Research Report
Institute of Aerospace Medicine 2023

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Preface

The Institute of Aerospace Medicine at the German Aerospace Center (DLR) comprises departments in Cologne and in Hamburg with an internationally unique research expertise and infrastructure. At DLR, our Institute serves as interface between sophisticated technology and life sciences research including biology, medicine, and psychology. We conduct our research in close collaboration with leading national and international research institutions and industry. The long-standing experience of the Institute in selecting and caring for pilots, air traffic controllers, and astronauts in particular directly after return to Earth provides a solid foundation guiding our research efforts. Mechanism-oriented human research, which is a particular strength of our Institute, is fostered by the state-of-the-art research infrastructure at the :envihab facility. Systematic ground-based studies in radiation, astro- and gravitational biology in dedicated simulation facilities are complemented by successful investigations in space. Our overarching goal is to conduct research that improves the human healthspan in space, in aeronautics, and on Earth. Knowledge and technologies generated at our Institute are transferred to applications that address important societal challenges and foster economic development.

We are proud to highlight some of our research activities in 2023, which addressed important medical, psychological, and biological issues with practical applications and transfer potential in space, in aeronautics, and in traffic. We investigated how new technologies such as single pilot operation, higher automation levels, and artificial intelligence affect operational safety and aerospace operator requirements, selection, training, and work. During the Artemis I mission to the Moon, our Institute conducted the Matroshka AstroRad Radiation Experiment (MARE). This collaboration with international agencies and industry is an important landmark in astronautical space exploration. In the MARE experiment, the anthropomorphic female phantoms Helga and Zohar were flown in crew seats onboard the Orion capsule around the Moon and back to Earth loaded with sophisticated radiation detector technology. Zohar was equipped with a novel radiation protection vest. We hope that the knowledge gained in this experiment will help to address medical risks associated with exposure to space radiation.

In 2023, we completed the NASA Spaceflight-Associated Neuro-Ocular Syndrome Countermeasures head-down bed rest study (SANS-CM) at :envihab. The study will guide development of preventive measures to maintain eye and brain health during long duration space travel.

Meanwhile, we further developed artificial intelligence-based methodologies that can be applied to monitor eye and brain health in future astronauts but also in patients on Earth. We assessed how insufficient sleep affects team performance, a highly relevant topic in space, in aeronautics, in traffic, and many other areas in which human performance is crucial to maintain safety.

We also investigated how new technologies such as single pilot operation, higher automation levels, and artificial intelligence affect operational safety and aerospace operator requirements, selection, training, and work.

Furthermore, we conducted a sophisticated study testing how nutrition affects the gut microbiome which in turn regulates inflammatory processes in the body. The study is an outstanding example how expertise and infrastructure for aerospace medicine can be applied to address important health challenges in people on Earth. The mid-term workshop of the DLR Graduate School GANDALF on Awareness and Fighting of Pandemic Threats in October 2023 showcased the progress of the doctoral students in their interdisciplinary projects aimed at improving microbial monitoring in public transport and risk assessment models and at developing countermeasures such as antimicrobial surfaces, air curtains and high-temperature air decontamination. GANDALF thereby develops solutions for mitigating effects of future pandemics on the transport sector. The Graduate School is led by our Institute and involves the DLR Institutes of Aerodynamics and Flow Technology, Vehicle Concepts, Software Technology, System Architectures in Aviation and Technical Physics.

Our biology program provided new insight in cellular responses to gravity changes and radiation exposure based on laboratory studies, experiments on various platforms including the drop tower in Bremen, DLR Mapheus sounding rockets and heavy ion accelerators. In 2023, the sounding rocket MAPHEUS-13 was successfully launched from the Esrange Space Center near Kiruna in Sweden. Within the seven minutes of microgravity exposure, experiments from life and material sciences were successfully performed, such as online measurements of the activities as well as inflight fixation dedicated for proteomic profiling of neuronal cells. Finally, we made great strides in applying bioregeneration technologies developed for space to dispose biological waste on Earth in a sustainable fashion.

We are very grateful for all the support from collaborators, funding agencies, and industry which made this research possible and look forward to tackle future challenges.

Jens Jordan, Head of the Institute of Aerospace Medicine, DLR

Ruth Hemmersbach, Acting Head of the Institute of Aerospace Medicine, DLR

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Cardiovascular Aerospace Medicine

Cardiovascular Aerospace Medicine

Prof. Dr. med. Jens Tank (Head)

Dr. rer. nat. Darius Gerlach (Deputy)

The Department for Cardiovascular Aerospace Medicine investigates gene-environmental influences on the human cardiovascular system. We focus on real and simulated weightlessness, atmosphere conditions, nutrition, and exercise. The major aim is to elucidate mechanisms of cardiovascular structural and functional adaptation and how these responses are integrated by the autonomic nervous system.
Human space experiments are flanked by highly controlled terrestrial studies in healthy persons and in patients in close collaboration with leading university medical faculties. Combination of physiological or pharmacological challenges with high-fidelity human phenotyping and biomedical engineering is our particular strength. Moreover, we translate observations in patients with rare cardiovascular conditions and defined genetic variants to astronauts confronting spaceflight and vice versa. The ultimate goal is to improve diagnostics, cardiovascular countermeasures, and treatments in space, in aeronautics, and on Earth.

Teams

Advanced Functional Imaging (Dr. rer. nat. Darius Gerlach)

- Probing the brain-heart axis with brain and cardiac imaging
- Functional MRI assessment of the brainstem and hypothalamus, the centers of autonomic control
- Autonomic nervous system testing within the MRI scanner, for the characterization of functional and neuroplastic adaptations to immobilization, diseases, and life style
- Cardiac real-time MRI under extreme environments, including hypoxic condition and immobilization for the detection of cardiovascular deconditioning
- Unique combinations of cardio vascular challenges such as lower body negative pressure during real-time MRI and physiological monitoring
- Individual phenotyping with dynamic functional cardiovascular real-time MRI

Cardiovascular Control in Health and Disease (PD Dr. med. Karsten Heusser)

- High fidelity cardiovascular phenotyping including direct measurements of muscle sympathetic nerve activity in healthy subjects and in patients with rare autonomic disorders as model for spaceflight conditions
- Inflight experiments (parabolic flights and ISS missions)
- Validation of certified non-invasive methods under extreme environment conditions
- Application and development of physiological and pharmacological methods and challenges, e.g. head-down tilt bed rest studies
- Determine the efficacy of drug therapy as well as nonmedical treatments including countermeasures and physical training
- Improving early detection of cardiovascular disease in space and in terrestrial medicine

Study subject during tilt-table testing
Microneurographic recordings of sympathetic nerve fiber activity in the peroneal nerve at the level of the knee. The therapy dog 'Olli' creates a relaxed atmosphere. The picture was taken during an experiment in the ProANS study.

Genetic ganglionic nicotinic acetylcholine receptor defect

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The inability to maintain blood pressure with standing or with other gravitational challenges is a medical issue in astronauts following spaceflight, in fighter pilots, and in patients on Earth. We were referred an 18-year-old woman with a number of symptoms such as pronounced orthostatic intolerance with inadequate reflex tachycardia, profoundly prolonged gastrointestinal transit, and impaired bladder emptying. In her history, she also had episodes of hypoglycemic coma. Magnetic resonance imaging showed a massively dilated colon. Her eyes could not adapt and accommodate adequately. Her skin was warm and dry. The clinical picture made us suspect a dysfunction of the ganglionic nicotinic acetylcholine receptors which transmit autonomic signals from spinal to peripheral neurons.

During the standing test without compression pants, blood pressure decreased markedly within 1 min and heart rate failed to increase. She had to sit down to prevent syncope (Fig. 1). With compression pants, she was able to stand for 10 min without symptoms. Further autonomic function testing revealed profound impairments consistent with severe autonomic failure. Direct recordings from several peroneal nerve fiber bundles innervating the lower leg showed normal activity except for efferent sympathetic traffic. Norepinephrine, the peripheral transmitter of sympathetic fibers was profoundly reduced in the supine and standing position. However, normal plasma concentrations of dihydroxyphenylglycol, which is largely formed from norepinephrine leaking from sympathetic nerve fibers showed normal plasma concentrations. Likewise, cardiac 123-I-mIBG uptake was normal (Fig. 2). The tracer is taken up by sympathetic nerve fibers. These findings corroborated our suggestion that sympathetic nerves are intact but fail to secrete norepinephrine. Residual function of the suspected receptor can be amplified by inhibiting the enzymatic degradation of acetylcholine. Yet, the acetylcholinesterase inhibitor pyridostigmine did not rescue autonomic functions but decreased blood pressure (Fig. 3).

Ganglionic nicotinic receptors are composed of five subunits. Pathogenic variants of the alpha-3 subunit have been identified in rare patients with autonomic failure and severe orthostatic hypotension. The subunit is encoded by the CHRNA3 gene. We performed trio whole exome sequencing and detected a paternally inherited frameshift variant and a maternally inherited deletion of exons 5 and 6 (Fig. 4).

Both variants were classified as pathogenic. This compound heterozygous variant has not been described before. The disorder results in a rare hereditary form of life-long autonomic failure by disconnecting peripheral autonomic nerves from central nervous input such that electrical signals required for neurotransmitter

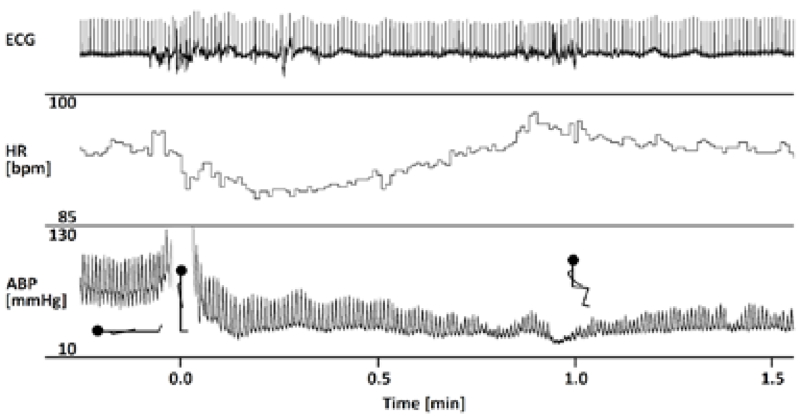

Fig. 1: Standing results in orthostatic hypotension and presyncopal symptoms within 1 min. ECG: Electrocardiogram; HR: Heart rate; ABP: Arterial blood pressure.

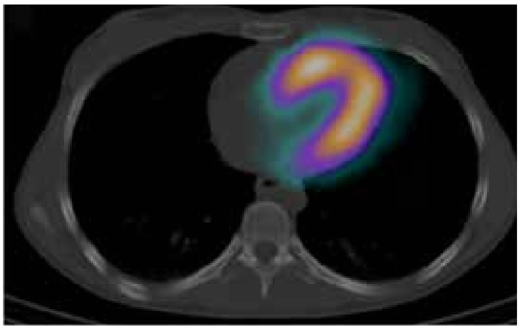

Fig. 2: The 123-I-mIBG scan reveals intact homogeneous sympathetic nerve fibers in the heart.

release are not produced. CHRNA3 gene mutations should be considered in patients with early-onset autonomic dysfunction.
Moreover, the study identified a molecular pathway that is indispensable for maintaining blood pressure in the face of gravitational challenges.

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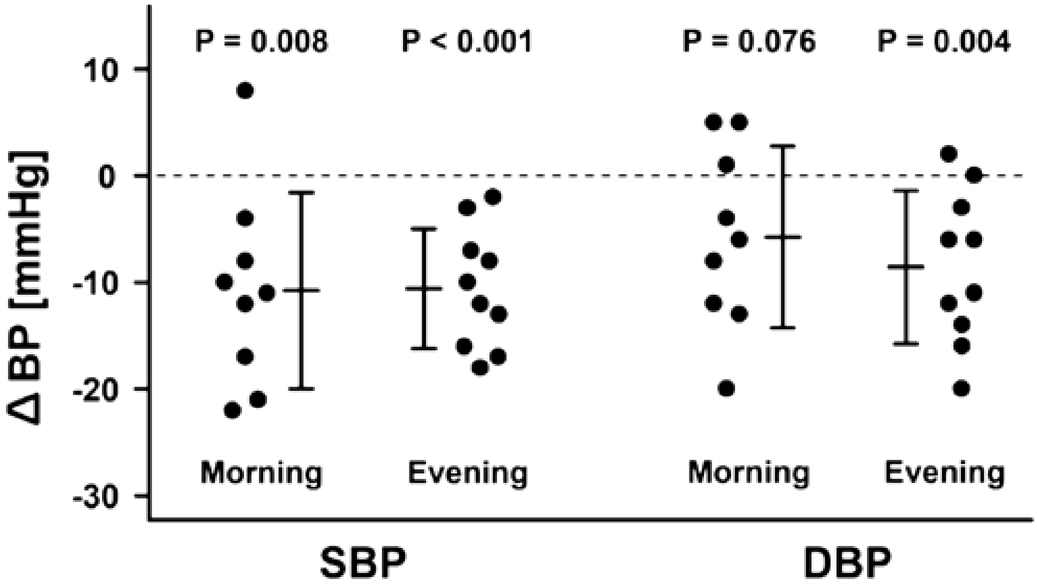

Fig. 3: Blood pressure (BP) reactions to single-blind pyridostigmine or placebo on 20 different days. The blood pressure lowering effect of pyridostigmine indicates a near-complete interruption of transmission in cardiovascular autonomic ganglia. SBP: Systolic blood pressure; DBP: Diastolic blood pressure.

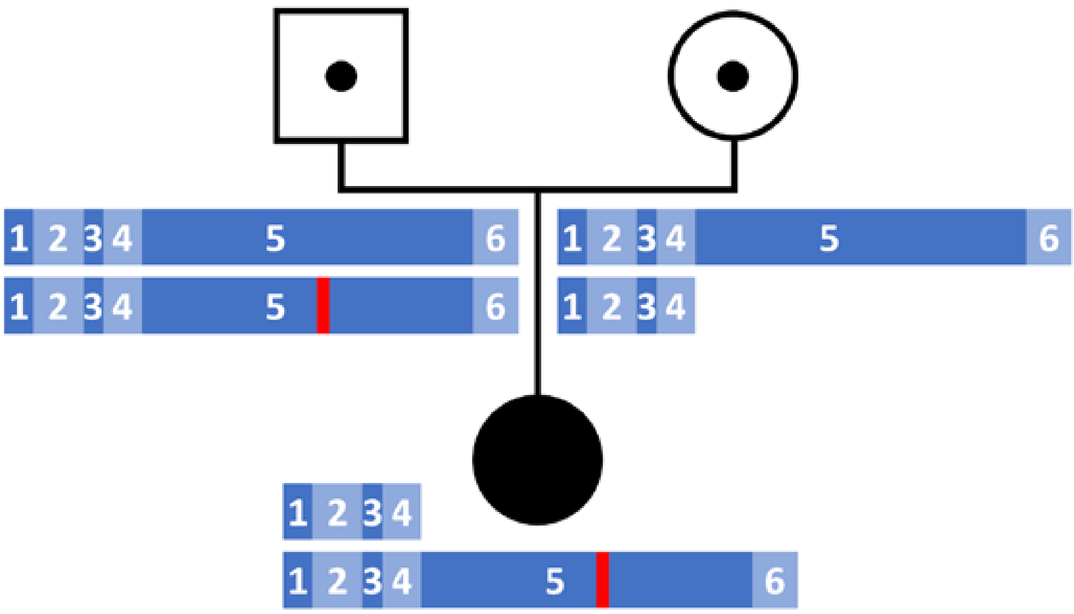

Fig. 4: Pedigree and cDNA representation of the CHRNA3 gene in the patient and both parents. Exons are shown in shades of blue. On the paternal allele, the position of the c.907_908delCT frameshift variant in exon 5 is marked in red. On the maternal allele, exons 5 and 6 are deleted.

The role of left ventricular contractility in orthostatic tolerance testing

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Introduction

Orthostatic intolerance represents a major medical risk in astronauts transitioning from space to Earth or another celestial body. Head-down tilt bedrest (HDTBR) mimics cardiovascular deconditioning in space. We hypothesized that daily six hours lower-body-negative-pressure (LBNP, -25 mmHg) or 60 minutes of cycling followed by 6 hours of venous thigh occlusion mitigates orthostatic intolerance, plasma volume loss, and reductions in left ventricular stroke volume during HDTBR.

Methods

We enrolled 47 healthy persons (20 women,27 men, 35±9 years, 23.7±2.6 kg/m2) to 30 days of strict HDTBR (SANS-CM study). Subjects were assigned to 6 hours upright seating (positive control, n=11), -25 mmHg LBNP (n=12) per day, 60min supine cycling followed by 6 hours of thigh cuff venous occlusion on 6 days per week (n=6), or no countermeasure (negative control, n=12). We measured orthostatic tolerance, and echocardiographic left ventricular stroke volume index in 80° head-up tilt testing (HUT) with incremental LBNP until presyncope before and after HDTBR. We determined plasma volume with carbon monoxide rebreathing two days before and at day 27 of bed rest.

Results

Time to presyncope did not differ at baseline between groups. Following HDTBR orthostatic tolerance decreased 289±89 s in the seat-

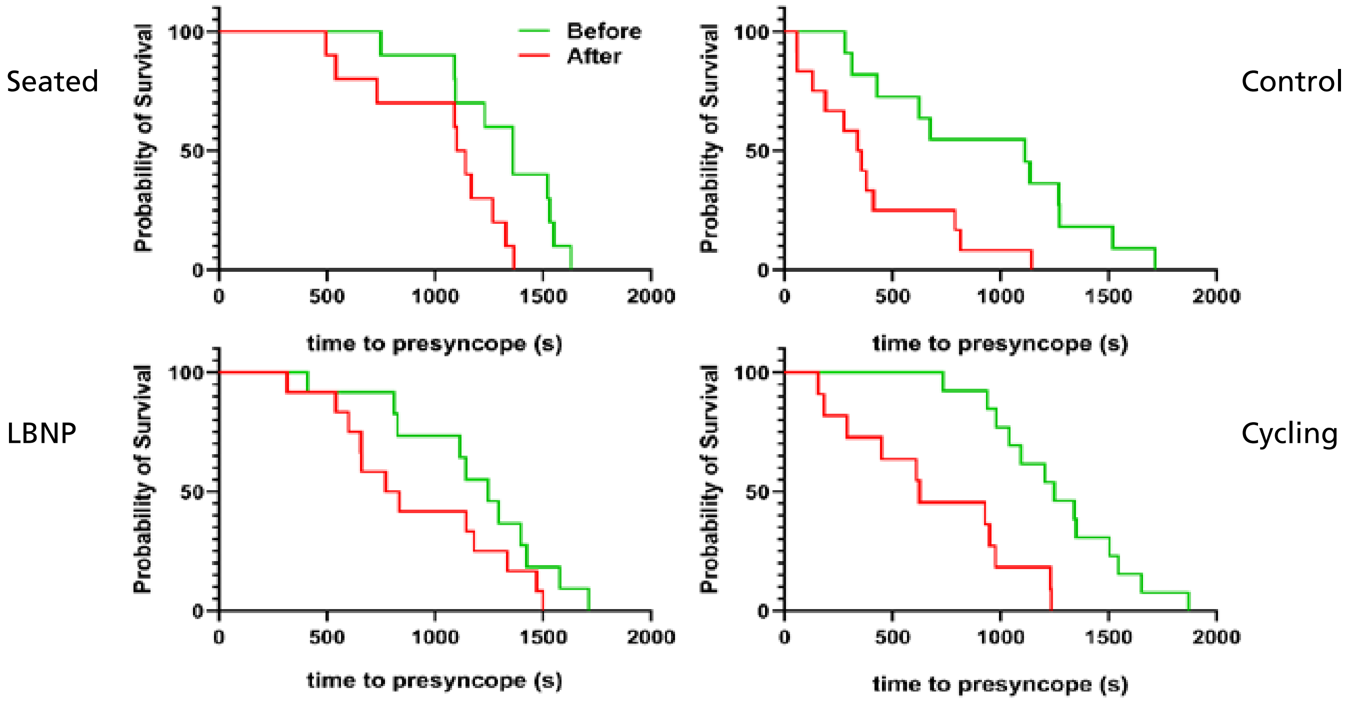

Fig. 1: Kaplan-Meier curves presenting a reduction of orthostatic intolerance, which was computed by the time to presyncope in tilt table testing, in all groups, except in the LBNP group.

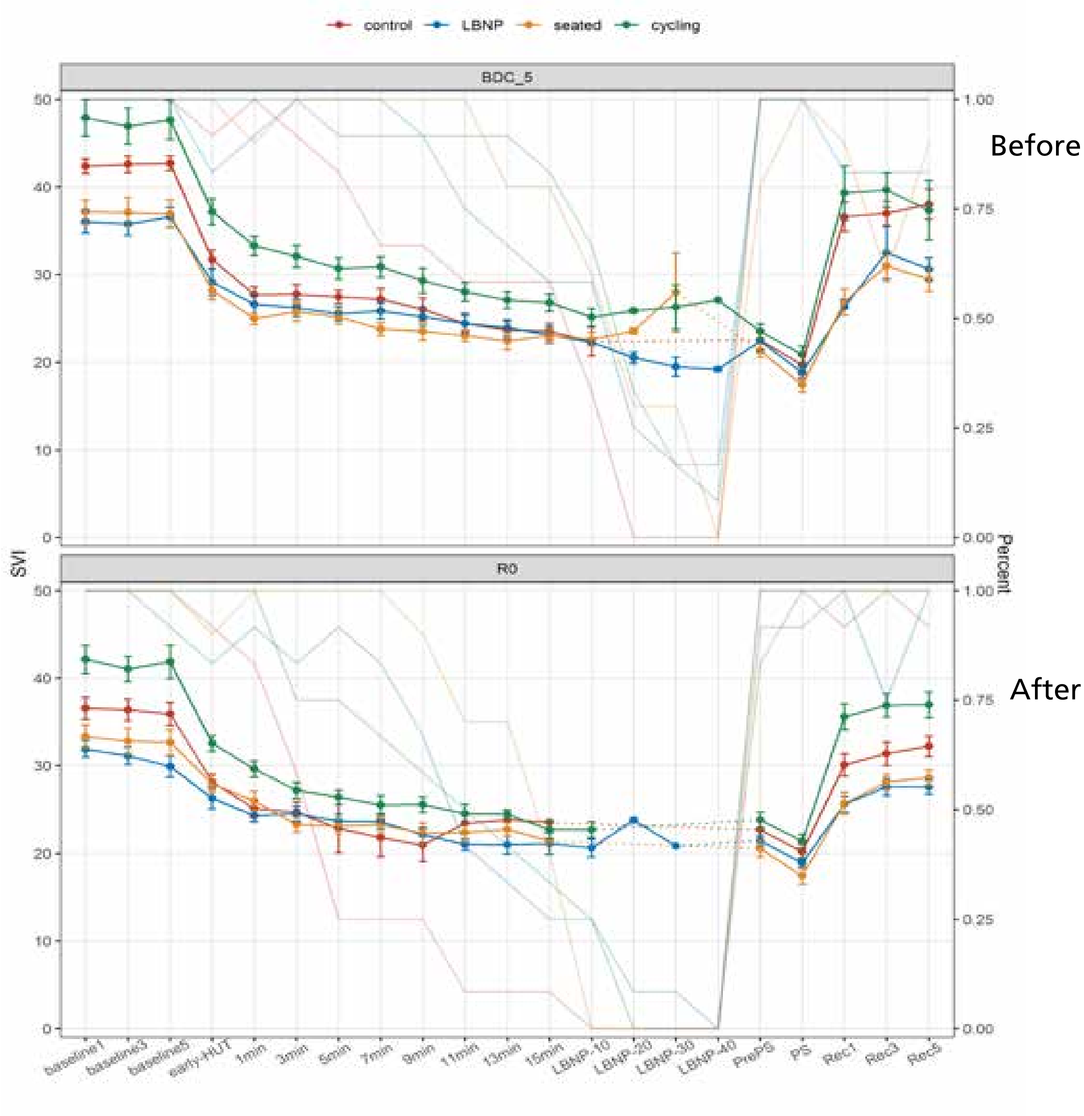

Fig. 2: Course of left ventricular stroke volume index (mean ± standard deviation) in all groups before at both times of tilt table testing in addition to relative values of orthostatic tolerance (semi-transparent lines). Bed rest led to a reduction in baseline stroke volume index and it also decreased in 80° head up tilt. However, at presyncope stroke volume index did not differ before and after bed rest.

ed, 284±95 s in the LBNP group, 539±235 s in cycling, and 540±457 s in the control group. Plasma volume decreased 569±212 ml in the seated and 604±407 ml in the LBNP group, 147±95 ml in cycling, and 286±153 ml in control group. Left ventricular stroke volume index was reduced in all groups following bed rest, but did not differ at presyncope before and after bed rest (p=0.4930).

Conclusions and perspectives

Our study suggests that six hours LBNP per day attenuate reductions in orthostatic tolerance during HDTBR while daily endurance exercise followed by venous occlusion appears to be less effective. Remarkably, there is a dissociation between efficacy in maintaining orthostatic tolerance and plasma volume between interventions. In addition, we observed no beneficial effect of the countermeasures on stroke volume following bed rest. However, stroke volume appears to contribute to the induction of presyncope.

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Impact of 30-day head-down-tilt bed rest on endothelial function

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Introduction

Head down tilt bed rest and space flight lead to cardiovascular deconditioning and impact systemic inflammation, which could worsen endothelial function. The mechanism may predispose to cardiovascular disease, both, in astronauts and in persons on Earth. Flow mediated dilatation (FMD) is an established approach to measure endothelial function in human beings. Therefore, we determined how 30 days head-down tilt bed rest affect FMD and proand anti-inflammatory cytokines.

Methods

In the SANS-CM study, we submitted 47 healthy persons (20 women,27 men, 35±9 years, 23.7±2.6 kg/m2) to 30 days of strict HDTBR. They were assigned to to 6 hours upright seating (positive control, n=11), -25 mmHg LBNP (n=12) per day, 60min supine cycling followed by 6 hours of thigh cuff venous occlusion on 6 days per week (n=6), or no countermeasure (negative control, n=12). We measured FMD 5 days before and after 28 days of bed rest. To account for possible confounders, we performed all measurements in a specific time slot (10am to 15 pm) and implemented a fasting period of 2 hours before measurements. We measured FMD on the brachial artery in a room with dimmed lighting and an initial resting phase of 15 minutes. We selected an occlusion pressure of 200 mmHg over a period of 5 minutes, which represented a difference of more than 50 mmHg to the systolic blood pressure. The selection of annotated episodes of FMD was in accordance on the current recommendations of the European Society of Cardiology. We collected venous blood samples for measurement of proand antiinflammatory cytokines (Essay: Simoa®)14 days before, day 28 day of bed rest and at day 13 of recovery.

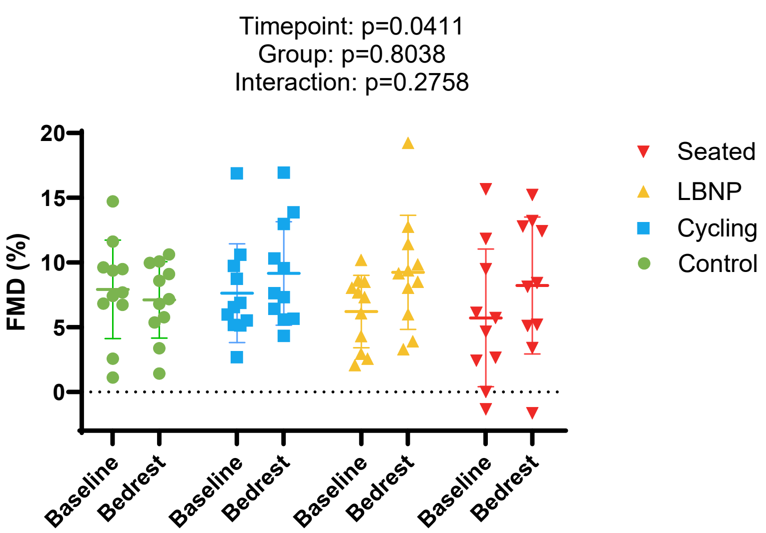

Fig. 1: We measured flow mediated dilatation (FMD) based on current recommendations of the European Society of Cardiology. Six hours of daily lower body negative pressure (-25%; LBNP) and 1 hour of cycling followed by 6 hours of thigh cuff inflation revealed no affection of the FMD in contrast to negative control and positive control (six hours upright seated per day).

Results

FMD increased in the countermeasure groups but not in the control group (seated baseline: 5.7±5.3%; after bedrest: 8.2±5.3%; LBNP: 6.2±2.8% and 9.2±4.4%; cycling: 7.6±3.8% and 9.2±4%; control 7.9±3.8% and 7.1±2.9%; timepoint: p=0.0411; group: p=0.8038, interaction: p=0.2758). Several cytokines revealed different concentrations at baseline or presented an increase through bed rest, but there was no evidence for a clinically relevant inflammatory response. Examples for proand anti-inflammatory responses including p-values are provided in figure 2.

Conclusions and perspectives

We did not observe worsened FMD following 30 days strict head-down tilt bedrest. In fact, FMD increased in the countermeasure groups.

