**Spaceflight effect on white matter structural integrity**

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Recent reports of elevated brain white matter hyperintensity (WMH) counts and volume in postflight astronaut MRIs suggest that further examination of spaceflight’s impact on the microstructure of brain white matter is warranted. To this end, retrospective longitudinal diffusion-weighted MRI scans obtained from 15 astronauts were evaluated. In light of the recent reports of microgravity-induced cephalad fluid shift and gray matter atrophy seen in astronauts, we applied a technique to estimate diffusion tensor imaging (DTI) metrics corrected for free water contamination. This approach enabled the analysis of white matter tissue-specific alterations that are unrelated to fluid shifts, occurring from before spaceflight to after landing. After spaceflight, decreased fractional anisotropy (FA) values were detected in an area encompassing the superior and inferior longitudinal fasciculi and the inferior fronto-occipital fasciculus. Increased radial diffusivity (RD) and decreased axial diffusivity (AD) were also detected within overlapping regions. In addition, FA values in the corticospinal tract decreased and RD measures in the precentral gyrus white matter increased from before to after flight. The results show disrupted structural connectivity of white matter in tracts involved in visuospatial processing, vestibular function, and movement control as a result of spaceflight. The findings may help us understand the structural underpinnings of the extensive spaceflight-induced sensorimotor remodeling. Prospective longitudinal assessment of the white matter integrity in astronauts is needed to characterize the evolution of white matter microstructural changes associated with spaceflight, their behavioral consequences, and the time course of recovery. Supported by a grant from the National Space Biomedical Research Institute, NASA NCC 9-58.