Rewiring of the brain in space
What happens to the brain due to spaceflight?

Prof dr Floris Wuyts
University of Antwerp
Lab for Equilibrium Investigations and Aerospace, UA
European Institute for ORL - St Augustinus Hospital, Wilrijk
Floris.Wuyts@uantwerpen.be


proxima
Thomas Pesquet
esa

Neuroplasticity = the brain’s ability to reorganize itself by forming new neural connections.

Objectives BRAIN-DTI
ESA project/Roscosmos – initiated in 2009

- Determine biomarkers of neuroplasticity by means of advanced MRI techniques

- comparison of the brain before and after spaceflight

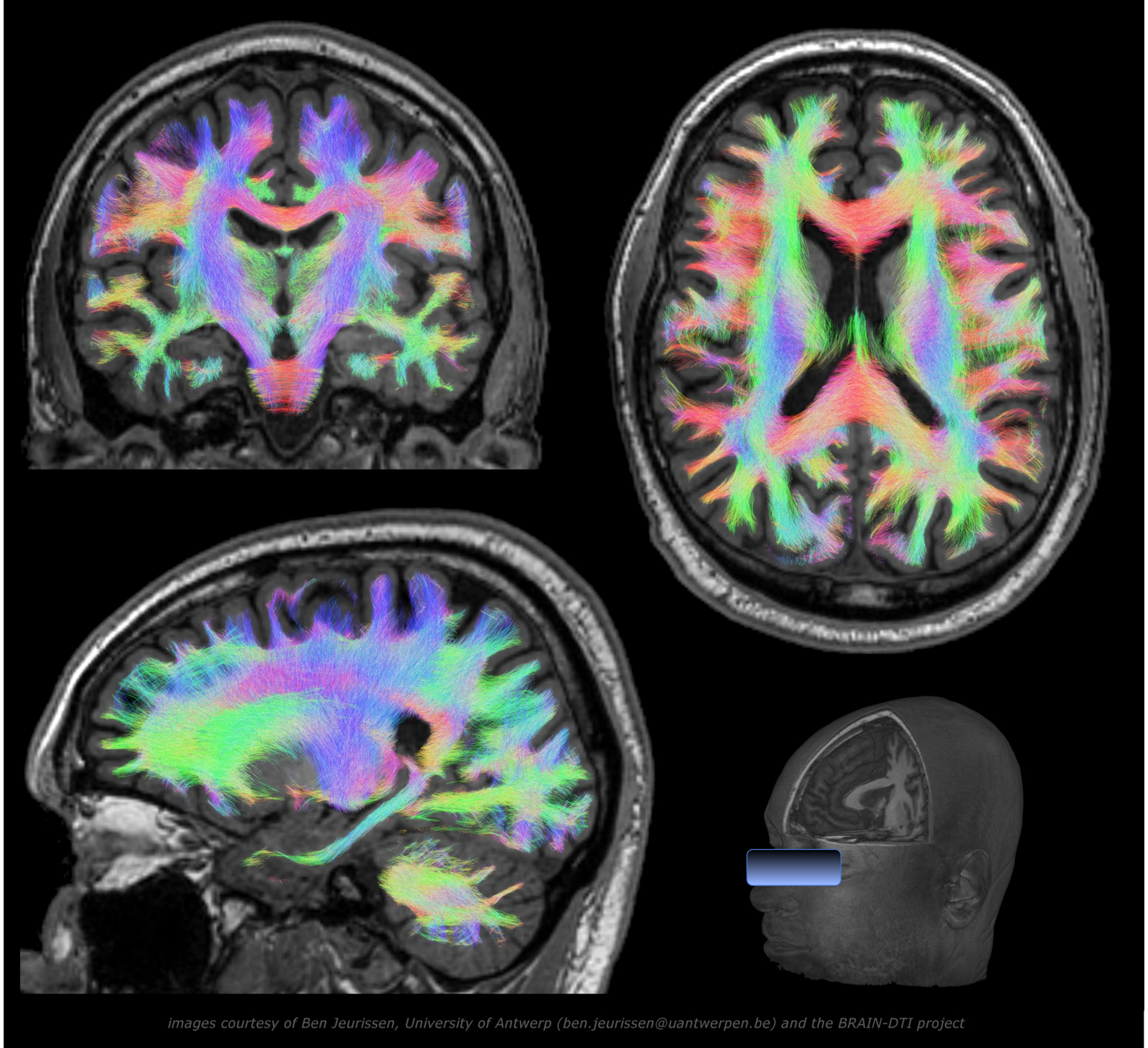
- Which specific regions of interest (ROI) are involved

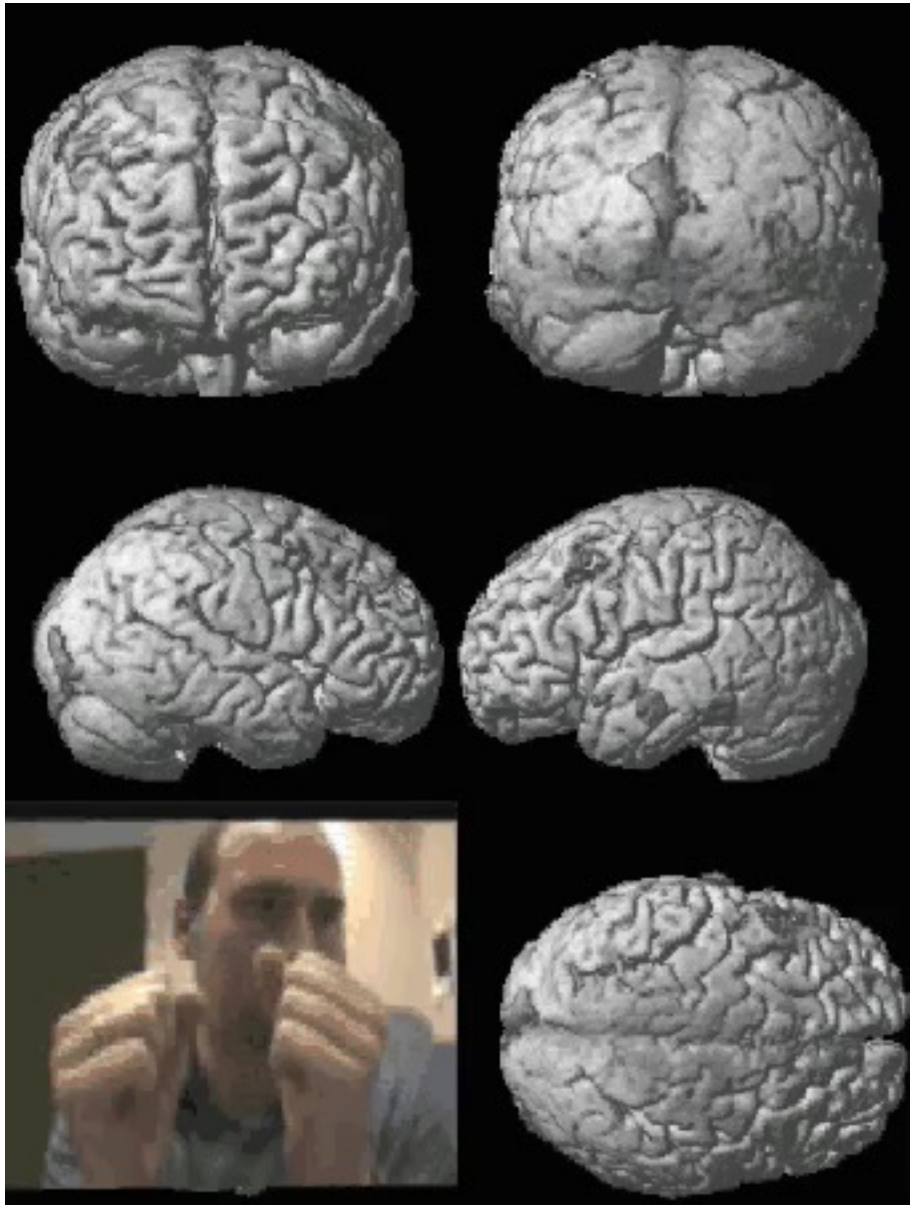
- Relate insight to patients with vestibular dysfunction and the elderly.