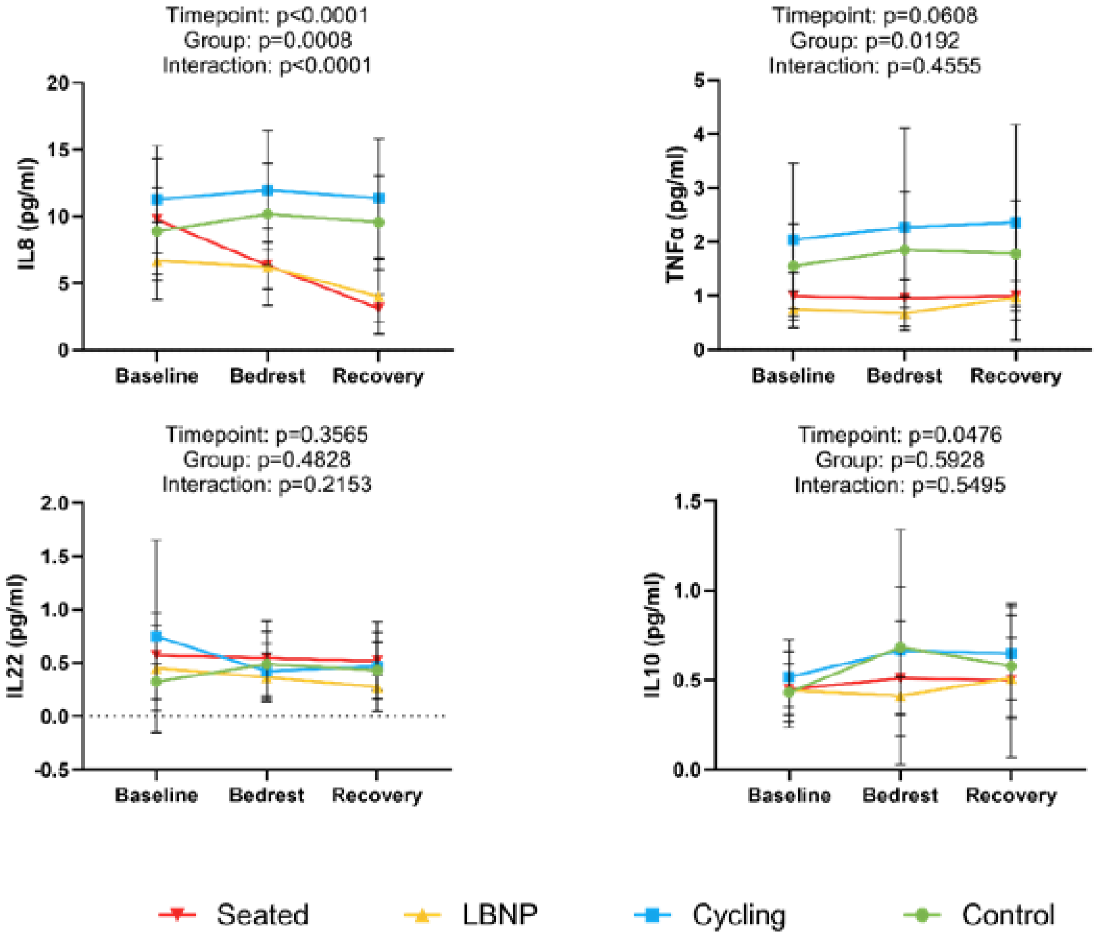

Fig. 2: Figure 2: Presentation of central cytokine levels at the first study day, after 28 days bed rest, and day 13 of recovery. We observed a reduction of interleukin 6 (IL6) in bed rest and recovery, which is considered as a central parameter of vascular inflammation. Same was observed while bed rest in LBNP group. Tumor necrosis factor-α (TNFα), a further prominent marker of vascular inflammation, was not affected by bed rest, but values where higher in LBNP than control while baseline and bed rest. Interleukin 22 (IL22) is a key contributor to adhesion of immune cells to the endothelium and remained stable over the whole study phase. In addition, interleukin 10 (IL10) increased in all groups and harbors a crucial role in anti-inflammatory regulation in blood vessels.

Yet, there were no significant group differences. Bed rest did not induce a relevant inflammatory response despite some changes in cytokine plasma levels. In upcoming analyses, the influence of plasma volume, catecholamine release and orthostatic tolerance will be correlated with changes in FMD. The FMD data from day 13 of the recovery phase will also be analyzed. Nevertheless, the current analyses already provide insight into the vascular adaptations to bed rest. The fact that endothelial function did not worsen is encouraging.

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AI-based analysis of real-time MRI in univentricular hearts

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Background

The special nature of the Fontan circulation is that, the univentricular heart performs the function of the left ventricle with a direct connection of the veins with the pulmonary arteries. The Fontan procedure is performed in children born with congenital heart conditions such as hypoplastic left heart syndrome, tricuspid atresia, and double outlet right ventricle. Evaluating the Fontan circulation using using currently available methods is difficult. Patients with this condition have limited breathholding capacity, especially when exposed to low oxygen levels. Cardiac real-time MRI, which enables rapid image acquisition during breathing, provides a novel approach to gaining a deeper understanding of the hemodynamics and the unique cardiac anatomy in these cases. Univentricular hearts can present a wide range of appearances, making it challenging for conventional tools to accurately assess clinical parameters related to heart function in patients with this special heart anatomy. Moreover, this challenge is exacerbated by the dynamic changes in heart shape throughout the cardiac cycle and influences of respiratory movements. Therefore, our goal is to train an artificial intelligence network using pre-segmented images to address this complex task.

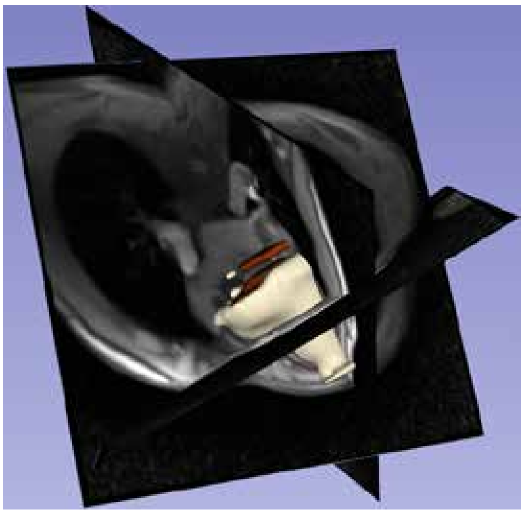

Fig. 1a: This image shows a univentricular heart with a hypoplastic right heart. The heart was scanned with cardiac real-time MRI in short axis direction (transverse to the longitudinal axis) during spontaneous breathing. The cardiac short axis slices were segmented with artificial intelligence sorted automatically for their cardiac and respiratory phase to create and 3D stack representing end-diastolic and end-expiratory phase. The cross-sections in the image are shown in figure 1b.

Material and Method

We recruited 18 patients with Fontan circulation (9 females) (24.8±6.3 years; 23.0±3.6 kg/m^2) and performed real-time cardiac MRI in normoxia and in normobaric hypoxia (24 hours of 15.1 % O_2). We acquired conventional cine MRI (25 phases) during normoxia and real-time cardiac MRI (temporal resolution of 33 ms over 10 seconds) in the short axis during both, normoxia and hypoxia.

We used expert annotations of cardiac short axis images of the univentricular hearts to teach the U-net [1] based AI for segmentation. We defined a sorting algorithm to solve the problem that slices are acquired one after the other and thus, heart phases and respiration phases need to be aligned.

Results

Cine cardiac short axis from 54 patients were segmented by experts which are in total are 1095 images. In addition, real-time acquisition of 8 patients (580 images) were initially segmented by the AI and corrected by experts. The cine and the corrected real-time cardiac short axis images were used for training the U-net. Based on the segmented real-time images (Figure 1) we developed an algorithm for the automatic detection of systole, diastole, inspiration and exspiration and sorting the images according the heart and respiratory phase in a 3D volume (Figure 2). The automatic detection was compared with

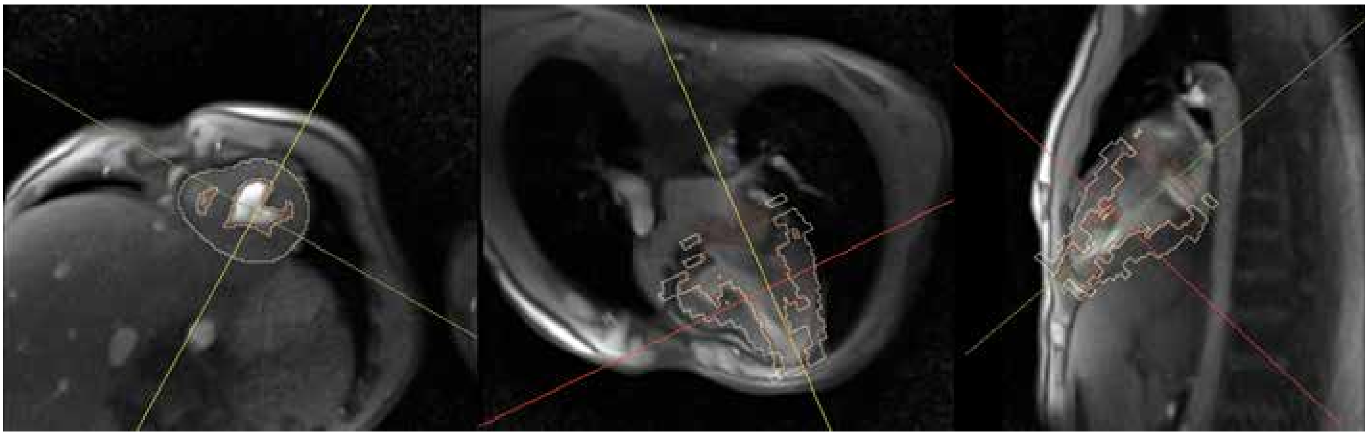

Fig. 1b: The left image depicts the acquired short-axis image with segmentation of blood pool (red outline) and myocard (yellow outline). The middle and right images are reconstructed clinically relevant views, which represent the long axis view.

the corresponding time points in the physiological recordings. During U-net training, the data set was split into 1340 training data and 335 validation data. The latter was then used to test the performance of the network in each training iteration. Our so-called dice score at the end of the training is on average 0.84 on the validation data. State-of-the-art for large standard data sets such as ACDC (i.e. healthy heart MRIs) are dice scores of 0.9. The Fontan hearts are comparatively highly complex in their anatomy, require significantly more detailed labels and have a higher variance among the patients. For medical validation, we retained a third of the patients as pure test data, which the network has never seen.

Conclusion

The goal of the joint artificial intelligence project is to automatically segment these challenging hearts and reconstruct the hearts in 3D models from a series of 2D real-time MRI acquisitions, allowing straightforward computation of all necessary parameters. This comes with the advantage that clinical parameters can be estimated in a robust way independently of human examiners. In particular, the approach offers insight during different breathing periods, which are not captured by conventional means. In the Fontan circulation, breathing augments preload and pulmonary blood flow, however, the detailed mechanism is not understood. Future studies will use cardiac real-time MRI to assess diastolic filling and cardiovascular testing which potentially enhances diagnostics other than CINE breath hold cardiac MRI.

References

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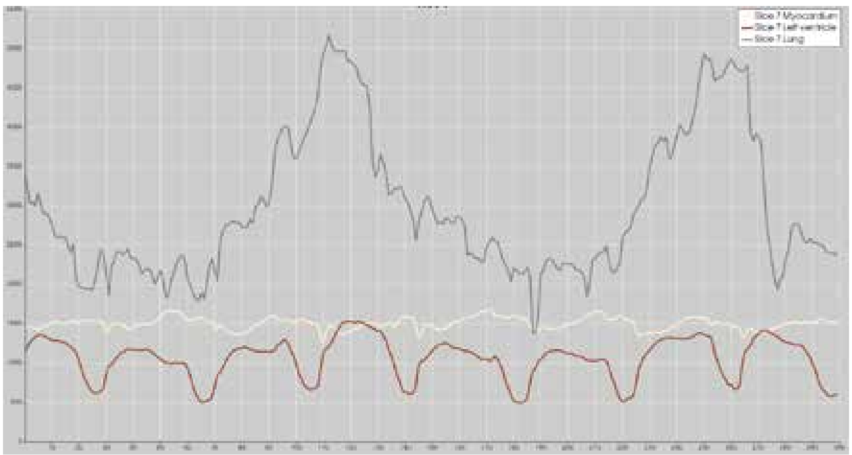


Fig. 2: This image illustrates the sorting algorithm. The AI segments the blood pool (red), the myocardium (yellow) and the lung (gray) in all short axis images. The number of pixels in the respective image is plotted over time (x-axis). The maximum of the blood pool represents the end of diastole and the minimum the end of systole. In addition, the maximum of the lung voxel gives us the information when the end-inspiration is and the minimum the end-expiration. Now you can search for the minimum distance between systole and end expiration, for example, in order to sort all images in this phase. This is necessary because the recordings are made layer by layer over several breathing cycles and are staggered in time. This allows us to determine the clinically relevant time points: end-systole and end-expiration, end-diastole and end-expiration and, in addition, during the inspiration phase.

Sleep and Human Factors Research

Sleep and Human Factors Research

Prof. Dr. sc. nat. Daniel Aeschbach (Head)

PD Dr. med. Eva-Maria Elmenhorst (Deputy)

Our mission is to maintain optimal human performance, sleep, and wellbeing for operators working under the specific challenges and risks of a mobile 24-hour society. Shift work is highly prevalent in operators working in the field of aeronautics, space, and transport exposing a large number of persons to its negative short-term (cognitive decline) and long-term (health) consequences. We apply our highly advanced and controlled laboratory environment to systematically study how homeostatic and circadian processes regulate cognitive performance as well as the quality, duration, and timing of sleep and how they are impacted by disturbances like acute and chronic sleep loss or circadian misalignment. In a unique combination of molecular neuroimaging and behavioral research, we strive to uncover mechanistic pathways that help us understand why some individuals show stronger cognitive decline and negative health consequences due to sleep loss than others.

Our society's need for mobility is in conflict with local residents' need for undisturbed recreation and sleep. In order to ease this conflict, we investigate how sleep, cognitive performance, and annoyance are affected by air, rail, and road traffic noise, and share protection concepts with stakeholders. Aircrews and astronauts work and sleep under conditions of hypobaric hypoxia or hypercapnia. Thus, we have a specific interest in studying systematically in the lab or inflight how barometric and atmospheric alterations affect performance, sleep and well-being. Digital health expertise provides medical support for patients and research through remote applications.

Working Group

Performance and Sleep (PD Dr. med. Eva-Maria Elmenhorst)

- Effects of sleep loss, irregular timing of sleep, adverse work hours, and workload
- Effectiveness of flight time limitations
- Effect of environmental conditions (e.g. hypoxia)
- Neuromolecular mechanisms conveying individual (trait) vulnerabilities
- Developing individualized countermeasures

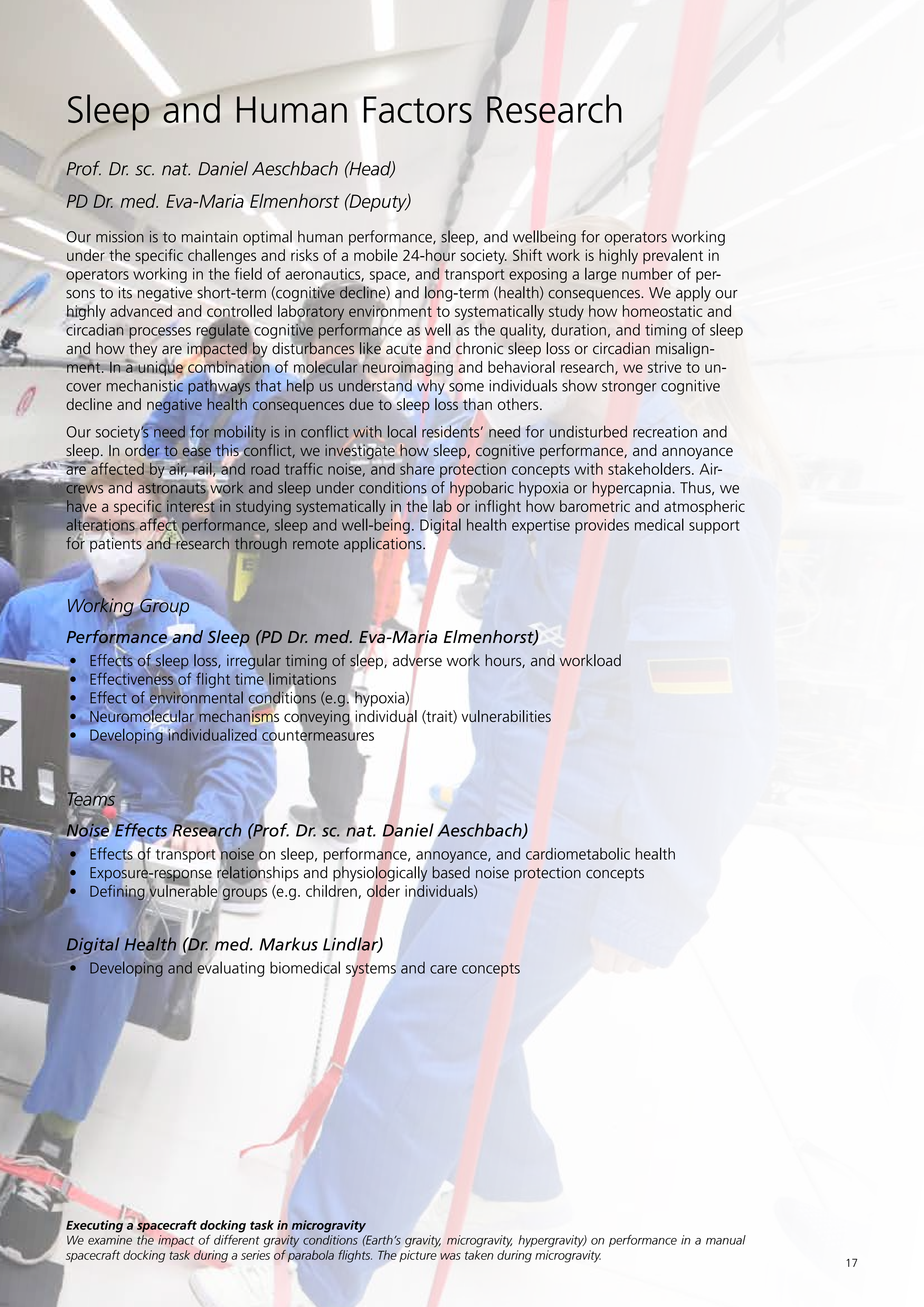
Teams

Noise Effects Research (Prof. Dr. sc. nat. Daniel Aeschbach)

- Effects of transport noise on sleep, performance, annoyance, and cardiometabolic health
- Exposure-response relationships and physiologically based noise protection concepts
- Defining vulnerable groups (e.g. children, older individuals)

Digital Health (Dr. med. Markus Lindlar)

- Developing and evaluating biomedical systems and care concepts



Executing a spacecraft docking task in microgravity
We examine the impact of different gravity conditions (Earth's gravity, microgravity, hypergravity) on performance in a manual spacecraft docking task during a series of parabola flights. The picture was taken during microgravity.

Effect of nocturnal low-sonic boom noise of future civil supersonic aircraft on annoyance

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Traffic noise-induced disturbance of nighttime sleep over a longer time and the associated secondary effects such as annoyance are considered as effect modifiers of the relationship between noise and health risks [1]. Currently, the National Aeronautics and Space Administration (NASA) as well as commercial companies are pursuing the goal of relaunching civil supersonic aircraft. New aircraft designs (low-boom design) and flight procedures (Mach cut-off) are being developed to minimize the intensity of the sonic boom perceived on the ground and thereby to reduce the noise impact (Figure 1). Findings from the literature on noise effects of conventional civil and military supersonic aircraft are applicable only to a limited extent. Therefore, research on the effects of these new types of sonic booms on sleep as well as on physiological and psychological reactions is needed.

A double-blind laboratory study was carried out on behalf of the German Environment Agency (Umweltbundesamt – UBA), in which 42 healthy participants (mean age 36 ± 12.5 SD, 21 women) spent three consecutive nights in the sleep laboratory (M5, :envihab). The first night served as a quiet control night (*quiet condition*). During each of the following two randomized nights, 40 low-sonic boom events based on simulations of a demonstrator for future civil low-boom aircraft (*low-boom condition*) and using the Mach cut-off flight procedure (*Mach cut-off condition*) were played back as they would be expected to sound on the ground inside a building. Ratings of the short-term annoyance caused by nocturnal noise events were collected on the following morning via questionnaires (ICBEN scale from 0 = "not at all" to 10 = "extremely"). In addition, non-acoustical factors (e.g. individual's attitudes, personality traits) potentially influencing the annoyance judgments were captured.

Fig. 1: Supersonic aircraft planned by Boom Supersonic.

Analyses revealed that the highest annoyance resulted from the low-boom condition, followed by the Mach cut-off condition and the quiet condition with the lowest annoyance (Figure 2).

Annoyance after the night with *low-boom condition* was significantly higher compared to both the *quiet condition* (MD = 3.93, 95% CI (5.09, 2.77)) and the *Mach cut-off condition* (MD = 3.62, 95% CI (2.51, 4.73)) (both $p < .001$, post-hoc t-tests, Bonferroni corrected). Analyses with mixed linear models showed the best model fit (in terms of the Akaike Information Criterion, AIC) when self-assessed sleep quality, control and coping capacity as well as the ability to adapt to noise were included. These variables were added to the prediction model by a stepwise forward selection process as non-acoustical predictors in addition to the noise condition (Table 1). Low subjective sleep quality correlated with higher levels of annoyance. A low self-rated general ability to cope with noise and to adapt to it was associated with higher levels of annoyance.

The present results provide a first estimate of the prospective impact that nocturnal sonic booms from a future civil supersonic aircraft might have on short-term annoyance. According to a general rule by which annoyance values can be transferred into the categories "highly annoyed", "annoyed" and "(at least)

Factor	Estimate (SE)	p-value	AIC after inclusion
Intercept	6.864 (1.131)	< 0.001	
Condition			554
quiet	Reference		
low-boom	4.117 (0.424)	< 0.001*	
Mach cut-off	0.806 (0.452)	0.078	
Subjective sleep quality in the previous night	-0.052 (0.0178)	0.004*	550
Control and coping capacity	-0.115 (0.046)	0.016*	543
General adaptation capacity to noise	-0.640 (0,313)	0.048*	539

*Tab. 1: Mixed linear model with regard to the effect of acoustical and non-acoustical predictors on short-term annoyance. * = significant difference, SE = standard error.*

a little annoyed", a value of ~5 caused by the low-boom aircraft can be classified as at least a little annoying [2]. Whereas, the Mach cut-off flight procedure resulting in an annoyance value of ~1 can be classified as not annoying. Therefore, applying the noise-reducing Mach cut-off flight procedure during a flight over land with a low-boom-aircraft may reduce annoyance reactions. In addition, the importance of non-acoustical predictors on the annoyance judgment is highlighted for these new types of sonic booms. In the present study, subjective sleep quality, self-assessed ability to cope with noise and adapt to noise were found to be relevant for short-term annoyance. These results are consistent with findings from studies on other conventional traffic noise sources [3, 4, 5].

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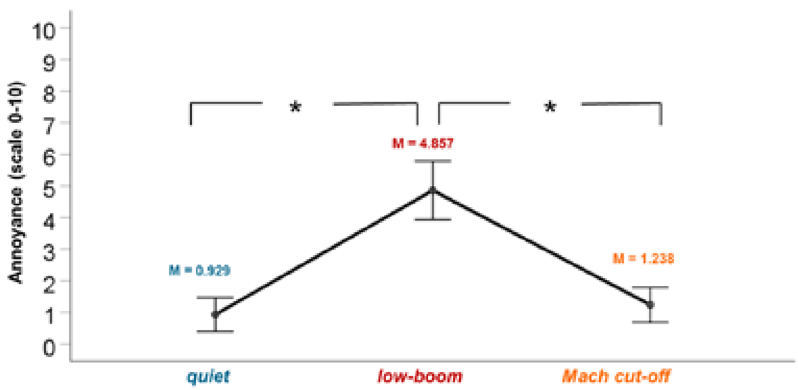

*Fig. 2: Effect of noise conditions on short-term annoyance. The error bars represent the 95% confidence interval, * = significant difference.*

The effects of different gravity conditions on manual spacecraft control performance: a parabolic flight study

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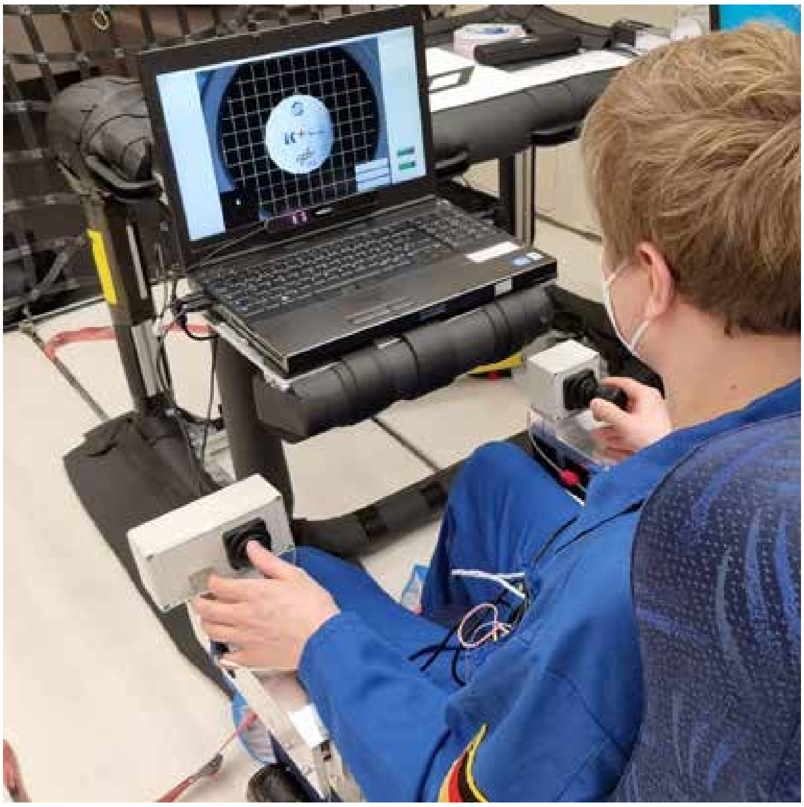

Fig. 1: Experimental setup of the 6df simulation in the aircraft.

Background

Microgravity can affect cognitive performance, spatial orientation, and the precision of previously trained motor responses which are based on force vectors and vestibular signals in normal gravity (Carriot et al., 2021; De la Torre, 2014; Strangman, Sipes, & Beven, 2014). Additionally, it is hard to determine whether reported performance decrements originate in microgravity or in unspecific stress factors associated with space flight (Arshad and Ferré, 2023). Experimental evidence on the influence of microgravity on complex operational tasks comprising motor and cognitive demands is especially scarce, although performance in tasks such as robotic or vehicle control might be particularly vulnerable to the extreme conditions in space (Seidler & Mulavara, 2021). Therefore, we investigated the influence of varying gravitational levels during parabolic flights on performance in the simulated manual control of a spacecraft, a safety-relevant operational task.

Methods

During parabolic flights, 27 trained participants (8 women and 19 men, 18-61 years old, 9 previously exposed to a parabolic flight) performed 15 manual control tasks of varying difficulty based on the docking simulation *6df* (Fig. 1). Within this simulation, a spacecraft had to be aligned continuously with a rotating space station in a fixed distance by controlling six degrees of freedom with manual levers. Each task encompassed 80 seconds centered around either the incoming or outgoing hypergravity segment of a parabola and thus included to equal parts a 0 g, 1 g, and 1.8 g phase (Fig. 2). Average deviations from the perfect distance and alignment with the station were z-transformed and aggregated into an overall manual control deviation score. We compared manual control deviation between phases of microgravity, hypergravity, and normogravity during the parabolic flight by using a linear mixed effects model and subsequent pairwise contrasts of estimated marginal means. Additionally, we assessed the effects of task difficulty (rotation of the target station along one, two, or three axes) and previous exposure to parabolic flights on *6df* performance.

Results

We observed a significant main effect of gravitational phase on manual control deviation (Fig. 3; $p < .001$): performance was worse in microgravity compared to 1 g ($p < .001$) and 1.8 g ($p < .001$), whereas there was no differ-

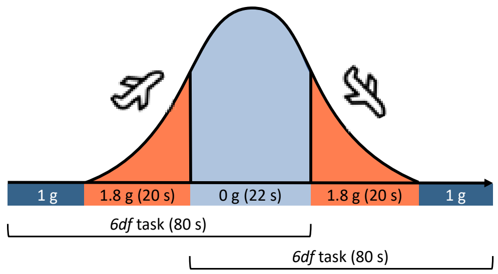

Fig. 2: Gravitational phases during parabolic flights. 6df tasks lasted 80 seconds per parabola and comprised one 1 g, 1.8 g, and 0 g phase in counterbalanced order.

ence between 1 g and 1.8 g ($p = .95$). Manual control deviation increased with increasing task difficulty ($p < .001$), but there was no interaction of task difficulty with gravitational phase ($p = .28$). Prior experience with parabolic flights had no influence on manual control performance ($p = .43$), regardless of the gravitational phase ($p = .51$).

Discussion

Microgravity had detrimental effects on manual control accuracy of six degrees of freedom that appear to be unrelated to unspecific stress effects. The increase of manual control deviation in microgravity, but not during hypergravity, suggests a higher relevance of impaired spatial orientation due to confounding vestibular signals compared to the mere change in force vectors. Even during easier tasks, participants were not able to compensate for the effects of microgravity. The results were independent of prior parabolic flight exposure, indicating that novelty or increased stress are unlikely sources of impairment. As a consequence, impairments in spatial perception due to microgravity should be considered in the development of effective training interventions for complex manual tasks in human space flight.

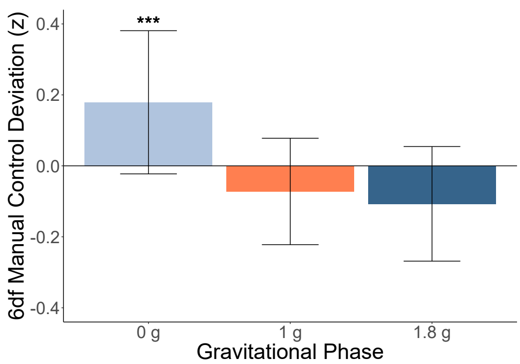

Fig. 3: Bar plot showing the average z-transformed manual control deviation from optimal alignment with the target station during the gravitational phases of the parabolic flight. Positive values indicate larger deviations, negative values smaller deviations than the sample average. Whiskers are representative of the standard error.

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Effects of chronic sleep restriction and repeated caffeine intake on A_1 adenosine receptor availability in the human brain

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The neuromodulator adenosine decreases cerebral neuronal activity and promotes sleep via binding at adenosine receptors. Adenosine levels and A_1 adenosine receptor (A_1AR) availability in the brain have been shown to increase with elapsed wake duration reflecting the rising sleep pressure during total sleep deprivation (Porkka-Heiskanen et al. 2000, Elmenhorst et al. 2007, Elmenhorst et al. 2017). Caffeine unfolds its wakefulness promoting effect via blocking A_1AR, thus preventing adenosine from binding at its receptor (Elmenhorst et al. 2012). To date it is unclear, 1) whether chronic sleep restriction and total sleep deprivation induce similar responses – i.e., increases in A_1AR availability, and 2) whether repeated daily caffeine intake under conditions of sleep restriction induces lasting alterations in A_1AR availability.

To investigate these questions we examined 71 healthy volunteers aged 20 to 40 years in the Sleep and Simulation Lab of the DLR :envihab. Participants were randomly (but stratified by age, sex, and BMI) assigned to one of four groups. All groups had one adaptation and two baseline nights with 8 h time in bed (TIB) with following adaptation and baseline days (B1, B2). Sequentially, 5 experimental nights and days (E1-E5) were scheduled and one final recovery night with 8 h TIB and one recovery day (Rec). (1) The rested control group (n=15, 5 female, mean age ± SD 28 ± 6 years) was not sleep restricted and continued with 8h TIB during nights prior to E1 through E5. (2) The restriction group (n=21, 9 female 26 ± 4 years) was scheduled to 5 h TIB during nights prior to E1 through E5. (3) The caffeine group (n=19, 8 female, 30 ± 5 years) followed the same sleep schedule as the restriction group, but received standardized 600 ml coffee per day (in total ~300 mg caffeine: morning dose 200 mg, early afternoon dose 100 mg) double-blind on E1 through E4 and 400 ml coffee (~200 mg caffeine, morning dose only) on E5. (4) The decaffeinated coffee group (n=16, 7 female, decaff, 28 ± 5 years) underwent the same schedule as the caffeine group, but consumed decaffeinated coffee. We chose a naturalistic caffeine administration of brewed coffee consumed twice a day – in the morning and in the early afternoon. Participants of the caffeine (76% C/C) and decaff (88% C/C) groups predominantly carried the caffeine-sensitive genotype of the A_{2A} adenosine receptor (ADORA2A c.1976). We measured A_1AR availability with 18F CPFPX positron emission tomography in the control group and sleep restriction group on E5 and Rec, and in the caffeine group and the decaff group on B2 and Rec. Ten brain regions were located and analysed.

