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Replacement of daily load attenuates but does not prevent changes to the musculoskeletal system during bed rest

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ABSTRACT

The dose-response effects of exercise in reduced gravity on musculoskeletal health have not been well documented. It is not known whether or not individualized exercise prescriptions can be effective in preventing the substantial loss in bone mineral density and muscle function that have been observed in space flight and in bed rest. In this study, typical daily loads to the lower extremities were quantified in free-living subjects who were then randomly assigned to control or exercise groups. Subjects were confined to 6-degree head-down bed rest for 84 days. The exercise group performed individually prescribed 1 g loaded locomotor exercise to replace their free-living daily load. Eleven subjects (5 exercise, 6 control) completed the protocol. Volumetric bone mineral density results from quantitative computed tomography demonstrated that control subjects lost significant amounts of bone in the intertrochanteric and total hip regions ($p < 0.0125$), whereas the exercise group showed no significant change from baseline in any region ($p > 0.0125$). Pre-and post-bed rest muscle volumes were calculated from analysis of magnetic resonance imaging data. The exercise group retained a larger percentage of their total quadriceps and gastrocnemius muscle volume ($-7.2\% \pm 5.9$, $-13.8\% \pm 6.1$, respectively) than their control counterparts ($-23.3\% \pm 5.9$, -33.0 ± 8.2, respectively; $p < 0.01$). Both groups significantly lost strength in several measured activities ($p < 0.05$). The declines in peak torque during repeated exertions of knee flexion and knee extension were significantly less in the exercise group than in the control group ($p < 0.05$) but work done was not significantly different between groups ($p > 0.05$). The decline in VO_{2max} was $17\% \pm 18$ in exercising subjects ($p < 0.05$) and $31\% \pm 13$ in control subjects ($p = 0.003$; difference between groups was not significant $p = 0.26$). Changes in blood and urine measures showed trends but no significant differences between groups ($p > 0.05$). In summary, the decline in a number of important measures of musculoskeletal and cardiovascular health was attenuated but not eliminated by a subject-specific program of locomotor exercise designed to replace daily load accumulated during free living. We conclude that single daily bouts of exposure to locomotor exercise can play a role in a countermeasures program during bed rest, and perhaps space flight, but are not sufficient in their own right to ensure musculoskeletal or cardiovascular health.

1. Introduction

The detrimental effects of spaceflight on the musculoskeletal system have been known for almost half a century (LeBlanc et al., 2007). Pharmacological countermeasures have been recently explored (Leblanc et al., 2013), but exercise has been the mainstay of both the U.S. and Russian countermeasures programs (Macias et al., 2005). Although questions about bone strength and integrity remain, recent findings suggest that heavy resistance exercise and good nutrition help maintain bone mineral density (Smith et al., 2012; Smith et al., 2014). Other evidence shows that exercise alone has not been completely successful in preventing bone and muscle loss during flight (Orwoll et al.,

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2013). An excellent analog for the study of on-orbit musculoskeletal changes that occur during long-duration spaceflight is head-down bed rest (Pavy-Le Traon et al., 2007). The purpose of the present study was to determine whether individualized mechanical load replacement through locomotor exercise can serve as a countermeasure to losses in bone mineral density, bone quality (including cortical and trabecular components), and muscle atrophy during 84 days of bed rest.

2. Materials and methods

2.1. Subjects

Twelve subjects were enrolled in an 84-day bed rest study that was approved by the Institutional Review Boards at NASA Johnson Space Center, the Cleveland Clinic, and the University of Washington. Six men and six women (76.5 ± 13.6 kg, 174.5 ± 7.2 cm, and 30.2 ± 6.8 years; and 66.9 ± 6.9 kg, 165.5 ± 7.3 cm, and 31.3 ± 9.9 years, respectively) provided written informed consent before they participated. There was no significant difference in weight, height, or age between treatment groups. One female subject was lost after 5 weeks of bed rest because of a pre-existing medical condition that had not been detected during screening.

Subjects were required to pass a rigorous screening protocol before they were considered for inclusion in the study. They were required to pass psychological and physical examinations. Subjects took both the clinical and validity sections of the Minnesota Multiphasic Personality Inventory-2 (MMPI-2) and completed an interview with the study psychiatrist. Subjects were medically cleared via a modified Air Force Class III physical examination, including screening for cardiovascular issues with a Bruce treadmill stress test. Subjects were required to have a whole-body bone mineral density (BMD) Z-score within 1 standard deviation of age-adjusted normal. Additional exclusion criteria included metabolic disease, a medical or orthopaedic condition, certain medications, pregnancy, gastroesophageal reflux disease, and a history of renal stones or thrombosis. Subjects were also tested for tuberculosis, hepatitis B, and HIV. Female subjects who were taking hormonal birth control or hormone replacement therapy or were perimenopausal or menopausal were excluded from participation. Subjects were non-smokers or had not smoked or used tobacco products in 6 months, as confirmed by urine cotinine testing. Subjects were interviewed about their activity levels, and only mild to moderate nonhabitual exercisers were accepted into the study.