MRI
MR
Positioning Kit

Tractography

Diffusion MRI





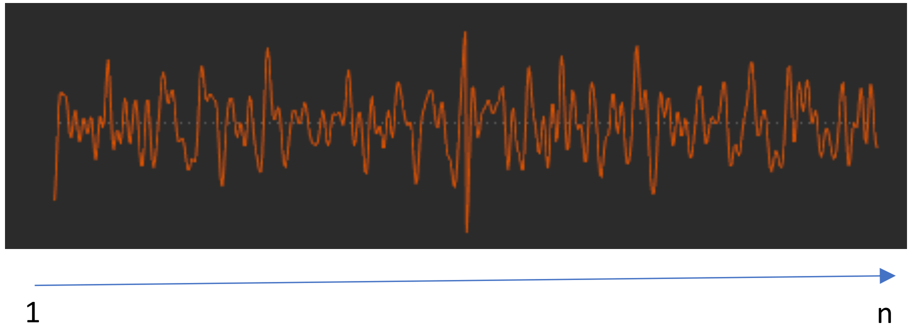
Measure **blood oxygenation as marker for neural activity** (blood-oxygenation level dependent: BOLD signal). Courtesy of Stefan Sunaert

Resting-state functional MRI

→ Resting-state: no instruction

→ Measure signal changes in time = timeseries

BOLD fMRI timeseries



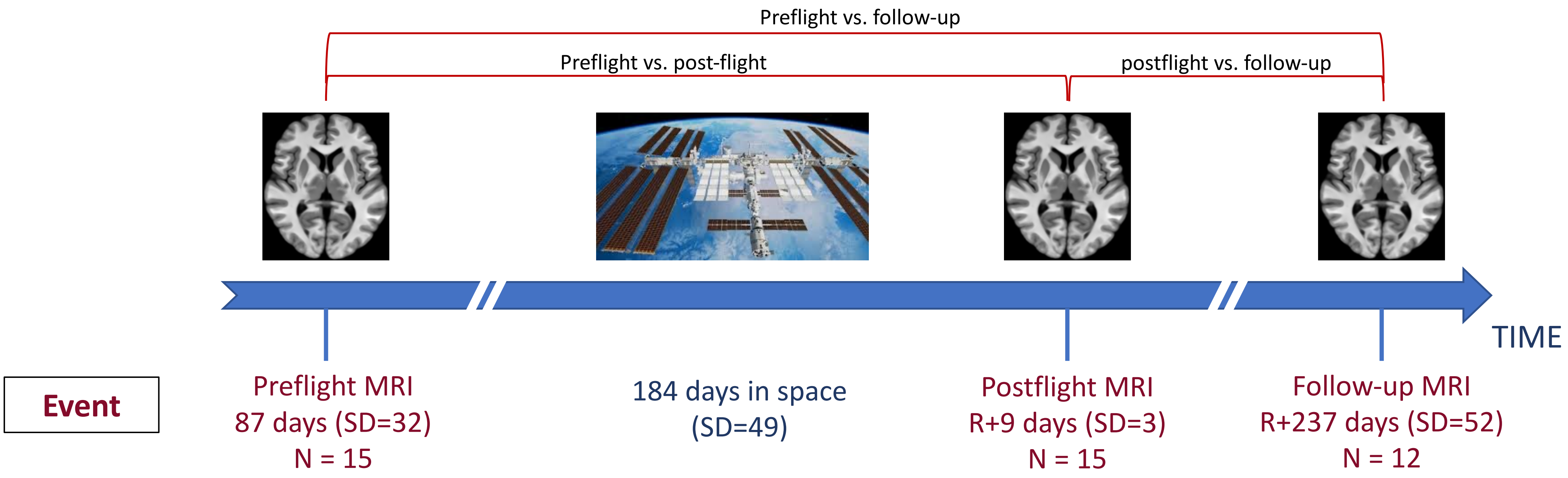
→ Timeseries acquired for each voxel

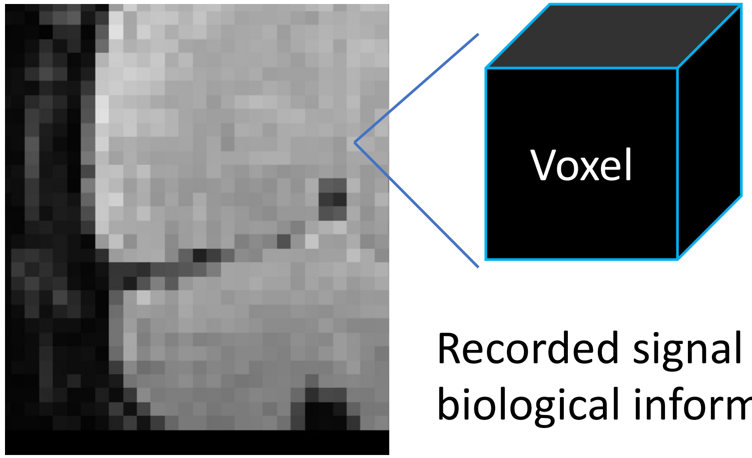
→ Correlate timeseries between voxels

→ Perform statistical analysis of connectivity profile between groups and/or timepoints

Functional connectivity = correlation between the signal changes in time across distinct brain areas

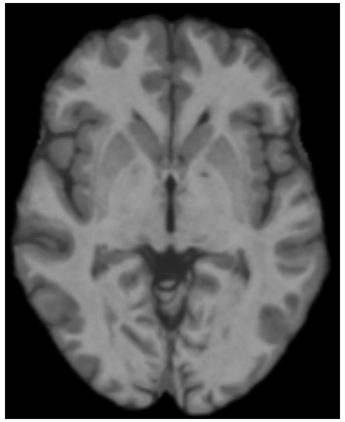
The BRAIN-DTI project overview





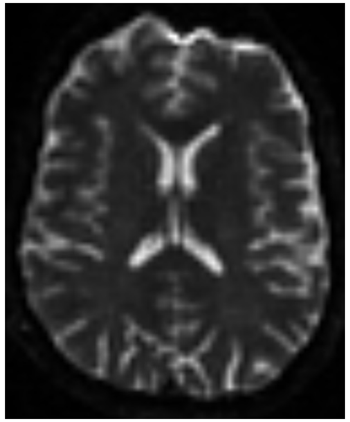
Recorded signal reflects biological information

Anatomical MRI



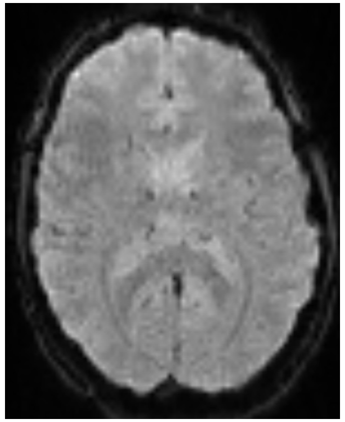
Anatomy and volume

Diffusion MRI



Microstructure

Functional MRI



Functional connectivity

Brain Struct Funct
DOI 10.1007/s00429-015-1054-3

SHORT COMMUNICATION

Cortical reorganization in an astronaut's brain after long-duration spaceflight

Athena Demertzi[1] · Angelique Van Ombergen[2] · Elena Tomilovskaya[3] · Ben Jeurissen[4] · Ekaterina Pechenkova[5] · Carol Di Perri[1] · Liudmila Litvinova[5] · Enrico Amico[1] · Alena Rumshiskaya[5] · Ilya Rukavishnikov[3] · Jan Sijbers[4] · Valentin Sinitsyn[5] · Inessa B. Kozlovskaya[3] · Stefan Sunaert[6] · Paul M. Parizel[7] · Paul H. Van de Heyning[2] · Steven S. L. Laureys[1] · Floris L. Wuyts[2]

Received: 8 April 2015 / Accepted: 30 April 2015

Abstract To date, hampered physiological function after exposure to microgravity has been primarily attributed to deprived peripheral neuro-sensory systems. For the first time, this study elucidates alterations in human brain function after long-duration spaceflight. More specifically, we found significant differences in resting-state functional the underlying neural basis for the observed physiological deconditioning due to spaceflight and are relevant for future interplanetary missions and vestibular patients.

Keywords Microgravity · Functional MRI · Motor behavior · Cortical reorganization · Vestibular cortex

A. Demertzi & A. Van Ombergen et al. *Brain Struct Funct* (2016).

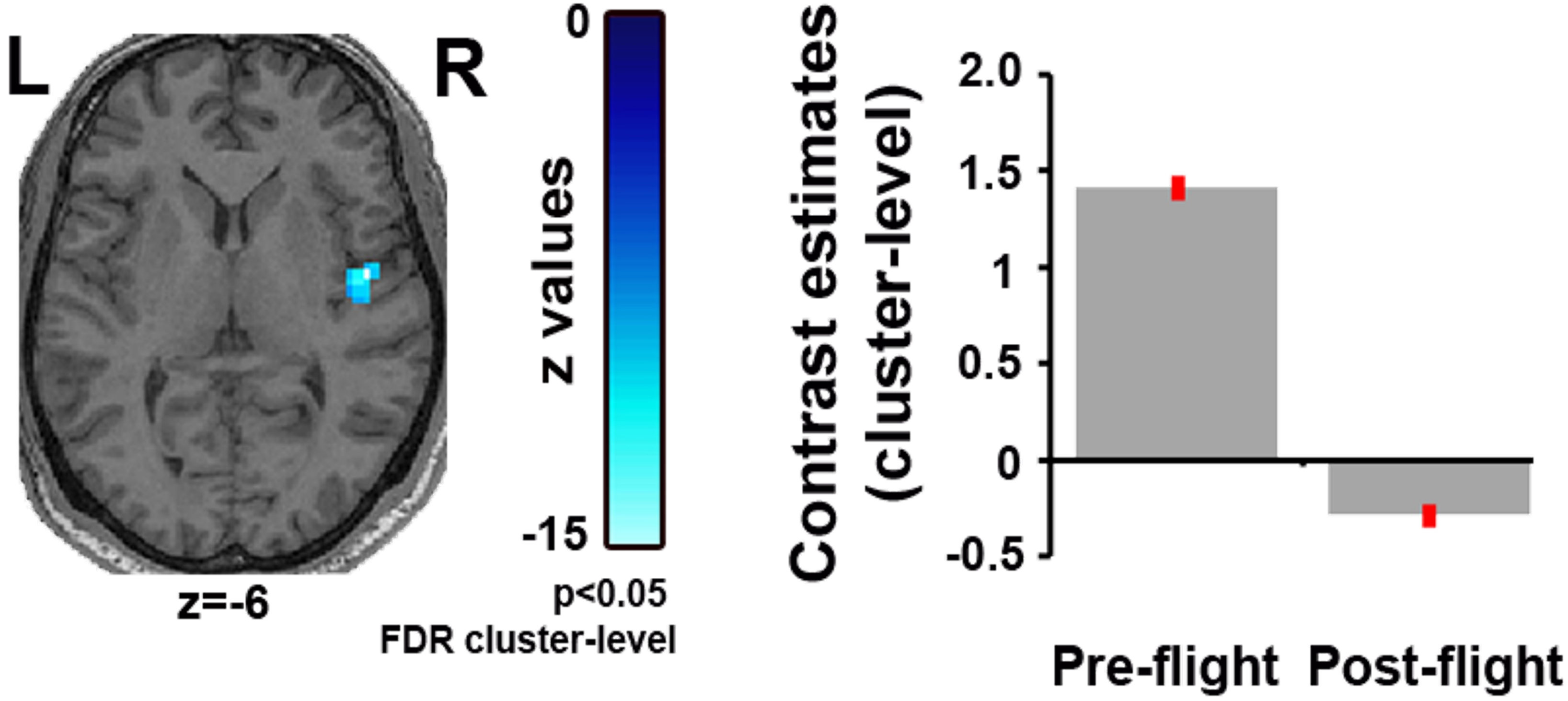


Fig. 1 a The hypothesis-free exploration of connectivity changes (voxel-to-voxel connectivity analysis) indicated that, compared to preflight scan, at post-flight the cosmonaut had **reduced intrinsic connectivity in the right insula and ventral posterior cingulate cortex**. The figure summarizes the results for the right insula, as this region is a critical part of the vestibular system.