In all examined brain regions, A_1AR availability did differ neither between the control and the sleep restriction group on E5 and Rec, nor within each of these groups when comparing E5 with Rec (all $p>0.35$; Figure 1, 2). In all examined brain regions, A_1AR availability did also differ neither between the decaff and the caffeine group on B2 and Rec, nor within each of these groups when comparing B2 with Rec (all $p>0.7$; Figure 2).

Five nights with chronic sleep restriction did

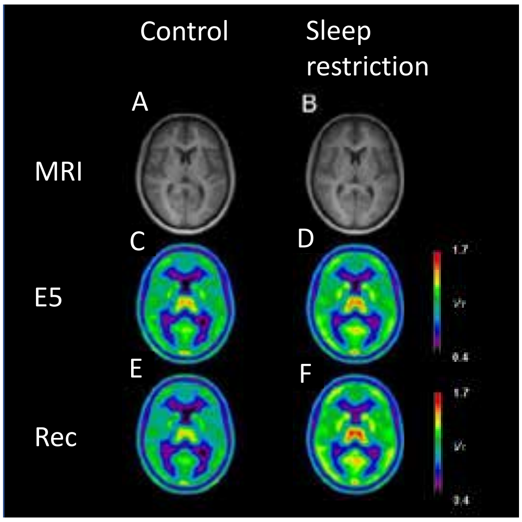

Fig. 1: Average images of anatomy (MRI, A and B) and A1 adenosine receptor availability (PET: C, D, E, F) after spatial normalization of the control group and the sleep restriction group. E5, experimental day 5 (C and D); Rec, recovery day (E and F). Axial views; coordinates according to the Montreal Neurological Institute Brain Atlas were 55, 55, 40 (x, y, z).

not alter the availability of A_1AR. This finding indicates fundamental differences in the homeostatic responses to acute sleep deprivation and chronic sleep restriction. The result is consistent with recent evidence of non-additive interactions of distinct acute and chronic sleep loss effects on performance (Aeschbach et al. 2023). Repeated coffee intake during chronic sleep restriction did not induce lasting changes or adaptive processes of A_1AR availability. The observation that acute caffeine withdrawal leads to symptoms such as headache and sleepiness suggests adaptive processes in response to chronic caffeine consumption. However, our results indicate that these processes are not mediated by A_1AR. They might be mediated by different receptors such as A_2A adenosine receptors.

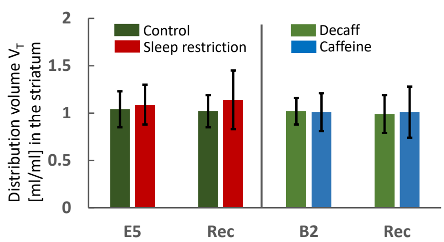

Fig. 2: A_1 adenosine receptor availability measured as distribution volume V_T in the striatum. E5, experimental day 5; B2, baseline day 2; Rec, recovery day.

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Long-term simulation of microgravity with 60-day 6° head-down tilt bed rest impairs sleep duration and quality

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Sleep duration and sleep quality are important factors for the recuperative function of sleep. In space astronauts report disrupted and short sleep episodes. The few objective measures that were taken in space confirm that sleep duration is shorter than on Earth lasting on average 5.96 hours (Barger et al. 2014) to 6.5 hours (Dijk et al. 2001). Thus, the daily amount of sleep is clearly shorter than recommended (Watson et al. 2015). The accumulation of such sleep loss has been shown to result in performance impairment on Earth (van Dongen et al. 2003) and has been associated in epidemiological studies with adverse health outcomes (Cappuccio and Miller 2017). Sleep stages and arousals of neuronal brain activity provide information about the quality of sleep, but can only reliably be determined with polysomnography. Such data have rarely been acquired from astronauts in space, so information rely on small sample sizes and results are inconclusive. On Earth the 6° head down tilt (HDT) bed rest has been shown to induce multiple physiologic alterations that are typical for a stay in microgravity (e.g. fluid shift, bone and muscle loss, space-flight associated neuro-ocular syndrome). We used this space analogue to examine its impact on sleep.

Twenty-four healthy volunteers (8 female; mean age: 33 ± 9 (SD) years) were included in a 60-day 6° HDT bed rest study. In the DLR :envihab facility, baseline data were collected 15 days (BDC) prior to the 60 days in HDT and recovery data for 14 days thereafter. Polysomnography was recorded during 8 nights. Mixed analyses of variance (ANOVA, SAS: proc mixed) with post-hoc Bonferroni adjust-

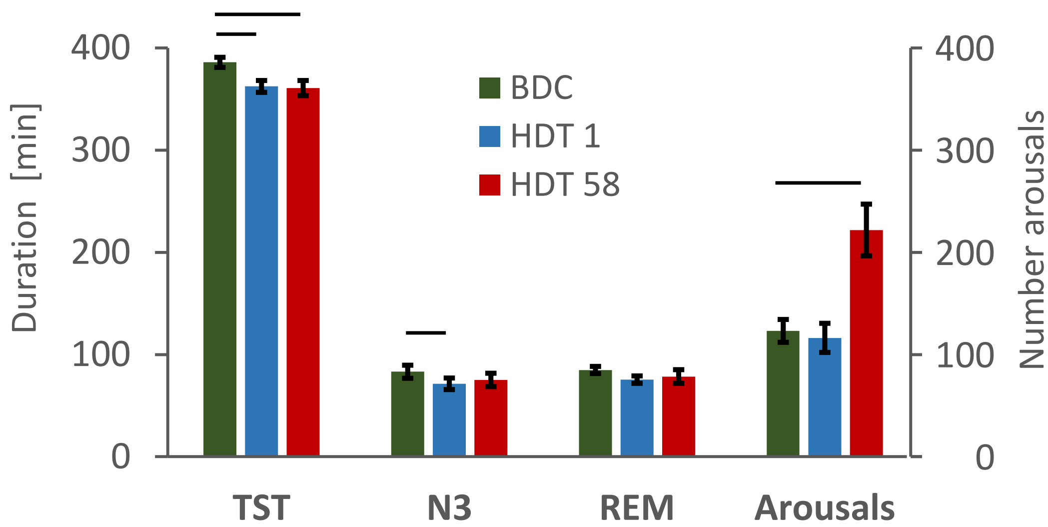

Fig. 1: Sleep duration and quality during 6° HDT bedrest. TST, Total sleep time; stage N3, duration of slow-wave sleep; REM, duration of rapid eye movement sleep. Green bars represent data from BDC, blue bars from HDT 1 and red bars from HDT 58 expressed as means and standard errors. Horizontal bars indicate significant differences between conditions (p<0.05).

ment were used for comparison of HDT and recovery sleep data to baseline.
We report here the acute (at HDT 1) and long-term effects (at HDT 58) of 6° HDT bed rest on sleep duration (total sleep time; TST) and on sleep quality measured as number of arousals from sleep, as slow-wave sleep (stage N3, also called deep sleep) and REM (rapid eye movement) sleep duration (Figure 1).
As an acute response to the HDT posture, sleep duration was 24 min shorter at HDT 1 ($p=0.008$) and contained 12 min less slow-wave sleep (N3 duration $p=0.02$) than at baseline. REM sleep duration and number of arousals were not different. After 58 days in HDT, sleep duration was 25 min shorter at HDT 58 ($p=0.009$) and 99 more arousals were recorded ($p<0.001$) than at baseline. Slow-wave sleep and REM sleep duration were not different.
Our study accurately reproduced the findings from space on short sleep duration and confirmed that this effect is long-lasting. Sleep quality was impaired, which was acutely detectable as reduced slow-wave sleep duration and increased arousal frequency after longer exposure to HDT. Our results highlight the importance of monitoring the impact of long-duration spaceflight on astronauts' sleep. To date – corroborated by the current laboratory studies – we have no reason to assume that sleep sufficiently adapts to the space environment. This is worrisome with respect to astronauts' safety and health. Even though we seem able to reproduce the effects of microgravity on Earth through 6° HDT bedrest, long-term polysomnographic measurements in space with sufficient statistical power are needed to reliably quantify sleep and its role for astronauts' health and wellbeing during extended missions.

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Clinical Aerospace Medicine

Clinical Aerospace Medicine

Dr. med. Claudia Stern (Head)

Dr. med. Martin Trammer (Deputy)

The Department of Clinical Aerospace Medicine is responsible for medical qualification and individual health prevention strategies in aviation, spaceflight, and other occupational settings. We primarily target private and professional pilots, aircrew members, astronauts as well as personnel in the other areas of aerospace, air traffic control and transportation. Additionally, we apply our experience in medical qualification examinations supporting the Institute's departments in selecting test subjects for various clinical and physiological trials.

Our aim is to maintain flight safety as part of the flight medicine community. One key factor for flight safety is a healthy and well-trained cockpit and cabin crew. One centerpiece of this process is the medical qualification examination according to national and international requirements. In addition, we care for other operators with different responsibilities and tasks contributing to flight safety including air traffic controllers, airplane technicians, mechanics, and ramp agents. Indeed, flying and non-flying tasks are equally important to maintain flight safety in aviation. We translate our findings to other occupational settings like spaceflight, terrestrial medicine, scientific research, traffic, and transportation among others.

We serve as the occupational health service for DLR sites in the western region (> 3000 employees), all new DLR Institutes without an occupational health service and the residencies abroad (Brussels, Paris, Tokyo and Washington D.C.). We are certified for medical specialist training in occupational health and are responsible for all hygiene related topics.

Our overall goal is to support aerospace safety and maintain the health of aerospace personnel during their working life time. To attain this goal, we closely collaborate with the Institute's research departments to foster the translation of science to applications in aerospace medicine.

The scientific emphasis focuses on research of numerous eye changes in astronauts in the scope of the Spaceflight associated Neuro-ocular Syndrome (SANS).

In summer 2023 the department moved to building 2.

Teams

Aeromedical Center (Dr. med. Martin Trammer)

- Examination and certification of aviation personnel, certified physician for patient information due to the federal genome diagnostic act of electrodes (Gendiagnostikgesetz GenDG)

Aerospace Ophthalmology (Dr. med. Claudia Stern)

- Ophthalmological research and examinations of astronauts, aviation personnel and test subjects

Occupational Medicine (Peter Tuschy)

- Prevention and managing health of DLR staff and test subjects, medical specialist
- training in occupational medicine
- responsible physician for hygiene related topics
- certified physician for patient information due to the federal genome diagnostic act (Gendiagnostikgesetz GenDG)

Building #2
The new home of the department Clinical Aerospace Medicine and the Study Ambulance.

Eye examinations during bed rest studies to explore Spaceflight Associated Neuro-ocular Syndrome in astronauts

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Department Clinical Aerospace Medicine, Institute of Aerospace Medicine, German Aerospace Center (DLR), Cologne, Germany

Fig. 1: Eye ultrasound examination

Spaceflight Associated Neuro-ocular Syndrome (SANS) describes different possible eye pathologies that can include optic disc edema, globe flattening with hyperopic shift, optic nerve sheath distension and chorioretinal folds, as well as cotton wool spots. About 2/3 of all long-term astronauts are affected during their mission. The intensity of ocular changes increases with mission duration and the number of missions. After return to gravity changes can rapidly or slowly disappear or in some cases also remain. Astronauts usually realize the shortening of the eye by a reduced near vision, which normally can be corrected by additional glasses. The first seven cases have been published in 2011. Since then researchers are trying to find the origin for these ocular changes, especially because they are seen as the red risk number two behind radiation for longterm space travel to Mars.

-6° head down tilt bedrest (HDTBR) is an established method of simulating the effects of microgravity on the human body. During the VAPER study in 2018 we could show for the very first time that a strict head down tilt bedrest can produce optic disc edema. Since then we performed five 30-60 days head down tilt bed rest campaigns with the main

Fig. 2: Electroretinography in head-down-tilt

focus on ocular changes which have been sponsored by NASA.

To ensure test subjects safety and a qualitative excellent research outcome, we perform a thorough selection process and several eye safety examinations in addition to many ocular research examinations. We exclude test subjects with an astigmatism above 3 diopters because of OCT image quality. We also exclude test subjects with a high intraocular pressure or a reduced retinal nerve fiber layer for safety reasons. We also do not accept test subjects after corneal refractive surgery because measured parameters such as intraocular pressure changed after the procedure and after LASIK there is the possibility of late flap complications because of many eye examinations. The eye safety examinations include testing of visual acuity, visual field, objective refraction, slit lamp, fundoscopy and performing tonometry. Visual acuity testing is important to find out whether the acuity dropped during or after the bed rest, which also happens in professional astronauts. Visual field testing is necessary because the blind spot can enlarge in case the optic disc is swollen, as happened also inflight. Objective refraction is important to get knowledge about a hyperopia induced by globe flattening. In addition to that bed rest international standard measures need to be performed which include ocular ultrasound examinations (Figure 1), optical coherence tomography (OCT) and tonometry. The research part of the last four bed rest studies included additional OCT examinations (including OCT Angiography and Multicoulour Imaging), electroretinography (image 2), pneumatonometry, intravenous fluorescein angiography and dynamic vessels analysis. These very special eye examinations will give us new insides into the development of SANS.

The selection criteria and safety measurements were successful in keeping the test subjects eyes healthy, apart from the SANS typical changes and should be applied in all head down tilt bedrest studies.

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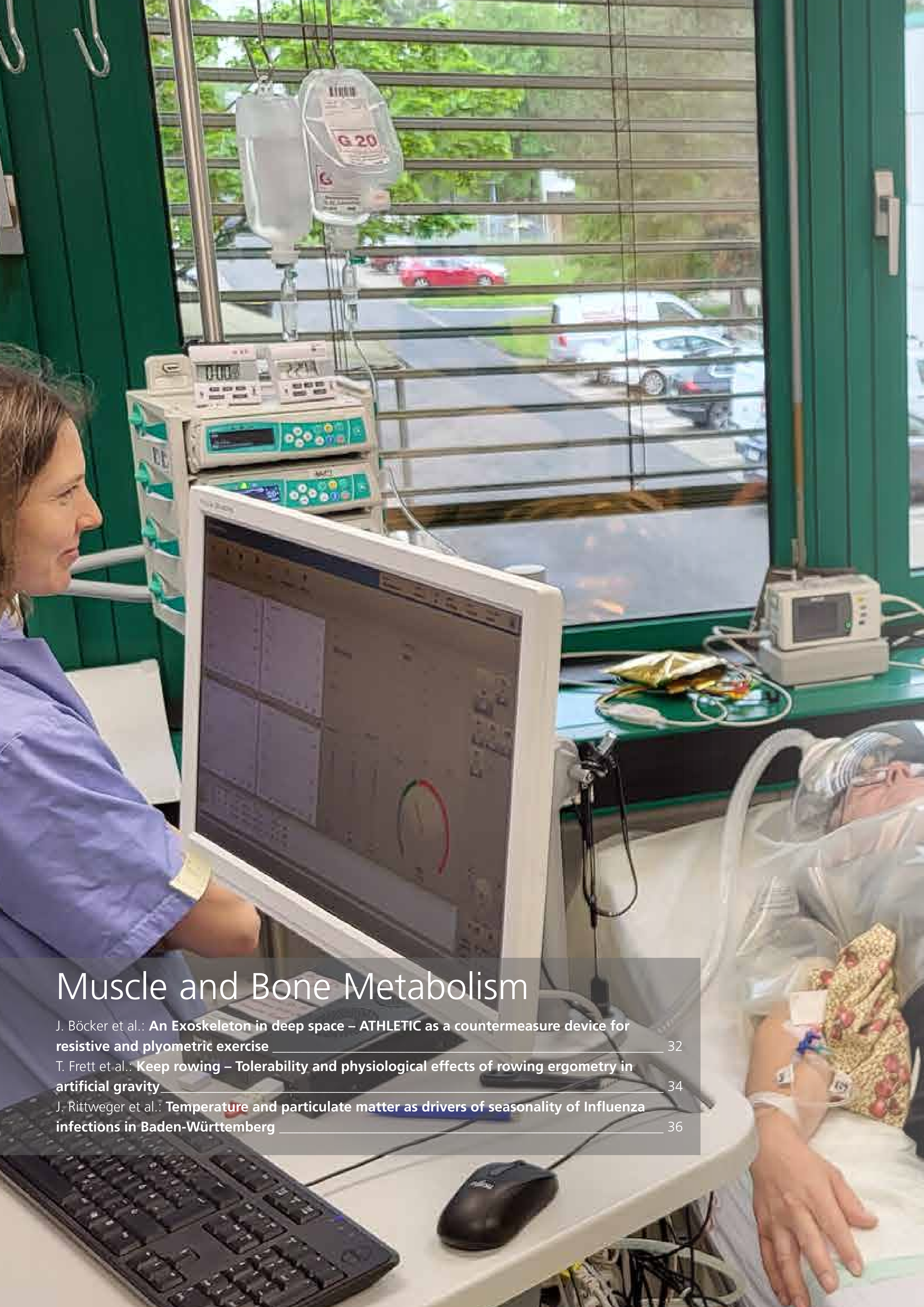

Muscle and Bone Metabolism

Muscle and Bone Metabolism

Prof. Dr. med. Jörn Rittweger (Head)

Prof. Dr. rer. nat. Dominik Pesta (Deputy)

Humans have evolved as a species that is uniquely capable of enduring physical performances. Long periods of physical inactivity, conversely, lead to deconditioning, to untoward metabolic consequences, and to compromised health. The Muscle and Bone Metabolism department therefore examines the effects of physical activity, and of the lack thereof in the context of mission-related environmental conditions, such as microgravity, atmospheric challenges, nutrition, circadian disruption and radiation. Genetic predisposition and the ageing process are taken into account as well.

Our ultimate goals are to screen for immobilization-related musculoskeletal disorders, to prevent them where possible and to rehabilitate them where needed. To this purpose, we aim to define valid muscle test protocols, to develop efficient measures to counteract muscle atrophy, bone loss and metabolic derailment in space and on Earth. We aim at these goals in a rational approach that ranges from cellular to organismic levels.

Researching the biomechanics and mechanophysiology of muscles and bones are a prerequisite to understand the physiological effects of muscle contractions and exercise. This is seconded by research into skeletal muscle's metabolism and its systemic interactions. Combining this knowledge with genetic model systems allows us to develop exercise and other countermeasures that are purpose-optimized for space and specific Earth-based applications.

Working Group

Translational Metabolism Research (Prof. Dr. rer. nat. Dominik Pesta)

- Metabolic studies, euglycemic hyperinsulinemic clamp testing, biosample management
- Evaluation of artificial gravity achieved through short-arm centrifugation alone or in combination with physical training or virtual reality applications as potential counter-measure for health issues during space travel

Teams

Mechano-Physiology (Prof. Dr. med. Jörn Rittweger)

- Biomechanical testing, biomechanical modeling, technology development, data management

Training and Countermeasures (PD Dr. rer. nat. Jochen Zange)

- Exercise training studies, musculoskeletal imaging, exercise countermeasure development

Resting metabolism
Measurement of gas exchange at rest allows assessment of resting metabolic rate and an estimation of substrate utilization.

An exoskeleton in deep Space – ATHLETIC as a countermeasure device for resistive and plyometric exercise

Jonas Böcker[1], Jochen Zange[1], Torsten Siedel[2], Guillaume Fau[2], Sebastian Langner[3], Thomas Krüger[4], Jörn Rittweger[1]

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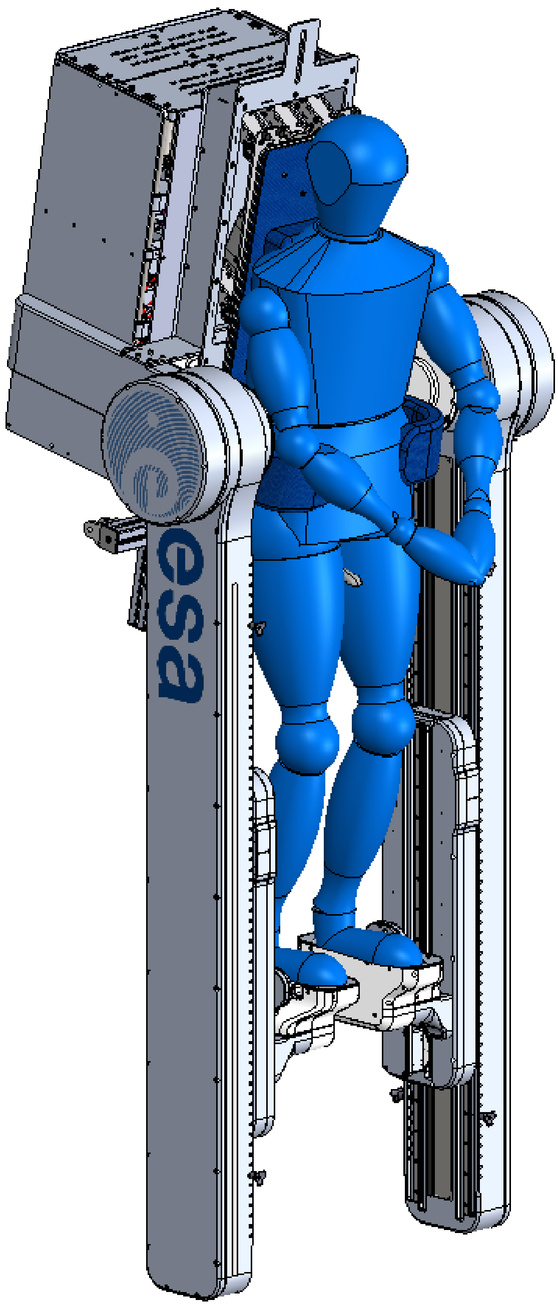

Fig. 1: The ATHLETIC device based on an exoskeleton concept as a novel countermeasure device for future deep-space missions

Introduction

During a long-term mission to space, the musculoskeletal system of astronauts still experiences bone losses and muscle wasting despite of an almost daily performance of endurance and strength training as countermeasure. Future long-term deep space missions e.g. towards Mars will increase the challenges to exercise countermeasures: The training must become more effective, more reliable and smaller, as the new spacecrafts will afford less space for training equipment. Therefore, new approaches to training devices are imperative. ATHLETIC (AstronauT HeaLth EnhancemenT Integrated Countermeasure; ESA Contract No. AO/1-9473/18/NL/RA) is based on the concept of an exoskeleton. A passive constant force mechanism generates weight-analogous forces and an inertial module combine to produce sufficiently high loads that enable both intense resistance training and plyometric training (Figure 1). An evaluation study was conducted to test the functionality of this approach.

Methods

Ten participants (5 female, 5 male) completed reference exercises consisting of strength training (squats and heel raises with 50% additional load using barbells i.e. 150% body weight) and plyometric training (countermovement jump, reactive hopping with 100% body weight) on a jumping platform. Afterwards, participants were asked to perform the same exercises on ATHLETIC in supine horizontal posture. Notably, the horizontal posture misaligns the body's long axis with the gravity vector and thus abolishes the normal gravitational loading. During squats and countermovement jumps ATHLETIC allowed natural joint motion of the hips, knees and ankles. As in reference exercise, the ground reaction force (constant force + inertial force) during squats and countermovement jumps on ATHLETIC acted on the forefeet, which were

Fig. 2: Subject performing squats on the ATHLETIC device.

placed in line with the subject's centre of gravity. Intensity on the movement sequence during exercise on ATHLETIC was compared with reference exercise using mechanical variables like ground reaction force, contact times, motion speed, joint angles etc. and the activity of selected leg and trunk muscles recorded by electromyography (EMG).

Results

When testing ATHLETIC by their own, the constructors were able to perform leg press exercise in a fixed upright seated posture operating with the maximum possible constant force of 300 kp. Therefore, this type of exercise was not further tested on subjects.

In the study, all participants could perform all types of reference exercise as given. On ATHLETIC, especially during squats and countermovement jumps, participants struggled with the coordination of motion. Participants must familiarize with the circumstance that on ATHLETIC exercise started in horizontal posture. To facilitate the exercise, we started with constant forces lower than the reference force until subjects were able to perform the respective exercise with almost correct movement coordination.

Squats on ATHLETIC were performed with a constant force of only 65 ± 8 %RE (% of the corresponding value measured at reference exercise, mean ± standard deviation). The vastus lateralis muscles representing the group of knee extensor muscles reached EMG amplitudes of 70 ± 28 %RE on the right and 79 ± 21 %RE on the left leg, respectively.

Heel raises were performed on ATHLETIC with a constant force corresponding with 76 ± 13 %RE. The gastrocnemius lateralis muscles representing the plantar flexion muscles reached EMG amplitudes of 78 ± 15 %RE on the right and 86 ± 22 %RE on the left leg.

Countermovement jumps on ATHLETIC were performed at a constant force of 90 ± 14 %RE. However, the participants could not always execute the jump in a fluid movement of dropping and jumping off. In consequent the jump height on Athletic was only 25 ±13 %RE. Peak EMG amplitudes of the vastus lateralis muscle were highly variable with 77± 63 %RE on the right and 94 ± 76 %RE on the left leg.

Forefoot hopping on ATHLETIC was performed with a constant force of 89 ± 11 %RE. The ground contact time in between the hops was 3.5 ± 4 times longer than in the reference exercise). This was too long to utilize elastic energy storage in calf muscles and the Achilles tendon. In consequence average hopping height was only 21 ± 12%RE. However, peak EMG amplitudes of the gastrocnemius lateralis muscle were 100 ± 36 %RE on the right and 100 ± 23 %RE on the left leg.

Conclusions

The present study confirms the principal functionality of ATHLETIC as a countermeasure exercise device. Types of resistive exercise, with low challenges on motion coordination are possible with high training loads. Further improvements of the device are needed to improve the correct performance of plyometric training. Above all, the way participants are attached to the device needs to be improved to allow for sufficient body stiffness, which is required to utilize muscle and tendon elasticity in plyometric exercise. In general, subjects need a proper familiarization to learn the different modes of exercise in the new environment.

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Keep rowing – tolerability and physiological effects of rowing ergometry in artificial gravity

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Despite daily microgravity countermeasures, such as treadmill running or resistance training, long-term exposure to microgravity during spaceflight is associated with bone loss, muscle atrophy (1), and reduced exercise capacity (2). These physiological changes can result in significant health risks for astronauts during and after space missions. The daily provision of passive 1g via short-arm human centrifugation, although well tolerated (3) seems insufficient to counter physiological deconditioning induced by head-down bed rest—an analogue of microgravity—suggesting concurrent exercise is necessary (4). High-intensity whole-body exercises, such as rowing during centrifugation, promoting both aerobic fitness and intensive musculoskeletal loading, are preferable for spaceflight to counter muscle and bone loss and cardiovascular deconditioning (5). However, the effects of cross-coupled moments and g-gradient during training while rotating upon hemodynamic, biomechanics and motion sickness remain unclear. Therefore, we evaluated the tolerability, rowing performance, muscular activity and cardiopulmonary response to upright seated rowing during centrifugation with 0.5 g at the individual center of mass, comparing it to an equivalent resultant g vector in terrestrial gravity. Eight men and four women (27.2 ± 7.4 yrs, 179 ± 0.1 cm, 73.7 ± 9.4 kg), experienced rowers, started self-paced rowing at 30 W, increasing by 15 W every three minutes until exhaustion. Motion sickness, rating of perceived exertion (BORG), rowing performance and cardiopulmonary responses (ECG, blood pressure, spirometry and blood lactate concentration) were compared between conditions. Participants completed all sessions without serious adverse events, dropouts or exercise-related problems. The average centrifuge spin rate was 15.4 ± 0.4 rpm. There was no significant difference in motion sickness ($p = 0.38$) between conditions. While the BORG score increased in both conditions (Earth $p < 0.0001$; SAHC; $p < 0.0001$), there was no difference post conditions ($p = 0.76$). Motion sickness ratings slightly increased after centrifugation ($p = 0.0074$) but was generally low. Total distance ($p = 0.003$) and average wattage ($p = 0.\ 0001$) were significantly lower during centrifugation (Table 1), but no difference in heart rate ($p = 0.50$, Figure 1), lactate ($p = 0.11$, Figure 2), or blood pressure responses (systolic: $p = 0.65$, diastolic: $p = 0.99$, figures 3-4) were observed between conditions. Maximal heart rate values were 181 ± 10 BPM during centrifugation and 186 ± 9 BPM during terrestrial control. All participants reached their calculated VO2max. We did not find a significant effect of condition in the cardioventilatory response except for a higher ventilation (V´E) during terrestrial rowing ($p < 0.0001$) that tended to interact with the longer rowing duration in this condition.

We demonstrate for the first time that graded rowing to exhaustion during centrifugation is feasible and tolerable—with BORG and motion sickness comparable with the matched Earth condition. While total distance and average wattage during centrifuge-based row-

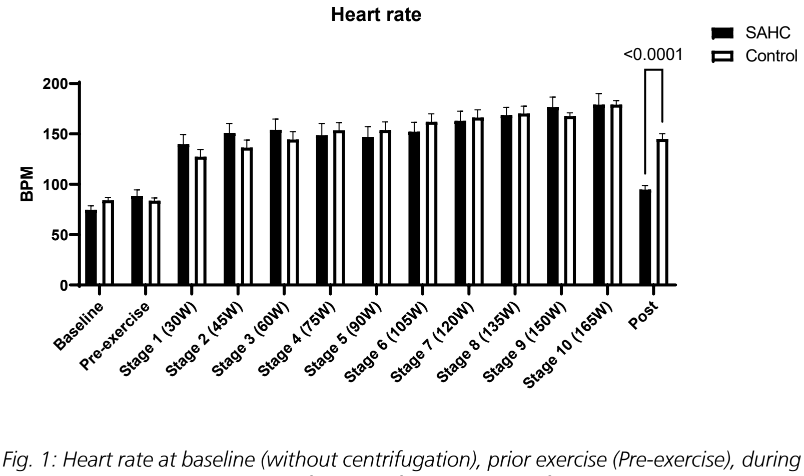

Fig. 1: Heart rate at baseline (without centrifugation), prior exercise (Pre-exercise), during gradually increased rowing and after end of rowing (POST) for both groups.

ing were lower, the cardiovascular responses—and thus aerobic stimulus—were similar. Thus, biomechanical (kinematic and kinetic) and electromyographic evaluation of rowing is warranted to assess musculoskeletal suitability. It seems likely, that active training during centrifugation even in a steeper gradient field are more tolerable than expected. Our results are in line with others testing physical exercises on a short arm centrifuge (6, 7).