2.2. Procedures

2.2.1. Before bed rest

One to 2 months before the start of the bed rest phase of the study, subjects began participating in study activities. Subjects were asked about any changes in their physical activity and weight in the previous 12 months. They filled out activity logs for about 1 month, recording their daily activity in 30-minute increments on the activity log sheets. Four representative days were selected from each subject's activity logs for collection of ambulatory data recording (ADR) while the subject was still free-living in their normal environment. On an ADR day, the subject arrived at the laboratory immediately after waking and performing their morning routine. The subjects were outfitted with a Novel Load Monitor system (Novel GmbH, Munich, Germany), a non-encumbering long-duration data logger that measured the net vertical force during each foot contact under the right and left feet individually at 100 Hz. The unit was attached to a pair of rubber-sealed insoles, which were sized to the subject's shoes. The subject wore the system for all waking hours and performed shut-down and doffing procedures just before preparing for bed, resulting in 12.70 ± 1.31 h of data. This provided a comprehensive record of the subject's daily force profile. The subject returned to the clinic the next day for data download and system re-initialization. Four to five days of ADR data were collected for each subject. The collected foot forces were analyzed via a series of custom MATLAB (MathWorks, Natick, MA, USA) scripts using the enhanced daily load stimulus (EDLS) algorithm (Genc et al., 2009) to calculate the subject's total stimulus value for each day. These values were used in the calculation of the subject's exercise prescription (Genc et al., 2015).

Subjects underwent magnetic resonance imaging (MRI) and quantitative computerized tomography (QCT) scans so that their muscle volumes and bone mineral density could be assessed. Before the subject was scanned in the MRI, a pair of water-filled cylinders was scanned for calibration purposes. All scans were performed using a 1.5-tesla magnet, with a 3-mm slice thickness, no inter-slice gap, and a 512 × 512 acquisition matrix. T2-weighted and short TI inversion recovery (STIR) scans of the lumbar spine were taken from the endplate of T12 to the endplate of L3 using a surface acquisition coil. The remaining regions—thigh, shank and upper extremity—were scanned using T1-weighted spine echo sequence and STIR, and a body coil was used. The thigh was scanned from the superior aspect of the femoral head to the inferior border of the patella, and the shank was scanned from the superior border of the patella to the distal end aspect of the lateral malleolus. For the calculation of BMD, a series of scans using a Siemens Somatom Sensation 16 CT scanner (Siemens AG, Munich, Germany) was performed and analyzed using specialized Mindways bone densitometry computer software (Mindways Software, Inc., Austin, TX, USA). Before a subject was scanned, a rectangular calibration phantom was scanned longitudinally, with a quality assurance phantom placed perpendicularly at its longitudinal midpoint. The subject was then scanned while lying atop the rectangular calibration phantom. Volumetric scans of the lumbar spine and both hips were performed. The left hip was used for analysis. Both scans used a spiral acquisition technique with a peak kilovoltage of 120 kVp at 180 mA, and a 3-mm slice thickness.

Maximal isokinetic torque measurements were recorded for the hip, knee, ankle, and elbow using an isokinetic dynamometer (Biodex Medical Systems, Inc., Shirley, NY, USA). Subjects underwent a familiarization session to ascertain their correct dynamometer positions and ranges of motion, which were used for both pre- and post-bed rest testing sessions. During testing, each movement was performed five times with a 2-second pause at the end of each motion. Bilateral testing was performed. For the knee and elbow, peak concentric and eccentric torques were determined at a velocity of 60 °/s during extension and flexion. Peak concentric and eccentric torques at the hip during flexion and extension and abduction and adduction were also determined at 60 °/s. Peak ankle concentric and eccentric torques were determined during plantarflexion and dorsiflexion performed at 30 °/s. Isometric testing was performed for each joint at set angles of 0°, 45°, 45°, and 90° for the ankle, knee, hip, and elbow, respectively. Additionally, endurance was assessed while subjects performed 21 reciprocating, maximal knee extension and flexion contractions at 180 °/s. Changes in torque and work were evaluated.

Measures of postural stability were assessed while subjects stood quietly for 30 s on a force plate (AMTI, Watertown, MA, USA) mounted flush with the floor. Subjects stood barefoot, with their arms at their sides, heels placed 15 cm apart, feet each rotated externally 10°, and wore a fall safety harness attached to an overhead rail. Measures of postural stability were quantified by measuring total center-of-pressure excursion during the 30-second period. Subjects were tested under three experimental conditions: (1) eyes open, head upright; (2) eyes open, head back; and (3) eyes closed, head upright. For the eyes-open conditions, subjects fixed their gaze on a stationary target in the center of their field of vision. For the head-back condition, the head-neck angle was standardized to 45 degrees of extension. The conditions were ordered using a randomized balanced design. Each subject performed three 30-second trials per condition, which were averaged.

Aerobic capacity was assessed via cycle ergometry. Subjects performed a graded exercise test while cycling upright. First, peak heart