



Research Report  
Institute of Aerospace Medicine 2021



# 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. Moreover, the 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 2021, which addressed important medical, psychological, and biological issues in space, in aeronautics, and in traffic. Suffice it to say that planning and executing scientific projects was by no means trivial in the face of the Covid19 pandemic. Human investigations were particularly challenging and required strict safety measures for staff members and study participants. However, the pandemic with all its personal and professional hardships also inspired our research. For example, we applied our knowledge in aerospace microbiology and astrobiology to better understand the spread of pathogens and to develop strategies to cope with the current and future pandemic threats in collaboration with partners at DLR and other leading institutions. We also analyzed how the pandemic affected psychological selection procedures. Furthermore, many of us experienced the psychological and medical challenges imposed by isolation and confinement first hand. This experience provides an impetus to study these unresolved risks to astronauts and people on Earth, particularly the elderly, and to find technological solutions ameliorating consequences of isolation and confinement on wellbeing.

In 2021, we carried out the first campaign of the NASA Spaceflight-Associated Neuro-Ocular Syndrome Countermeasures head-down bed rest study (SANS-CM) at :envihab. The study will guide the development of preventive measures maintaining eye and brain health during long-duration space travel. We also conducted sophisticated human studies on cardiac regeneration in patients following myocardial infarction and on caffeine's mechanisms of action in the brain. Furthermore, we conducted investigations on muscle and bone, target tissues affected by weightlessness, in patients with a rare genetic disease affecting phosphate metabolism.

We completed a study in patients with glaucoma to test whether gravity can be exploited to ameliorate elevated pressure levels in the eye, a hypothesis that directly arose from our space medicine research. We also conducted exciting studies in the field be it a sleep investigation conducted in the bedroom of people affected by traffic noise, radiation measurements on long-haul airplane flights, or an investigation onboard the International Space Station. ESA Astronaut Thomas Pesquet initiated experiments testing antimicrobial metal surfaces under spaceflight conditions. Subsequently, the German astronaut Matthias Maurer successfully started biomedical experiments including artificial intelligence-based diagnostic testing of eye health. Our biology program provided new insight in cellular mechanisms responding in gravity and radiation based on laboratory studies and experiments on various platforms including the drop tower and Mapheus sounding rockets. 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

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# Cardiovascular Aerospace Medicine

*Prof. Dr. med. Jens Tank (Head)*

*PD Dr. med. Karsten Heußer (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 (Prof. Dr. Jens Tank)***

- State of the art neuroimaging methods
- Functional MRI assessment of the brainstem and hypothalamus, the centers of autonomic control
- Autonomic nervous system testing within the MRI scanner, to characterize the function and neuroplastic adaptations in response to immobilization, diseases, and life style
- Cardiac MRI under extreme environments, including hypoxic condition and im mobilization
- Detection of cardiovascular deconditioning and impairment in immobilization and diseases
- Probing the brain-heart axis with brain and cardiac imaging
- Unique combinations of novel methods in the MRI setting such as lower body negative pressure during neuro imaging

### ***Cardiovascular Control in Health and Disease (PD Dr. 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 cardiovascular disease in space and in terrestrial medicine

*Photo: Preparing a subject with a univentricular heart for magnetic resonance imaging (MRI) under hypoxic conditions.*

# Limited effect of 60-days strict head-down tilt bed rest on vascular ageing

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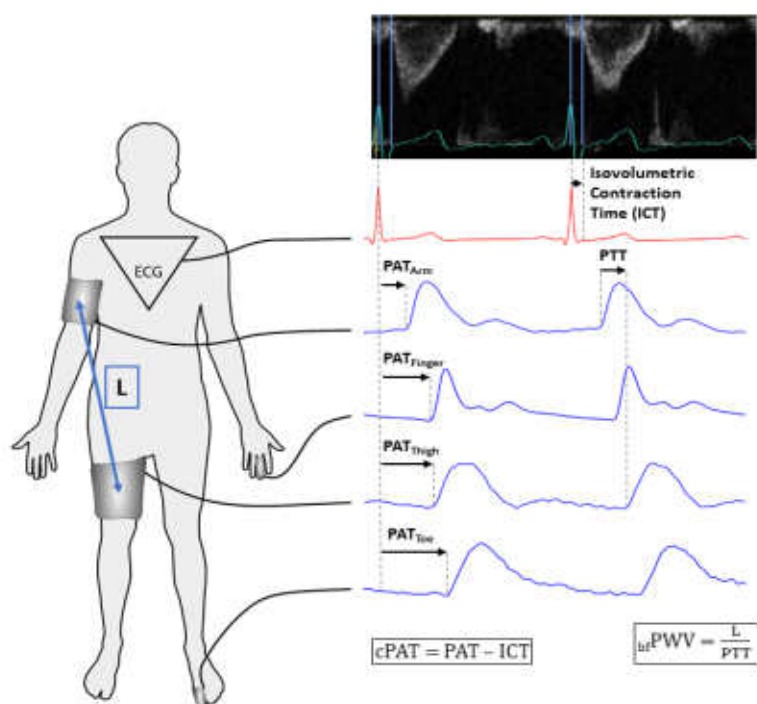