Van Ombergen, Zu Eulenburg and Wuyts, 2018

CORRESPONDENCE

Brain Tissue–Volume Changes in Cosmonauts

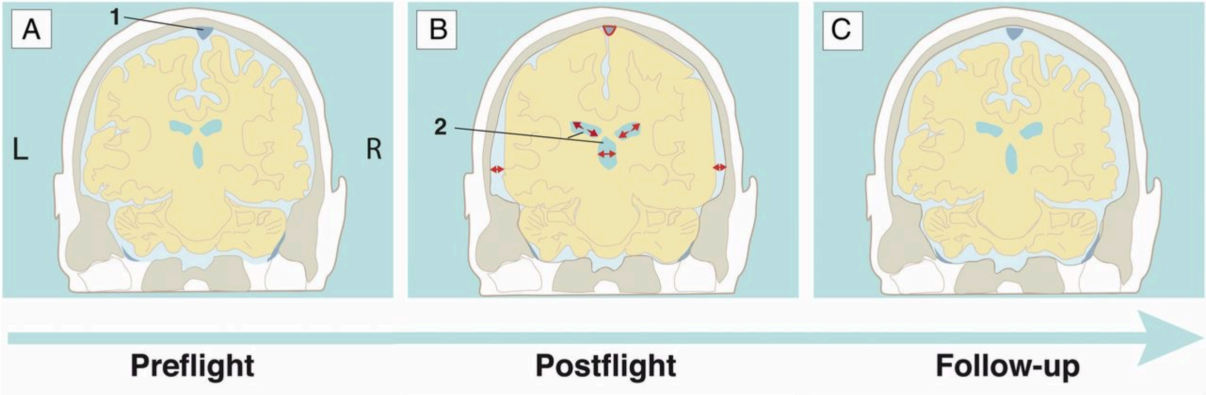
TO THE EDITOR: Long-duration spaceflight has detrimental effects in several physiological systems. Several studies have shown an upward shift of the cerebral hemispheres, a decrease in frontotemporal volume, and an increase in ventricle size after spaceflight.[1-3] However, information is limited about the effects of microgravity on brain volume, particularly regarding changes that are evident more than 1 month after spaceflight.

We prospectively studied data from T_1-weighted magnetic resonance imaging (MRI) that was performed in 10 male cosmonauts (mean age, 44 years; average space-mission duration, 189 days) at three time points: preflight (in 10 cosmonauts), short-term postflight (average, 9 days postflight; in 10), and long-term postflight follow-up (average, 209 days postflight; in 7). The volumes of gray matter, white matter, and cerebrospinal fluid (CSF) were analyzed with the use of voxel-based morphometry. (The complete methods and additional analyses are provided in the Supplementary Appendix, which is available with the full text of this letter at NEJM.org.) Aging effects that may occur over the interval between preflight and postflight were accounted for by longitudinal data from matched controls.

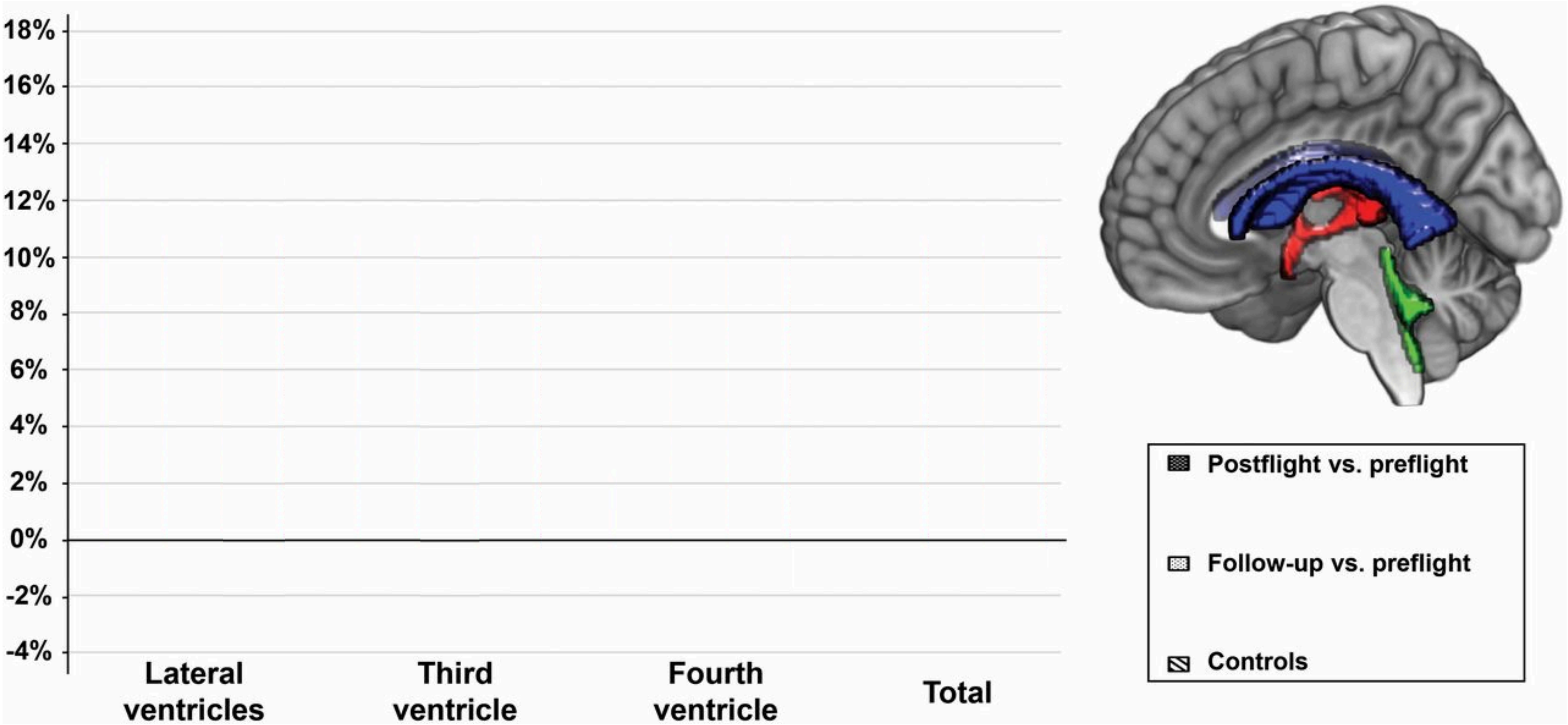
THIS WEEK'S LETTERS

The gray-matter volume postflight as compared with preflight showed a widespread decrease in the orbitofrontal and temporal cortexes; the maximal decrease was 3.3% in the right middle temporal gyrus. At long-term postflight follow-up, most reductions in gray-matter volume had recovered toward preflight levels (e.g., a 1.2% reduction in gray-matter volume persisted in the right temporal gyrus). The white-matter volume postflight as compared with preflight was reduced along a longitudinal tract of the left temporal lobe, but there was a global reduction of cerebral white-matter volume at long-term follow-up as compared with postflight. The ventral CSF spaces of the cerebral hemispheres and the ventricles had increased in volume postflight as compared with preflight (maximal increase, 12.9% in the third ventricle), while CSF volume below the vertex decreased. At long-term follow-up, the CSF volume in the ventricles had returned toward preflight values, while the CSF volume in the entire subarachnoid space around the brain had increased. Changes in the volumes of gray matter and CSF are shown in Figure 1.

