

## EXERCISE EFFECTS ON THE COURSE OF GRAY MATTER CHANGES OVER 70 DAYS OF BED REST

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**BACKGROUND** Long duration spaceflight affects posture control, locomotion, and manual control. The microgravity environment is an important causal factor for spaceflight induced sensorimotor changes through direct effects on peripheral changes that result from reduced vestibular stimulation and body unloading. Effects of microgravity on sensorimotor function have been investigated on earth using bed rest studies. Long duration bed rest serves as a space-flight analogue because it mimics microgravity in body unloading and bodily fluid shifts. It has been hypothesized that the cephalad fluid shift that has been observed in microgravity could potentially affect central nervous system function and structure, and thereby indirectly affect sensorimotor or cognitive functioning. Preliminary results of one of our ongoing studies indeed showed that 70 days of long duration head down-tilt bed rest results in focal changes in gray matter volume from pre-bed rest to various time points during bed rest. These gray matter changes that could reflect fluid shifts as well as neuroplasticity were related to decrements in motor skills such as maintenance of equilibrium. In consideration of the health and performance of crewmembers both in- and post-flight we are currently conducting a study that investigates the potential preventive effects of exercise on gray matter and motor performance changes that we observed over the course of bed rest. Numerous studies have shown beneficial effects of aerobic exercise on brain structure and cognitive performance in healthy and demented subjects over a large age range. We therefore hypothesized that an exercise intervention in bed rest could potentially mitigate or prevent the effects of bed rest on the central nervous system. Here we present preliminary outcomes of our study.

**METHODS** Fourteen subjects were assessed at 12 and 7 days before-, at 7, 30, and ~70 days in-, and at 8 and 12 days post 70 days of bed rest at the NASA bed rest facility in UTMB, Galveston, TX, USA. Each subject was randomly assigned to either a control group or an exercise group. Exercise consisted of daily aerobic and resistance exercise (e.g. squat, heel raise, leg press, cycling and treadmill running). Exercise participants started exercising 20 days before the start of bed rest; the first ~20 days of exercise included orientation to supine exercise and a gradual increase in intensity; the full exercise program began with the start of bed rest. All exercises were executed in supine position. At each time point structural T1-weighted MRI scans were obtained using a 3T Siemens scanner. Focal changes over time in gray matter density were assessed using the voxel based morphometry 8 (VBM8) toolbox under SPM. In addition, gray matter volume was measured per brain lobe, the cerebellum, and the third and lateral ventricles. Functional mobility was assessed by measuring time to complete an obstacle course. The subject's ability to use input from the vestibular system to maintain balance was measured using the sensory organization test. Behavioral measures were assessed pre-bed rest, and 0, 8 and 12 days post bed rest. Repeated measurement analysis was used to test for time, group, and group-by-time interactions.

**RESULTS** There were significant group-by-time interactions for third ventricle volume and functional mobility performance. Increase in third ventricle volume was larger in control subjects than in exercise subjects. Functional mobility performance was less affected by bed rest in exercise subjects than in control subjects. In addition, post bed rest, exercise subjects recovered faster than control subjects. VBM further revealed significant differences in changes from pre bed rest to 70 days in bed rest between the exercise and control group in bilateral primary motor cortex regions, and vermis IX of the cerebellum. Though the latter were significant at  $p < .001$ , these observations were no longer significant after correction for multiple comparisons.

**DISCUSSION** Aerobic exercise in bed rest mitigates the adverse effect of bed rest on functional mobility and increase of third ventricle volume. In addition, exercise could result in differential brain structural changes in motor regions such as the primary motor cortex and the cerebellum. Whether these structural changes precede the functional changes warrants further investigation, ideally including functional MRI sequences.