Fig. 1: Data acquisition for vascular measurements. Left panel: Recording sites and length (L) determination for brachial-femoral pulse wave velocity (bfPWV) assessment. Right panel – top: ECG and Doppler flow curves in the left ventricular outflow tract. We measured isovolumetric contraction time (ICT) from the R-peak to aortic valve opening indicated by flow onset. Right panel – bottom: Pulse wave arrival time (PAT) is defined as the time from the ECG R-Peak to pulse wave arrival at a certain landmark. By dividing L by pulse transit time (PTT) between arm and thigh cuffs, we obtained bfPWV. We obtained measurements from every heartbeat recorded during a 60-s period. For the sake of clarity, PAT and PTT are shown for two consecutive heartbeats. We calculated corrected PAT (cPAT) by subtracting ICT from PAT.

## Background

Cardiovascular risk may be increased in astronauts after long-term space flights based on biomarkers indicating premature vascular ageing. We tested the hypothesis that 60 days of strict 6° head-down tilt bed rest (HDTBR), an established space analogue, promotes vascular stiffening and that artificial gravity training ameliorates the response.

## Methods

Within AGBRESA, we studied 24 healthy participants (8 women, 24 - 55 years, BMI = 24.3 ± 2.1 kg/m<sup>2</sup>) before and at the end of 60 days HDTBR. 16 subjects were assigned to daily artificial gravity. We applied echocardiography to measure stroke volume and isovolumetric contraction time (ICT), calculated aortic compliance (stroke volume/aortic pulse pressure), and assessed aortic distensibility by MRI. Furthermore, we measured brachial-femoral pulse wave velocity ( $v_{bf}$ PWV) and pulse wave arrival times (PAT) in different vascular beds by blood pressure cuffs and photoplethysmography (see Fig. 1). We corrected PAT for ICT (cPAT).

## Results

In the pooled sample, diastolic blood pressure (+8 ± 7mmHg, p < 0.001) and heart rate (+7 ± 9 bpm, p = 0.002) increased during HDTBR. Stroke volume decreased by 14 ± 15 ml (p = 0.001). Aortic area tended to increase (p = 0.05) but  $v_{bf}$ PWV, aortic compliance and aortic distensibility remained unchanged. In contrast, the uncorrected arrival times at brachial and femoral artery, which include the ICT, increased by 9 ± 13 ms (PAT<sub>Arm</sub>, p = 0.002)



