

# Focal gray matter plasticity as a function of long duration head-down tilt bed rest

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## Introduction:

Long duration spaceflight (i.e., 22 days or longer) has been associated with changes in sensorimotor systems, resulting in difficulties that astronauts experience with posture control, locomotion, and manual control. The microgravity environment is an important causal factor for spaceflight induced sensorimotor changes. Whether these sensorimotor changes may be related to structural and functional brain changes is yet unknown. However, increased intracranial pressure that by itself has been related to microgravity-induced bodily fluid shifts [1] has been associated with white matter microstructural damage [2]. Thus, it is possible that spaceflight may affect brain structure and thereby cognitive functioning. Long duration head-down tilt bed rest has been suggested as an exclusionary analog to study microgravity effects on the sensorimotor system [3]. Bed rest mimics microgravity in body unloading and bodily fluid shifts. In consideration of the health and performance of crewmembers both in- and post-flight, we are conducting a prospective longitudinal 70-day bed rest study as an analog to investigate the effects of microgravity on brain structure [4]. Here we present results of the first eight subjects.

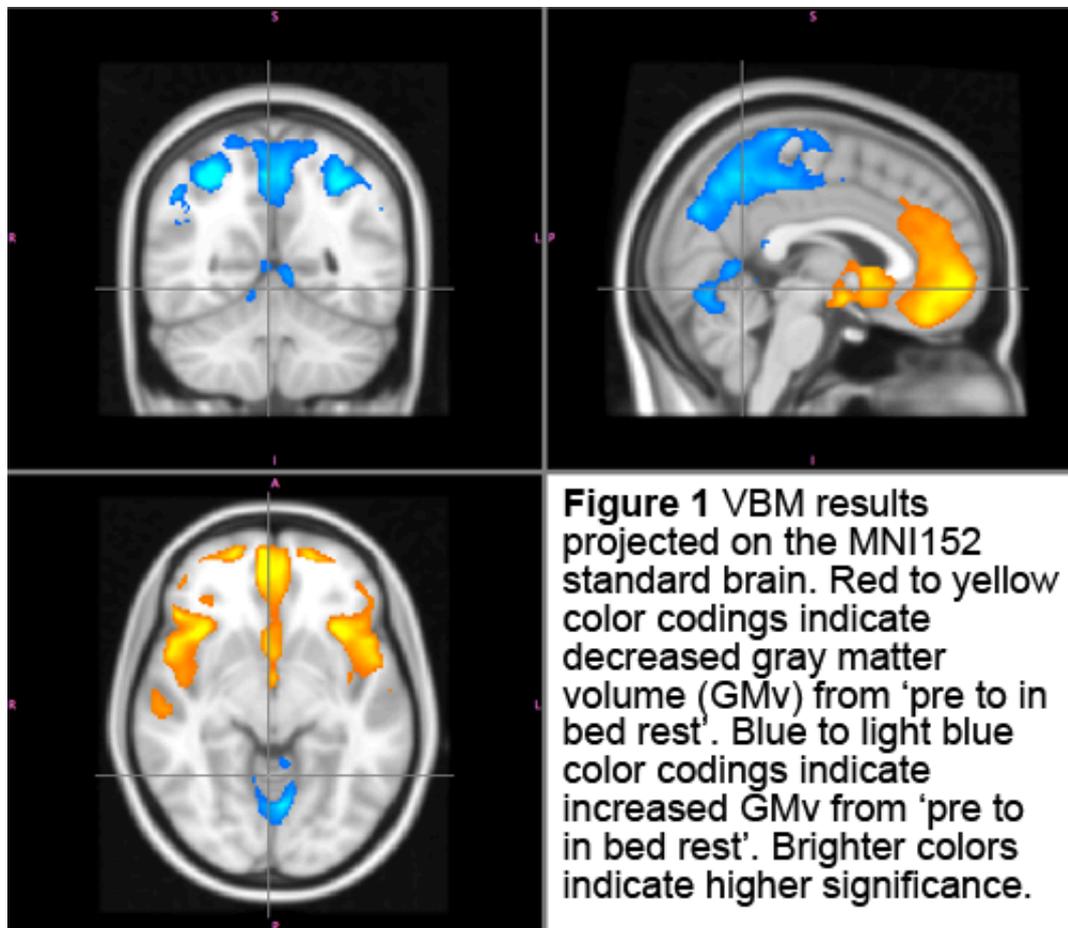
## Methods:

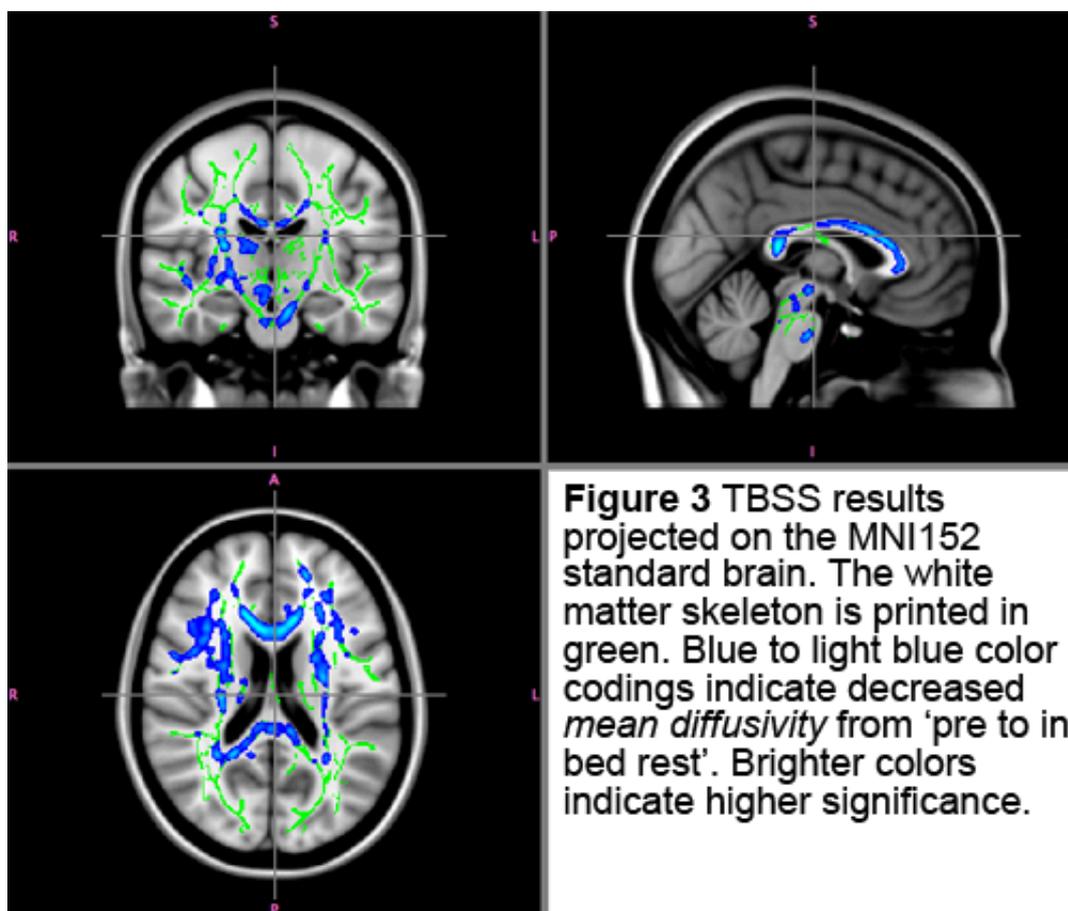
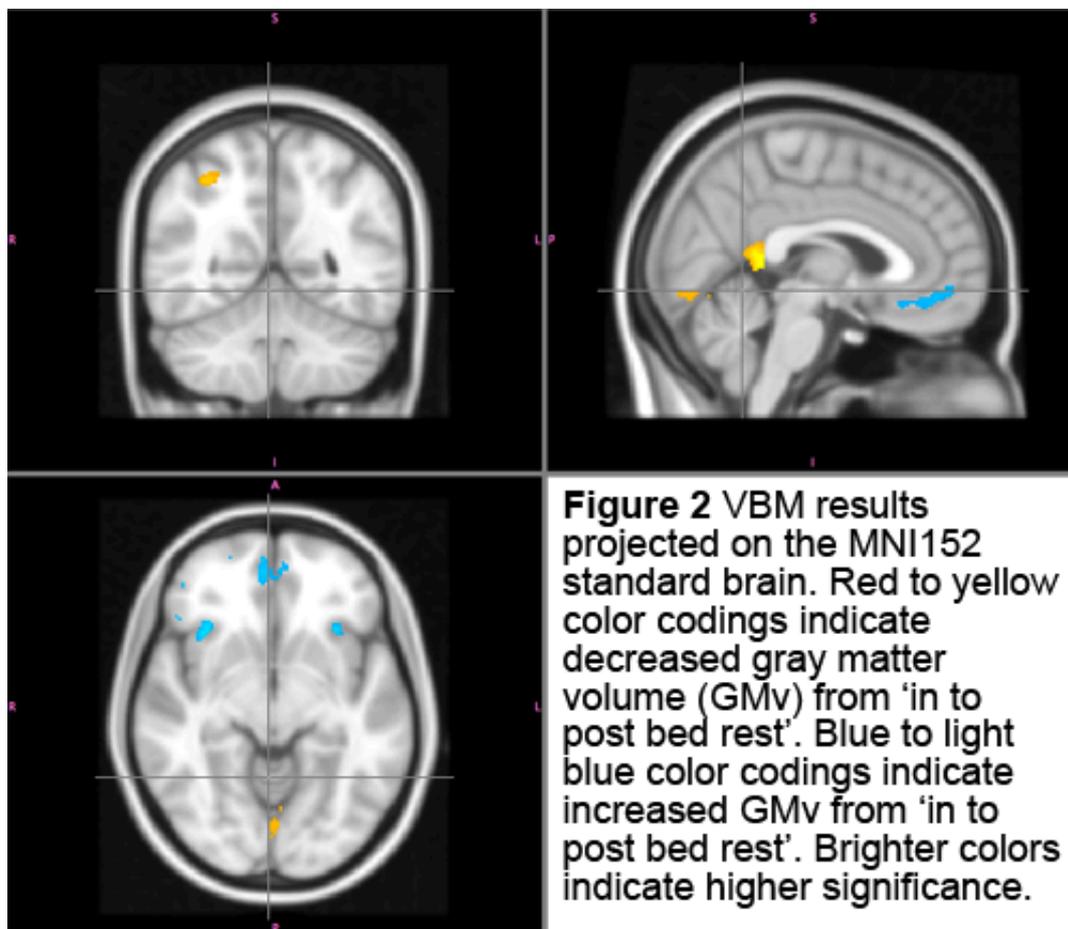
Eight subjects were assessed at 12 and 7 days before-, at 7, 30, and ~70 days in-, and at 8 and 12 days post 70 days of bed rest at the NASA bed rest facility at UTMB, Galveston, TX, USA. At each time point structural MRI scans (i.e., high resolution T1-weighted imaging and Diffusion Tensor Imaging (DTI)) were obtained using a 3T Siemens scanner. Focal changes over time in gray matter volume were assessed using the voxel based morphometry 8 (VBM8) toolbox under SPM. Longitudinal processing in VBM8 includes linear registration of each scan to the mean of the subject and subsequently transforming all scans in to MNI space by applying the warp from the mean subject to MNI to the individual gray matter segmentations. Modulation was applied so that all images represented the volume of the original structure in native space. Finally, all images were smoothed. Focal changes in white matter microstructural integrity were assessed using tract based spatial statistics (TBSS) as part of the FMRIB software library (FSL). TBSS registers all DTI scans to MNI space. It subsequently creates a study specific white matter skeleton of the major white matter tracts. For each subject, for each DTI metric (i.e. fractional anisotropy (FA), mean, axial, and radial diffusivity (MD; AD; RD)), the maximum value in a line perpendicular to the skeleton tract is projected to the skeleton.