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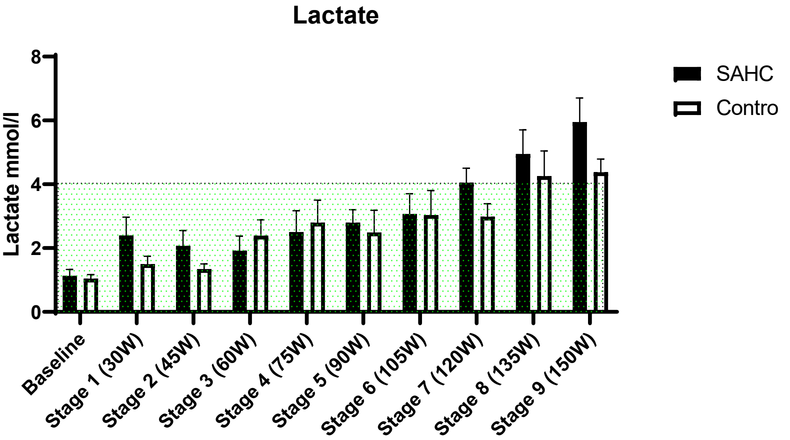


Fig. 2: Blood lactate during baseline and after each stage of self-paced rowing. Anaerobic threshold (> 4 mmol/l) marked in green.

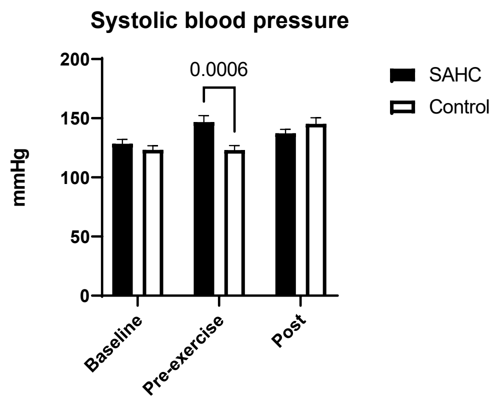
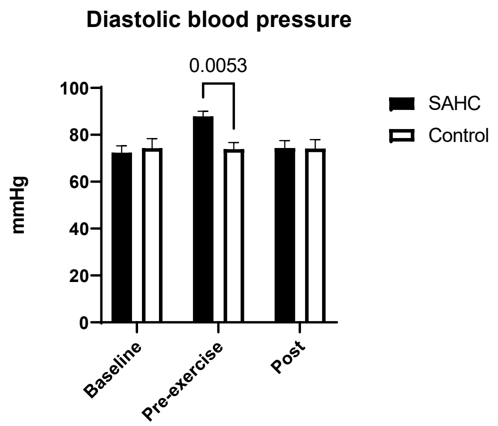


Fig. 3: Systolic blood pressure at baseline, prior exercise and after end of rowing.



Fig, 4: Diastolic blood pressure at baseline, prior exercise and after end of rowing.

	SAHC	CONTROL	Paired t-test
Stroke rate (spm)	20.0 ± 1.5	23.1 ± 2.0	t (6) = 1.606, p = 0.16
Watt (W)	61.4 ± 7.9	88.3 ± 7.8	t (6) = 8.616, ***p < 0.0001
Power (W x kg1/3)	182.0 ± 46.1	363.6 ± 38.8	t (9) = 4.678, **p = 0.001
Total distance (m)	3006 ± 652.8	5135 ± 839.0	t (7) = 4.402, **p = 0.003
Total duration (s)	1202 ± 193.9	1761 ± 232.0	t (6) = 2.986, *p = 0.024

Table 1: SAHC Short arm human centrifuge; Earth terrestrial control; spm strokes per minute; W· kg1/3 Watt per corrected body weight; s seconds; m meter p < 0.05 *** p < 0.001*

Temperature and particulate matter as drivers of seasonality of Influenza infections in Baden-Württemberg

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Background

Seasonality of Influenza Infections seasonality is well established, but its mechanism is not clear. Thus, even in tropical zones without clear-cut seasons, there are seasonal peaks in Influenza incidence (1). Previous studies have mostly been based on urban in-situ studies, linking influenza to single or selected meteorological or pollutant stressors (1, 2). Only few studies have so far examined rural and less polluted areas in temperate climates. In a co-operation between DLR and AOK, one of the largest health insurers in Germany, we want to overcome that limitation.

Objective

We investigated the effects of quarterly residential exposure to particulate matter (PM2.5), NO2, air temperature, and precipitation on influenza incidence with full coverage of Baden-Württemberg (a Federal state in the southwest of Germany).

Methods

We modeled environmental exposure from the Copernicus Atmospheric Monitoring Service (CAMS) and from the Copernicus Climate Change Service. This was done by computing spatiotemporal aggregates that represent quarterly mean values at the zip code level. In addition, we retrieved health insurance data to capture influenza cases from January 2010 to December 2018 by identifying new cases as ICD-10 codes J09, J10 or J11. For statistical analyses, we used generalized additive models with Gaussian Markov random field smoothers for the spatial input. Four different models were run that either included 'quarter' or not, and which either used all data from 2010 to 2018, or only data from 2012 to 2018. Statistical analyses were performed with the R/Rstudio environment, using the R-package 'mgcv' for creating general additive models and the function 'predict' for predictions of stressor effects.

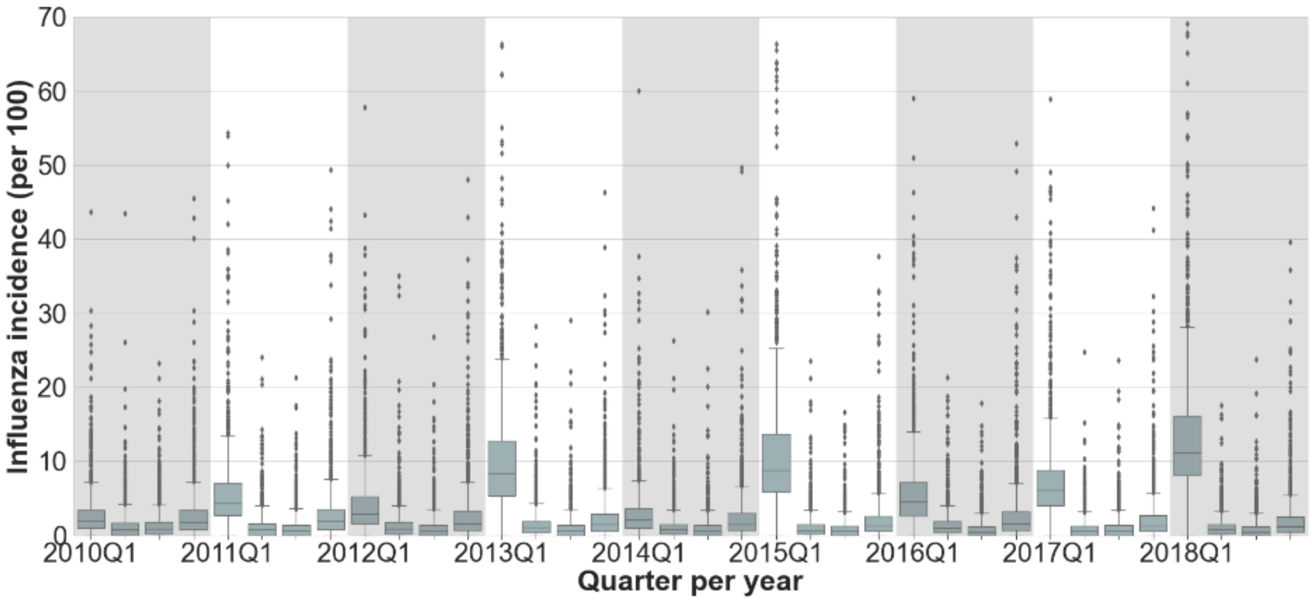

Fig. 1: A boxplot showing influenza incidence by postcode for each quarter from 2010 to 2011. The y-axis has been truncated to 70 to better illustrate the data. Figure reproduced from (3)

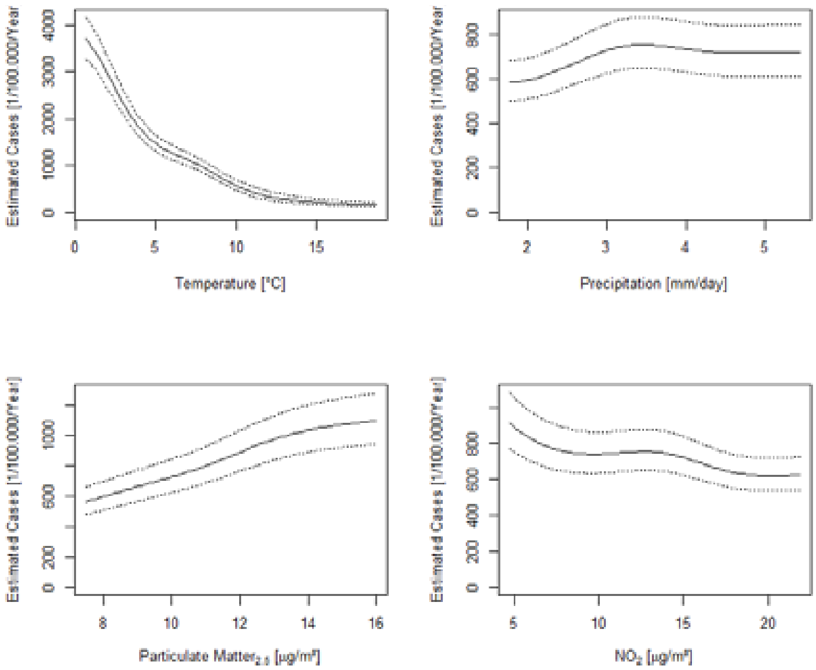

Fig. 2: Predictions (and their 95% confidence intervals) for the effects of temperature, precipitation, PM2.5, and NO2 on Influenza incidence. Here we show the curves for a restricted model (excluding quarter as an independent variable) with the previous season set (2012/13 onwards). Note that the other 3 statistical models yielded the same trend curves as the models shown here. Also, interaction terms such as temperature and PM2.5 had no obvious effect on the trend curves. Figure reproduced from (3)

Results

The cohort comprised 3.85 million people, and there were a total of 513,404 cases of influenza occurred over 9 years. Of these cases, 53.6% in the 1st quarter (January–March) and 10.2%, 9.4%, and 26.8% in the 2nd, 3rd, and 4th quarter (see Figure 1). Statistical modeling showed significant effects of air temperature, precipitation, PM2.5 and NO2. Calculation of stressor-specific effects revealed 3,499 infections per 100,000 AOK clients per year that are attributable to a reduction in mean ambient air temperature from 18.71°C to 2.01°C (Figure 2). Stressor-specific effects were also found for particulate matter, with 502 attributable infections per 100,000 client-years by an increase from 7.49 mcg/m³ to 15.98 mcg/m³. For NO2, an inverse relationship was found (Figure 2).

Discussion

The strongest statistical effect upon Influenza incidence was exerted by temperature, regardless of whether 'quarter' was included as independent variable into the gam model or not. This implies that temperature is a driver for seasonality of influenza incidence, and the same is true for particulate matter. However, whilst good pathophysiological evidence is available to explain as a direct effect of particulate matter, the fact that people spend most of their time indoors in summer and winter alike (4) suggests that temperature exerts its statistical effect in an indirect fashion. Future research should therefore clarify the mediating mechanisms. Finally, we also regard this study as proof-of-principle for epidemiological studies that use Earth observation-based modeling in combination with health insurance data.

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Aerospace Psychology

Aerospace Psychology

Dr. Dipl.-Psych. Viktor Oubaid (Acting Head since 06-2022)

Pilots, air traffic controllers, astronauts, and operators in other skilled professions are, both, an asset and a liability regarding safety in aerospace. Indeed, proper decisions together with functioning human-machine and human-human interactions enhance the reliability of technical system tenfold. Yet, operators are also responsible for the majority of aviation incidents and accidents. By developing, validating, and implementing comprehensive selection systems, the Department of Aviation and Space Psychology makes a significant contribution to safety in aerospace. Research in the field of performance under (simulated) microgravity, flight cockpit design, flight operation of aircrafts and drones, virtual reality and passenger comfort in trains and aircraft expands the research range of the department and promotes cooperation with operators and manufacturers for the benefit of travellers and crews.

Given the importance of human factors, our work will help attaining the goals of Flightpath 2050, an 80% reduction in accidents. Our safety-related research program is of high scientific, economic and societal value, contributes to employment security and job satisfaction of selected candidates, and supports economic development of aerospace industry by reducing training costs and minimizing errors. An additional part of our research addressed acceptance of new technologies, which is a critical barrier for economic success of novel technology.

Working Groups

Air Traffic Control (Dr. phil. Yvonne Pecena)

- Job requirements of controllers and UAS operators
- Selection of air traffic controllers
- Inter team cooperation
- Eye tracking methods
- Urban air mobility
- Acceptance of aviation systems

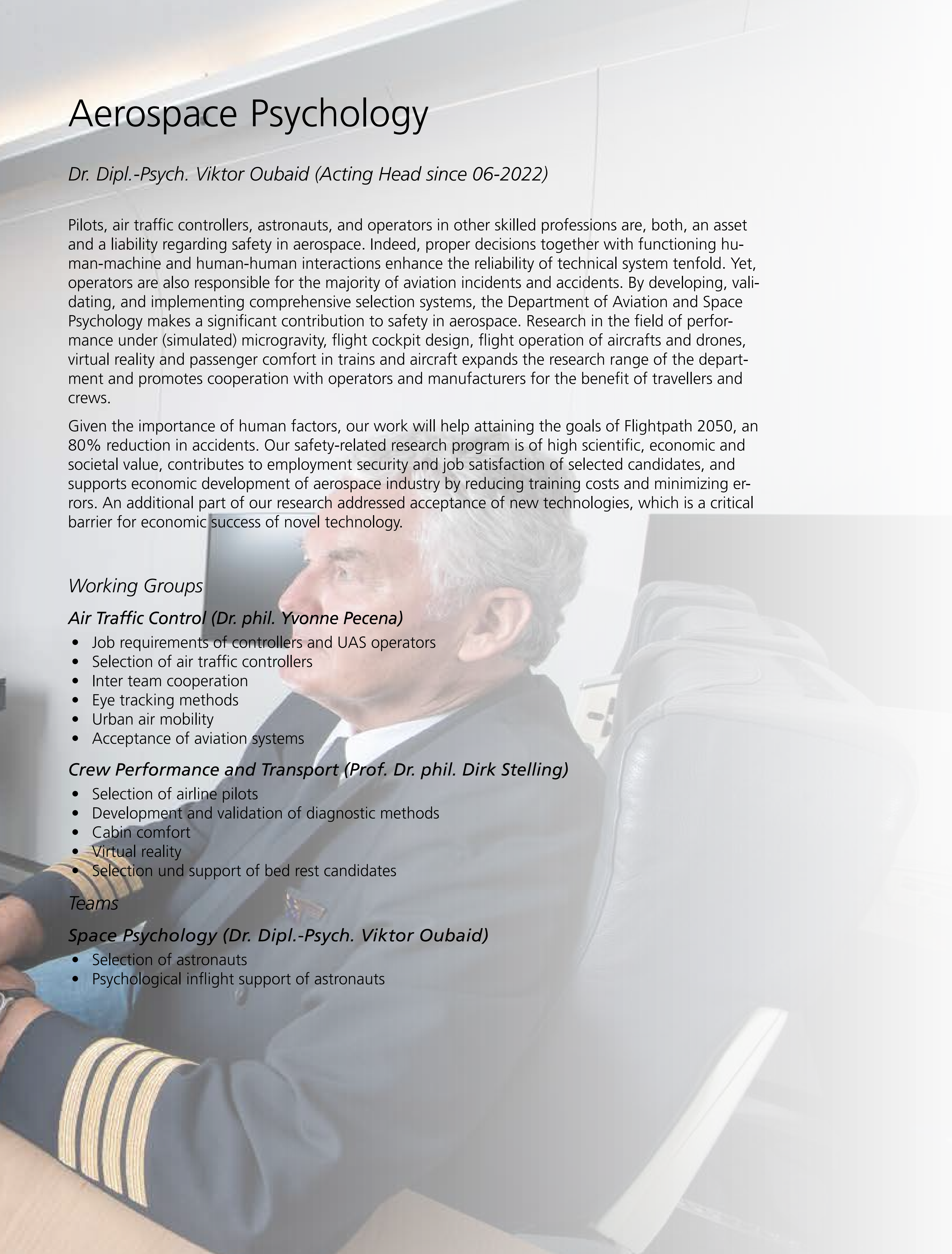
Crew Performance and Transport (Prof. Dr. phil. Dirk Stelling)

- Selection of airline pilots
- Development and validation of diagnostic methods
- Cabin comfort
- Virtual reality
- Selection und support of bed rest candidates

Teams

Space Psychology (Dr. Dipl.-Psych. Viktor Oubaid)

- Selection of astronauts
- Psychological inflight support of astronauts



An Airline training captain assessing pilot performance in an evidence based training unit under fully digital remote conditions developed by DLR
We are developing and evaluating a system with which the prescribed regular checks and training units of airline pilots can be assessed with significantly higher objectivity and ergonomics than with the existing solutions in the airlines.

Social acceptance of civilian drones and air taxis – a large-scale telephone survey

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Introduction

Within the project HorizonUAM, 11 DLR institutes and facilities collaborated under the leadership of the Institute of Flight Guidance in Braunschweig from 2020 to 2023 to assess chances and risks of future urban air mobility (UAM; Pak et al., 2023). In this context, concepts for possible use of unmanned aerial vehicles (drones) for passenger transport in urban airspace were developed. Importantly, the project focused not only on technological aspects such as vehicles, cybersecurity, and ground infrastructure, but also on public acceptance.
Acceptance research was led by the Department of Aviation and Space Psychology in Hamburg and realized in collaboration with colleagues from Braunschweig. At the heart of the acceptance research was a large-scale telephone survey among German citizens to gain insights into the prevailing opinions on civilian drones in general and air taxis in particular (for a detailed report, see End et al., 2023).

Method

The institute BIK ASCHPURWIS + BEHRENS GmbH was commissioned to conduct N = 1001 computer-assisted telephone interviews on behalf of DLR at the end of 2022. The interviews took on average 21 minutes (median). To ensure the representativeness of the results for the German population with respect to key demographic characteristics (e.g., gender, age, highest educational degree), both design and adjustment weighting were applied to the data.

Results

Attitudes towards civilian drones in general were rather positive among the German population. In contrast, attitudes towards the use of drones as air taxis were more balanced, with slightly more very negative than very positive responses (Fig. 1). Concerns about the misuse for criminal purposes (85%) and concerns about the violation of privacy (84%) were the most common assessed concerns about civilian drones, while concerns about noise were least common (46%).

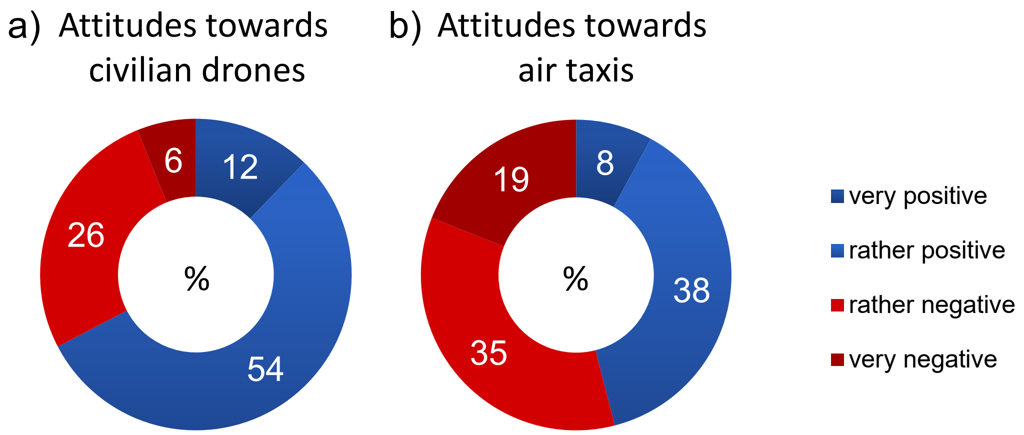

Fig. 1: a) Question "Based on what you know about this so far: How would you describe your general attitude towards civilian drones?" (Values missing to 100%: „do not know"/ „refused"). b) Question "Based on what you know about it so far: How would you describe your general attitude towards air taxis?". Note: Figure adapted from End et al. (2023).

Dataset	Predicted variable	Prediction accuracy (%)
Full	Drones	60.14
	Air taxis	37.87
Binarized	Drones	68.38
	Air taxis	58.14

Tab. 1: Accuracies of the classification and regression tree algorithm (CART) predicting attitudes towards civilian drones and air taxis by concerns, separately for the full dataset (four variable levels from very positive to very negative) and a dataset with binarized variable levels (positive vs. negative). Note: Table adapted from End et al. (2023).

Statistical analyses revealed a large number of factors associated with attitudes towards civilian drones and air taxis. For example, demographic variables (e.g., age), interest in other topics such as environmental protection, and general noise annoyance in the past year were found to be significantly associated with attitudes towards civilian drones and air taxis ($p < .05$).

In addition, the application of machine learning algorithms, such as a classification and regression tree algorithm (CART), demonstrated that respondents' attitudes towards civilian drones and air taxis could be predicted by the assessed concerns above chance level (Tab. 1).

Discussion

The current study provides a comprehensive overview of drone acceptance with representative insights into current opinions in Germany, statistical analyses of possible influencing factors, and models for predicting attitudes. Integrating a substantial number of questions from the previous survey by Eißfeldt et al. (2020) conducted in 2018 made it possible to look at changes in the prevailing opinions over the last four years. In this context, a slightly positive trend in attitudes towards civilian drones was found compared to 2018.

While the current study was critical to gain representative insights into the prevailing opinions, a key challenge for research on drone acceptance is that a substantial number of citizens have not yet encountered drones in real life, let alone air taxis. Virtual reality studies can help overcome this challenge. In this context, two studies were conducted within HorizonUAM providing virtual experience to participants and examining their well-being in different UAM scenarios (Papenfuss et al., submitted; Stolz & Laudien, 2022).

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Validating air traffic controller selection and training

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Introduction

Validating selection and training is an important part of quality assurance in recommending suitable applicants. In order to maintain the quality of the DLR selection for ab initio air traffic controllers (ATCOs) and to investigate relevant psychological assessment questions, comprehensive validation studies of the entire selection process are regularly conducted (Conzelmann, Heintz & Eißfeldt, 2011; Conzelmann & Keye, 2014; Damitz et al., 2000; Eißfeldt & Maschke, 1991; Eißfeldt et al., 2013, Pecena et al., 2013).

In the current validation study (Project ValiS) funded by and in cooperation with the DFS Deutsche Flugsicherung GmbH, the predictive validity of the DLR ATCO selection for the DFS ATCO training was investigated (see Fig. 1). The goal was to identify potentials and deduct appropriate measures to further optimize ATCO selection and training. One main research question was whether ATCO training performance and ATCO training success can be predicted by the selection tests.

Method

The validation sample consisted of N = 603 applicants (72.3 % male, 27.7 % female, mean 20.0 years, SD = 1.9, range 18–25 years) that were selected as trainees for DFS ATCO training. They took part in the selection from 24th November 2008 to 14th May 2013 and were trained from 11th January 2010 to 20th September 2018. Thus, this was the largest DLR validation sample that has been investigated.

As a reference sample served N = 13,133 applicants (59.9 % male, 40.1 % female, mean 20.1 years, SD = 1.9, range 18–25 years) who took part in the selection in about the same time period as the validation sample.

The selection procedure is a multi-phase, multi-modal process. It starts with cognitive performance tests and is completed by an interview with a selection board (see Fig. 2).

The DFS ATCO training consists of two phases: The initial training (IT) with theoretical lessons and simulations at the DFS Academy in Langen, Germany, and the unit training (UT) at the respective DFS Tower or Center with supervised training on live traffic (see Fig. 3).

For this study, comprehensive quantitative and qualitative DLR selection data and biographical information were used. Comprehensive training data on the performance and success of ATCO trainees were provided by DFS. For the first time, training performance data from UT were available for validation. The final data set encompassed about 900 variables. To investigate the main research question, we calculated correlation analyses, regression analyses and if adequate Chi²-tests.

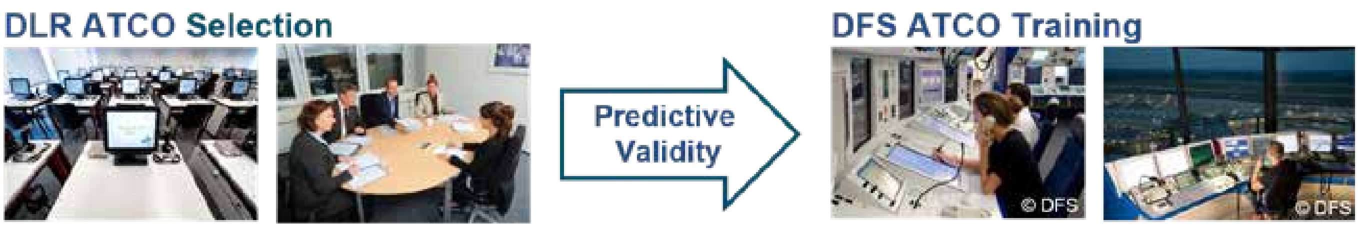

Fig. 1: Main goal of the validation study with example pictures from the DLR selection procedure and the DFS ATCO training

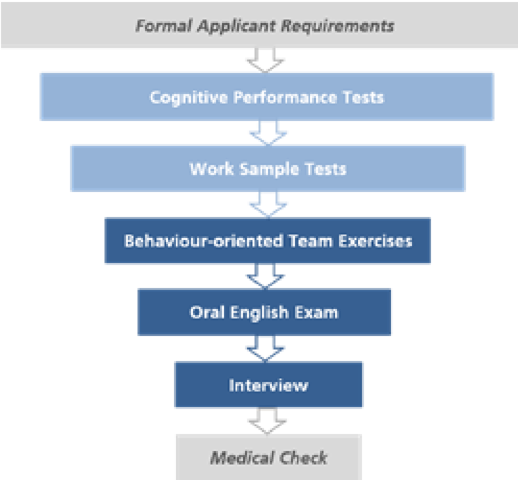

Fig. 2: DLR ab initio ATCO Selection Procedure

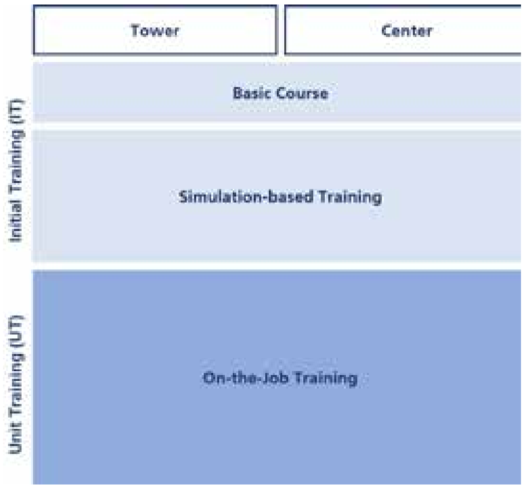

Fig. 3: DFS ATCO Training Structure

Results

Due to the great number of results, a summary of the main results for each selection phase is given. For each selection phase, primarily systematic significant predictive validities across a number of predictors and criteria are reported.

The cognitive performance tests were predictive of IT performance and IT success, whereas work sample tests and interview were predictive of both performance and success in both IT and UT. For the behavior-oriented team exercises no systematic predictions were found. However, performance data of this phase generate hypotheses for the interview. They are therefore included in the final selection board assessment on social competence which partially predicted UT performance and UT success.

Conclusion

In general, validation studies are impacted by several methodological challenges such as restriction of variance. As only 6% of the applicants pass all selection phases, data for both unsuccessful applicants and trainees are lacking which generally impedes the occurrence of significant correlations.

Overall, the results of the validation study confirmed the predictive validity of the DLR selection process for ATCO training success and performance. Furthermore, for the first time, performance in the UT could be predicted. We used the validation results to further optimize specific aspects of the selection tools, and implemented the findings in the work of the selection board.

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Acknowledgment

The former colleagues Markus Neumann, Dietrich Grasshoff and Verena Vogelpohl contributed substantially to data processing and data analyses and are therefore named as authors.

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Psychological evaluation of oxygen masks for pilots – The project PROTECTeD

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Background

The objective of the project "New flight crew PROTECTive Device concept for prolonged use in civil aircraft" (PROTECTeD) was to evaluate a prototype of a new oxygen system for pilots in civilian aircraft. PROTECTeD was part of platform 3 in the EU Clean Sky 2 funding program. The new oxygen system was developed by the cooperation partner Safran Aerosystems (https://www.safran-group.com/) and the evaluation comprised usability, comfort and human performance. Key features of the new oxygen system are that it is controlled automatically or via a display instead of fully manually, like conventional masks. Also, the facepiece of the new mask is lighter and designed more ergonomically.

Methods

A Human Factor test campaign (HFTC) with a sample of 20 pilots (CPL or ATPL holders) was performed in Plaisir, France at Safran Aerosystems. The candidates had to work on various flight tasks (cruise flight, two different emergency situations) in a demonstrator. They also had to answer several questionnaires regarding usability and comfort. Another part of the experiment was to work on different cognitive tasks: the so-called Deary-Liewald reaction time task (Deary et al., 2010), a visual search task (Treisman & Gelade, 1980) and a Nback acoustical memory task (Jaeggi et al., 2010). The behavior in all tasks was observed (cf. Figures 1 and 2).The candidates had to perform the tasks without mask (baseline), while wearing the prototype of the new oxygen system (new mask) and while wearing a conventional aircraft oxygen mask (legacy mask).

Results

Analyses of variance showed that the new oxygen mask was evaluated better in all flight tasks (Figure 3). 77.8% of the subjects stated that they would prefer to wear the new oxygen mask on a real flight. Several sub-measures showed that usability and comfort of the new oxygen system were better compared to the legacy mask. The questionnaires also revealed many starting points for further refinements of the new system. Results of the cognitive tasks showed that wearing a mask seems to be a general impediment for human performance, there were comparable performance detriments with both types of masks.

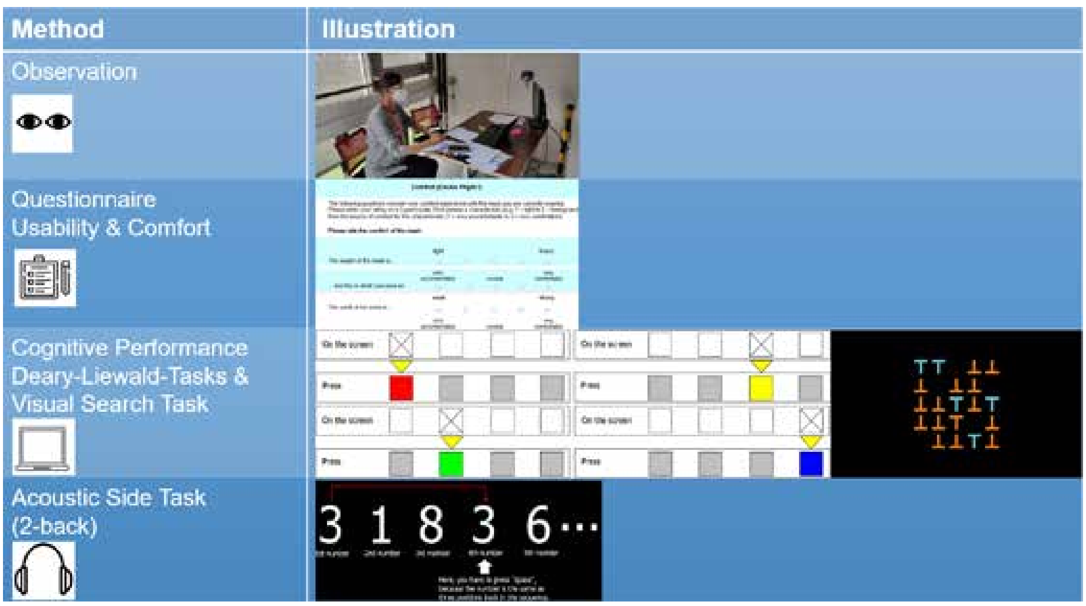

Fig. 1: Depiction of methods in the Human Factors Test Campaign

Fig. 2: Candidate in the experimental setting

Conclusion

The HFTC has been successful and the results with their practical implications have a solid base because the external and ecological validity with a sample of professional pilots was given. The superior usability and comfort of the new oxygen mask have been shown and starting points for further development were revealed. The examination of the effects of the new mask on human cognitive performance has shown that its deteriorating effect is not larger than that of a conventional mask.