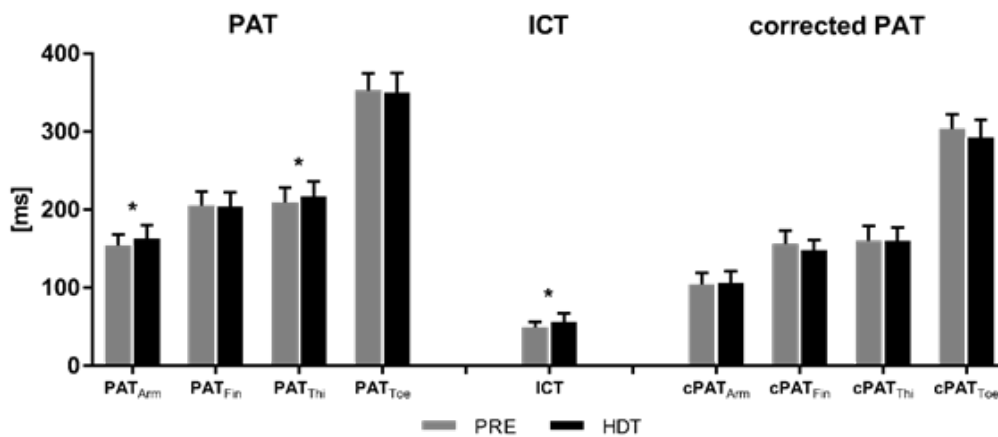


Fig. 2: Pulse wave arrival times (PAT) increase with greater topological distance from the heart to arm, finger, thigh, and toe, all indicated by subscripted acronyms. PAT<sub>Arm</sub> and PAT<sub>Thigh</sub> significantly increased after 60 days HDTBR (black bars) compared to baseline recordings 6 days before HDTBR (gray bars). Isovolumetric contraction time (ICT) also increased with HDTBR. Corrected PAT did not change with HDTBR. Results are represented as mean values from 24 subjects with error bars indicating the first standard deviation; \* < 0.05.

and  $8 \pm 15$  ms (PAT<sub>Thigh</sub>,  $p = 0.022$ ), respectively. PAT<sub>Finger</sub> and PAT<sub>Toe</sub> remained unchanged ( $p = 0.898$  and  $0.957$ ). However, ICT increased by  $8 \pm 13$  ms ( $p = 0.036$ ) after 60 days in HDTBR and the corrected PAT values (see Fig. 2) for the femoral and brachial artery (cPAT<sub>Thigh</sub> and cPAT<sub>Arm</sub>) were unaffected by HDTBR. In contrast, cPAT<sub>Finger</sub> and cPAT<sub>Toe</sub> tended to decrease by  $8 \pm 5$  and  $11 \pm 13$  ms, without reaching significance after correction for the increased ICT. None of the parameters showed significant interaction between HDTBR and artificial gravity training.

## Conclusion

60 days HDTBR, while producing cardiovascular deconditioning and cephalad fluid shifts akin to weightlessness, did not worsen vascular stiffness. Artificial gravity training did not modulate the response. We conclude that only ICT corrected PAT values should be used as vascular biomarkers.

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# Short-term hypercaloric diet decreases hypothalamic and brainstem functional connectivity in humans

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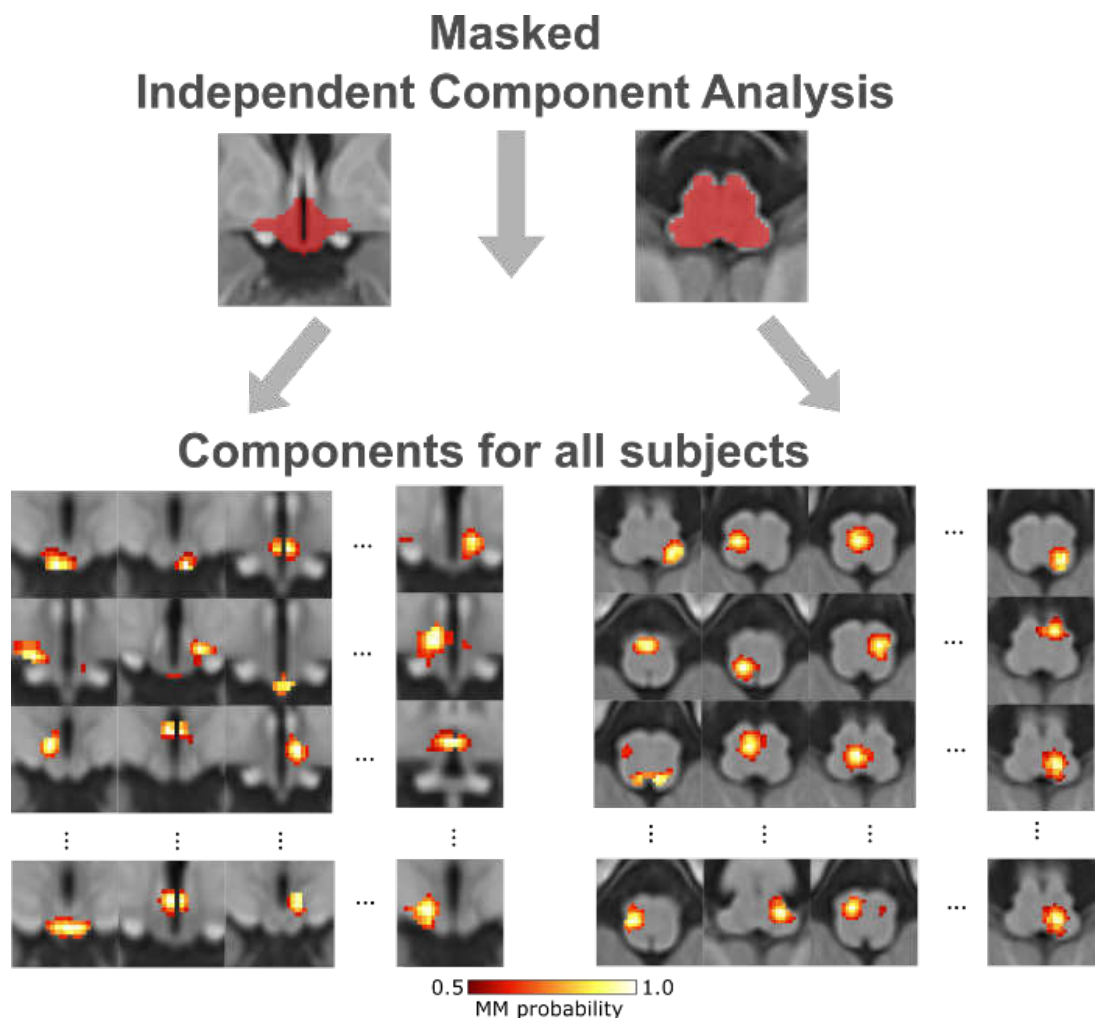


