ESA crew member Andre Kuipers during his first orbital Neurospat session. Kuipers wears an Electroencephalogram (EEG) cap to investigate the effect of spaceflight on visual and spatial perception. NASA ID: iss030e022627.

Publication Highlights

Human Research

ISS research includes the study of risks to human health that are inherent in space exploration. Many research investigations address the mechanisms of these risks, such as the relationship to the microgravity and radiation environments as well as other aspects of living in space, including nutrition, sleep, and interpersonal relationships. Other investigations are designed to develop and test countermeasures to reduce these risks. Results from this body of research are critical to enabling missions to the lunar surface and future Mars exploration missions.

The CSA investigation Bone Marrow Adipose Reaction: Red Or White? (MARROW) assesses the effect of space environment, microgravity in particular, on bone marrow.

Reduced red blood cell (RBC) count, known as space anemia, was reported during the early days of spaceflight. Researchers initially thought that the decrease in RBC was a sudden adaptive response to the fluid shift changes experienced in space. However, recent reports have challenged these early views, showing increased concentration of cell elements in the blood through the entire duration of a flight and positive correlations between anemia severity, recovery time, and flight duration.

Using a new technology that combines breath and blood samples to precisely measure carbon monoxide as a direct indicator of hemoglobin degradation, researchers found increases in RBC destruction that persisted through the duration of the space mission.

Results were published in a recent study in *Nature Medicine*. Relative to preflight, elimination or expiration of carbon monoxide from the body increased by 54% in space. Destruction of RBCs sharply decreased upon astronauts' return to Earth. Moreover, researchers discovered that the hormone erythropoietin, which is involved in the stimulation of new red blood cells, was over-produced during spaceflight. Increased erythropoietin indicated the presence of anemia in astronauts during spaceflight and about 6 months postflight.

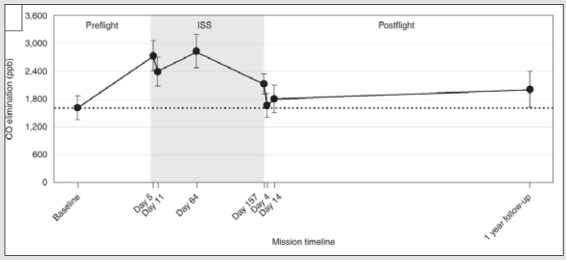

Figure 12. Exhalation of carbon monoxide increased during spaceflight and had not returned to baseline levels one year after spaceflight. Image adopted from Trudel, Nature Medicine.

These results demonstrate that early RBC count changes are not an adaptive response. Instead, it indicates that RBC degradation is a primary effect of being in space, and longer exposure to spaceflight worsens space anemia. Anemia is tightly linked to fatigue, dizziness, and an inability to stand upright or exercise; close monitoring of RBC destruction in space is necessary to ensure the health of astronauts and space tourists for safer space exploration.

Trudel G, Shahin N, Ramsay T, Laneuville O, Louati H. Hemolysis contributes to anemia during long-duration space flight. Nature Medicine. 2022 January 14; 1-4. DOI: 10.1038/s41591-021-01637-7.

Findings from various research studies tracking astronaut health in space are archived in our ISS medical monitoring investigation. This collection contains a wealth of knowledge regarding the effects of spaceflight on multiple body systems. In a collaboration between ESA and ROSCOSMOS, a new study classified as ISS

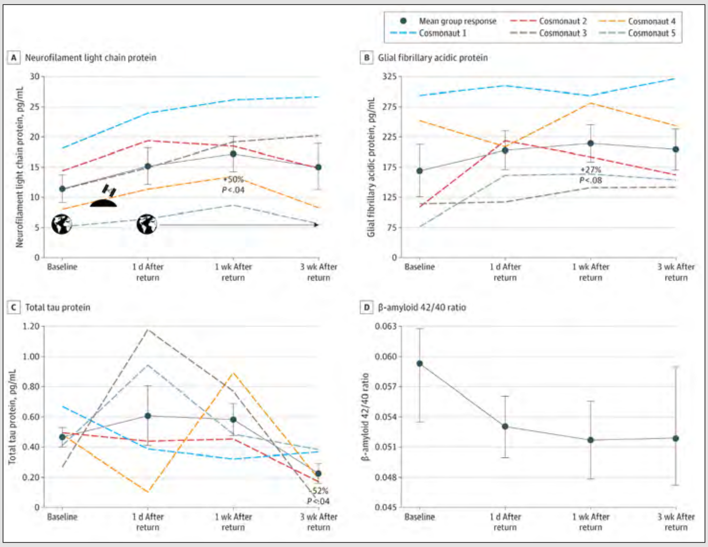

Figure 13. Line graphs of blood-based indicators assessed. Image adopted from zu Eulenburg, JAMA Neurology.

medical monitoring reported recent findings in the journal *JAMA Neurology*.