PROTECTeD bore a sound approach to a multi-facet psychological and ergonomic evaluation of oxygen masks and other devices for the flight deck. Also, the methods developed can be used in other scientific contexts. A comprehensive report of the project has been published (Maier et al., 2022).

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Funding

This project has received funding from the Clean Sky 2 Joint Undertaking (JU) under grant agreement No. 945583, CS2-LPA-GAM-2020-2023-01. The JU receives support from the European Union's Horizon 2020 research and innovation programme and the Clean Sky 2 JU members other than the Union.

Fig. 4: Funding and project partners

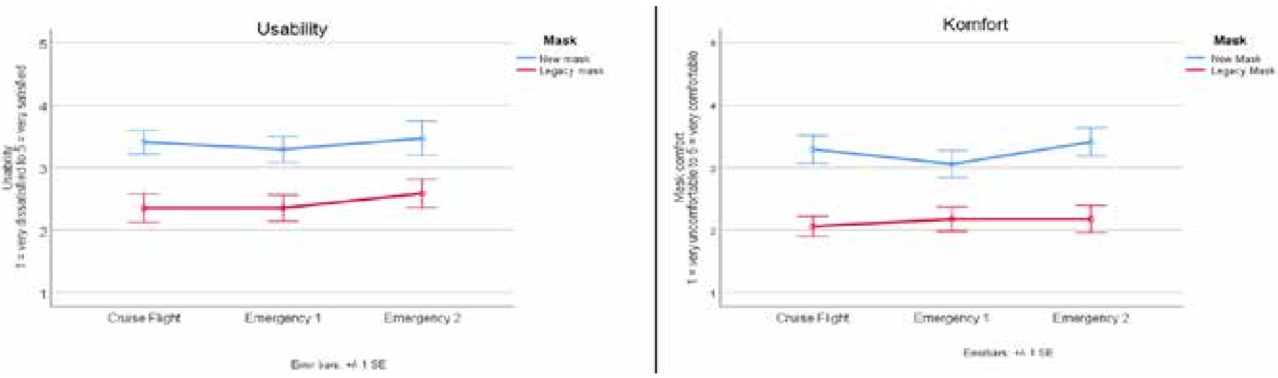

Fig. 3: Usability and comfort measures in comparison between the both oxygen mask systems

Using basic flight simulators for selection of unlicensed pilots

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Fig. 1: The setup of the SIM with the test monitor in the foreground and the candidate in the back inside the test booth.

Simulators offer a safe and effective method for predicting real aircraft performance and present a cost-efficient and valid means for evaluating the flying abilities of pilot candidates in a work-sample context during flight training selection (Darr, 2009). However, administering simulators as a selection tool remains comparatively expensive and time-consuming. A test instructor who is familiar with the requirements is necessary to monitor and evaluate each candidate's performance during the mission tasks. The simulator hardware and test scenarios must be customized to the candidate's level of experience to ensure appropriate testing. Off-the-shelf test devices are not available (Gress & Willkomm, 1996). Thus, many civil aviation companies are disinclined to employ complex work sample tests, like low-fidelity flight simulators, and prefer using less costly computerized group tests (Hoermann, Stadler, & Wium, 2022). This raises the question of whether these tests are as effective in predicting flight training performance as basic flight simulators.

Methods

The Department of Aerospace Psychology utilizes a simplified flight simulator that has been suitable for ab initio pilot candidates without any previous flight experience for many years. It consists of an enclosed cabin that simulates a single-pilot cockpit, control instruments such as yoke, throttle, and stopwatch, and the instruments altimeter, gyrocompass, airspeed indicator, tachometer (RPM), vertical speed indicator, and artificial horizon. Figure 1 offers a visual representation of the simulator setup. The objective of the

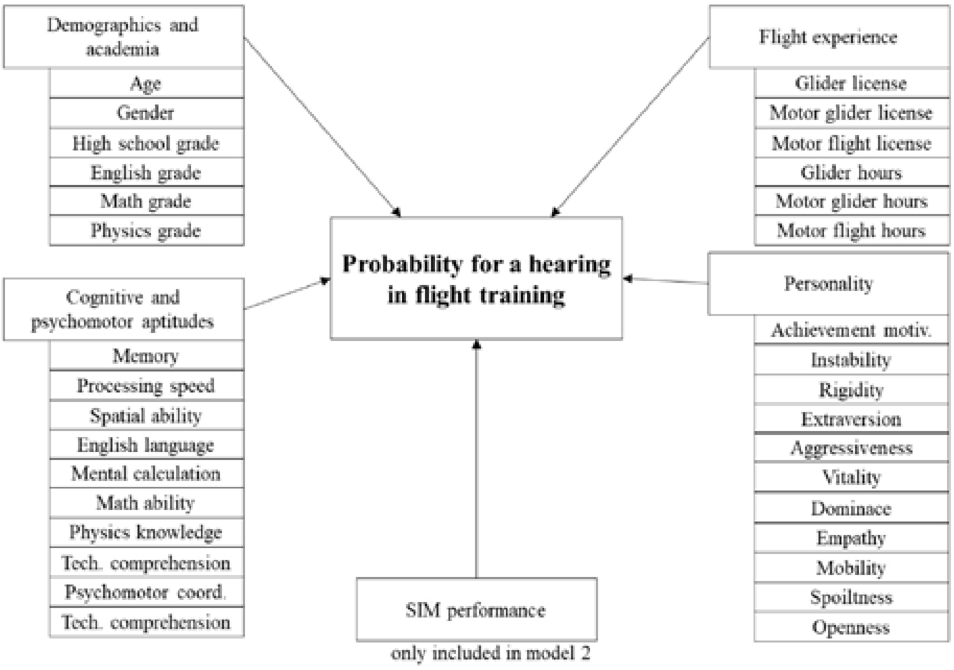

Fig. 2: Graphical representation of the two logistic regression models with all variables included.

test is to pilot an aircraft under instrument flight conditions by executing a predetermined sequence of maneuvers including level segments, standard turns, and climb/descent legs. In addition, candidates have to actively monitor their aircraft position, compute optimal headings and flight levels for upcoming segments, and provide standardized announcements of their next maneuvers. The test monitor evaluates performance on a standardized set of criteria using a scale ranging from 1 to 9.

Results

We used a sample of 1753 candidates who passed the selection procedure between 2006 and 2014. Of these, 218 (33 females, 185 males) were called to a hearing because of problems in their flight training. Based on this data, we computed two logistic regression models: 1) a model that predicted the likelihood of a hearing case considering demographic, personality, and cognitive testing data, and 2) the previously mentioned model with the addition of the SIM performance. Figure 2 displays all the predictive factors included in the models.

When comparing the two models, the likelihood ratio test indicated a significant gain in predictability by including the SIM performance ($\chi^2(1) = 4.45$; $p = .035$). According to the prediction, candidates who did not pass the SIM would, on average, have a 9.8% higher chance of receiving a hearing than those who passed.

Discussion

Despite conceptual similarity to other tests, most notably multiple task ability tests (Martinussen, 1996), basic simulators have incremental validity in predicting success in flight training compared to a cognitive and psychomotor test battery, personality scale and demographic data. Given the immense cost of training a student to obtain a commercial multi-pilot license, the use of basic flight simulators in the selection of pilots seems justified, even if less expensive multiple task ability tests are also part of the selection process. With higher predictive validity of selection tests, the number of training failures can be limited and training costs can be reduced.

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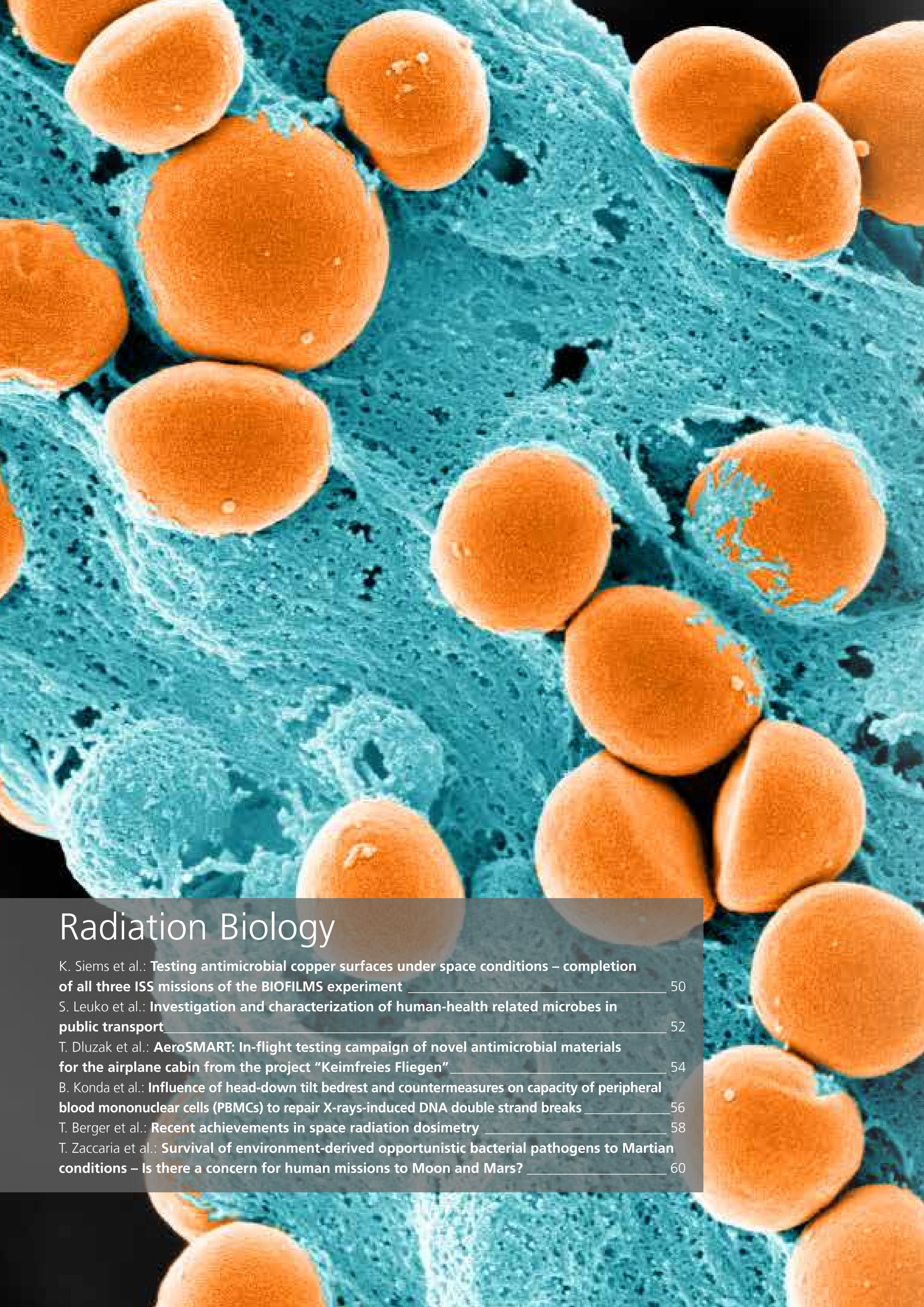

Radiation Biology

Radiation Biology

PD Dr. med. vet. Christine E. Hellweg (Head)

Dr. rer. nat. Petra Rettberg (Deputy)

The Radiation Biology department conducts biophysical and cell biological research to elucidate mechanisms of cell damage and repair following radiation exposure. The goal is to improve individual risk prediction for space missions, in aeronautics, and on Earth. Radiation exposure can initiate and promote carcinogenesis and cause cell death, cellular senescence, and genetic defects, or even acute radiation sickness. Therefore, cosmic radiation remains a major limiting factor for long-term space missions and an important occupational health issue at aviation altitudes.

Our findings are applied to improve radiation protection in aviation and spaceflight. Moreover, we closely collaborate with leading medical partners to translate our findings from space radiobiological research to advance the knowledge of aging-associated diseases and oncologic radiotherapy. Another focus of our department is microbiology which in addition to providing cell models for radiation biology research is applied to elucidate biotic and abiotic factors limiting microbiological life and adaptation to extreme conditions. We apply this knowledge to develop novel approaches to limit the spread of infectious agents, to investigate the human microbiome, and to support the search for extraterrestrial life and habitable environments on other celestial bodies.

Working Groups

Aerospace Microbiology (Prof. Dr. rer. nat. Ralf Möller)

- Radiation response of microorganisms
- Human microbiome research, biofilm formation, antimicrobial materials and decontamination approaches

Astrobiology (Dr. rer. nat. Petra Rettberg)

- Life in extreme environments and microbiome of confined habitats

Biodiagnostics (PD Dr. med. vet. Christine E. Hellweg)

- Molecular mechanisms of space radiation effects in CNS and other target organs, modifiers of radiation response and radiosensitivity

Biophysics (Dr. rer. nat. Thomas Berger)

- Space radiation dosimetry and modeling from ISS to Moon and Mars

Genome Maintenance Mechanisms in Health and Disease (Prof. Dr. rer. nat. Boris Pfander)

- DNA break repair and genome maintenance of eukaryotes
- Methodology development for quantification of DNA breaks and radiation damage

Team

Radiation Protection in Aviation (N. N.)

- Radiation effects in the atmosphere
- Development of products and services for the aviation industry and the society

Scanning electron microscope image of a biofilm formed by the human-associated bacterium Staphylococcus capitis
The image was taken as part of the BIOFILMS ISS experiment and has been artificially coloured to show the bacteria in orange and the matrix of the biofilm in blue.

Testing antimicrobial copper surfaces under space conditions – completion of all three ISS missions of the BIOFILMS experiment

Katharina Siems[1], Andrea Schröder[1], Erika Muratov[1], Stella Koch[1], Carolin Krämer[1], Yen-Tran Ly[1], Marta Cortesao[1], Katharina Runzheimer[1], Gudrun Holland[2], Michael Laue[2], the BIOFILMS research teams at ESA/NASA/Kayser Italia/BIOTESC, Ralf Moeller[1]

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Microorganisms are closely linked to the human body and, thus, automatically travel with astronauts on space missions is can jeopardize astronaut health and compromise structural integrity of the spacecraft. Especially biofilms, the most natural microbial lifestyle, are a particular problem. Biofilms are accumulations of microorganisms that envelop themselves in a slime layer which offers protection from external environmental influences. They are known to degrade equipment and can harbor pathogenic species. The presence of biofilms on the International Space Station (ISS) has been reported already [1] and there is a there is a presumption that space conditions might even promote biofilm formation [2].

Antimicrobial active metal surfaces such as copper can rapidly inactivate microorganisms and have shown promising results in clinical settings already, reducing microbial contamination and the spread of antibiotic-resistant microorganisms [3]. Applying such surfaces to spacecrafts may mitigate both astronaut health risks and equipment integrity issues. However, research is needed on the effect of antimicrobial surfaces in microgravity, which is why the BIOFILMS experiment was launched [4]. "BIOFILMS" stands for "Biofilm Inhibition on Flight equipment and on board the ISS using microbiologically Lethal Metal Surfaces". The experiment was accepted in an open call for experiments by ESA in 2014 and is an interdisciplinary microbiology (DLR) and material science (Saarland University) experiment. Ultimately, BIOFILMS comprised three consecutive flight missions to the ISS in 2021 (SpX-23), 2022 (SpX-25) and 2023 (SpX-27).

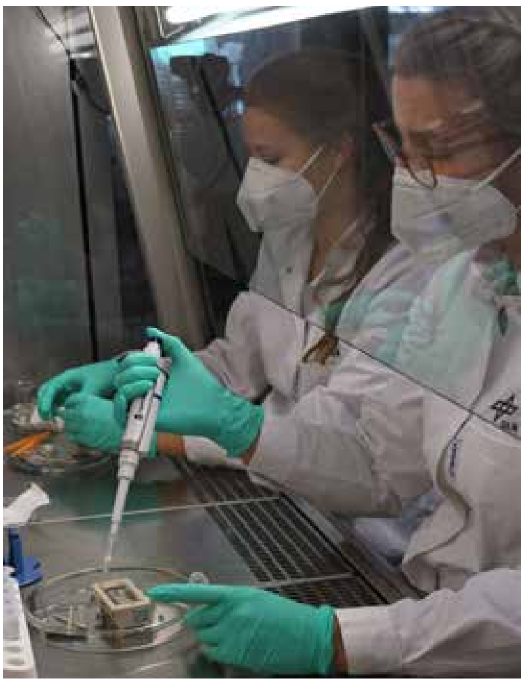

Fig. 1: Aerospace Microbiology Team during the disassembly of the experiment units from the second BIOFILMS mission. An experiment unit contained five metal surfaces (in the case shown in the picture, polished stainless steel). Before the surfaces can be removed, the liquid is pipetted off and transferred to reaction tubes for later analysis.

In BIOFILMS, the antimicrobial efficacy of functionalized copper-containing surfaces against three bacterial species was tested in different gravity conditions. The selected bacterial species (*Staphylococcus capitis*, *Acinetobacter radioresistens* and *Cupriavidus metallidurans*) were exposed to topographically functionalized metal surfaces in a specific experiment container (Figure 1). This container allowed automated activation and termination of the experiment as well as controlled incubation conditions with direct contact of bacteria and metal surface. The tested surfaces were copper and brass (antimicrobial) as well as stainless steel (control). The topography of the surfaces was modified by "Direct Laser Interference Patterning" using ultrashort laser pulses. With this method, interfering laser beams create as surface topography that can be adapted for particularly enhanced or reduced adhesion possibilities for bacteria. In BIOFILMS, grid topographies with a periodicity of 3 µm and 800 nm were tested with polished surfaces as control. All surface-types were tested with the bacterial species under microgravity (µg), 0.4 × g and 1 × g by using the Kubik facility in the Columbus Module (Figure 1).

Fig. 2: Samantha Cristoforetti integrating a BIOFILMS experiment container (blue) into Kubik. The outer positions in Kubik allow incubation in microgravity. In the position inside the rotor in the middle, centrifugation is used to set different gravitational conditions. BIOFILMS samples were incubated at 20 °C for 14 days at µg, 0.4 × g and 1 × g in cubes. Image copyright: ESA.

For all three BIOFILMS missions, the experiment containers were assembled in the DLR laboratories in Cologne due to the COVID-19 pandemic. Despite several challenges that came along with the remote preparation of the experiment, all three missions launched successfully to the ISS and were integrated into Kubik before the predefined "expiry date" of the bacterial suspensions. The astronauts who integrated the BIOFILMS experiment into Kubik were Thomas Pesquet, Samantha Cristoforetti (Figure 2) and Francisco Rubio. Since May 2023, all samples have been retrieved from the three BIOFILMS missions. Among other methods, scanning electron microscopy is used to examine the attached bacteria and the morphology of the biofilms. Initial results show the effectiveness of the topographically altered copper surfaces in microgravity (Figure 3), however, detailed post-flight analyses have not yet been fully completed. The results will provide insights into antimicrobial efficacy in reduced gravity and give an outlook on the possibility of the future use of antimicrobial surfaces in space travel.

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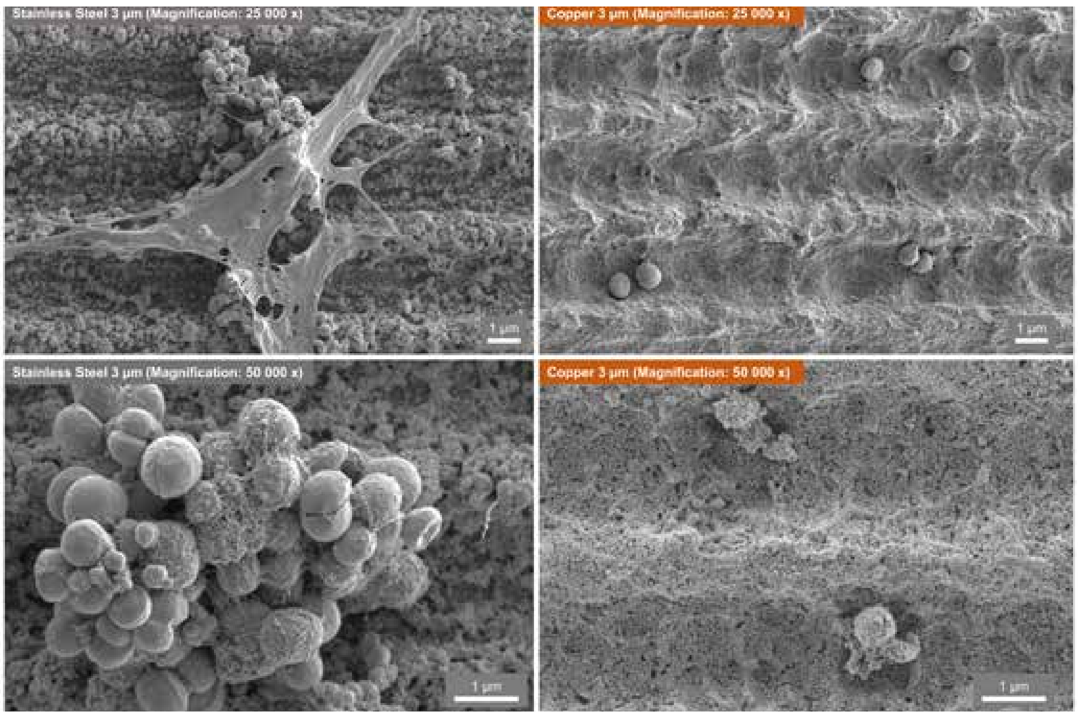

Fig. 3: Scanning electron microscopic images of microgravity samples of Staphylococcus capitis on stainless steel (left) and copper surfaces (right) with a 3 µm surface topography. On stainless steel, bacteria started forming small aggregates and production of biofilm matrix. On copper, only single cells, that were covered in particles and appeared damaged, were attached to surface.

Investigation and characterization of human-health related microbes in public transport

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Institute of Aerospace Medicine, German Aerospace Center (DLR), Cologne, Germany

Microorganisms are an essential part of the human body and our surroundings. Wherever we are or go, they accompany us. For the most part, microorganisms are beneficial and harmless to us. However, some fungal spores, bacteria, and viruses can be harmful to both sick and healthy passengers. Therefore, an evaluation of the microbial inventory in local and long-distance transport is necessary. In 2021, over 8,000 million individuals used public transportation in Germany (bus, tram, train) [1]. The COVID-19 outbreak has demonstrated that a virus can trigger a global pandemic at any time, and as a society, we need to be prepared for the possibility of another pandemic occurring at any moment.

As part of the DLR Research projects "VMo4Orte" and "RoSto", we are investigating the microbial inventory of the Regional Express (RE6) train from the company National Express. Every second month, samples are taken via swabs at 10 different spots in the train (Fig 1). During one campaign, a focus was put on the viable microbial cells at different sampling locations including the toilet. The analyzed samples from the commuter train showed a variety of environmental microorganisms, such as the most frequently isolated microorganism *Micrococcus luteus*. In addition, large amounts of microbes from the human microbiome were found, especially those found on the skin. These include numerous staphylococci such as *S. epidermidis* and *S. hominis*. Some microbes of the human gastrointestinal tract were also detected, such as *Enterobacter cloacae, Citrobacter freundii* and *Escherichia coli*. These occurred more frequently in the samples in the immediate vicinity of the toilet. Although most of the samples analyzed contained microorganisms from the environment or the human microbiome, there is still the possibility that these can cause disease in humans.

To monitor microbial diversity over a longer period of time and to gain further detailed insights, the samples were analyzed in detail using Next-Generation-Sequencing (NGS). For this purpose, 10 different locations on this train were sampled using swabs, the DNA was extracted using commercially available kits. The result is shown in Fig. 3. Using this method, it is possible to obtain a very detailed insight into

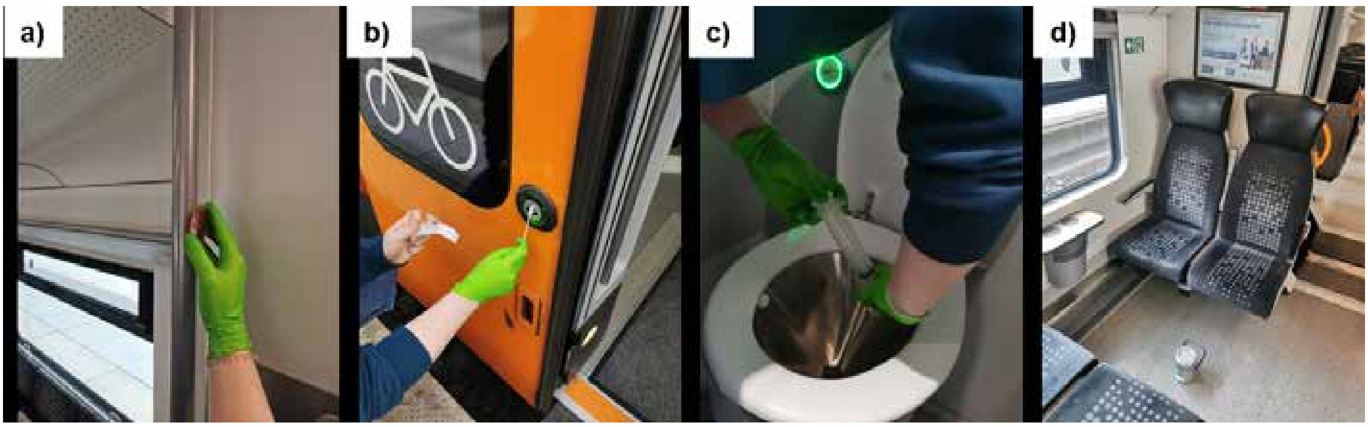

Fig 1. Photographs of the sampling in the local train RE6 on 28 March 2023. Picture a) shows the sampling by means of a blood agar contact plate on a stop bar, picture b) illustrates the sampling of the train door opener by means of a swab, picture c) shows the sampling of water from the train toilet, while picture d) shows the sampling of the air inside a seating group by means of the air sampler MAS-100 Eco.

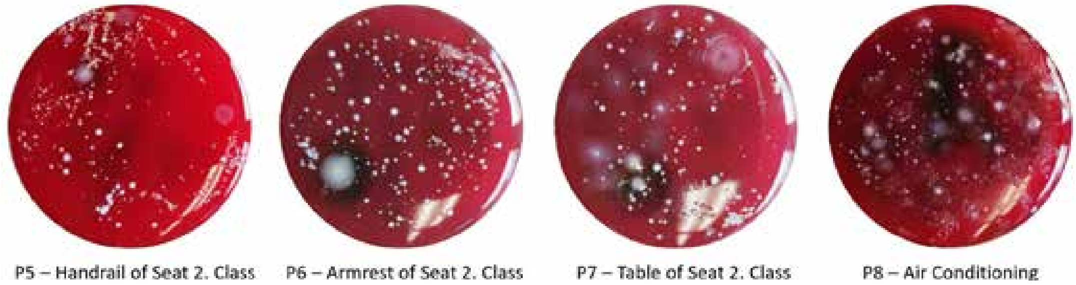

Fig. 2. Results of cultivation from different spots on the train

the microbial inventory. Similar to the cultivation methods, most of the organisms identified are human-associated such as *Staphylococcus* spp., *Cutibacterium* spp., and *Corynebacterium* spp. Environmental organisms such as *Deinococcus* spp. could also be detected. However, in contrast to the cultivation-based method, organisms that are present in smaller quantities and grow at different temperatures as well as nutrient conditions are also detected. It is also important to mention that this method cannot distinguish whether the microbes are still alive or not. Despite these limitations, a very precise insight into the microbial inventory is obtained and, if necessary, the number of bacteria can be reduced somewhat with the measures described below.

The knowledge and techniques gained from research into microbial contamination in local transport provide a basis for transfer to other types of transport (e.g. long-distance transport). They not only contribute to current safety, but can also help to better manage future pandemics. Continuous monitoring of the germ load enables those responsible to act at an early stage, interrupt chains of infection and minimize the spread of pathogens. Ultimately, it is crucial that these efforts lead to a broader understanding of microbial ecology in different environments. This will not only allow us to better respond to potential health risks, but also to develop long-term strategies to protect public health and population mobility.

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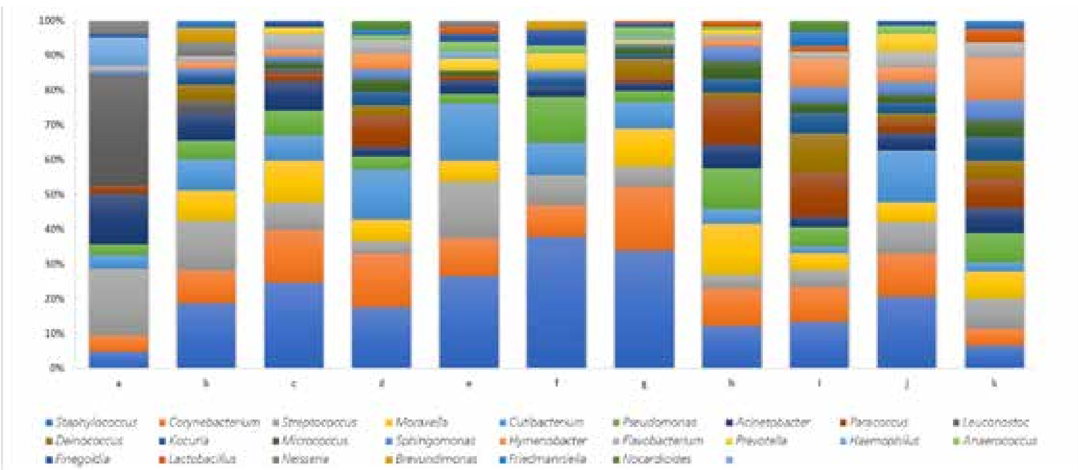

Fig. 3: The 25 most commonly found bacterial genera in commuter trains. a) 1st class table, b) 2nd class table, c) 2nd class armrest, d) 2nd class headrest, e) inner door knob, f) outer door knob, g) 2nd class orange handles, h) air vents, i) 1st class bottom handle, j) door handle bar, k) air sampler.