Fig. 1: Masked independent component analysis (mICA) decomposes the BOLD signal into spatially independent components where each independent component consists of voxels that show similar signal fluctuations.

Hypothalamic and brainstem pathways, particularly the leptin melanocortin system, regulate energy balance through adjustments in autonomic efferent activity. Disordered regulation of the system predisposes to obesity and obesity-associated arterial hypertension. We applied high-resolution subcortical functional magnetic resonance imaging (fMRI) to test whether short-term increase in energy intake elicit functional connectivity changes between and within hypothalamus and brainstem nuclei in human beings.

We submitted 20 subjects (7 women, 26.7±8 years; 22.6±2 kg/m<sup>2</sup>) to 5 days hypercaloric (25% increase of energy intake by fat) or normocaloric diets in a randomized crossover fashion with a washout period between interventions. We obtained high resolution brainstem and hypothalamus fMRI (3T PET/MRI, Siemens mMR Biograph). Then, we applied masked independent component analysis for resting state measurements and defined functional connectivity changes using dual regression between and within relevant regions.

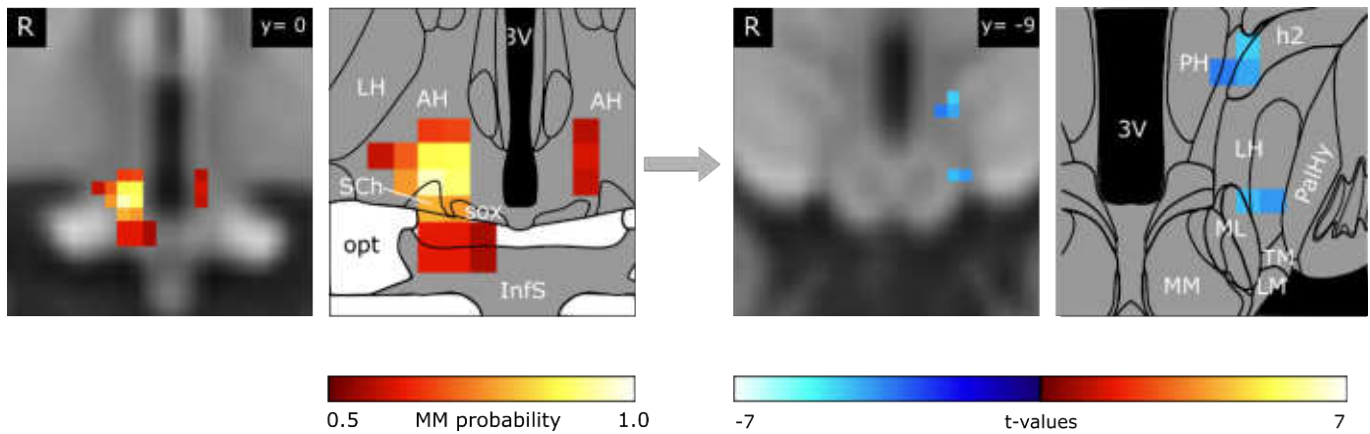


Fig. 2: We observed significantly decreased functional connectivity after hypercaloric compared to normocaloric diet. Connectivity changes obtained were  $P < 0.05$  and threshold-free cluster enhancement (tfce) corrected. Regions that are involved in metabolic regulation: arcuate nucleus (InfS), mammillary bodies (ML), and lateral and posterior hypothalamic areas (LH and PH).