Despite the knowledge gained in the last decade regarding brain health after spaceflight (i.e., ventricular enlargement at the expense of gray and white matter), neuroscientists for the first time have conducted a full assessment of brain tissue integrity after cosmonauts' extended exposure to microgravity.

Blood-based indicators of brain health (i.e., neurofilament light chain, glial fibrillary acidic protein, tau protein, and two amyloid-ß proteins) were collected from cosmonauts before and after spaceflight.

Biochemical tests showed a significant increase in neurofilament light chain, tau, and amyloid-ß three weeks after flight, indicating axonal injury and increased astrocytic response. Furthermore, a ratio of the two amyloid-ß proteins showed a downward trajectory typically associated with poor brain health outcomes. Researchers hypothesize that the increased levels of amyloid proteins observed after spaceflight may represent an unresolved cleansing from months of accumulated proteins in space.

Further investigation of the subject is necessary to understand the relationship between spaceflight and brain health. A robust understanding of the effects of spaceflight on the human brain supports the safety of astronauts and mission success.

zu Eulenburg P, Buchheim J, Ashton NJ, Vassilieva G, Blennow K, et al. Changes in blood biomarkers of brain injury and degeneration following long-duration spaceflight. JAMA Neurology. 2021 October 11; 78(12): 1525-1527. DOI: [10.1001/jamaneurol.2021.3589](https://doi.org/10.1001/jamaneurol.2021.3589).

Findings from various research studies tracking astronaut health in space are archived in the [ISS medical monitoring](#) investigation. This collection contains a wealth of knowledge regarding the effects of spaceflight on multiple body systems. In a new study sponsored by ROSCOSMOS, researchers take advantage of the connections and influences that exist between the cardiovascular and nervous systems to understand spaceflight-induced changes in human physiology.

The autonomic nervous system (ANS), involved in the unconscious regulation of bodily functions, impacts the frequency of each heartbeat. When under stress or high alert, the sympathetic branch of the ANS signals the heart to beat faster. In a relaxed state, the parasympathetic branch of the ANS signals the heart to beat more slowly. In this study published in *Frontiers in Physiology*, researchers examined preflight-to-postflight concentration changes of 125 blood plasma proteins associated with heart beating frequency in cosmonauts grouped as sympathetic (i.e.,

Publication Highlights

Human Research

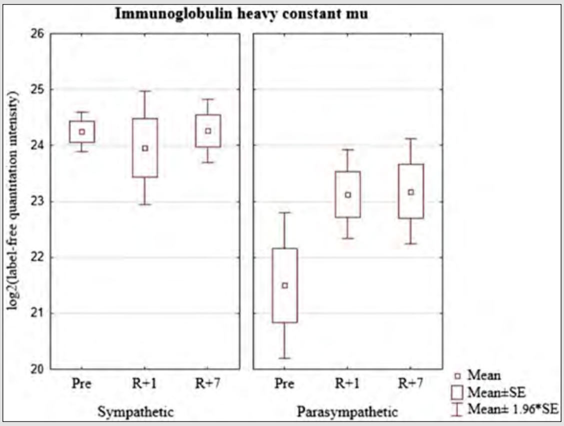

Figure 14. Differences in immunoglobulin heavy constant mu – a measure of autonomic regulation – between sympathetic and parasympathetic crew members before and after spaceflight. Image adopted from Pastushkova, Frontiers in Physiology.

stressed state) or a parasympathetic (i.e., calm state) based on an electrophysiological measure obtained before data analysis. Identification of each group's sympathetic and parasympathetic state prior to analysis was important to accurately reveal how spaceflight impacted the cardiovascular system of the cosmonauts. The proteins examined were indicators of cardiovascular regulation. Researchers used liquid chromatography along with mass spectrometry to examine the blood samples.

