A first insight in regional brain changes after parabolic flight: a voxel-based morphometry study.

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Target audience: Researchers interested in the vestibular system, space researchers, neuroradiologists, ENT doctors, neurologists.

Purpose: The effect of microgravity experienced during spaceflight on the human body has already been studied quite thoroughly and include cardiovascular, muscle and bone physiology[1,2]. Furthermore, it has been proposed that weightlessness can impair processes at the level of the central and peripheral nervous system[3]. However, changes of brain morphology associated with spaceflight have not yet been investigated. The purpose of this study was to investigate possible effects of short-term gravity transitions on brain connectivity and morphology. This study is part of a larger, ongoing study were we investigate neuroplasticity in astronauts after spaceflight[4,5]. We hereto use, among other MRI techniques, voxel-based morphometry (VBM)[6], an unbiased and automated technique, to assess anatomical differences throughout the brain.

Methods*:* *Data acquisition:* Data were acquired on a 3T GE MR 750 W (GE Healthcare, Milwaukee, Wisconsin, USA) scanner, located close to the parabolic flight (PF) site in Bordeaux, using a 32-channel head coil. 3D IR-prepared FSPGR images with a FOV of 256mm x 256mm and 176 slices were acquired with a spatial resolution of 1 x 1 x 1 mm^3 and with following acquisition parameters: TR = 8.2 ms, TE = 2.52 ms, TI = 450 ms, flip angle = 12°. *Data processing:* The data for the VBM-analysis was processed in accordance with a pipeline that relies on an improved version first proposed by Ashburner et al[6]. It mainly consists of three steps. First, a segmentation of the brain tissues is conducted in native space to classify the intensities of the original images as gray matter (GM), white matter (WM), cerebrospinal fluid (CSF), skull and an outlier class. Prior to the segmentation, the MR-image intensity is corrected for non-uniformity, using a 60mm FWHM threshold for the assumed Gaussian distribution of the bias field[7]. In a second phase, the GM and WM images are brought to the same stereotactic space, using an iteratively created template where the images are non-linearly registered to using a diffeomorphic image registration algorithm[8]. Finally, all the segmented and registered images were affinely transformed to Montreal Neurological Institute (MNI) space and smoothed using a Gaussian FWHM kernel of 8mm. As the output of this phase is very likely to be influenced by anatomical irregularities such as atrophy, we took into account the guidelines presented in Henley et al.[9]. All intermediate results were visually inspected for gross misregistration or mis-segmentation. *Subjects:* Sixteen first-time parabolic flyers were included and underwent a MRI scan before (L-2) and immediately (2-4 hours, R+0) after the parabolic flight. Gray matter (GM) differences were assessed by means of VBM. *Parabolic flight*: The parabolic flight tests were done during the 60 and 61st ESA parabolic flight campaigns in Bordeaux with the A300 Zero-G airbus. During a parabolic flight mission, once the airplane is at cruising altitude, it is 31 times consecutively subjected to phases of 1.8 g, 0 g and 1.8 g each lasting approximately 22 seconds and constituting the parabolas. In between these parabolas, the plane flies level at 1 g for 1 to 5 minutes. A mission typically lasts 3 hours.

Results: Significant clusters (p<0.001, uncorrected) of GM volume decrease (L-2 > R+0) were located in the middle frontal gyrus, the occipital lobe (cuneus included) and the middle temporal gyrus (with V5/MT area). We also found a significant increase (p<0.001, uncorrected) in GM volume (L-2 < R+0) in the anterior lobe of the cerebellum and the superior frontal gyrus (see **Fig. 1**). We did not find any significant clusters when we corrected for false discovery rate (FDR).

Discussion: The changes found above are similar to the ones earlier described in vestibular patients[10-12] having dizziness problems and this could imply that the absence of gravity or the shifts in gravity mimic a vestibular failure. The similarity between vestibular failure patients and parabolic flight participants consists among others a neurosensory mismatch. Patients lack coherent information due to a failure of the vestibular end organ, leading to a conflict between visual, proprioceptive and vestibular information. Likewise do parabolic flyers experience a sensory mismatch each time they are subjected to the gravity transitions, and in particular during the free floating phase. Additionally, most of the regions described are also involved in the cortico-limbic network and changes in these areas have been shown to be stress-related[13]. A parabolic flight is an event with a high stress load and earlier studies have already shown an increase in stress hormones and stress-related changes in electrocortical activity[14,15]. Increasing the number of subjects and including experienced PF subjects (low stress load) could help to get better insight in this matter.

Conclusion: These results suggest that alteration of gravity has an impact on brain morphology in regions that are known to play a pivotal role in the integration of neurosensory information matching vestibular, visual and proprioceptive inputs. Future research and the parallel linking of these results to long duration spaceflight is necessary to support and extend these preliminary findings and to get a first insight in the effects of spaceflight on the function and morphology of the central nervous system. This is the first experiment studying possible changes in brain morphology due to gravity alterations. It shows that short lasting gravity transitions are sufficient to induce neuroplasticity, similar to the ones experienced by vestibular patients. Identification of the regions of interest will allow better understanding of the processes involved in adaptation to microgravity environments, and this becomes more and more important in view of commercial space flight, as well as for future long duration flights e.g. interplanetary space missions and space habitats.

References

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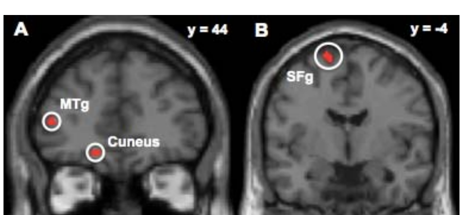

Figure 1: Brain areas showing a significant decrease (A + B) in gray matter after parabolic flight. Data are presented in normalized stereotactic space, overlaid on a high-resolution anatomical MR image with the right side of the brain shown on the left (numerical labels, y coordinates of coronal slices).