

Functional brain connectivity changes in head-down tilt bedrest-induced orthostatic intolerance

Jorge Manuel¹, Alex Hoff¹, Anja Bach¹, Edwin Mulder¹, Jens Jordan^{1,2}, Jens Tank¹, Darius A. Gerlach¹

¹Institute of Aerospace Medicine, German Aerospace Center (DLR), Cologne, Germany

²Chair of Aerospace Medicine, University of Cologne, Cologne, Germany

Key words

fMRI; head-down tilt bedrest; hypothalamus; brainstem; orthostatic tolerance

Introduction

Both, returning astronauts and bedridden patients, often experience orthostatic intolerance. Plasma volume changes and cardiovascular deconditioning cannot fully explain the severity of the symptoms. To test the hypothesis that neural changes in cardiovascular control centers in the brain contribute to orthostatic intolerance, we applied functional magnetic resonance imaging (fMRI) during an orthostatic challenge before and after head-down tilt bedrest.

Methods

48 healthy individuals (21 women; 34 ± 8 years; 23.5 ± 2.6 kg/m²) underwent 30 days of strict head-down tilt bedrest. They were assigned to one of four intervention groups: lower body negative pressure (LBNP) (6 h/d; n = 13), sitting (6 h/d; n = 11), supine cycling (1 h/d) followed by venous thigh occlusion (6 h/d; n = 12), and a negative control (n = 12). All underwent orthostatic tolerance testing through combined head-up tilt and LBNP.

At baseline, at day 28 of bedrest, and four days into recovery, we acquired fMRI measurements using a 3 T scanner during three different LBNP conditions (without pressure, -10 mmHg, -30 mmHg). We determined changes in functional connectivity by applying independent component analysis followed by a dual regression using an F-test and post-hoc two-sample t-tests.

Results

In all groups, orthostatic tolerance substantially decreased albeit to various degrees. After 28 days of bed rest, mainly five hypothalamic nuclei showed functional connectivity changes: the lateral and anterior hypothalamic areas, the ventromedial and the medial preoptic nuclei, and the mamillary bodies. The visual cortex also showed functional connectivity changes with the hypothalamus. The connectivity change between the medial preoptic nucleus and the ventromedial hypothalamic nucleus and the anterior hypothalamic area correlated negatively with the change in time to presyncope ($R^2 = 0.20$; $p = 0.02610$).

Conclusion

In addition to cardiovascular deconditioning and plasma volume changes, head-down tilt bedrest elicits neuroplasticity in cardiovascular control centers of the brain. The mechanism may contribute to orthostatic intolerance in real or simulated weightlessness.