AeroSMART: In-Flight Testing Campaign of novel antimicrobial materials for the airplane cabin from the project "Keimfreies Fliegen"

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Fig. 1: Logos of the Aerospace Microbiology projects "Keimfreies Fliegen" and "AeroSMART".

In the interconnected world we live in, public transportation has become increasingly indispensable. Even during episodes of public lockdown in Germany within the year 2021, around 3.5 million journeys were taken with German public transportation only between January and June 2021 according to the Federal Statistical Office (Destatis). As a passenger taking a journey on a public transport, one finds herself/himself in a confined space with regularly high passenger densities. Throughout the year we face the seasonal upcoming of diseases like influenza and now also SARS-CoV-2. Especially places like airplane cabins can then pose an elevated risk for not only the rapid spread but the transmission over long distances of potentially harmful microbes. Particularly during long-haul flights, conditions can be very favorable and conducive to microbe transmission.

With increased awareness of health following the COVID-19 pandemic, global society as well as industry is more conscious of potential infection risks when using public transportation. It is, therefore, in the interest of public health to take sustainable measures in order to mitigate the spread of human pathogens in airplane cabins in the future. When thinking about long-term preventive means to effectively avoid the risk of an infection occurring while flying within an airplane cabin, the integration of antimicrobial materials in key-areas and frequently touched surfaces within the environment of new cabin designs is a highly relevant research objective. The main advantage of applying antimicrobial materials is, that we could decrease the immediate need of manual disinfection and could still guarantee a safe microbial hygiene over the term of a flight.

In our research on "Keimfreies Fliegen" we tested the efficiency of already available "off-the shelf" antimicrobial materials but mainly developed completely novel light – weight functional materials with antimicrobial properties (Institute of Lightweight Systems (SY)). Generally, any antimicrobial material on the market is commonly coated or enriched with compounds that have antimicrobial properties e.g. copper, silver or zinc. As we know of the effectiveness of those metals, the materials scientists (SY) developed fully functional

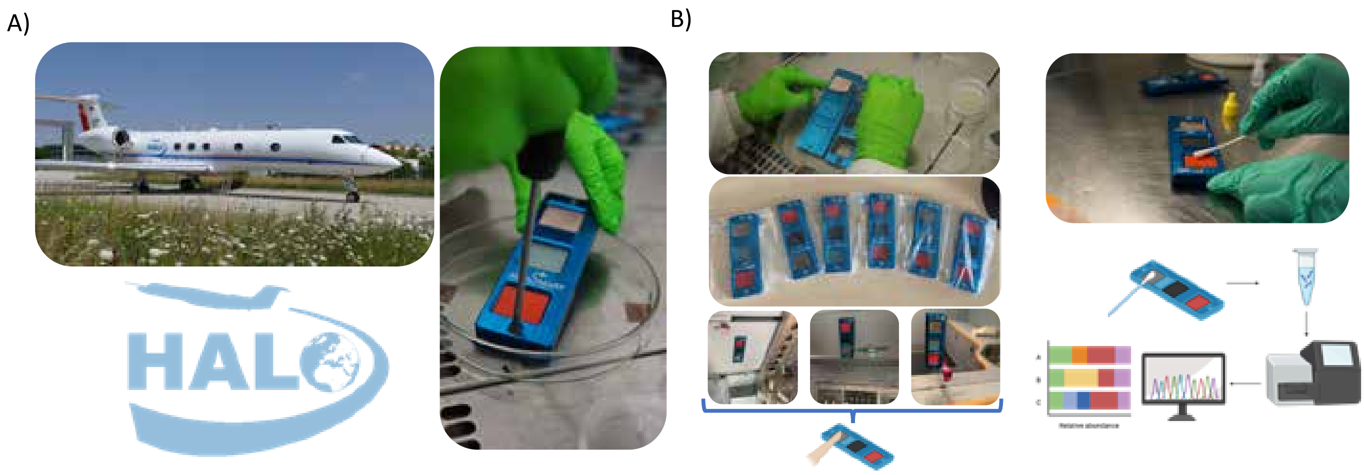

Fig. 2: A) Hardware assembly and microbial analysis of AeroSMART Touch Arrays - a device that allows to test microbial deposition in different selected materials in real airplane cabin conditions. First In-Flight Campaign in cooperation with DLR Flight Experiments in the HALO aircraft. B) Exposition of Hardware In-Flight during the recent HALO campaign. The microbial follow – up analysis is based DNA isolation and 16S sequencing. The data is then bioinformatically processed.

multi-composite materials that are either 3D printed, manufactured in a "Resin Transfer Mould" process (RTM) or in an "Additive Layer Manufacturing (ALM)". Additionally, sustainable materials with industrial waste products (e.g. carbon black) or natural polymers like chitosan were developed and tested for antimicrobial activity.
In contact-killing experiments with Phi 6 phages, SARS-CoV-2 and Monkeypox virus, the materials are tested for their antimicrobial effectiveness after different contact times.
In collaboration with the DLR's flight squadron several materials were installed in a sled – developed hardware (AeroSMART) and mounted within different locations in the HALO aircraft for a long-term exposure over 1 month. The surfaces were touched and all touch events were counted. The subsequent analysis will be 16S sequencing to determine the microbial load on the surfaces qualitatively and quantitatively. Another post-exposure aspect is the resilience of the materials, which will be analyzed through imaging techniques such as scanning electron microscopy (SEM).
It is expected that the microbial diversity in the aircraft cabin will resemble the microbiome of other means of public transportation, such as buses or trains, consisting primarily of skin microbiome microbes. Moreover, the tested surfaces are expected to reduce microbial contamination in aircraft cabins and can potentially decrease the risk of infection during flights. The cost and energy efficiency of these materials make their integration into aircraft surfaces realistic, providing a means to control microbial contamination in aviation in the future.

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Influence of head-down tilt bedrest and countermeasures on capacity of peripheral blood mononuclear cells (PBMCs) to repair X-rays-induced DNA double strand breaks

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Introduction

Major limiting factors in human spaceflight are deleterious effects of reduced gravity and of space radiation exposure on health and performance. Radiation-induced cellular DNA damage, if not repaired or not correctly repaired, increases the risk of cancer and degenerative diseases. Likewise, reduced gravity may lead to musculoskeletal and cardiovascular deconditioning without appropriate countermeasures. We hypothesize that deconditioning could possibly hinder the recovery of cells from radiation damage. We aimed to develop a terrestrial *ex vivo* model to investigate cellular DNA repair while simulating microgravity effects using head-down-tilt (HDT) bedrest during the Spaceflight-Associated Neuro-Ocular Syndrome Countermeasures (SANS-CM) studies.

Methods

The SANS CM campaigns comprised three experimental phases: 1) a 14-days baseline data collection (BDC) phase (BDC-14 through BDC-1); 2) 30 days of 6° HDT bedrest phase (HDT1 through HDT30); and 3) a 14-days recovery (R+) phase (R+0 through R+13). Twelve participants enrolled in each campaign were healthy non-smoking men and women of 24-55 years with body height of 153-190 cm and body mass index of 19-30 kg/m^2. In the study, the countermeasure applied was either lower body negative pressure (LBNP) or upright sitting, both 2 x 3 h per day. Blood samples were obtained from the subjects 14 days before the bedrest (BDC-14), 10 and 28 days into head-down tilt bedrest (HDT-10 and HDT-28) and after 10 days of recovery (R+10). Peripheral blood mononuclear cells (PBMC) from the venous blood were isolated by density gradient centrifugation using Greiner Leucosep™ tubes. We studied the ex vivo induction and repair of DNA double strand breaks, for which the cells were exposed to 1 and 4 Gy of X-rays and harvested after 0.5, 1, 2, 4 and 24 h after irradiation. DNA double strand breaks were detected via immunofluorescence staining of γH2AX that was quantified using flow cytometry.

Results

We successfully established an ex-vivo model to study DNA damage induction and repair in human cells. γH2AX fluorescence intensity indicating DNA double strand breaks induced by X-rays reached a peak value after 2 h of X-rays irradiation (Fig. 1). The peak increased dose-dependently. γH2AX fluorescence reached baseline levels after 24 h in cells exposed to 1 Gy X-rays, and it was slightly above the baseline in cells irradiated with 4 Gy X-rays indicating incomplete repair after 24 h. For all blood collection time-points during the study, BDC-14, HDT-10, HDT-28 and R+10, the γH2AX fluorescence intensity did not differ significantly. Also, there was no significant difference between the two countermeasure groups, LBNP (n=12) and upright sitting (n=12). Furthermore, there was no significant interpersonal variance of DNA double strand break repair capacity.

Conclusion

DNA double strand break repair activity in PBMC remained unaffected by one month of HDT bedrest combined with the countermeasures LBNP or upright sitting, suggesting that the physical deconditioning does not modulate DNA repair capacity in case that daily countermeasures are applied.

Acknowledgement

The study was funded by the National Aeronautics and Space Administration (NASA) and the German Aerospace Center, and performed at the :envihab research facility of the DLR Institute of Aerospace Medicine. The authors wish to gratefully acknowledge the bedrest participants who volunteered their time, without whom this project would not have been possible. We also thank the SANS CM study staff for their dedicated work and tireless effort.

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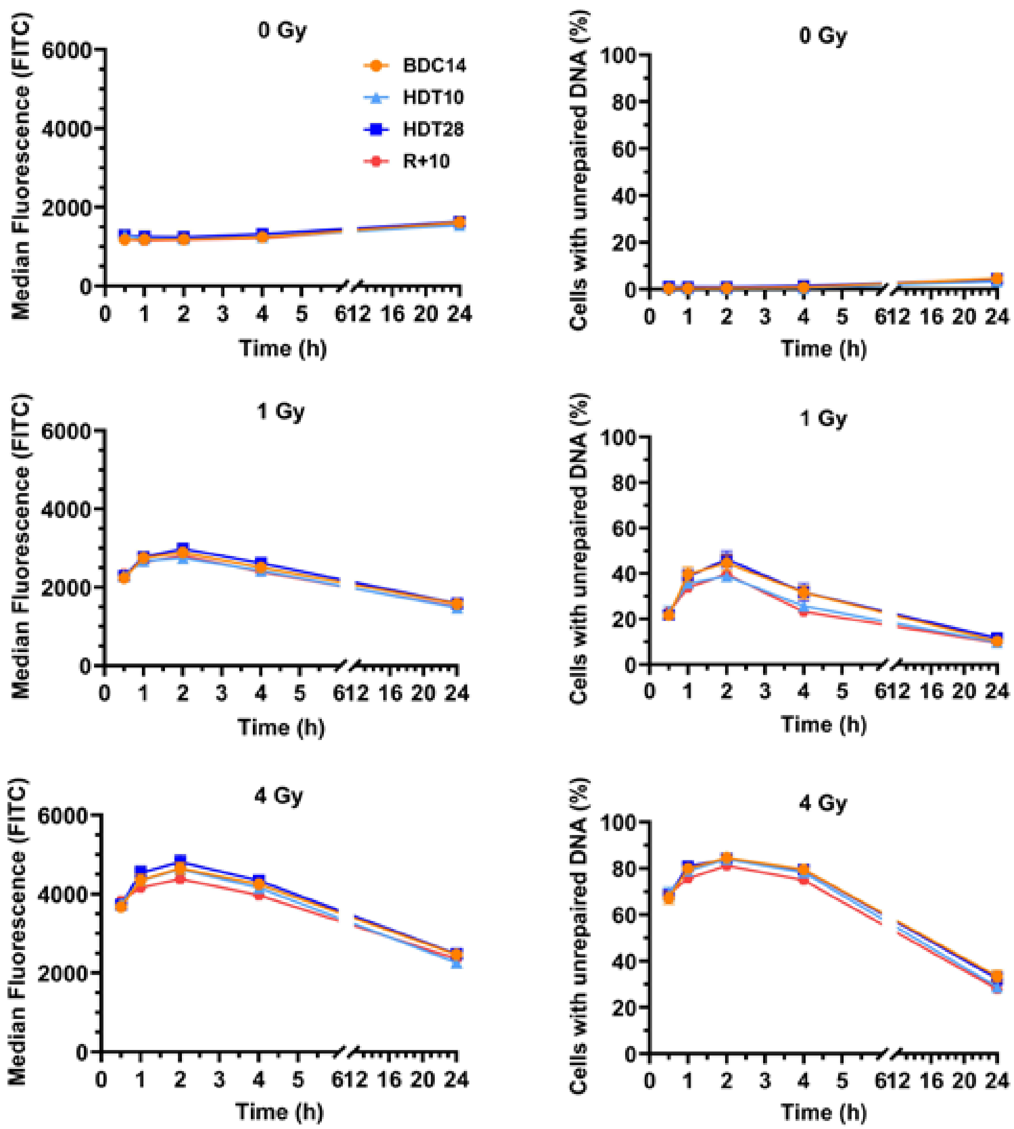

Fig 1: DNA repair kinetics in PBMCs from subjects of the SANS-CM 1&2 studies. PBMCs from the subjects (n=24) were isolated at different phases of study (BDC14, HDT10, HDT28 and R+10), exposed to 1 and 4 Gy of X-rays and incubated at 37 °C for 0.5, 1, 2, 4 and 24 h to allow DNA repair. The graphs in column A provide the median fluorescence intensity of the γH2AX signal which correlates to X-rays-induced DNA double strand breaks. Column B gives the information on the percentage of cells with unrepaired DNA damage for the different repair times.

Recent achievements in space radiation dosimetry

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Space radiation dosimetry and the measurement of the space radiation environment as for example on-board the International Space Station (ISS) as well as on satellite missions and in preparation for human exploration missions Beyond Low Earth Orbit (LEO) is one of the main topics of the Biophysics Group in the Radiation Biology Department. In the last years various experiments have been performed to gain a better understanding of the changes in the radiation environment on the ISS, on the DLR Eu:CROPIS satellite, on the DLR MAPHEUS missions, on NASA balloon experiments as well as and especially during the NASA Artemis I mission to the Moon and back.

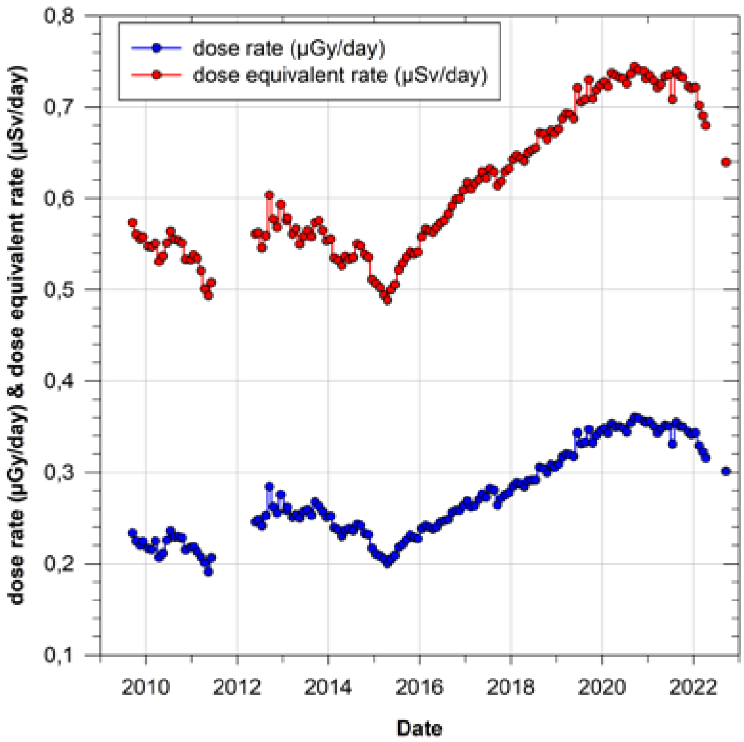

Fig. 1. The absorbed dose (µGy/day) and the dose equivalent (µSv/day) as measured with the DOSTEL-2 instrument inside the Columbus Laboratory of the ISS from mid of 2009 to end of 2022.

On-board the ISS and here especially inside the European Columbus Laboratory data has been generated already from mid of 2009 onwards to determine the radiation dose levels with active (DOSTEL) and passive radiation detectors in the frame of the DOSIS and sub-sequent DOSIS 3D experiment. Highlighted data for the long-term measurement of the radiation environment with the DOSTEL instrument, in cooperation with CAU, Kiel is provided in Figure 1. Figure 1 shows the long-term variation of the absorbed dose rate (µGy/day) as well as the biological relevant dose equivalent rate (µSv/day) starting in mid of 2009 (in solar minimum) extending this data over the following solar maximum (2014-15) going to the next solar minimum in 2020 and again measuring the declining phase due to the increase in solar modulation from 2021 onwards, thereby covering more than one solar cycle of data [1].

In addition to the data generated within DOSIS 3D in Columbus work was performed for the development of a DLR in-house built radiation detector system the DLR M-42 detector family [2]. Not only were the DLR M-42 detectors flown as part of the MARE experiment on the NASA Artemis I mission in late 2022 – to the Moon and back – it was also possible within DLR internal cooperation's to launch the M-42 system on up to now five MAPHEUS missions to free space. In a joint effort with TUM, Munich, Germany one M-42 instrument is flying, as the DLR radiation sensor, as part of the RadMap instrument since April 2023 on-board the ISS [3]. One goal of this experiment will be the mapping of the changes of the radiation environment in dependence on the location of the instrument. As an example, Figure 2 shows the count rate profile measured with the RadMap M-42 system in the Japanese JEM Module of the ISS for a duration of two days clearly showing the nominal variation of galactic cosmic radiation

(GCR) and the passing's of the Earth Van Allen radiation belts. Further mapping was and is currently performed in NODE 3 and the US-LAB and from 2024 onwards the Columbus Laboratory of the ISS. This will offer a perfect opportunity to compare the DOSTEL instruments from DOSIS 3D with the RadMap instrument data.

Still ongoing – and now we are leaving the ISS and going to higher orbits is the data generation with the DLR RAMIS instrument as flying on the DLR Eu:CROPIS satellite. RAMIS started its mission in December 2018 and will soon have five full years of data in a polar orbit. This enables especially now during the increasing solar activity the possibility to measure Solar Particle Events (SPEs) with RAMIS, since the detector is sitting behind very low shielding and the satellite covers orbits up to 83° latitude. One highlight over the last years was the measurement of the SPE in late October 2021. Figure 3 provides for this event the count rates (cts/sec/cm²) as well as the absorbed dose rates (µGy/day) for polar orbits as seen by RAMIS. This was also the first SPE which was measured on Earth and on the lunar as well as the Martian surface [4], making it a really special event in space radiation dosimetry.

This was just a short snapshot of radiation dosimetry data gathered within the current cooperation's and experiments as performed by the Biophysics Group at DLR. Further data evaluation especially for the NASA Artemis I mission and new developments in terms of radiation detectors are on their way.

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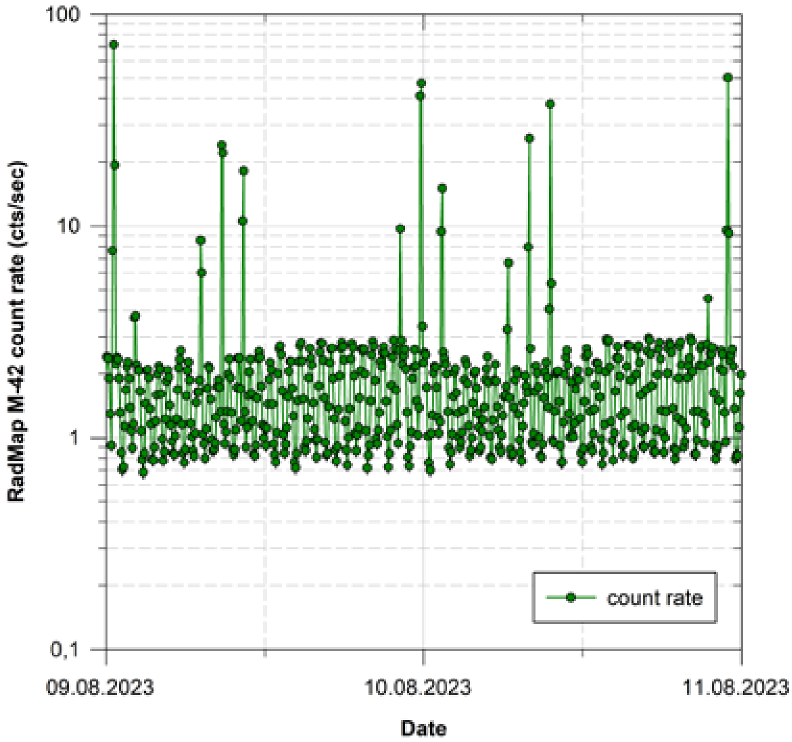

Fig. 2. The count rates (cts/sec) as measured with the RadMap DLR M-42 instrument inside the Japanese JEM module of the ISS for two days in August 2023

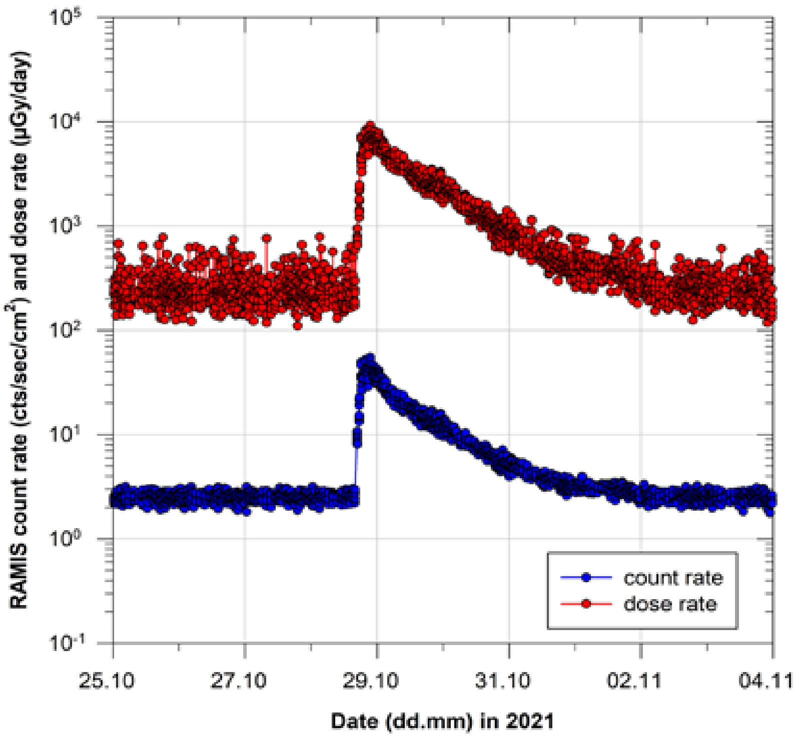

Fig. 3. The Solar Particle Event in late October 2021 as measured over the Earth North and South Pole with the RAMIS instrument on the DLR Eu:CROPIS satellite.

Survival of environment-derived opportunistic bacterial pathogens to Martian conditions – Is there a concern for human missions to Moon and Mars?

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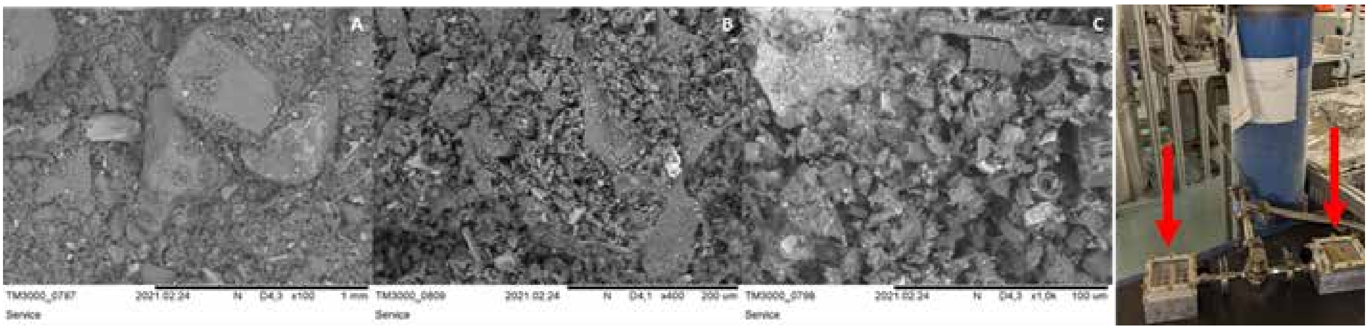

Fig. 1. Scanning electron microscopy (SEM) pictures of MGS-1 at x100 (A), x400 (B) and x1000 (C) magnification and experimental set up of the exposure of the bacteria to Mars atmosphere and pressure in the TREX-boxes (red arrows).

Background

The health of astronauts during space travel to new celestial bodies in the solar system, is a critical factor in the planning of a mission. Despite cleaning and decontamination protocols, bacteria and fungi from Earth have been and will be identified on spacecraft especially when human travelers will be involved. This raises concerns for both human safety and for planetary protection. Bacteria and fungi which have been isolated on the ISS and other spacecraft not only include environmental isolates but human pathogens as well. Many of which make up the human microbiome and therefore will be travelling with astronauts during space travel. Due to the presence of these potentially dangerous microorganisms, in this study we therefore decided to examine the tolerance of clinically relevant non-fastidious bacterial species (*Burkholderia cepacia, Klebsiella pneumoniae, Pseudomonas aeruginosa and Serratia marcescens*) to simulated Martian conditions. We were able to show how these remarkable species are able to grow in minimal media with only one carbon source, gluconic acid – a carbon source which was also identified in carbonaceous meteorites which have arrived on Earth and which is presumably also present on Mars.

Materials and Methods

Our research evaluated the survival of the four bacteria to Mars like conditions including exposure to perchlorates (NaClO4), desiccating conditions, UV radiation, growth with Mars regolith simulant (MGS-11) and exposure to Martian atmospheric composition and pressure (Figure 1).

Results

Our initial hypothesis was that the Mars regolith simulant, MGS-1, would be toxic to the bacteria. However, when we conducted our experiments, we saw that this was not the case and instead the Martian soil simulant stimulated the growth of the bacteria. Furthermore, it was thought that the bacteria grown minimal media, would not tolerate a great deal of Mars-like conditions. Yet, all the species showed a tolerance to desiccation on glass disks, to UV-C (254 nm at a maximum fluence of 250 J/m^2) and polychromatic UV radiation (200-400 nm at a maximum fluence of 1200 J/m^2) as well as exposure to desiccation combined with Mars atmosphere and pressure of 6 hPa (Figure 2).

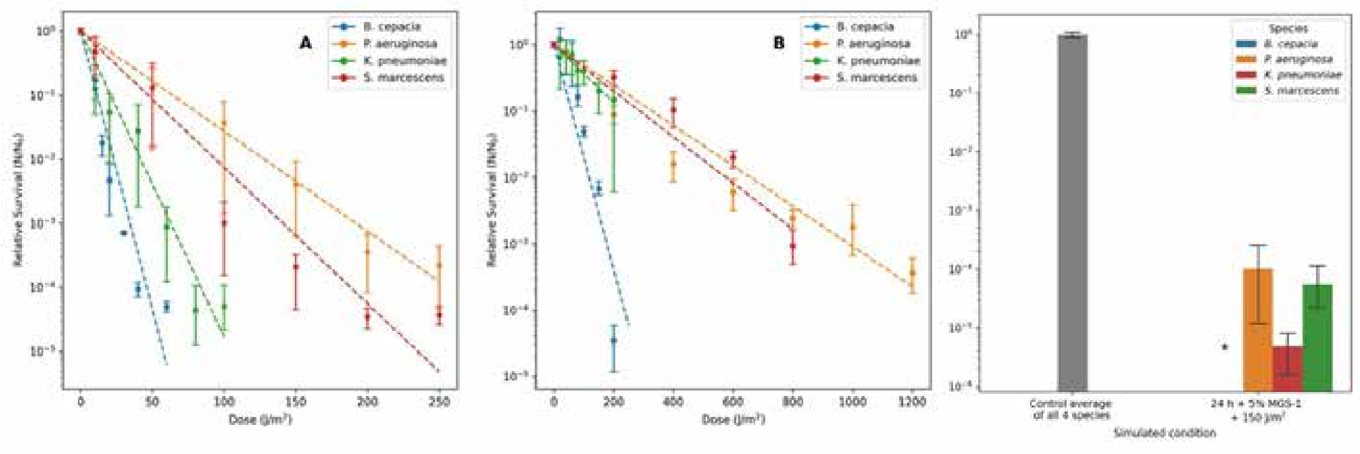

Fig. 2. Relative survival of the bacteria exposed to UV-C (254 nm) (A), polychromatic (200-400 nm) Mars-like (B) UV radiation and bacteria grown with MGS-1 exposed to desiccation, polychromatic UV radiation and Mars atmosphere and pressure for 24 hours (C). All the bacterial species were able to survive these combined conditions with the exception of B. cepacia (*).

Outlook

Our results show that the selected bacterial species are able to survive to an extent to Mars simulated conditions. These results coupled to the vast quantity of research which identified bacteria and fungi on and in spacecraft make human health a priority for long-term space missions. Furthermore, the fact that the regolith simulants supports rather than impedes bacteria growth, the spread of bacterial contamination must be avoided when travelling to sites of interest. Additionally, the toxic effects of the regolith when breathed in, as reported by Apollo astronauts Figure 3, will make hardware challenging to use on the surface of the Moon and Mars.

Conclusion

Identifying the limits of survival of human pathogens to Mars-like conditions is an important step to understand the health threats astronauts could face during a space mission. The ability of the bacteria to grow in minimal media makes them a concern not only for human health but also for planetary protection. The increase in survival provided by MGS-1 under all simulated conditions further highlights the importance of the study. Certainly, further research into the mechanisms of survival of the species is warranted. In addition, the identification of survival mechanisms could support the targeted development of drugs for use on Mars, where a limited amount of supplies can be taken.