The findings from an average of 7 months after a return to Earth can be summarized as showing that most of the loss in the gray-matter volume that was seen immediately postflight had recovered to preflight levels, while CSF volume continued to increase in the subarachnoid compartment. The expansion of CSF spaces in light of postflight decreases in the gray-matter volume and a reduction in the white-matter volume at follow-up suggests a persistent disturbance in CSF circulation even many months after a return to Earth. These brain-volume changes may relate to clinical findings, such as ocular and visual abnormalities after long-duration spaceflight.[4,5] Future investigation is required in order to determine the overall clinical signifi-



Ventricular volume changes after spaceflight

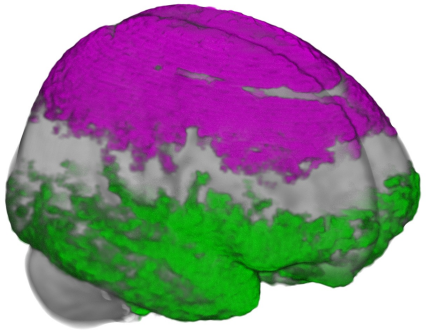


Ref: Van Ombergen et al, Brain ventricular volume changes induced by long duration spaceflight, PNAS, 2019

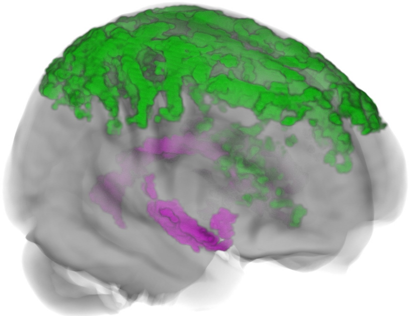
Main findings

Two other distinct effects

Fluid (CSF) redistribution

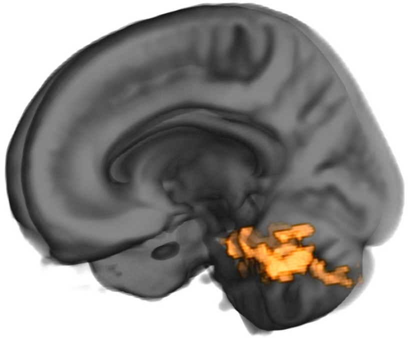


Cerebro spinal fluid (CSF) volume redistribution

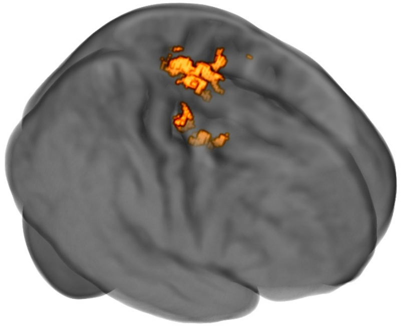


GM remodeling

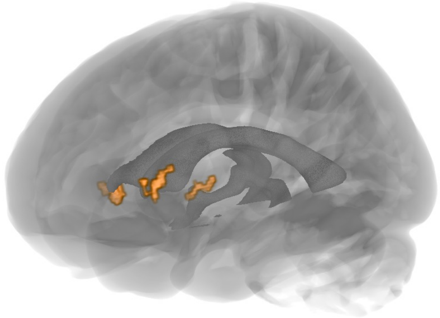
Sensorimotor adaptation / Neuroplasticity



Cerebellum



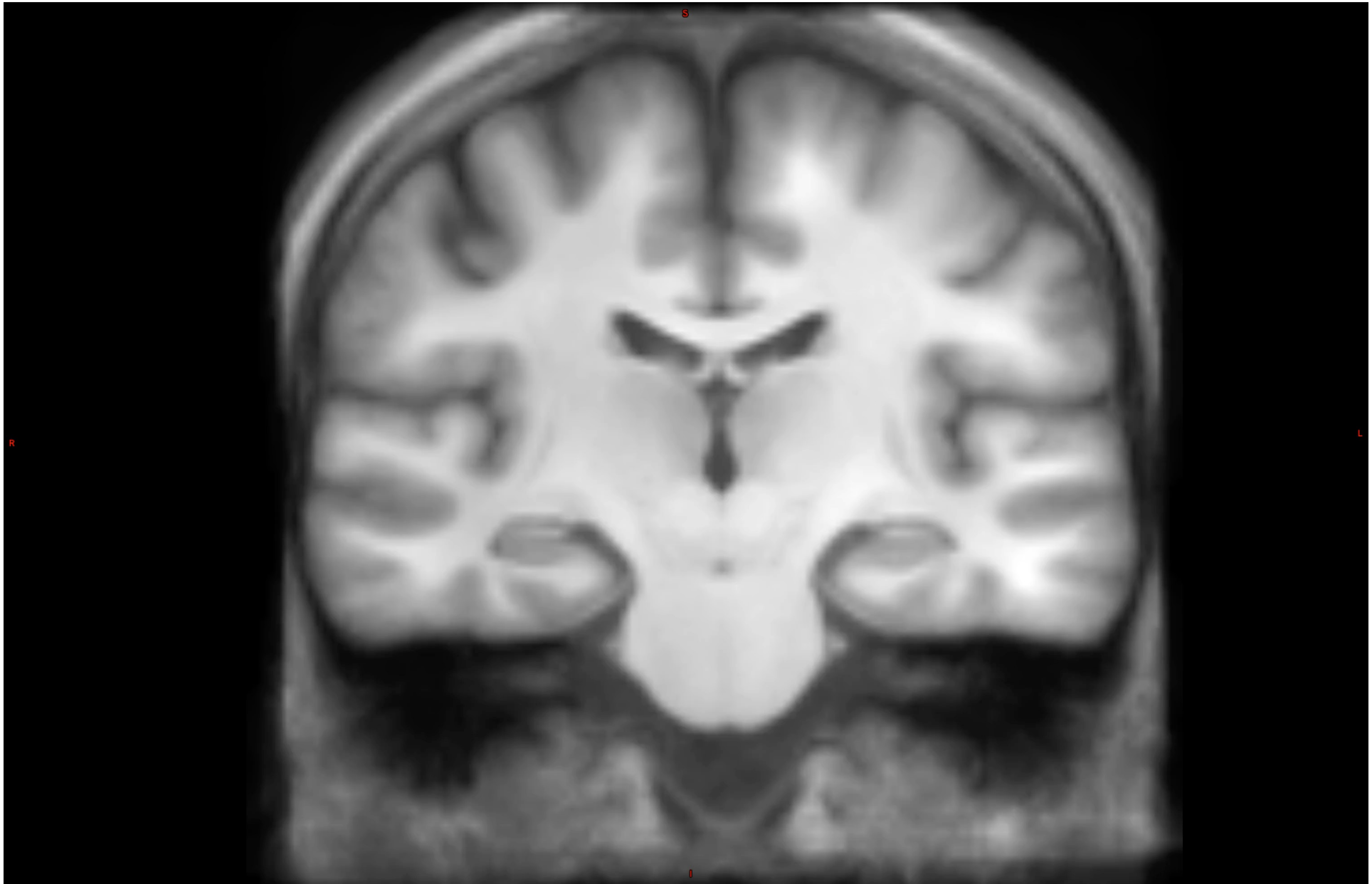
Sensorimotor cortex



Basal ganglia

(Jillings et al., *Science Advances*, 2020)

Diffusion MRI analysis N=18 cosmonauts pre and post flight, Increase FDC = Fiber Density and Cross section



Courtesy Ben Jeurissen

Brain MRI changes in astronauts & cosmonauts

- Narrowing of central sulcus and upward shift of the brain
  (Roberts et al., NEJM 2017)

- Increase of the ventricular volumes

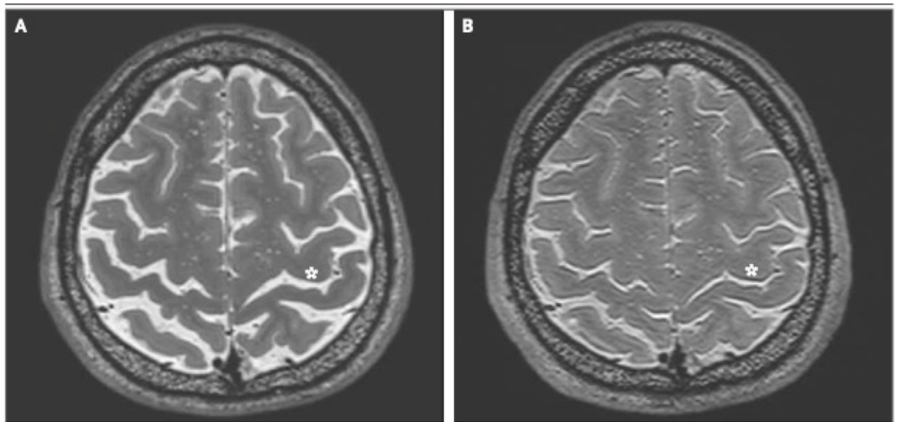
  (*Roberts et al., NEJM 2017, Roberts et al., AJNR, 2019,* Van Ombergen et al., *NEJM* 2018, Van Ombergen et al., PNAS 2019)

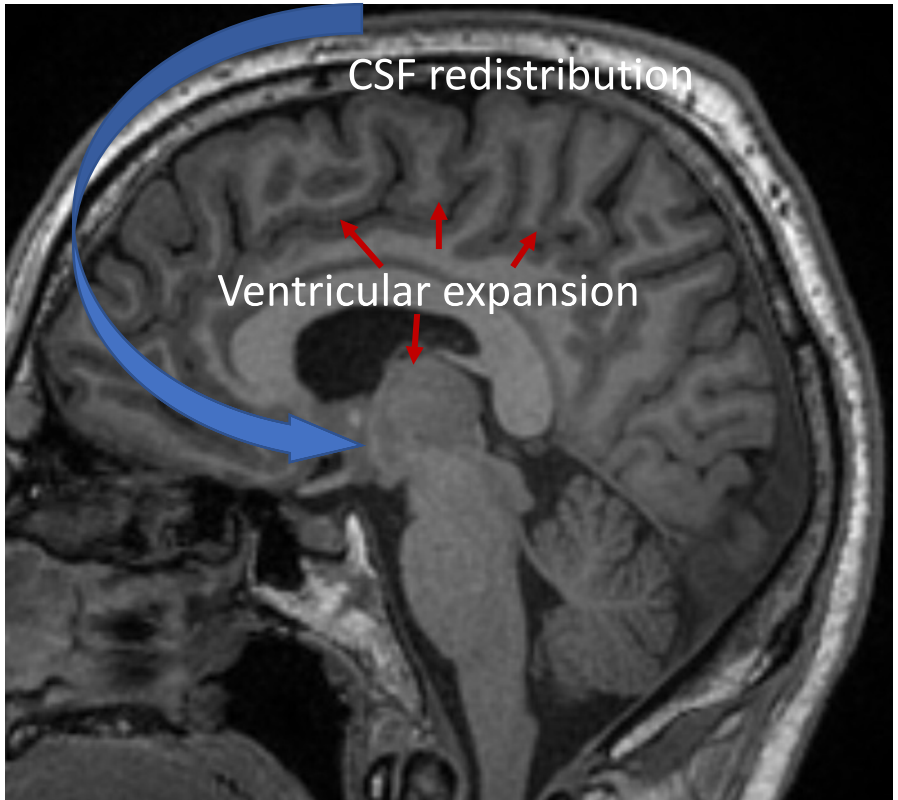
- ↑ pituitary deformation

  (Kramer et al., *Radiology* 2020)

