovascular effects of vibration exercise are not well understood, but may be related to an increase in vascular shear stress and muscle/tendon/skin stimulation (38). Therefore, the question that arises is whether whole body vibration alone can act on the autonomic nervous system. Whole body vibration stimulates the mechanoreceptors, especially plantar and muscular mechanoreceptors, and therefore influences the cardiovascular system.

Gladwell and Coote (22) have shown that in humans, small fiber muscle mechanoreceptor activation can inhibit cardiac vagal activity. Madhavan et al. (31) have shown that plantar stimulation by a vibration of ~44 Hz was able to decrease heart rate and blood pressure in sitting people. This micromechanical stimulation of the plantar surface could act on muscular mechanoreceptors and on the plantar cutaneous mechanoreceptors. Moreover, the skin Meissner corpuscles have a peak sensitivity in the range of 30–60 Hz (28). Therefore, it is possible that whole body vibration can influence the cardiovascular system and the autonomic nervous system directly through mechanoreceptors. The mechanisms by which very

### Table 2. LF/(LF + HF) and HF/(LF + HF) index during the orthostatic test

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<th>LF/(LF + HF)</th>
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<tr>
<td></td>
<td>Supine</td>
<td>Stand</td>
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<tr>
<td><strong>Control group</strong></td>
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<tr>
<td>Before HDT</td>
<td>0.54 ± 0.05</td>
<td>0.70 ± 0.03*</td>
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<tr>
<td>After HDT</td>
<td>0.64 ± 0.04$*</td>
<td>0.78 ± 0.04*$</td>
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<tr>
<td><strong>Vibration + exercise group</strong></td>
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<tr>
<td>Before HDT</td>
<td>0.39 ± 0.06</td>
<td>0.632 ± 0.06*</td>
</tr>
<tr>
<td>After HDT</td>
<td>0.49 ± 0.05$*</td>
<td>0.64 ± 0.04*</td>
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Values are means ± SE. HDT, head-down tilt bed rest; HF, high-frequency band; LF, low-frequency band (*vs. supine; $vs. before HDT).
low-magnitude mechanical signals, as we used in the present study, could improve musculo-skeletal and cardiovascular properties are currently unknown. We could hypothesize that small muscle afferent fibers may not be discharged by vibratory stimuli with the amplitude < 0.1 mm that might preferentially stimulate skin receptors of the soles. However, it has been shown that this kind of vibrations could increase bone and muscle mass in the weight-bearing skeleton of young women with low body mass density (21). In patients with Parkinson disease, a step synchronized, very low amplitude, vibration of sole improves locomotion (34).

**Why Countermeasure Had No Effect on Orthostatic Response**

Adaptation to orthostatic position needs an integrative blood pressure regulation. Simulated weightlessness alters several mechanisms maintaining blood pressure. Decreased central blood volume alters cardiac filling in standing position (7). An inadequate compensatory neurohumoral response (4) with a blunted carotid-cardiac baroreflex was also described with cardiovascular deconditioning (19). In humans, impairments of macro- and microcirculation are also involved in this downregulation (1). On rodent models, studies were carried out and showed that simulated weightlessness has negative effects on structural (13) and functional properties (8, 14) of vasculature. Another part of this downregulation is an alteration of equilibrium system (40). In our study, despite some effects on the autonomic nervous system, the whole body vibration with resistive exercise could not prevent orthostatic intolerance. Orthostatic intolerance is a multifactorial problem, and only preventing the autonomic nervous system dysfunction is not sufficient. Similarly, another study has shown that using thigh cuffs as a countermeasure also showed a beneficial (12) effect on the baroreflex function but did not improve orthostatic tolerance. So autonomic dysfunction might not be an obligatory component of orthostatic intolerance associated with bed rest.

Flywheel resistive exercise has already been tested as a countermeasure against orthostatic intolerance induced by 60 days of HDT and appeared unsuccessful (3). However, before conducting this study, we could have expected beneficial effects of daily whole body vibration on orthostatic tolerance, because whole body vibration training appeared to efficiently improve cardiorespiratory fitness and muscle strength in elderly individuals (6).

**Limitations**

This study had some limitations. Blood volume changes were not measured, and therefore we do not know whether this countermeasure had an effect on the plasma volume. The effect of vibrations on plasma volume is unknown. However, the effect on stroke volume was not significant; therefore, we could hypothesize that this countermeasure may not have preserved the plasma volume. In the present study, the subjects were allowed to stand daily for 10 min for hygienic requirements, which probably improved orthostatic tolerance in both groups compared with the studies that strictly imposed bed rest. It is important to mention that the short durations of daily standing might have acted as a countermeasure that maintained gravitational tolerance. Although the number of tolerant sub-
projects could appear high after this HDT, the proportion of abnormal responses to orthostatic stress is comparable to that observed after strict HDT. Custaud et al. (11) in 2002 showed that six out of eight subjects had an abnormal response (POTS) following a 7-day strict HDT. Thus a strong cardiovascular deconditioning was observed in both groups after 60 days of HDT together with the impairment of the baroreflex sensitivity and of the autonomic balance. Other weightlessness simulation studies where the subjects are allowed to stand daily for a short period of time have also shown severe cardiovascular impairment (25, 33). The number of subjects involved in the present study is low, and this could have impaired statistical power. We didn’t observe significant difference in some measurement, such as in cardiac output in the control group. We cannot exclude that if more subjects have been included, those results could became significant.

In conclusion, low magnitude whole body vibration with resistive exercise prevented an increase of the sympathetic index and limited the decrease of the spontaneous baroreflex induced by 60 days of HDT. We can hypothesize that whole body vibration may directly influence the autonomic nervous system through cutaneous and muscular mechanoreceptors, but the underlying mechanisms remain hypothetical. However, this countermeasure did not efficiently prevent orthostatic intolerance, which is a complex and multifactorial problem.

ACKNOWLEDGMENTS
We thank the volunteers who cordially took part in this HDT experiment and made this research successful. We also thank the scientists of the Astronaut Center of China, Beijing, China for the implementation of this experiment. Present address of Y. Li: Beijing Haidian District BeiQing Road 26, PO 5132, Branch 15, Beijing, 100094, China (acsmfa@gmail.com).

GRANTS
This work was supported by the French National Center of Space Studies and the Regional Council des Pays de la Loire, France. It was also supported by the China Manned Space Engineering Project, Advanced Space Medico-Engineering Research Project of China Grants 2005SSY200605, 2011SSY5406018, and SJ200801; State Key Laboratory of Space Medicine Fundamentals and Application, China Astronaut Research and Training Center Grant SMLFA09A02; Major State Basic Research Development Program of China, 973 Program Grants 2006CB705704 and 2011CB717704; and National High Technology Research and Development Program of China, 863 Program Grant HT09-5.

DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the author(s).

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