Functional connectivity changes after 28 days of head-down tilt bedrest

Poster #75

Jorge Manuel*[1], Alex Hoff[1], Anja Bach[1], Edwin Mulder[1], Jens Jordan[1,2], Jens Tank[1], Darius A. Gerlach[1]

[1]Institute of Aerospace Medicine, German Aerospace Center (DLR), Cologne, Germany
[2]Chair of Aerospace Medicine, University of Cologne, Cologne, Germany
*Jorge.ManuelSanchez@dlr.de

Introduction

Both, returning astronauts and bedridden patients, often experience orthostatic intolerance. Since cardiovascular deconditioning alone cannot explain the severity of the symptoms, we hypothesized contributory neural changes. We tested this hypothesis using functional magnetic resonance imaging (fMRI) during an orthostatic challenge following head-down tilt bedrest.

This study was part of the NASA 30 days bedrest study (SANS_CM), which investigated countermeasures for preventing spaceflight associated neuro-ocular syndrome.

Methods

Ethical approval
- North Rhine medical board

Location
- German Aerospace Center, Cologne, Germany

Demographics
- 47 healthy individuals (20 women; 34.7 ± 8.8 years; 23.6 ± 2.6 kg/m^2)

Study design
- 30 days of strict 6° head-down tilt bedrest
- Intervention groups
  - Lower body negative pressure (LBNP) (6 h/d; n = 12)
  - Sitting (6 h/d; n = 11)
  - Supine cycling (1 h/d) followed by venous thigh occlusion (6 h/d; n = 12)
  - Control (n = 12)

fMRI acquisition
- 3 T Siemens Biograph mMR; 32-channel head coil
- Functional sequence: 2 mm isotropic, T_R = 1.18 s; T_E = 32 ms; simultaneous multi-slice factor 6; partial Fourier 7/8
- LBNP conditions: without, -10, and -30 mmHg
- Time points: baseline, day 28 of bedrest, 4 days into recovery

Image preprocessing
- Motion and distortion correction
- Grand mean scaling
- High pass filter (0.01 Hz)
- Manual ICA-denoising
- Normalization to study template

Analysis
- Hypothalamic region identification
  - Masked independent component analysis of the hypothalamus
- Functional connectivity (temporal correlation) changes
  - Dual regression to hypothalamus, medulla oblongata and whole brain
  - ANOVA (time and LBNP condition) followed by post-hoc two-sample t-tests
  - Multiple comparison correction: family-wise-error and Bonferroni

Results

- Intrinsic (within a region) functional connectivity increases at day 28 of bedrest compared to baseline
  - LH, TuMM, PeF (Figure 1a) [control > sitting]
  - MM, LH (Figure 1b) [control > sitting]
  - LH, TuMM (Figure 1c)
- Functional connectivity increases between regions at day 28 of bedrest
  - MPO, SON, LH ⟶ VMH, PeVN, AH, DMH (Figure 1d)
  - AH, VMH, DMH, LH, PeF ⟶ LH, PVN (Figure 1e) [control > sitting]
  - LH ⟶ visual cortex (Figure 1f) [LBNP > sitting]