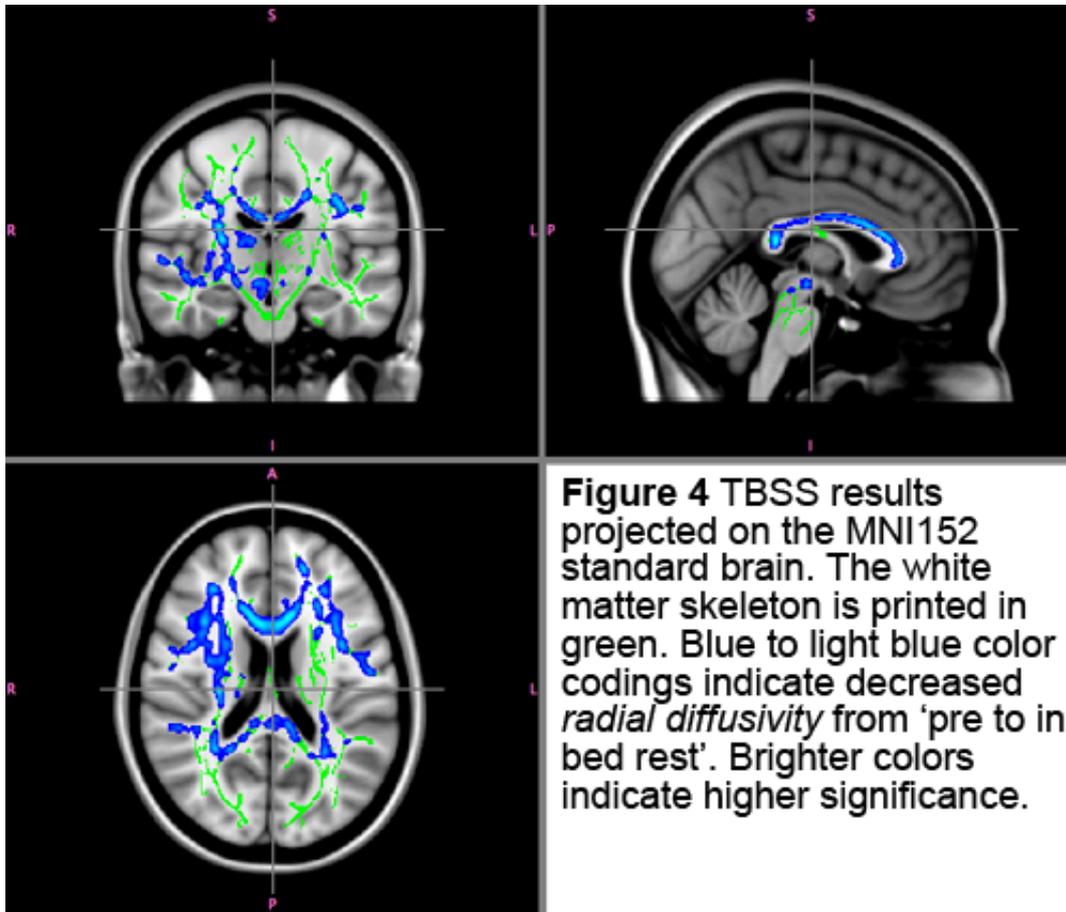
Non-parametric permutation based flexible factorial models (for VBM) and one sample t-tests of contrast images calculated from the tract maps (for TBSS) were used for voxel-wise, family-wise error corrected comparisons of the data.

**Results:**

VBM analysis revealed decreased gray matter density in bilateral areas including the frontal medial cortex, the insular cortex and the caudate (see Figure 1) from 'pre to in bed rest'. Over the same time period, there was an increase in gray matter density in the cerebellum, occipital-, and parietal cortex, including the precuneus (see Figure 1). The majority of these changes did not recover from 'during to post bed rest' (see Figure 2). TBSS analysis revealed significant widespread decreases from pre to in bed rest in MD and RD, but not FA or AD (see Figure 3 and 4). No significant changes in white matter integrity were observed from in bed rest to post bed rest.







### Conclusions:

Extended bed rest, which is an analog for microgravity, can result in gray matter changes and widespread microstructural white matter changes in areas that are important for neuromotor behavior and cognition. Most of these structural changes did not recover at two weeks post bed rest. Whether the effects of bed rest wear off at longer times post bed rest, and if they are associated with behavior are important questions that warrant further research.

### Motor Behavior:

Motor Planning and Execution

### Reference

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