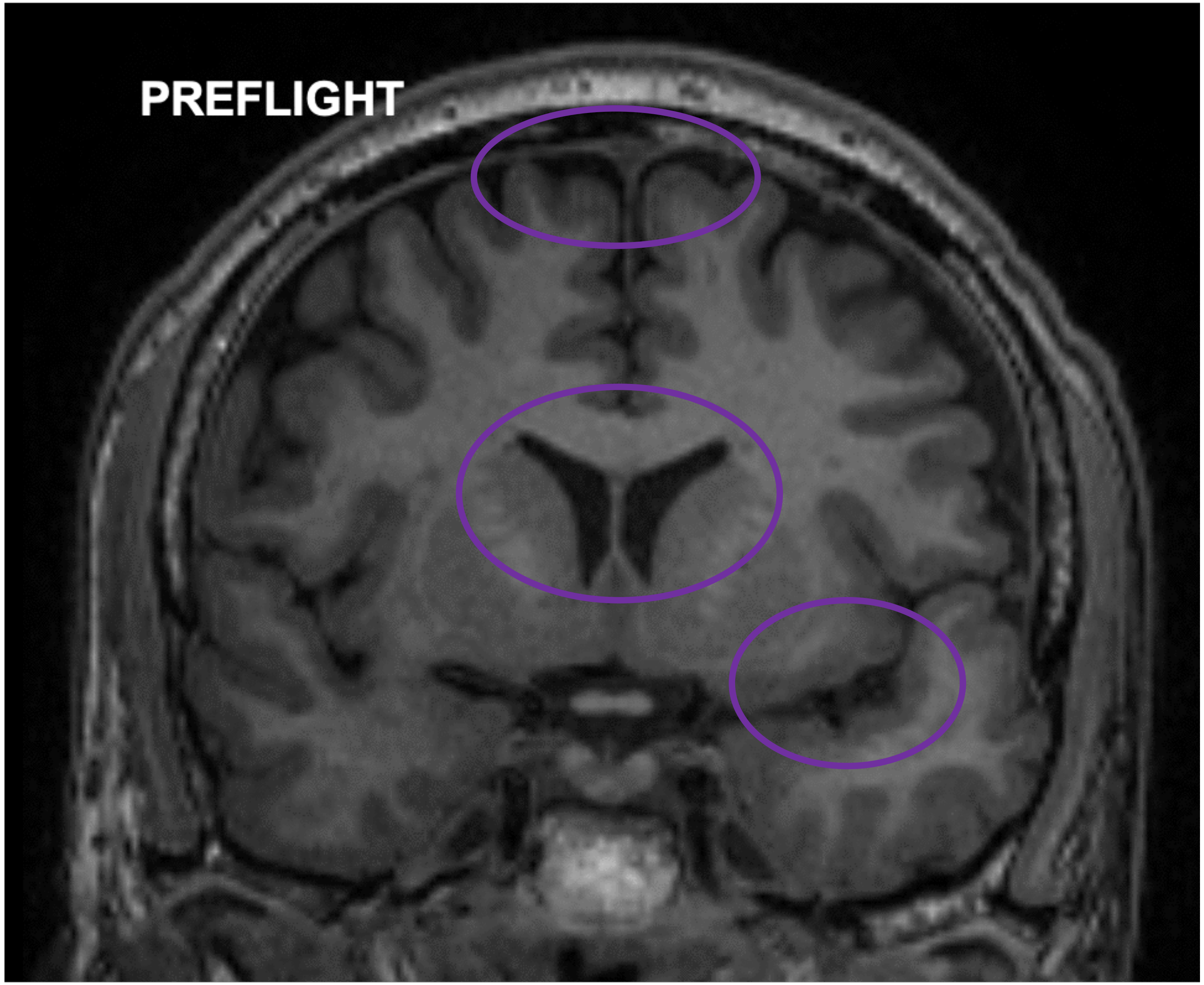
- White matter changes and redistribution of CSF

  (Jillings et al., *Science Advances*, 2020)





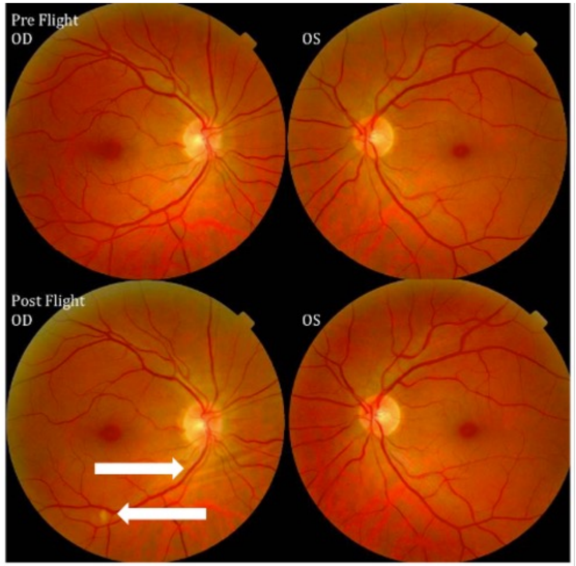
Upward brain shift

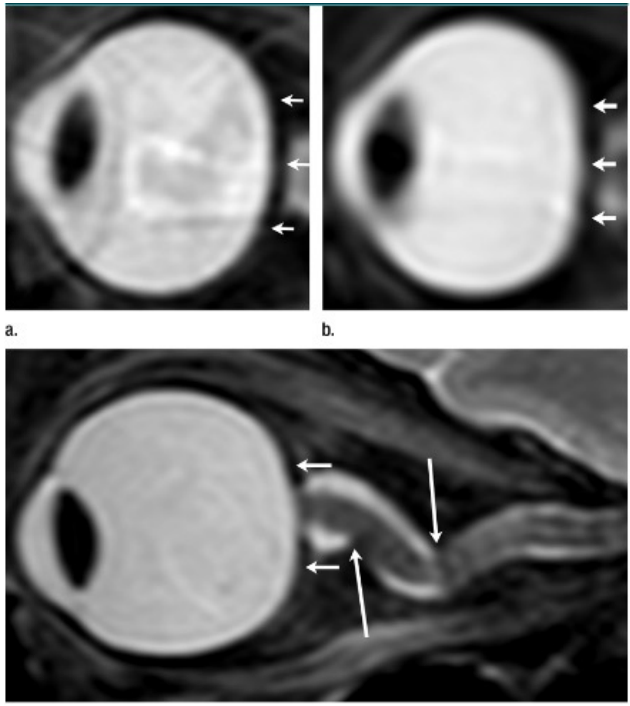


Courtesy Steven Jillings

Spaceflight-associated neuro-ocular syndrome (SANS)

- Optic disk edema
- Refractive changes
- Infarcts in the nerve-fiber layer
- Cotton wool spots
- Retinal folds
- ~40-60% of NASA astronauts experience vision changes



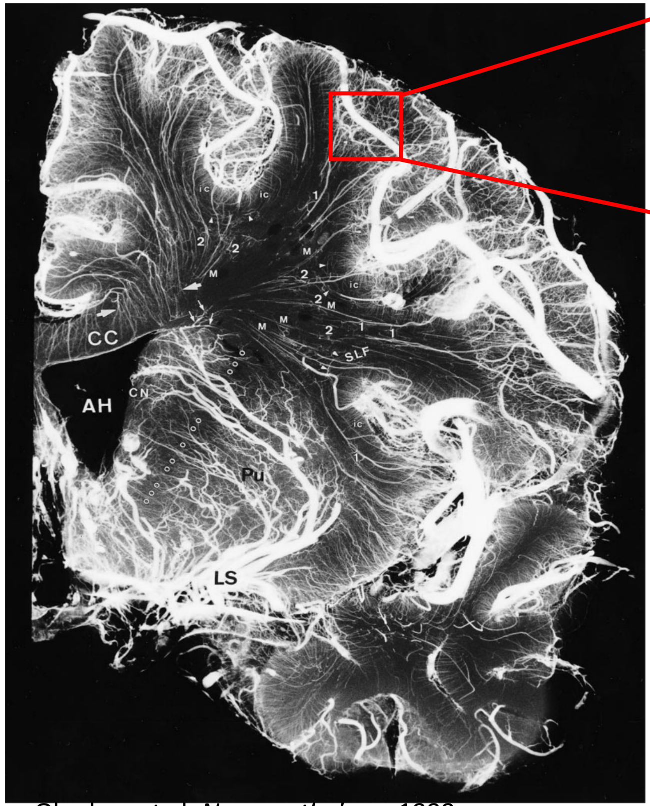


Source: NASA Risk of Spaceflight Associated Neuro-ocular Syndrome Evidence Report