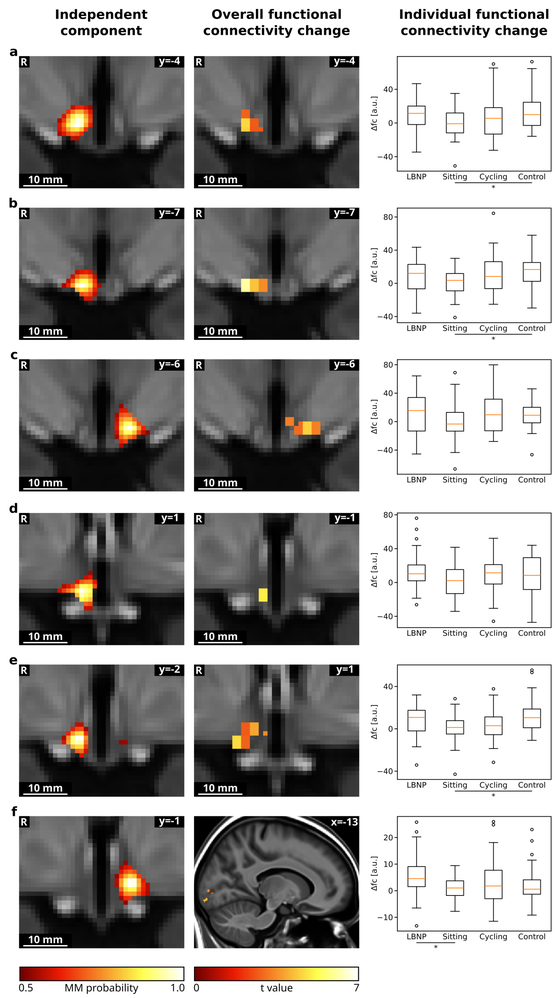

Figure 1. Functional connectivity increases at day 28 of bedrest compared to baseline. The left column shows the independent components from the hypothalamic segmentation, whereas the middle column depicts their significant functional connectivity changes over all interventions. The contribution of the different interventions is depicted in the right column.

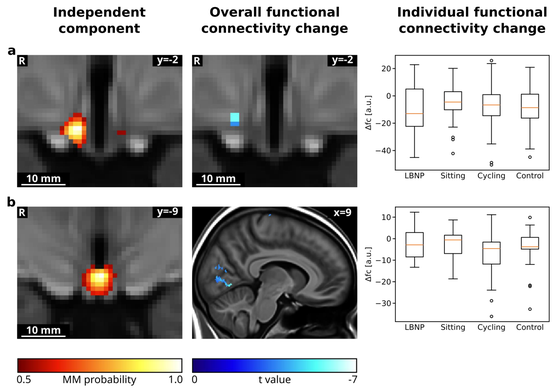

Figure 2. Functional connectivity decreases at day 28 of bedrest compared to baseline. Column distribution is identical to Figure 1.

- Functional connectivity decreases at day 28 compared to baseline
  - AH, VMH, DMH, LH, PeF ⟶ LH (Figure 2a)
  - MM ⟶ visual cortex, pre- and postcentral gyrus (Figure 2b)
- We did not observe functional connectivity changes at day 28 of bedrest between the hypothalamus and the medulla oblongata, or between the medulla oblongata and the rest of the brain.
- There was no interaction between countermeasures and bedrest.
- Orthostatic tolerance decreased in all groups (see poster #23).

Discussion

- We observed intrinsic functional connectivity increases, i.e within the independent component, in the LH, MM, TuMM and PeF at day 28. Intrinsic connectivity increases can be interpreted as increased activity.
- Sitting seems to be the strongest countermeasure, showing reduced functional connectivity changes compared to the control group.
- The lateral hypothalamic area (LH) seems to be strongly affected by prolonged bedrest as it shows connectivity changes to itself, as well as to different hypothalamic and cortical regions.
- The LH has been shown to regulate both, sympathetic and parasympathetic outflow [1].

Conclusion

Prolonged head-down tilt bedrest was associated with functional connectivity changes from hypothalamic regions, especially the Lateral hypothalamic area. We speculate that neuroplasticity may contribute to changes in cardiovascular regulation and orthostatic intolerance after real or simulated weightlessness.

Abbreviations

AH	Anterior hypothalamic area
DMH	Dorsomedial hypothalamic nucleus
LH	Lateral hypothalamic area
MM	Mamillary bodies
MPO	Medial preoptic nucleus
PeF	Perifornical nucleus
PeVN	Periventricular hypothalamic nucleus
PVN	Paraventricular hypothalamic nucleus
SON	Supraoptic nucleus
TuMM	Tuberomamillary nucleus
VMH	Ventromedial hypothalamic nucleus

References

[1] Dampney. The Hypothalamus and Autonomic Regulation: An Overview. In: Central regulation of autonomic Functions (2nd Edition). Oxford University press 2011.