Results showed that while protein concentrations between the cosmonaut groups differed significantly before flight – making it easier to distinguish the groups at the beginning – such protein concentration differences dissipated after flight. The sympathetic group remained equally stressed postflight compared to preflight, while the parasympathetic group's stress levels increased postflight. The change in autonomic regulation in only the parasympathetic group made the groups indistinguishable after spaceflight. The dynamic changes in protein concentrations after flight suggested that the autonomic nervous system reacts to internal and external factors to ensure the adaptation of the human body in space.

Proteomic analyses such as these can help researchers identify new biomarkers to better understand the connection between the cardiovascular and nervous systems as well as their influence on readaptation and rehabilitation after spaceflight.

Pastushkova LK, Rusanov VB, Goncharova AG, Nosovsky AM, Luchitskaya ES, et al. Blood plasma proteins associated with heart rate variability in cosmonauts who have completed long-duration space missions. Frontiers in Physiology. 2021; 12: 2011. DOI: 10.3389/fphys.2021.760875.

The JAXA investigation The effect of long-term microgravity exposure on cardiac autonomic function by analyzing 48-hours electrocardiogram for 1YM (Biological Rhythms 48 hrs) monitors heart health in crew members during flight for a continuous 48 hours to understand the effect of spaceflight on human biological sleep/wake cycles.

Recent studies conducted in microgravity for extended periods of time (12 months) suggest that upon adaptation of the organism to space, an anti-aging benefit emerges. For example, changes in the gene expression of C-elegans and fruit fly *Drosophila Melanogaster*, as well as lengthened telomeres observed in the Twins Study suggest that spaceflight could extend the lifespan. Improvements in heart rate, sleep quality, and infraslow oscillations (ISOs) in the brain involved in unconscious processing – all signs of possible adaptation – have also been reported in long-duration spaceflight. In this study published in *Scientific Reports*, researchers were particularly interested in checking for signs of adaptation in the cardiovascular and nervous systems after a prolonged period of time in space.

Publication Highlights

Human Research

An astronaut's cardiac activity – which included various frequency bands, some indicating brain activity in the medial prefrontal cortex, posterior parietal cortex, or posterior cingulate cortex, respectively – was examined before, during, and after a 12-month mission. Use of additional data of geomagnetic changes collected over the last 200 years allowed researchers to explore a potential contribution of the Earth's magnetic field to human adaptation in space.

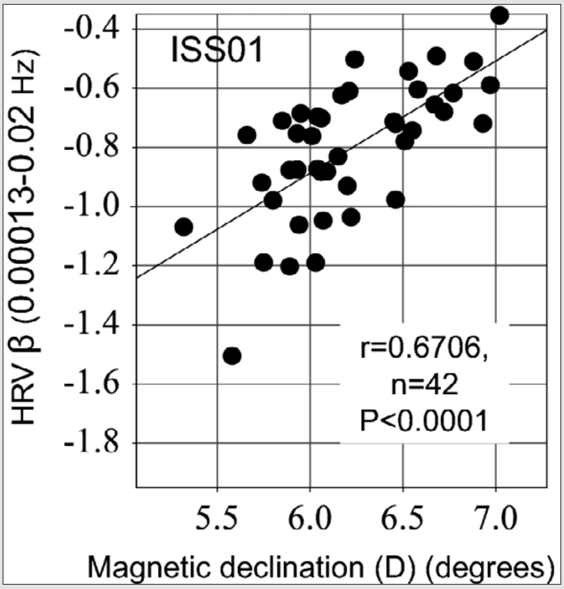

Figure 15. Relationship between Earth magnetic fluctuations and cardiovascular regulation. Results suggest that improved cardiac rhythms relate to magnetic changes in space. Image adopted from Otsuka, Scientific Reports.

Results showed that irregularity of the cardiovascular system improved 11 months later, during flight. Such improvement has not been observed in shorter missions. Researchers also noted that improvements in cardiovascular irregularities appear to be linked to increased ISOs in the brain. Moreover, geomagnetic fluctuations appear to have played a role in facilitating regulation of human systems. These results suggest that after a lengthy period of time in microgravity, joint adaptation of the cardiovascular and nervous systems takes place. These intriguing results shed light on the processes involved in neuro-cardiovascular coordination that potentially result in stable human adaptation during prolonged spaceflight.

Otsuka K, Cornelissen G, Furukawa S, Shibata K, Kubo Y, et al. Unconscious mind activates central cardiovascular network and promotes adaptation to microgravity possibly anti-aging during 1-year-long spaceflight. Scientific Reports. 2022 July 13; 12(1): 11862. DOI: 10.1038/s41598-022-14858-8.