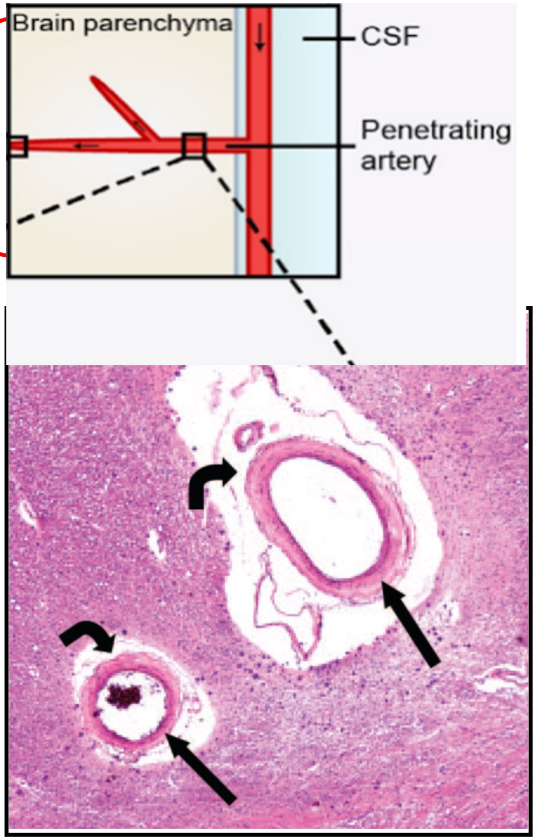
Mader et al., *Ophthalmology*, 2011
Bogomolov et al., *Aviakosm. Ekolog. Med.*, 2015

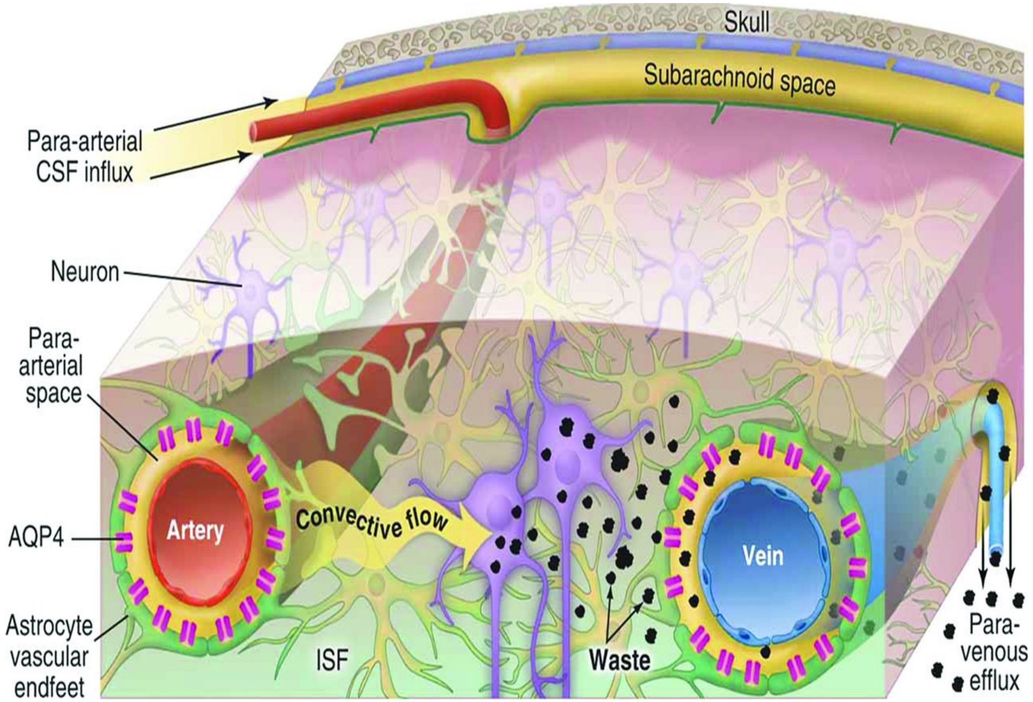
Perivascular spaces (PVS)

- Tubular fluid-filled structure around the blood vessels penetrating the brain parenchyma
- Clearance of waste products from the brain: the **glymphatic system**



Okudera et al, *Neuropathology,* 1999.