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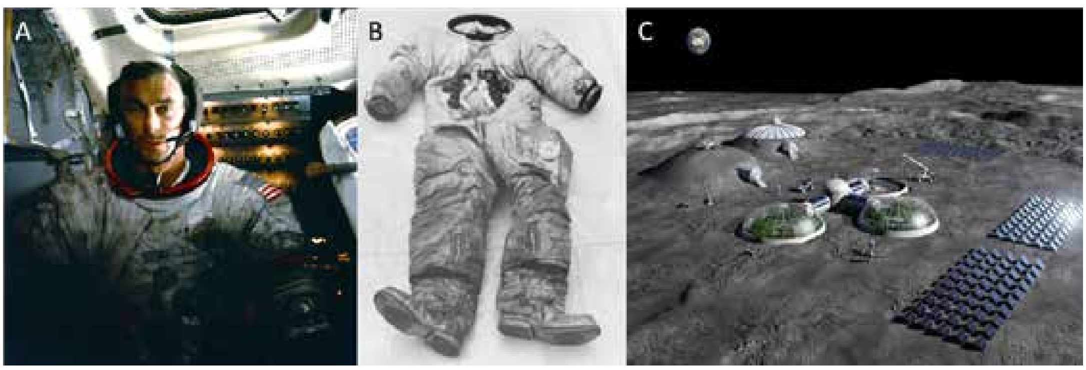
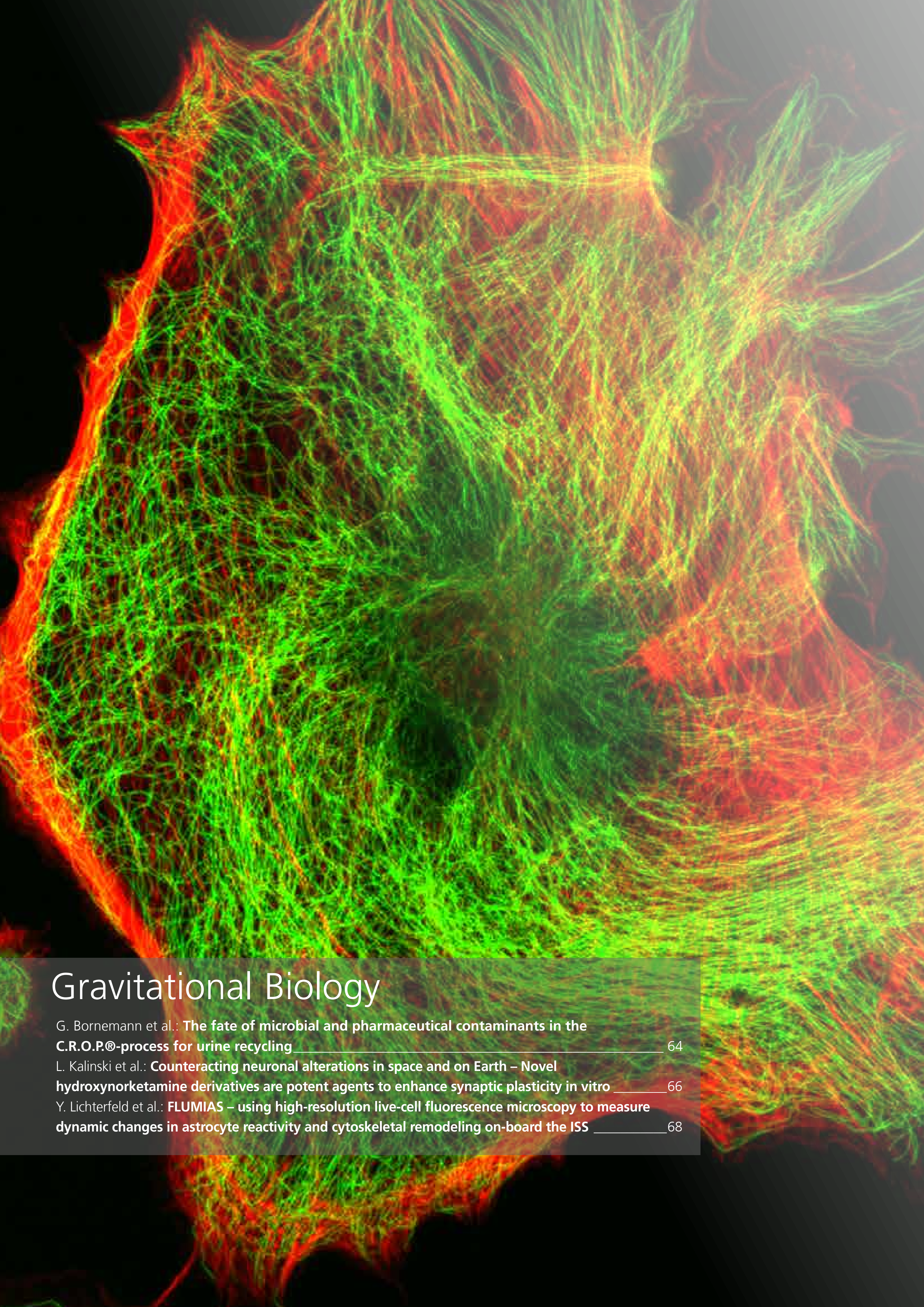


Fig. 3. (A) Apollo 17 mission commander Gene Cernan inside the lunar module on the Moon after his second moonwalk of the mission on 12/12/19723. (B) Spacesuit worn by Alan Bean on the surface of the Moon during Apollo 124. (C) Artist impression of a Moon Base concept5.



Gravitational Biology

Gravitational Biology

PD Dr. rer. nat. Ruth Hemmersbach (Head)

Dr. rer. nat. Christian Liemersdorf (Deputy)

Life evolved in terrestrial gravity, which is the only environmental factor that has remained constant for billions of years. The lack of gravity during space travel poses health challenges to astronauts while providing unique insight in the fundamental mechanisms of gravity and mechano-sensing. Indeed, biological systems perceive gravity directly and indirectly through mechanosensitive structures and pathways. The main scope of the Gravitational Biology Department is to better understand the impact of gravity on biological systems. Moreover, we assess implications of altered gravity on technology development.

Our goal is to elucidate molecular mechanisms of gravity perception and resulting biological responses ranging from single cells to human beings. We apply the acquired mechanistic knowledge to develop and refine countermeasures for space travel. Moreover, we translate findings on cellular mechano-sensing to terrestrial medicine in collaboration with medical departments in the Institute and elsewhere.

Another main focus is to improve closed biological life-support systems, which are a prerequisite for long-term human space missions. With our innovative DLR C.R.O.P.® (Combined Regenerative Organic food Production) technology we aim at optimizing waste recycling for food production. The technology is applicable for stations on Moon and Mars, but also for sustainable agricultural systems on Earth. Our Gravitational Biology research builds the basis for long-term human space exploration, guides human health research, and contributes to sustainable economic development on Earth.

Working Groups

Bioregeneration (Dr. rer. nat. Jens Hauslage)

- Analysis of biogenic waste degradation by microbial trickle filters, optimization of the filters to generate maximal efficiency in producing plant nutrients
- Conversion of the laboratory set-up to applications in space and on Earth with the goal to reclaim water while generating fertilizers for space travel and terrestrial agriculture (urine, slurry)

Cellular and Molecular Neuromuscular Research (Prof. Dr. med. Christoph Clemen)

- Biochemistry, genetically modified cells and organisms, cellular and animal studies
- Identification of gravity-sensitive responses of individual cell types that model various behavioral and physiological deconditioning phenotypes in humans with the focus on neurons, astroglia and skeletal muscle cells
- Verification of ground-based studies under hypergravity/simulated microgravity conditions in real microgravity using various platforms including DLR Mapheus sounding rockets, drop-tower, parabolic aircraft flights, and the Biolab-device on the ISS

Fluorescence microscope image of mouse astrocytes
Mouse astrocytes in a fluorescence microscope image: Tubulin is stained in the green channel, F-actin in the red channel.

The fate of microbial and pharmaceutical contaminants in the C.R.O.P.®-process for urine recycling

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Background

Urine recycling for fertilizer production is a key technology for closed-loop food production during long-term missions on and to moon or Mars. Although only few pathogens are excreted via urine, there is a risk of cross contamination with feces. In addition, when astronauts take medication, most of the un- or partially metabolized residues of the active ingredients are excreted in the urine. We examined the fate of these contaminants in the C.R.O.P.® laboratory.

Methods

We fed four C.R.O.P.® standard filters (trickling filters with 28 L tank and 6 L lava rock as growth media for nitrifying biofilm, figure 1) with human urine from a urological practice for 12 weeks. We sampled urine and treated urine solution in the filter tanks weekly and tested for pathogens and drug residues. For pathogen determination, we applied MALDI-TOF-MS (Biotyper® database) and quantified drug residues according to Gurke et al. (2015).

Fig.1: The four C.R.O.P.®-biofilters used in the experiment. The tubes contain lava rock as growth media. The grey tanks contain the urine solution. A pump circulates the solution continuously through the tubes thus bringing it repeatedly in contact with the biofilm in which nitrifying bacteria produce nitrate from the nitrogen compounds contained in the urine.

Results and Discussion

Table 1 shows that 16 species found in the urine fertilizer solution belong to risk group 2 and are considered facultative pathogens. Not all of these species could also be found in urine. Many are mainly found in soil and their presence in the filter can be explained by the fact that the filters were inoculated with garden soil when started. Urinating into a sample container is most comparable to using a urinal. The occurrence of species of human intestinal flora in the urine shows that cross-contamination takes place even if the urine is collected without contact with a toilet bowl.
A large number of drugs in the urine from the urological practice. These were partly degraded in the biological filters. Figure 2 shows as an example the content of Candesartan and Torasemid in the urine fertilizer solution Drug concentrations in the urine varied greatly. Accordingly, there was no uniform increase in drug concentrations in the urine solution. This is reflected in both, the curve of the estimated values and the curve of the measured values. The measured values of Candesartan concentrations were below the estimated concentration indicating that a partial degradation occurred in the filters. However, the experimental set-up does not allow a clear conclusion on a microbial degradation. It is also possible that the drug adsorbed to the growth media and was thus removed from the solution. Torasemid concentrations were not significantly reduced by the filters. In some samples, the measured concentration was even above the calculated expected value. This could have been caused by measurement inaccuracies or redissolution processes.

Species	In urine	In urine fertilizer	Species	In urine	In urine fertilizer
Achromobacter piechaudii		yes	*Lactococcus garvieae*	yes	
Achromobacter spanius		yes	*Lysinibacillus fusiformis*		yes
Alcaligenes faecalis		yes	*Lysinibacillus sphaericus*		yes
Bacillus licheniformis		yes	*Microbacterium esteraromaticum*		yes
Bacillus pumilus		yes	*Microbacterium paraoxydans*		yes
Bacillus thuringiensis		yes	*Morganella morganii*	yes	yes
Castellaniella defragrans		yes	*Proteus hauseri*	yes	
Citrobacter braakii		yes	*Proteus mirabilis*	yes	
Citrobacter freundii	yes	yes	*Proteus vulgaris*	yes	
Citrobacter youngae		yes	*Providencia rettgeri*		yes
Enterobacter cloacae		yes	*Pseudomonas aeruginosa*		yes
Enterococcus avium		yes	*Pseudomonas putida*		yes
Enterococcus devriesei	yes		*Raoultella terrigena*	yes	
Enterococcus faecalis	yes	yes	*Serratia marcescens*	yes	yes
Enterococcus faecium	yes		*Solibacillus silvestris*		yes
Escherichia coli	yes	yes	*Sphingobacterium mizutaii*		yes
Glutamicibacter creatinolyticus		yes	*Stenotrophomonas maltophilia*		yes
Glutamicibacter protoformiae		yes	*Streptococcus agalactiae*	yes	
Klebsiella aerogenes	yes	yes	*Streptococcus pneumoniae*	yes	
Klebsiella oxytoca	yes	yes	*Vagococcus fluvialis*	yes	
Klebsiella pneumoniae	yes				

Tab. 1: Bacteria species identified in the urine from the urological practice and in the urine fertilizer solution produced from it by the biological urine recycling plants. Species belonging to risk group 2 (TRBA 466) are highlighted in grey.

Conclusion

The important finding of our study is that the biological urine recycling process does not sufficiently remove potential pathogens or drug residues to provide a safe fertilizer. Additional process steps are likely required downstream to guarantee microbial and pharmacological decontamination.

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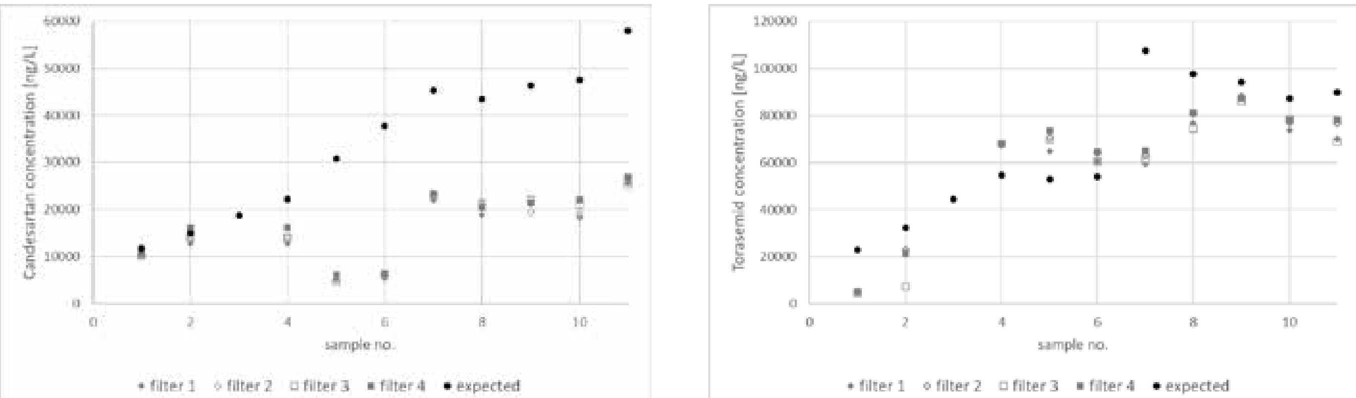

Fig. 2: Expected Candesartan (A) and Torasemid (B) concentrations in the filter tank calculated using the drug concentrations measured in the urine and the corresponding concentrations measured in the urine fertilizer solution produced by the biological urine recycling plants.

Counteracting neuronal alterations in space and on Earth – novel hydroxynorketamine derivatives are potent agents to enhance synaptic plasticity *in vitro*

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Space conditions impact neuronal structure and function, thus, providing a rational for development of neuroprotective agents for future manned space missions. Loss of synaptic plasticity in the brain has been linked to cognitive deficits, thus providing a promising target for therapeutic interventions (review: Fiala et al., 2002). Ketamine, a drug applied in treatment-resistant depression, rapidly induces synaptic plasticity via a BDNF-dependent mechanism. Nonetheless, ketamine features substantial side-effects due to its NMDA receptor interaction. Recently, ketamine´s most relevant metabolite, hydroxynorketamine (HNK), has been attributed a similar stimulating effect on synaptic plasticity, while its weak affinity to NMDA receptors leads to a mitigation of the psychotropic side effects. Aiming to utilize this enhancing effect of HNK on synaptic plasticity as a potential neuroprotective agent for astronauts and patients on Earth, novel HNK derivatives were synthesized. These derivatives were investigated for their use as preventative agents or neuro-stimulants while omitting psychotropic side-effects.

We applied ketamine, HNK and 19 different newly synthesized HNK derivatives at a broad range of concentrations (0.1-100 µM) and incubation durations (1h-72h) to primary hippocampal neurons in vitro. Evaluation of pre-synapse counts by VAMP2 immunostaining revealed that several candidate compounds enhanced synaptic plasticity in a concentration-dependent manner after incubation of 48h. HW-774 stood out as the best candidate compound with the highest stimulatory effect at the lowest dose (50x more potent than standard ketamine, Figure 1).

Enhancement of synaptic plasticity was further verified by STED (Stimulated Emission Depletion) super-resolution imaging of HW-

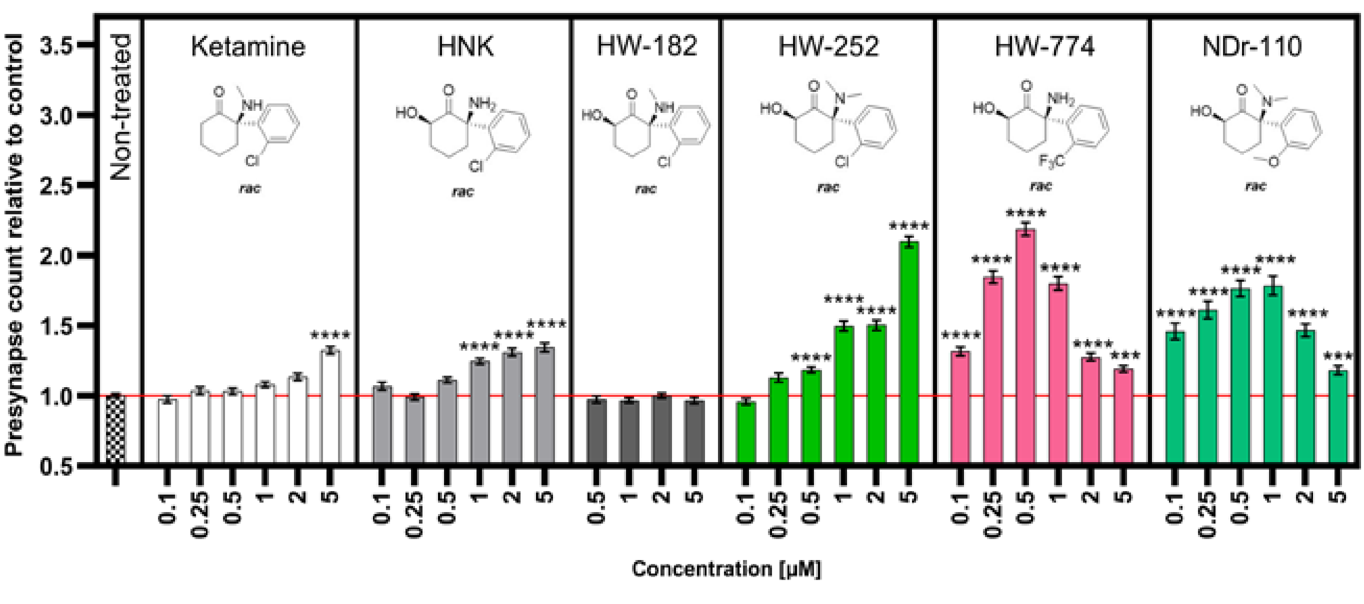

Fig. 1: Number of presynapses (VAMP2 immunostaining) of neuronal cells treated with ketamine, HNK and the best-performing derivatives at different concentrations relative to non-treated cells. Treatment for 48h, HW-182 cannot be metabolized and serves as a negative control. Mean + SEM, n ≥ 75 dendrite segments, Ordinary One-way ANOVA and multiple comparisons vs. non-treated neurons

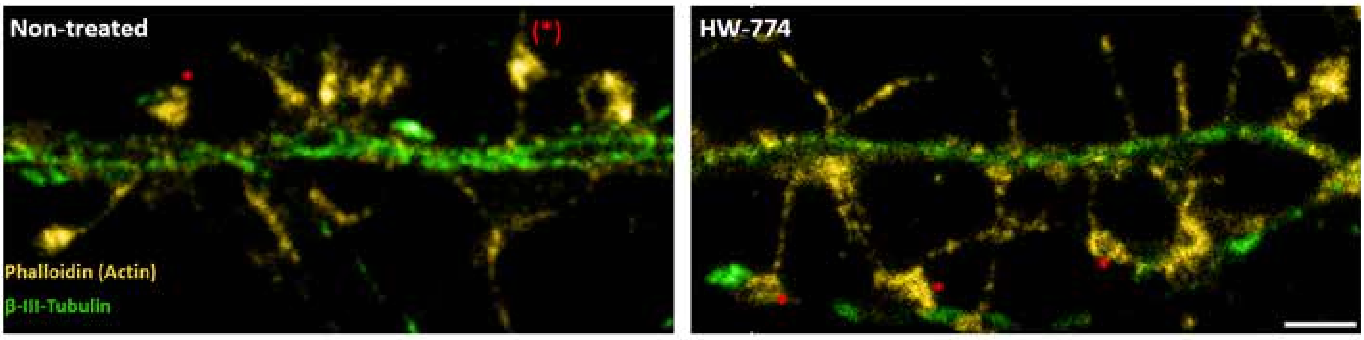

Fig. 2: STED images of dendrite segments of non- and HW-774-treated neurons stained with Phalloidin (yellow) and beta-III-Tubulin (green), red asterisks mark mushroom-shaped synapses, HW-774 treatment: 0.5 µM, 48h, Scale bar: 2 µm

774-treated neurons (Figure 2). Dendritic spines showed increased numbers of mushroom-shaped structures, which are commonly seen as mature, functional spines and are primarily responsible for signal transmission.

Additional experiments using Multielectrode Array (MEA) technology were carried out to assess effects on the functional electrophysiological activity of treated cells. A stimulating effect on firing activity was observed in neuronal cells treated with the compounds. For HW-774, stimulation reached its peak after incubation of 48 h (Figure 3).

In conclusion, we identified highly potent novel HNK derivatives, which effectively enhance functional neuronal synaptogenesis in a concentration-dependent manner. The beneficial effect on neuronal plasticity could pave the way for the development of new neuroprotective therapies.

We speculate that these novel compounds could be used as a countermeasure against synaptic loss induced by space conditions and especially microgravity. Therefore, we are planning to test HNK derivatives in simulated and real microgravity. Experiments utilizing MEA measurements during parabolic flights and in the MAPHEUS rocket program are scheduled for 2024 and 2025.

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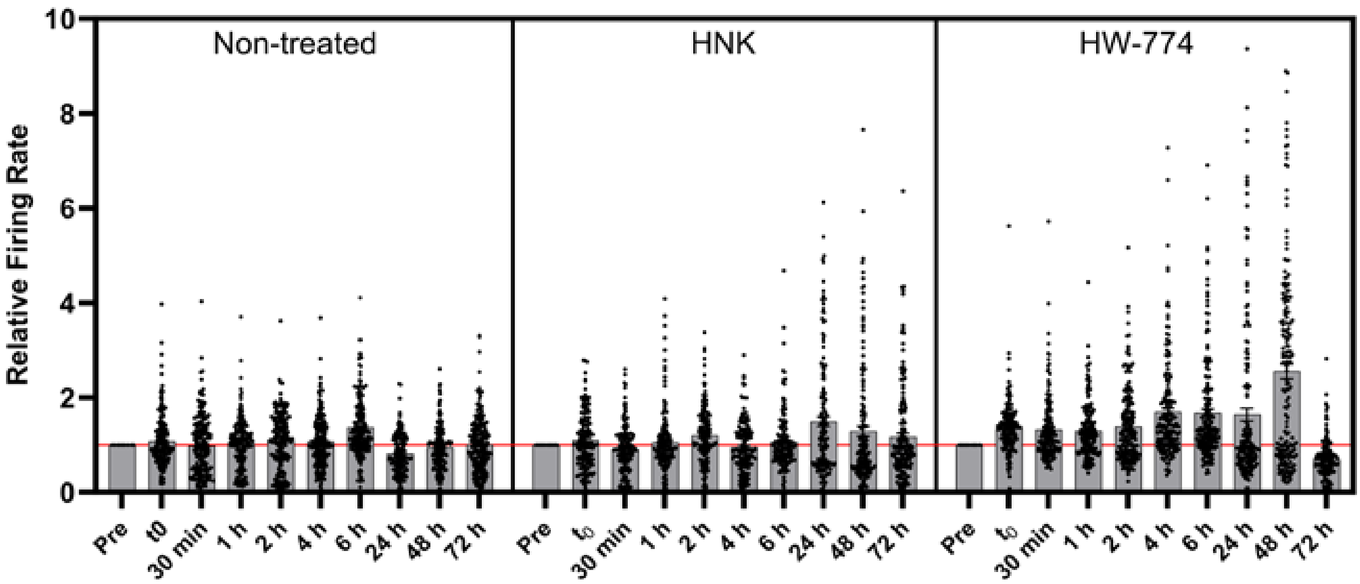

Fig. 3: Firing rate profiles for non-, HNK- and HW-774-treated neuronal cells over time relative to firing rates before treatment (Pre). HNK and HW-774 concentration: 0.5 µM

FLUMIAS – using high-resolution live-cell fluorescence microscopy to measure dynamic changes in astrocyte reactivity and cytoskeletal remodeling on-board the ISS

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Astrocytes are the prevalent type of glial cells in the central nervous system (CNS). These cells have two primary functions: in healthy tissue they support neurons by supplying nutrients via direct contact and by cleaning the extracellular space from excess neurotransmitters and waste products. In case of an injury to the CNS, astrocytes in the surrounding tissue change their phenotype and become reactive, they proliferate and migrate to the region of injury and form the glial scar by astrogliosis, inducing extracellular matrix synthesis and secretion of cytokines or neuronal growth inhibiting factors. The glial scar thus has an inhibitory effect on the regeneration of injured neural tissue. These processes are highly dynamic, subjecting neuronal cells to widespread morphological and therefore cytoskeletal rearrangements.

Our group previously discovered that astrocytes react to altered mechanical loading (hypergravity and simulated microgravity) with significant changes of their morphology, motility, cytoskeletal dynamics, and protein expression specific for reactivity. Hypergravity reduced hallmarks of astrocyte reactivity in vitro, whereas simulated microgravity led to an increase in reactivity proteins in cell culture. In the current study, we aim to decipher the adaptation processes of astrocytes under real microgravity conditions that could induce a reactive phenotype and astrogliosis ***in vitro*** (see Figure 1). Therefore, we will observe adaptation and cytoskeletal rearrangements of primary murine astrocytes to spaceflight and focus on factors related to astrocyte reactivity. The experiment will be executed using FLUMIAS* (FLUorescence MIcroscopic Analysis in Space), a newly developed research platform. FLUMIAS combines an automated microscope with a life support system and a centrifuge to apply variable gravitational loads up to 1*g* onboard the ISS.

Using FLUMIAS, long-term microscopic obser-

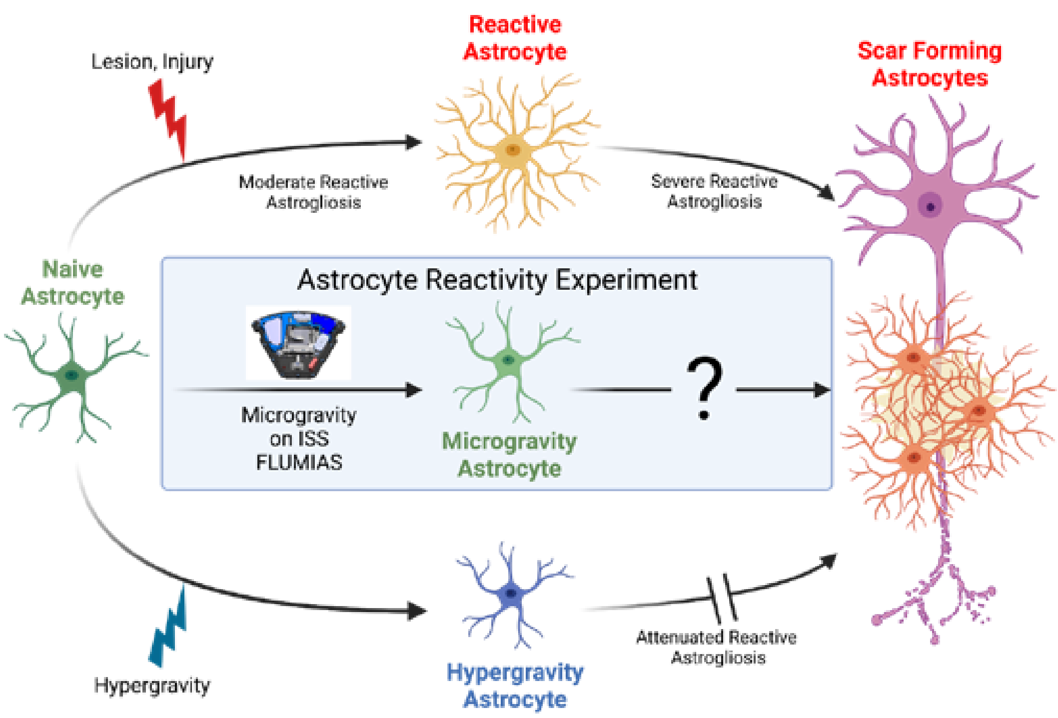

Fig. 1: Pre-studies identified a gravity-dependency of morphology and signaling in astrocytes. The Astrocyte Reactivity project aims to confirm these effects in prolonged timeframes of real microgravity.

vation of living cells using fluorescence is for the first time possible in microgravity. On orbit, the adaptation of the cytoskeleton to microgravity will be analyzed, taking several cell morphological features, migratory behavior, as well as the dynamics of intracellular actin fibers and the microtubule network as validation parameters. Cell behavior such as migration speed and direction, cell spreading, growth and general viability will be measured and compared to 1***g*** ground controls. Furthermore, astrocytes which have been adapted to microgravity will be measured during re-adaptation to 1***g*** (Earth), 0.16***g*** (Moon), and 0.38***g*** (Mars) gravity conditions via centrifugation on ISS FLUMIAS and further during the second adaptation phase back to microgravity to yield insight into adaptive changes of cytoskeletal components. By using the transgenic Life-Act-GFP mouse line additionally stained with a live cell tubulin staining, we are able to visualize live dynamic changes in the two major components of the cytoskeleton (see Figure 2). In addition, each parameter will be investigated in ground-based verification studies employing the FLUMIAS Science Reference Model (SRM) as well as simulated microgravity using the principle of fast 2D clinorotation (DLR 2D clinostat) and hypergravity (DLR incubator centrifuge MuSIC and DLR live cell Imaging centrifuge microscope, the Hyperscope).
If changes in astrocyte behavior occur under altered mechanical loading, a translation to a potential influence in astronaut cognition and motor performance can be carefully discussed. Moreover, a potential influence of altered gravity to astrocytic dysfunction could be used to further elucidate cognitive decline and neurodegenerative diseases that feature astrogliosis, such as spinal cord injuries, brain trauma, Alzheimer´s and Parkinson´s disease.

*FLUMIAS is a project of the German Space Agency at DLR (German Aerospace Center), developed by Airbus Friedrichshafen, based on an innovative microscope by TILL I.D., Martinsried. FLUMIAS will be handed over to ESA as national contribution to the SciSpacE programme for organizing European utilization and operation on ISS. The SciSpacE Research programme is organized via Announcements of Opportunities and international usage will be possible in future opportunities as well.

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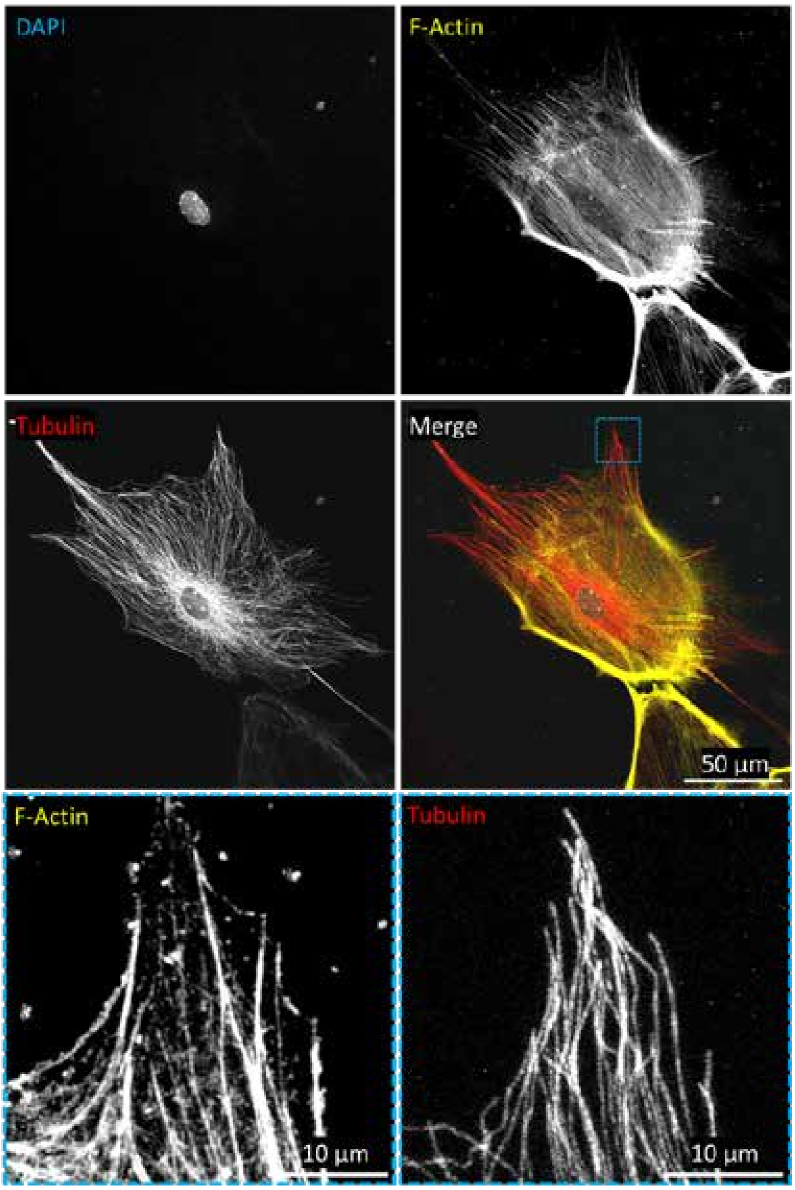

Fig. 2: Primary murine astrocytes imaged in the FLUMIAS breadboard model (SRM). Live cell imaging of astrocytes, stained: DAPI (blue), F-actin (yellow), tubulin (red) and a merged image. The nucleus, as well as the actin and tubulin cytoskeleton are imaged in a confocal-like resolution. Single microtubules were clearly discernible. For cytoskeletal analysis, individual microtubules and F-actin fiber meshworks could be clearly discerned as shown in the bottom row.

