

## **Increased brain activation for foot movement during 70-day 6° head-down bed rest (HDBR): evidence from functional magnetic resonance imaging (fMRI)**

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Bed rest has been widely used as a simulation of weightlessness in studying the effects of microgravity exposure on human physiology and cognition. Changes in muscle function and functional mobility have been reported to be associated with bed rest. Understanding the effect of bed rest on neural control of movement would provide helpful information for spaceflight. In the current study, we evaluated how the brain activation for foot movement changed as a function of bed rest. Eighteen healthy men (aged 25 to 39 years) participated in this HDBR study. They remained continuously in the 6° head-down tilt position for 70 days. Functional MRI was acquired during 1-Hz right foot tapping, and repeated at 7 time points: 12 days pre-, 8 days pre-, 7 days in-, 50 days in-, 70 days in-, 8 days post-, and 12 days post- HDBR. In all 7 sessions, we observed increased activation in the left motor cortex, right cerebellum and right occipital cortex during foot movement blocks compared to rest. Compared to the pre-HDBR baseline (1<sup>st</sup> and 2<sup>nd</sup> sessions), foot movement-induced activation in the left hippocampus increased during HDBR. This increase emerged in the 4<sup>th</sup> session, enlarged in the 5<sup>th</sup> session, and remained significant in the 6<sup>th</sup> and 7<sup>th</sup> sessions. Furthermore, increased activation relative to the baseline in left precuneus was observed in the 5<sup>th</sup>, 6<sup>th</sup> and 7<sup>th</sup> sessions. In addition, in comparison with baseline, increased activation in the left cerebellum was found in the 4<sup>th</sup> and 5<sup>th</sup> sessions, whereas increased activation in the right cerebellum was observed in the 4<sup>th</sup>, 6<sup>th</sup> and 7<sup>th</sup> sessions. No brain region exhibited decreased activation during bed rest compared to baseline. The increase of foot movement-related brain activation during HDBR suggests that in a long-term head-down position, more neural control is needed to accomplish foot movements. This change required a couple of weeks to develop in HDBR (between 3<sup>rd</sup> and 4<sup>th</sup> sessions), and did not return to baseline even 12 days after HDBR. The observed effect of bed rest on brain activation during a foot tapping task could be linked to HDBR-related changes in brain structure that we have recently reported. The relationship between pre- and post- HDBR changes in brain activation and performance in a functional mobility test will also be presented.

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