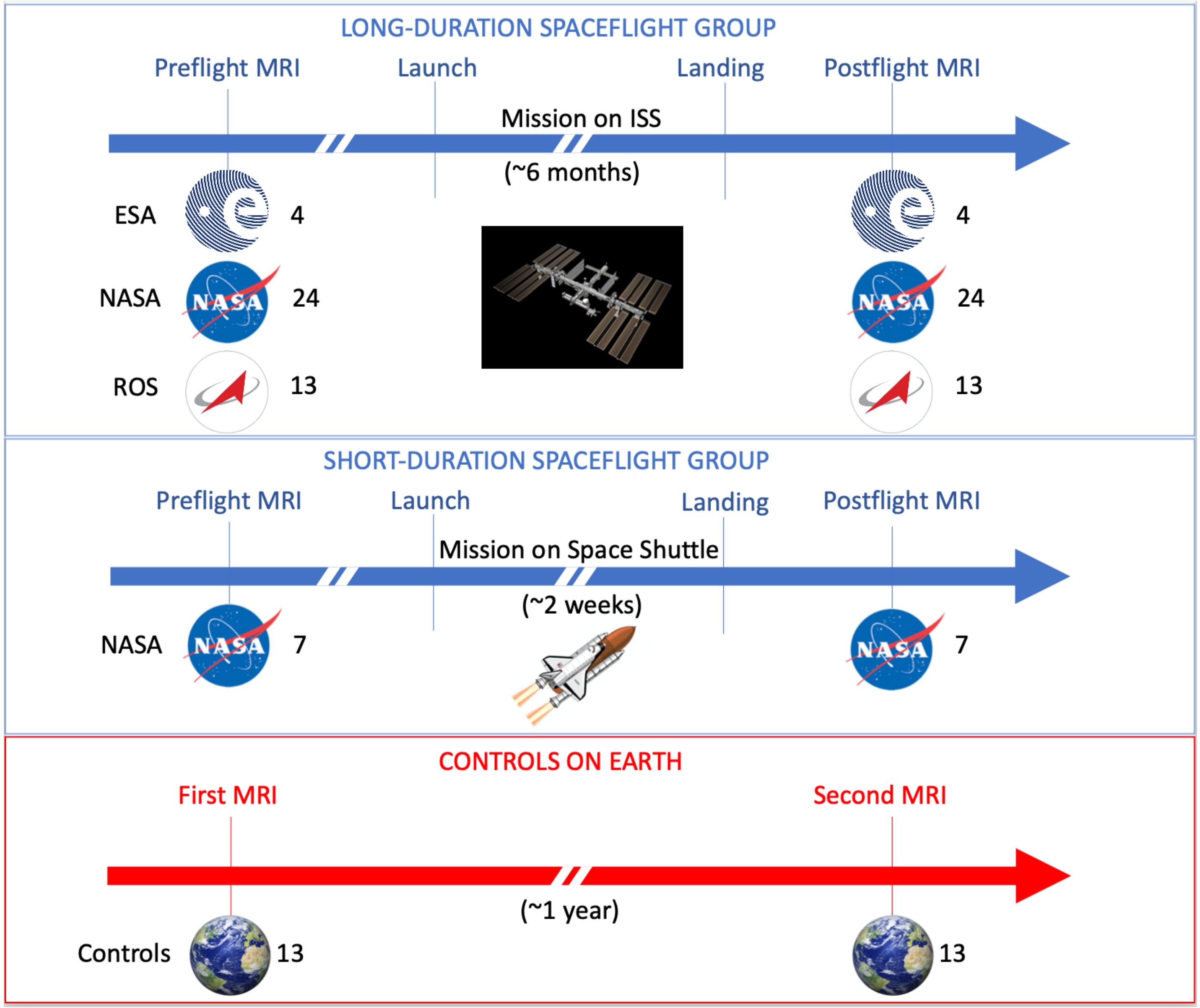


Mestre et al, *Clin Sci*, 2017

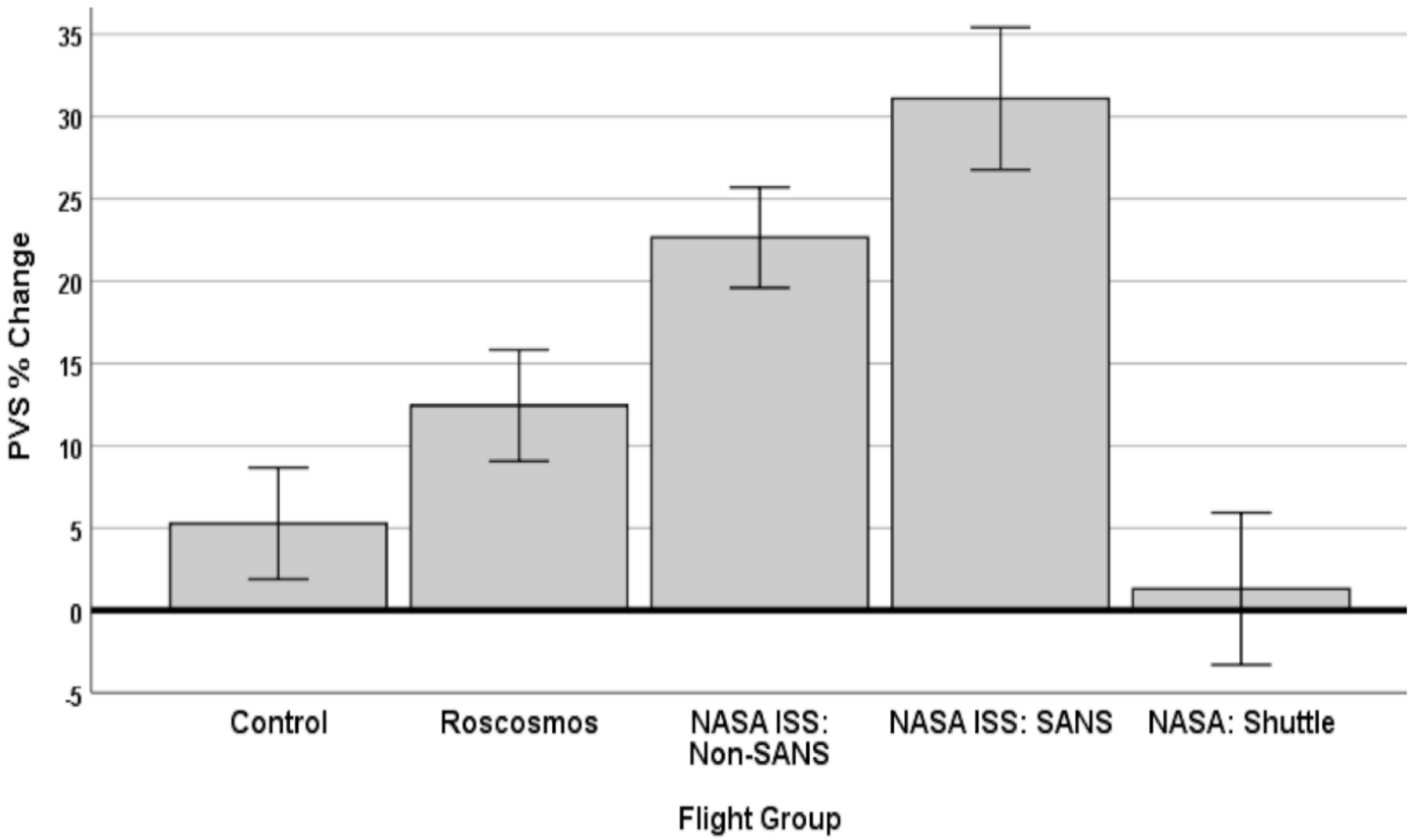
Study Design

- 3D T1-weighted MRI data
  (1mm isotropic resolution)

- 41 long-duration spaceflight on ISS
- 7 short-duration spaceflight on Space Shuttle
- 13 age-matched controls on Earth

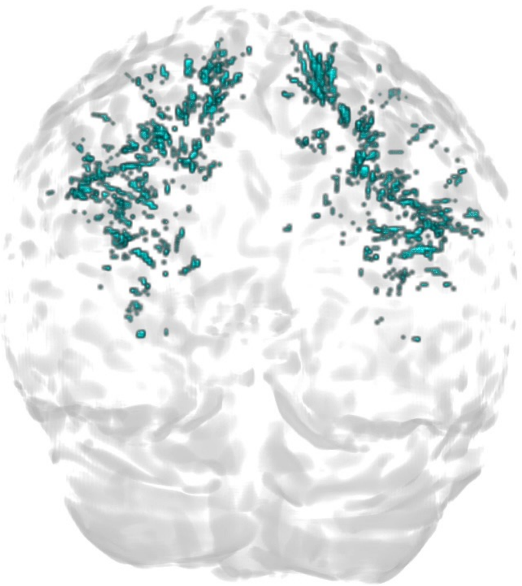


Results

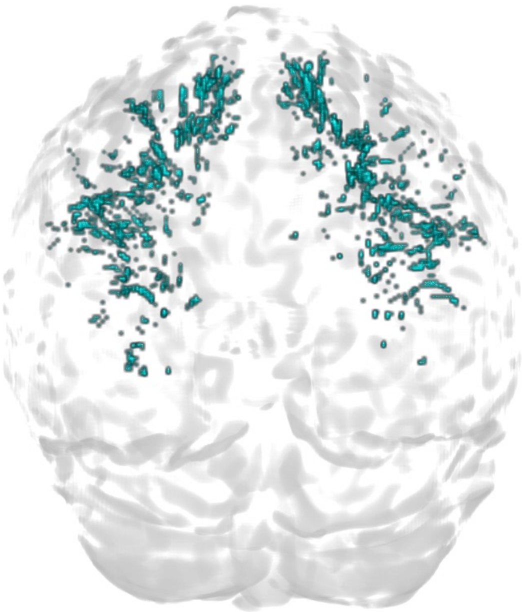


PVS volume changes are higher in NASA ISS astronauts compared with Roscosmos cosmonauts

White matter PVS



Before
long-duration spaceflight



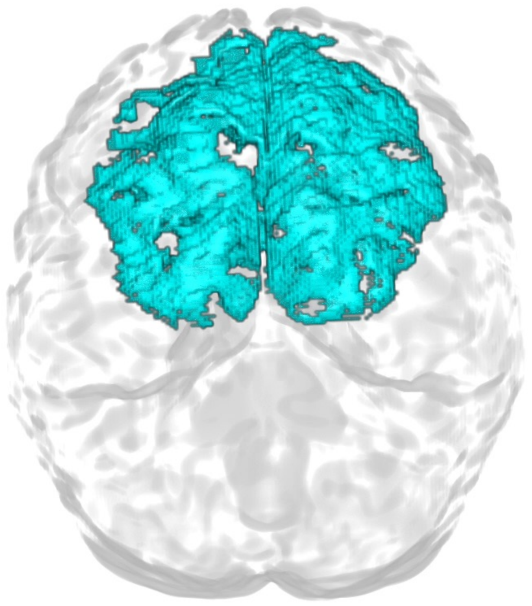
After
long-duration spaceflight

Basal ganglia PVS

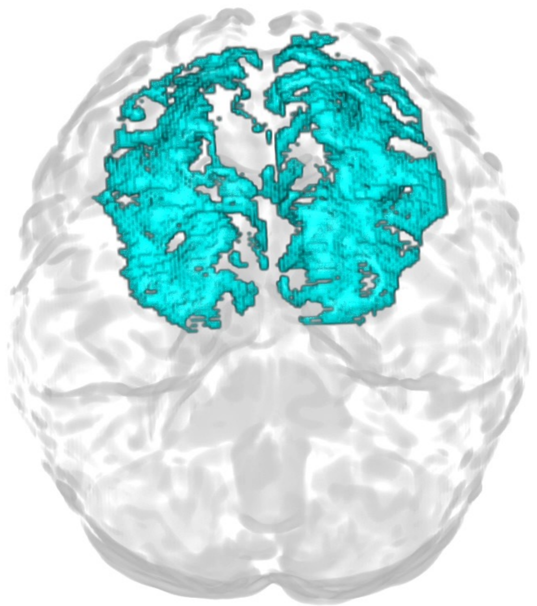
Before
long-duration spaceflight

After
long-duration spaceflight

Subarachnoid space at the vertex (VSA)

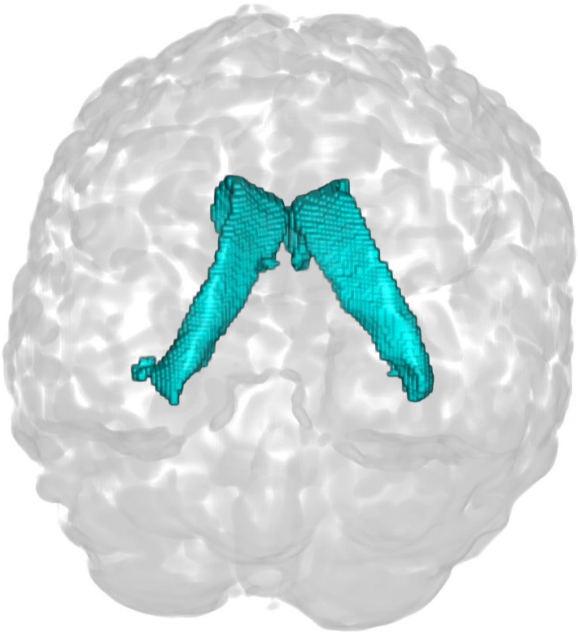


Before
long-duration spaceflight

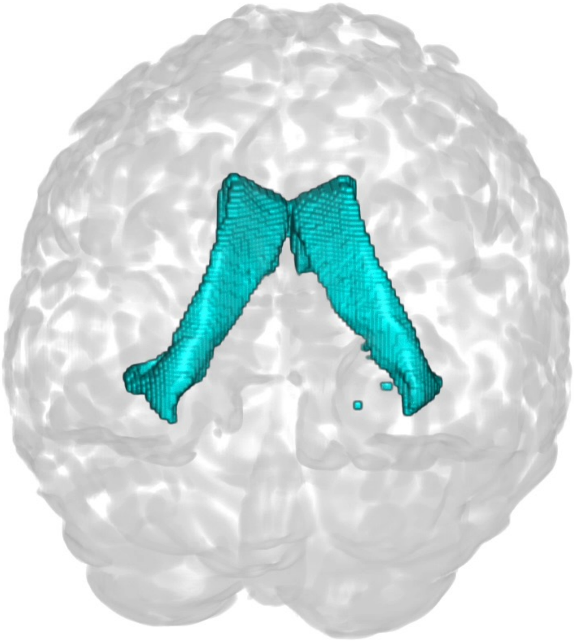


After
long-duration spaceflight

Lateral ventricles (LV)