Study Team

Study Team

The DLR study team comprises scientific and non-scientific employees with expertise in clinical research and management, neurology, human nutrition, and biology. The study team supports internal and external human investigations at the DLR and implements own scientific projects.

The team supports long-duration bed rest and isolation studies for ESA/NASA at the :envihab. In addition, the study team plans and realizes outpatient studies for internal and external researchers on a human short arm centrifuge developing e.g. new countermeasures for safe space travels. The team also coordinates the national centrifuge program enabling external researches to use the centrifuge for various scientific analysis, e.g. the perception of the body in a three-dimensional space during alterations of gravity.

Projects devoted to human neuroscience and clinical neurology are carried out in collaboration with the department of neurology at the university hospital Bonn, the German Center for Neurodegenerative Diseases (DZNE), the Dementia Research Institute at University College London, UK, the department of neurology at the university hospital Aachen, and the departments of cardiovascular aerospace medicine and of sleep and human factors research at the DLR. The different projects include clinical neurological assessments, orthostatic testings, cognitive testings, brain imaging, sleep studies, and biomarker analysis of patients with neurological disorders and of participants enrolled in human investigations at :envihab.

Moreover, the nutrition team within the study team devises standardized menu plans and nutrition concepts for outpatient and stationary studies. Those nutritional concepts often consider 32 single nutrients being kept in exact nutritional limits for each individual and in accordance with the study days. The team also carries out own nutritional studies and analysis scientific nutritional data together with internal and external researchers.

Main features of the working group

- General counselling for human physiological studies
- Support for application procedures (ethical protocol, insurance of subjects)
- Development and preparation of different required study documents (protocols, case report forms, and informed consent documents)
- Subject recruitment for human physiological studies
- Development, preparation and management of highly standardized nutrition schemes
- Project management for human physiological studies
- On-site management, with GCP/AMG-trained key personnel
- Preparation of internal reports/reviews
- Central management for scheduling studies in :envihab

Biological sample preparation
Sample preparation during the BMBF-funded TAhRget study.

Two weeks at 9.5% oxygen – state of emergency or doping for the human brain?

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Hypoxia refers to a condition in which there is a deficiency of oxygen in the body's tissues. Hypoxia can occur for various reasons, such as reduced oxygen supply to the tissues, impaired oxygen utilization, or decreased oxygen-carrying capacity of the blood. Hypoxia can have detrimental effects on organ function and can lead to serious health issues. However, low oxygen tensions maintain undifferentiated states of embryonic, hematopoietic, mesenchymal, and neural stem cell phenotypes and also influence proliferation and cell-fate commitment. Thus, researchers have also explored the therapeutic potential of targeting hypoxia-related pathways. Some studies have investigated methods to enhance the adaptive response to hypoxia or modulate hypoxia-inducible-factor (HIF) activity to promote cardiac repair. In this context, myocardial regeneration is of special interest. Myocardial regeneration refers to the process of repairing or replacing damaged heart tissue, particularly the myocardium, which is the muscular tissue of the heart responsible for pumping blood. This area of research is significant because heart diseases, such as heart attacks, can cause irreversible damage to the heart muscle. It has been shown, that exposure of mice to severe systemic hypoxemia (7% inspired oxygen, corresponding to 8000m altitude) for 2 weeks resulted in reactivation of cardiomyocyte mitosis.

It is currently unknown if the same effects can be expected in humans. We exposed patients with previous myocardial infarction to normobaric hypoxia corresponding to 6200m altitude investigating myocardial regeneration. However, translating these results into patients carries the risk of hypoxic damage to the central nervous system, although hypoxia can also be a positive factor for neurons, leading to axonal regeneration and increased plasticity. Therefore, we evaluated effect of prolonged reduced oxygen concentration on cognition and brain integrity in patients after myocardial infarction.

In this pilot study, three specially selected myocardial infarction patients (age 60±4 years) with anterior wall infarction after complete revascularisation (4, 5 and 10 years after the event) and one control subject (61 years) were gradually brought to their individual tolerance threshold for hypoxia. After slow acclimatisation over 5 weeks, the subjects were finally at 6200m during the day and 5300m at night for 2 weeks. During the entire study phase, neurological examinations, cognitive tests (CERAD, Basner Cognition Test) and cerebral 3T-MRI examinations were carried out. In addition, EDTA plasma was preserved in which neuronal and glial biomarkers (tau, glial fibre acidic protein (GFAP), amyloid-beta 40 (Aβ40), amyloid-beta 42 (Aβ42), neurofilament light (NfL)) were analysed on a Quanterix SIMOA analyser.

Clinical deficits occurred in the form of a mild intention tremor and bradydyskinesia that completely regressed after exposure to 21% oxygen. There was no decrease in cognitive performance during the entire study period. Subjects were able to maintain relatively constant arterial blood oxygen levels during hypoxia by increasing hemo-concentration from 15.1 g/dL (±1.3%) to 18.4 g/dL (±2.0%) and hyperventilating (SpO2 normoxia 97.3% (±1.1%), hypoxia 73.7% (±1.7%)), although

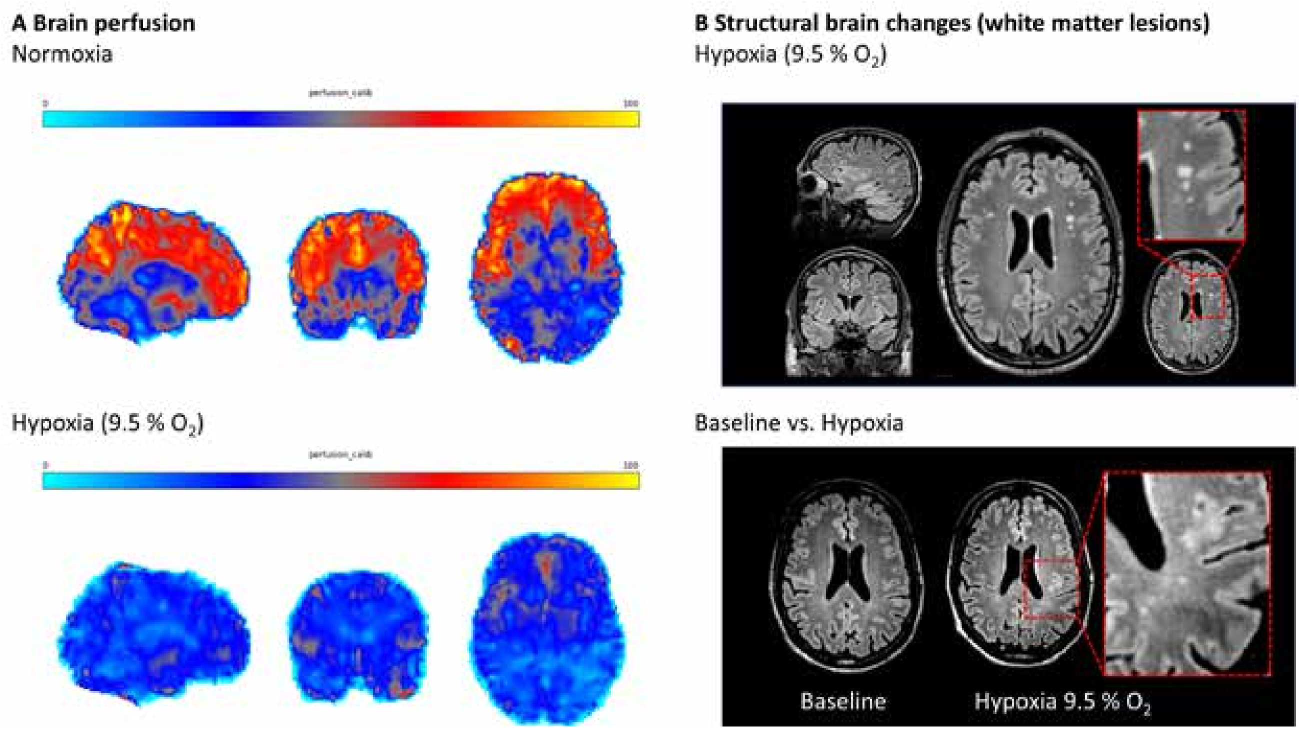

Fig. 1: A Cerebral brain perfusion measured by pseudocontinuous arterial spin labeling (pCASL) and proton density weighted image for calibration. Exemplary images of one subject. Brain perfusion is reduced under hypoxemia compared to normoxia. B Structural brain analysis shows white matter lesions under hypoxia of 9.5% O2.

brain perfusion decreased by an average of 15 ± 5 ml/100g/min (Fig. 1A). In cerebral MRI imaging, new, small white matter lesions were observed under hypoxia, which completely regressed within 30 days after cessation of hypoxia and were assessed as vasogenic oedema (Fig. 1B).
The neuronal biomarkers tau, Aβ40, and NfL increased only slightly under hypoxia (0.5 4pg/ml) and returned to their baseline values after cessation of hypoxia (Fig. 1A,B,D,E). GFAP increased by 10 pg/ml until 30 days after cessation of hypoxia and then fell back to baseline values (Fig. 1C).
These preliminary data demonstrate that neurological function and brain integrity of specially selected post-myocardial infarction patients are not adversely affected by weeks of severe normobaric hypoxia exposure in the context of trials.

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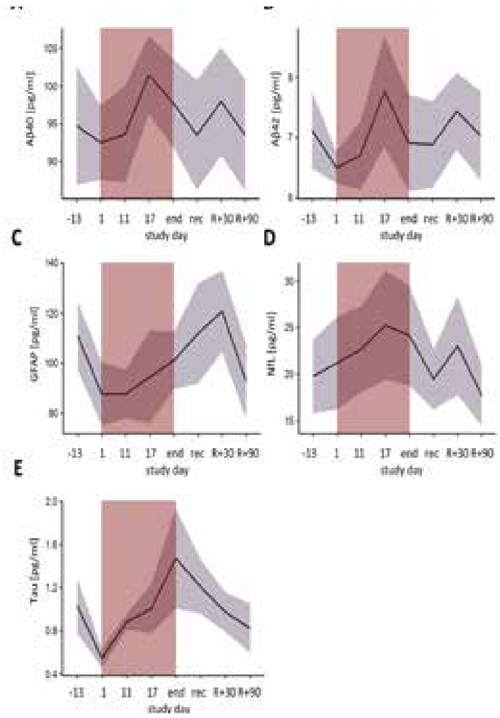

Fig. 2: Levels of neuronal and glial biomarkers in blood during baseline (study day -13), hypoxic conditions (red square, study day 1-end)) and follow up analysis. A Aβ40, B Aβ42, C GFAP, D NfL, E Tau. R+30=analysis 30 days post hypoxaemia, R+90=analysis 90 days post hypoxaemia, GFAP= glial fibre acidic protein.

Characterization of nutritional, AhR-dependent immune and inflammatory responses in healthy individuals – TAhRget-Study

Ann Charlotte Ewald[1], Anna Humer[1], Elisabeth Christa Ruth Wernick[2], Ralf Möller[1], Nicola Wilck[2], Alexandra Noppe[1], Anja Mähler[2], Laura de Boni[1], Melanie von der Wiesche[1]

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The collaborative TAhRget (Targeting AhR-dependent Inflammation for Organ Protection) study explores the impact of the aryl hydrocarbon receptor (AhR) on inflammatory and immunological processes, particularly within the realm of chronic kidney diseases (CKD) and multiple sclerosis (MS). The ultimate goal is to decipher the role of AhR in precipitating organ damage through a multifaceted approach that encompasses patient cohorts, animal models, cell cultures, single-cell analyses, microbiome studies, and nutritional studies. The study team of ME conducted one DLR subproject on healthy individuals of the TAhRget study and was an integral component of the TAhRget collaborative initiative, generously funded by the BMBF.

Inflammatory-induced organ damage constitutes a significant pathological factor in chronic illnesses like CKD and MS. The AhR, a ligand-activated transcription factor responsive to a spectrum of environmental and dietary ligands, is a central point of interest. The purpose of our study was to unravel the mechanisms of AhR-mediated immune responses and pathomechanism across diseases, especially Multiple Sclerosis (MS) and Chronic Kidney Disease (CKD). Many diverse organic molecules bind and activate AhR and these ligands are reported to either promote glomerular and tubular damage or protect against kidney injury. AhR crosstalk with estrogen, peroxisome proliferator-activated receptor-γ, and NF-κB pathways may contribute to the diversity of AhR responses during the various forms and stages of CKD. In MS, serum AhR agonist levels negatively correlate with disability in relapsing-remitting MS and progressive MS and decrease longitudinally in correlation with MRI markers of disease progression.

	2023	30. Jul.	31. Jul.	1. Aug.	2. Aug.	3. Aug.	4. Aug.	5. Aug.	6. Aug.	7. Aug.	8. Aug.	9. Aug.	10. Aug.	11. Aug.	12. Aug.	13. Aug.
		So	Mo	Di	Mi	Do	Fr	Sa	So	Mo	Di	Mi	Do	Fr	Sa	So
TAhRget DLR	H001	V1	V2	V3	V4	V5										
	H002	V1	V2	V3	V4	V5										
	H003	V1	V2	V3	V4	V5										
	H004		V1	V2	V3	V4	V5									
	H005		V1	V2	V3	V4	V5									
	H006		V1	V2	V3	V4	V5									
	H007								V1	V2	V3	V4	V5			
	H008								V1	V2	V3	V4	V5			
	H009								V1	V2	V3	V4	V5			
	H010									V1	V2	V3	V4	V5		
	H011									V1	V2	V3	V4	V5		
	H012									V1	V2	V3	V4	V5		

		Diet (plant based diet or western diet)	Samples / Experiments
V1	Arrival	-	faeces (baseline at home)
V2	Study day 1 at :envihab	diet 1	blood, BGA, spot urine, 24h urine, BodPod, BIA
V3	Study day 2 at :envihab	diet 1	blood, faeces, spot urine, 24h urine
V4	Study day 3 at :envihab	diet 1	blood, faeces, spot urine, 24h urine
V5	Study day 4 at :envihab / departure after stool sample	-	blood, BGA, faeces, spot urine, BodPod, BIA
V1	Arrival	-	faeces (baseline at home)
V2	Study day 1 at :envihab	diet 2	blood, BGA, spot urine, 24h urine, BodPod, BIA
V3	Study day 2 at :envihab	diet 2	blood, faeces, spot urine, 24h urine
V4	Study day 3 at :envihab	diet 2	blood, faeces, spot urine, 24h urine
V5	Study day 4 at :envihab / departure after stool sample	-	blood, BGA, faeces, spot urine, BodPod, BIA

Fig. 1: Study schedule

Fig. 2: A Study Office B Example western diet C Example plant-based diet D Lab E-F Preparation of PBMCs.

Our approach permits a comprehensive examination of AhR functions in the gut, blood, peripheral immune system, and inflammation-related organ damage in both conditions. We are particularly interested in AhR-dependent immune responses triggered by dietary ligands and intestinal bacterial metabolites, recognizing their potential to influence the underlying pathomechanisms.
In the DLR subproject, our objective is to understand how nutrition modulates AhR-dependent immune responses in healthy individuals. To achieve this, we conducted a three-day, tightly controlled, inpatient dietary intervention with 12 healthy volunteers (Fig.1, Fig. 2A). The subjects were assigned to one of two contrasting diets a western diet rich in pro-inflammatory nutrients like saturated fat, cholesterol, refined grains, and sugar, or a plant-based diet offering anti-inflammatory nutrients such as omega-3 fatty acids, fiber, and polyphenols (Fig. 2B,C). These dietary interventions were designed to elicit immediate and distinct effects on the gut microbiome composition and microbial metabolite production, which, in turn, influence the state of immune cells. By implementing these divergent diets, we sought to activate AhR across a wide physiological spectrum, with the overarching aim of deciphering the role of diet in AhR-associated inflammation. During this study, we collected various biological samples, including stool samples, blood, 24-hour urine, and peripheral blood mononuclear cells (PBMC, Fig.2 D-F). Our study design, featuring highly controlled, standardized diets and stringent environmental conditions, minimizes numerous confounding factors.
The outcomes of the initiative hold considerable significance for health policy, as AhR misregulation may extend to other chronic inflammatory conditions. The results could empower physicians to modulate disease progression and offer patients a means to positively influence their chronic illnesses.
The study was conducted in August 2023, and biological samples are presently undergoing analysis by the scientific consortium and the department of Aerospace Biology.

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Annex

Scientific activities

Teaching activities

Name	University	Subject
Anken, Ralf	University of Hohenheim	Space Biology
Belser, Nadine	University of Hamburg	Psychology
Berger, Thomas	International Space University, Straßburg	Master of Space Studies
Clemen, Christoph	University of Cologne	Biochemistry and Molecular Biology
de Boni, Laura	University Hospital Bonn	Neurology
Frings-Meuthen, Petra	International Space University Strasbourg	Nutrition in Space
Frings-Meuthen, Petra	University Kiel	Nutrition in Space
Gerlach, Darius	University of Cologne	Physiology
Goerke, Panja	FH Wedel University of Applied Sciences	Communication skills
Goerke, Panja	FH Wedel University of Applied Sciences	Communication skills
Hauslage, Jens	Hannover Medical School	Propaedeutics
Hauslage, Jens	University of Veterinary Medicine Hanover	Gravitational Biology
Hauslage, Jens	La Trobe University, Australia	Gravitational Biology
Hellweg, Christine	University of Bonn	Radiation Protection
Hellweg, Christine	Freie Universität Berlin	Immunology
Hellweg, Christine	Freie Universität Berlin	Pathology
Hellweg, Christine	University of Bonn	Radiopharmacy
Hemmersbach, Ruth	University of Bonn	Gravitational Biology
Heußer, Karsten	University of Cologne	Physiology
Liemersdorf, Christian	University of Bonn	Molecular Genetics
Mittelstädt, Justin Maximilian	University of Hamburg	Psychological assessment
Möller, Ralf	University of Applied Sciences Bonn-Rhein-Sieg	Microbiology
Möller, Ralf	University of Applied Sciences Bonn-Rhein-Sieg	Bachelor program: Space Microbiology
Möller, Ralf	University of Applied Sciences Bonn-Rhein-Sieg	Master program: Space Biotechnology / Medicine
Oubaid, Viktor	Universita San Raffaele, Milano IT	Advanced course in Aviation Psychology
Pesta, Dominik	University of Cologne	Research Track: Critical Reading

Pesta, Dominik	University of Cologne	Physiology Practical Course
Pfander, Boris	University of Cologne	Medicine
Pfander, Boris	University of Cologne	Research Seminar at the Institute of Genome Stability in Aging and Disease
Pfander, Boris	University of Cologne	Journal Club at the Institute of Genome Stability in Aging and Disease
Pfander, Boris	University of Cologne	Biology - M. Sc. - Molecular Mechanisms of Human Disease
Pfander, Boris	University of Cologne	Medicine - Research Track - DNA breaks
Pustowalow, Willi	University of applied sciences Bonn-Rhein-Sieg	Computer Science
Stelling, Dirk	Hochschule Fresenius	Psychology
Stelling, Dirk	Hochschule Fresenius	Psychology
Stelling, Dirk	Hochschule Fresenius	Psychology
Stern, Claudia	Technische Universität Braunschweig	Aerospace Medicine
Stern, Claudia	International Space University	Human Visual System
Stern, Claudia	School of Aviation Medicine	Ophthalmology
Zinn, Frank	University of Hamburg	Psychology

Graduations

Supervised Doctoral Students

University	Space	Aviation	Traffic
Justus Liebig University Giessen		1	
Radboud University	1		
Ruhr University Bochum	1		
Technical University of Darmstadt	1		
Technische Universität Braunschweig	1		
University Bern	1		
University of Bonn	5		
University of Cologne	11		
University of Duisburg-Essen	2		
University of Düsseldorf		1	
University of Oldenburg	1		

Doctorates

University	Space	Aviation	Traffic
Hannover Medical School	1		
Manchester Metropolitan University	1		
University of Bonn	1		
University of Cologne	3		
University of Cologne	1		

Bachelor Degrees

University	Space	Aviation	Traffic
Heinrich-Heine-University	2		
University of Applied Sciences Aachen,	1		
University of Applied Sciences Bonn-Rhein-Sieg		1	1

Diploma Theses/Master Degrees

University	Space	Aviation	Traffic
Hochschule Fresenius		1	
Rhine-Waal University	3		
Sorbonne University	1		
Technical University of Munich	1		
Universidade d Coimbra, Portugal	1		
University Mainz	1		
University of Bonn	1		
University of Cologne	1		
University of Geisenheim	1		
University of Naples Federico II	1		
Vrije Universiteit Amsterdam	1		

Scientific Exchange

Berger, Leonard	University Mainz
Bruder, Carmen	Universität zu Lübeck / Prof. Franke
Figueira, Joao	University of Porto, Portugal
Kramme, Johanna	University Hospital Cologne
Kremers, Stephan	Hospital of Cologne Merheim, Ophthalmology Clinic
Mack, Isa	University of Tübingen
Majmudar, Gauravam	International Space University
Oubaid, Viktor	Bundesanstalt für Strassenwesen
Oubaid, Viktor	BW / ZentrLuRMed Lw / A. Stevens
Oubaid, Viktor, Dr. Gayraud	TU Dresden / CETi / Prof. Sebastian Pannasch
Prior, Robert	University of Bonn
Rashid, Anas	University of Turin
Valetti, Alessandro	Università degli Studi di Torino
Zarus, Eleonora	International Space University

Awards

Berger, Thomas
DLR-Senior Scientist 2023

Böcker, Jonas
Orpea Award 2023, Special Award Research

Büscher, Finn-Marten
Cologne FortuneUniversity of Cologne

Frett, Timo
1. Platz Posterpreis, Jahrestagung DGLRM 2023

Krämer, Carolin
3rd Poster Award at the DGLRM Conference 2023, Cologne

Pavletic, Bruno
Best Poster Award at 8th European Congress of Virology 2023, Gdansk,

Pavletic, Bruno
Poland3rd Poster Award at the DGLRM Conference 2023, Cologne "Phages as tools in spaceflight virology research"

Piepjohn, Johanna
1st Poster Award at VAAM special group "Space Microbiology" Workshop BigBang…Microbes! Workshop on Cultivation of the Uncultivationables!, Cologne; "Horizontal gene transfer in space – preparation of the ISS experiment Bacterial Conjugation –"

Rettberg, Petra
2nd Poster Award at the DGLRM Conference 2023, Cologne; "Is the repair kinetics of radiation induced DNA damages influenced by microgravity? Preparation of the space experiment LUX-in-Space"

Team NUNOS (Paulke, Tim; Mierbach, Fabian; Sommerlad, H.; Stock, Johannes)
Innovationspreis Startup-Days der Andreas Hermes Akademie (AHA), Internationale Grüne Woche

Team NUNOS (Paulke, Tim; Mierbach, Fabian; Sommerlad, H.; Stock, Johannes)
Start-up-Preis Growth Alliance Networking Summit (GANS), Landwirtschaftliche Rentenbank

Team NUNOS (Paulke, Tim; Mierbach, Fabian; Sommerlad, H.; Stock, Johannes)
3. Platz Bio-Gründer Wettbewerb, Bio-Security Management GmbH

Team NUNOS (Paulke, Tim; Mierbach, Fabian; Sommerlad, H.; Stock, Johannes)
Gründungspreis Gründungswettbewerb – Digitale Innovationen, BMWK

Warkentin, Alena
2nd Poster Award at VAAM special group "Space Microbiology" Workshop BigBang…Microbes! Workshop on Cultivation of the Uncultivationables!, Cologne; "Beyond Gravity: Using gut microbiome insights in simulated weightlessness via SANS Studies as a first step to improve health in Astronauts".

Events, lectures, workshops at the Institute

14 January 2023
Hems Day Cologne 2023: Workshop together with ADAC Luftrettung

21 March 2023
Institute Seminar: Ana Ferreiro M.D., Ph.D., Translational research in congenital muscle disorders: from bedside to bench and back

3-4 March 2023
Kompetenznetzwerk Immobilisationsbedingte Muskelstörungen KNIMS (:envihab/Hybrid)

9 May 2023
Institute Seminar: Dr. Frederik Hammes, Advanced flow cytometric methods for drinking water analysis

23 May 2023
Institute Seminar: Dylan Buglewicz Ph.D, M.Sc, The impact of DNA repair pathways throughout the Carbon-ion Spread-out Bragg peak

22 August 2023
Institute Seminar (intern): Dr. Stefan Burauer, Technische Ideen schützen – Erfindungen immer (an)melden

26 September 2023
Institute Seminar: Dr. Sarah L. Castro-Wallace, Spaceflight Microbiology: From Apollo to Artemis

28-29 September 2023
VAAM-WS Big Bang… Microbes! – Workshop on Cultivation of the Uncultivables!

19-21 October 2023
61. Jahrestagung der Deutschen Gesellschaft für Luft- und Raumfahrtmedizin (DGLRM)

7 November 2023
Institute Seminar: Univ.-Prof. Dr. Dr. med. David Groneberg, The Masc - lessons learned from the pandemic

21 November 2023
Institute Seminar: Dr. Cyprien Verseux, Sustainable bioproduction on Mars

8 December 2023
8th Human Physiology Workshop

12 December 2023
Institute Seminar: PD Dr. med. Alexandra Ljimani, Advanced diagnostics of renal impairment in cardiometabolic syndrome by new MRI - based quantitative imaging biomarker

Publications

Publications with an impact factor above 10

Capri, M., Conte, M., Ciurca, E., Pirazzini, C., Garagnani, P., Santoro, A., Longo, F., Salvioli, S., **Lau, P., Moeller, R., Jordan, J.,** Illig, T., Villanueva, M.-M., Gruber, M., Bürkle, A., Franceschi, C., **Rittweger, J.** (2023) *Long-term human spaceflight and inflammaging: Does it promote aging?* Ageing Research Reviews. 2023;87:101909. Elsevier. doi: 10.1016/j.arr.2023.101909. ISSN 1568-1637.

Chacin, E., Reusswig, K.-U., Furtmeier, J., Bansal, P., Karl, L.A., **Pfander, B.,** Straub, T., Korber, P., Kurat, C.F. (2023) *Establishment and function of chromatin organization at replication origins.* Nature. 2023;616:836-842. Nature Publishing Group. doi: 10.1038/s41586-023-05926-8. ISSN 0028-0836.

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Hönemann, J.-N., Gerlach, D.A., Hoffmann, F., Kramer, T., Weis, H., **Hellweg, C.E., Konda, B.,** Zaha, V., Sadek, H., van Herwaden, A.E., Olthaar, A.J., Reuter, H., Baldus, S., Levine, B.D., **Jordan, J., Tank, J., Limper, U.** (2023) *Hypoxia and Cardiac Function in Patients With Prior Myocardial Infarction.* Circulation Research. 2023;132(9):1165-1167. Wolters Kluwer Health. doi: 10.1161/CIRCRESAHA.122.322334. ISSN 0009-7330.

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Simões, M.F., **Cortesão, M.,** Azua-Bustos, A., Bai, F.Y., Canini, F., Casadevall, A., Cassaro, A., Cordero, R.J.B., Fairén, A.G., González-Silva, C., Gunde-Cimerman, N., **Koch, S.M.,** Liu, X.Y., Onofri, S., Pacelli, C., Selbmann, L., Tesei, D., Waghmode, A., Wang, T., Zucconi, L., Antunes, A. (2023) *The relevance of fungi in astrobiology research – Astromycology.* Mycosphere. 2023;14(1):1190-1253. Guizhou Academy of Agricultural Sciences. doi: 10.5943/mycosphere/14/1/13. ISSN 2077-7000.

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Aeschbach, D., Cohen, D.A., Lockyer, B.J., Chellappa, S.L., Klerman, E.B. (2023) *Spontaneous attentional failures reflect multiplicative interactions of chronic sleep loss with acute sleep loss and circadian misalignment.* Sleep Health. 2023:Online ahead of print. Elsevier. doi: 10.1016/j.sleh.2023.07.013. ISSN 2352-7218.

Biaggioni, I., **Jordan, J.** (2023) *Orthostatic hypertension—too much of a good thing.* Clinical Autonomic Research. 2023;33(4):379-381. Springer. doi: 10.1007/s10286-023-00961-x. ISSN 0959-9851.

Blottner, D., Moriggi, M., Trautmann, G., Hastermann, M., Capitanio, D., Torretta, E., Block, K., **Rittweger, J., Limper, U.,** Gelfi, C., Salanova, M. (2023) *Space omics and tissue response in astronaut skeletal muscle after short and long duration missions.* International Journal of Molecular Sciences. 2023;24(4):4095. Multidisciplinary Digital Publishing Institute (MDPI). doi: 10.3390/ijms24044095. ISSN 1661-6596.

Borschert, A.L., Gauger, P., Bach, A., Gerlach, D., Johannes, B., Jordan, J., Li, Z., Elmenhorst, D., Bauer, A., Marshall-Goebel, K., **Tank, J., Zange, J., Rittweger, J.** (2023) *External to internal cranial perfusion shifts during simulated weightlessness: Results from a randomized cross-over trial.* npj Microgravity. 2023;9(1):25. Nature Publishing Group. doi: 10.1038/s41526-023-00267-2. ISSN 2373-8065.

Broussard, J.L., Knud-Hansen, B.C., Grady, S., Knauer, O.A., Ronda, J.M., **Aeschbach, D.,** Czeisler, C.A., Wright, K.P jr (2023) *Influence of circadian phase and extended wakefulness on glucose levels during forced desynchrony.* Sleep Health. 2023:Online ahead of print. Elsevier. doi: 10.1016/j.sleh.2023.10.010. ISSN 2352-7218.

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