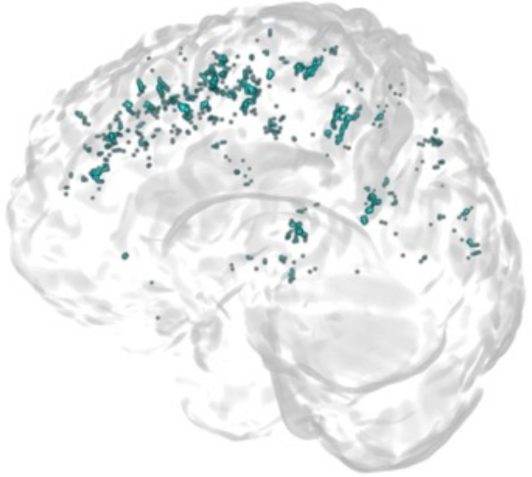
Before
long-duration spaceflight

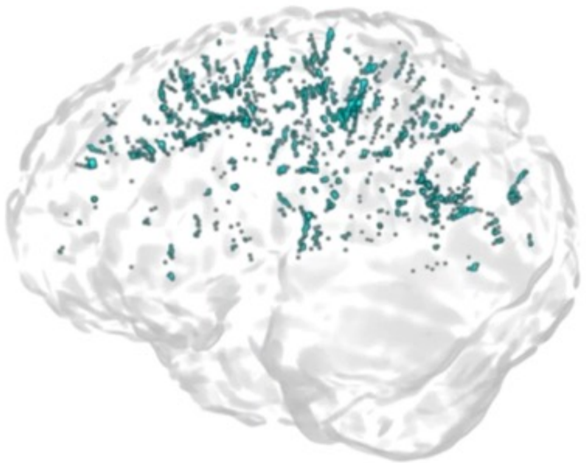


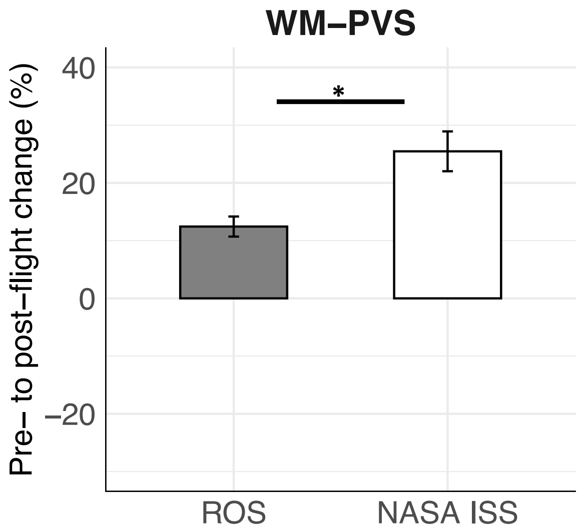
After
long-duration spaceflight

White matter PVS

Preflight MRI







What is the difference between NASA and Roscosmos crew?


esa
European Space Agency
Pesquet
Whitson
Novitsky
Kimbrough
Borisenko
Ryzhikov

Hypothesis 1: Lower body negative pressure

Hypothesis 2

ARED(advanced resistive exercise device)

PNAS

BRIEF REPORT | NEUROSCIENCE

OPEN ACCESS

Check for updates

The effect of prolonged spaceflight on cerebrospinal fluid and perivascular spaces of astronauts and cosmonauts

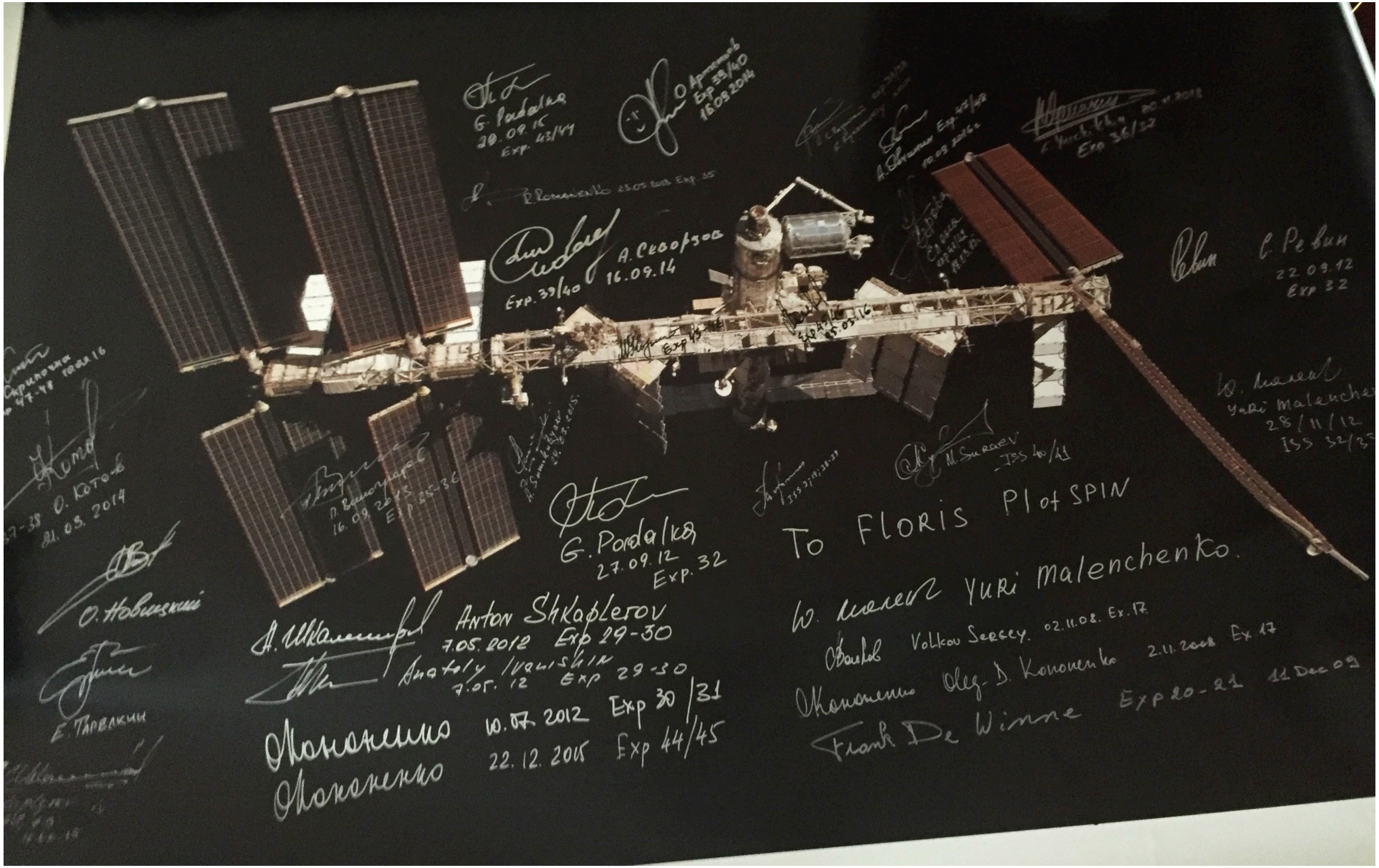
Giuseppe Barisano[a,1], Farshid Sepehrband[a], Heather R. Collins[b], Steven Jillings[c], Ben Jeurissen[d], James A. Taylor[b], Catho Schoenmaekers[c], Chloë De Laet[c], Ilya Rukavishnikov[e], Inna Nosikova[e], Liudmila Litvinova[f], Alena Rumshiskaya[f], Jitka Annen[g], Jan Sijbers[d], Steven Laureys[g], Angelique Van Ombergen[c], Victor Petrovichev[f], Valentin Sinitsyn[h], Ekaterina Pechenkova[i], Alexey Grishin[j], Peter zu Eulenburg[k], Meng Law[l], Stefan Sunaert[m], Paul M. Parizel[n], Elena Tomilovskaya[e,2], Donna R. Roberts[b,1,2], and Floris L. Wuyts[c,1,2]

Edited by Thomas Albright, Salk Institute for Biological Studies, La Jolla, CA; received December 3, 2021; accepted March 3, 2022

Take home messages

- Microgravity affects fluid redistribution in the brain.
- Microgravity affects the ventricles and perivascular space in the brain
- There is evidence for neuroplasticity (cerebellum,…)
- Further research crucial to tackle SANS

Thank you to all participating cosmonauts and astronauts



- Co investigators: E. Tomilovskaya, S. Jillings, A. Van Ombergen, B. Jeurissen, A. Demertzi, J. Sijbers, S. Sunaert, S. Laureys, A. Chouker, P.M. Parizel, E. Pechenkova, A Rumshiskaya, I. Koslovskaya, D Glukhikh, L Kornilova, P-F Migeotte, S Moore, H MacDougall, K Buytaert, A. Weerts, J. Annen, I. Nosikova, AM Van der Linden, M Verhoye, P zu Eulenburg, C. De Laet, C. Schoenmaekers, H. R. Collins, A. Grishin, A. J. Taylor, M. Law, G. Barissano, F Sehperband, D. Roberts

Thank you for your attention – any questions

Thanks to all collaborators of this project

Thanks to all participating cosmonauts, pilots and volunteers

Thanks to the Prodex funding program of the Belgian Science Policy

Lab for Equilibrium Investigations and Aerospace

Thomas Pesquet in the international space station