We observed significantly decreased functional connectivity after hypercaloric compared to normocaloric diet. In particular, connectivity decreased between hypothalamic regions involved in metabolic regulation such as ventromedial and arcuate nuclei, mammillary bodies, and lateral and posterior hypothalamic areas. In the brainstem, functional connectivity decreased between rostral ventrolateral medulla and the inferior olive; two regions involved in sympathetic regulation. Moreover, connectivity decreased between hypothalamus and brainstem involving several nuclei: ventromedial, arcuate and supraoptic nuclei in the hypothalamus; as well as the solitary, raphe and inferior olivary nuclei in the brainstem.

We conclude that several days hypercaloric dieting produces significant resting state functional connectivity changes within and between hypothalamus and brainstem areas known to regulate efferent autonomic activity. The methodology may have utility in elucidating how metabolic and cardiovascular autonomic control are integrated in human beings and how perturbed regulation contributes to cardiometabolic disease.

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# Prolonged hypoxia exposure in fully revascularized patients with prior myocardial infarction

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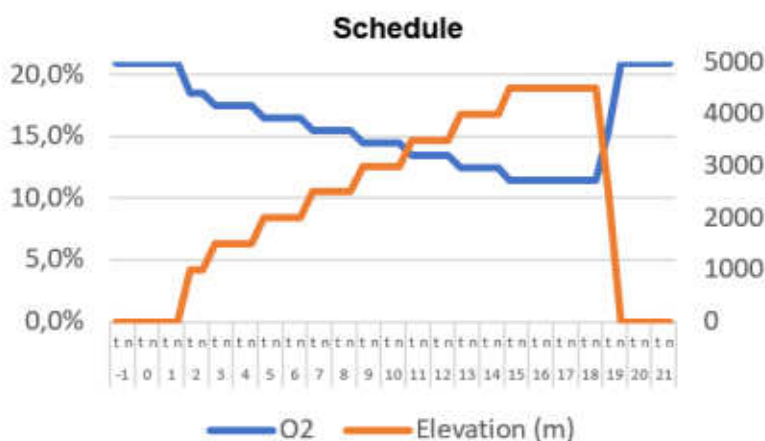


Fig. 1: Gradual adaptation of subjects to a FiO<sub>2</sub> of 11.5% (corresponding to 4500 altitude meters) followed by recovery.

Treatments improving cardiac regeneration could transform clinical management of ischemic cardiomyopathy. In mice with experimental myocardial infarction, prolonged normobaric hypoxia exposure corresponding to around 8,000 m altitude induced myocardial mitosis and improved left ventricular function. We determined whether a similar approach could be feasible and safe in patients.

We included four highly selected men with myocardial infarction in their history (3x STEMI, 1x NSTEMI). Patients had coronary 1-vessel disease with a fully revascularized LAD stenosis as culprit lesion. The study, which was conducted at the :envihab facility, included a two-day baseline, 19 days normobaric hypoxia, and a two-day recovery period. Atmospheric oxygen was gradually lowered to 11.8% and maintained at that level for 4 days. We obtained transthoracic echocardiography, magnetic resonance imaging of the heart and the brain at baseline, during 11.8% oxygen, and recovery, and daily 12-lead ECG.

Except for symptoms of acute mountain sickness, which improved over time, hypoxia was well tolerated and severe adverse reactions did not occur. Echocardiography revealed hypoxia

induced pulmonary hypertension, which rapidly abated during recovery. Mean left ventricular ejection fraction was  $50.7 \pm 11.0$  % (mean $\pm$ SD) at baseline,  $57.6 \pm 11.2$  % during hypoxia, and  $57.3 \pm 11.2$  following recovery ( $p=0.045$ ). Cardiac magnetic resonance imaging confirmed the finding. In patients with elevated NTproBNP at baseline, the measurement was decreased during hypoxia and following recovery. Troponin I concentrations remained in the reference range throughout the study.

In a small number of fully revascularized, highly selected patients with prior myocardial infarction, prolonged exposure to substantial normobaric hypoxia was feasible and safe despite reversible increases in pulmonary artery pressure. In fact, left ventricular ejection fraction and NTproBNP were improved during and following hypoxia exposure. Our findings provide critical information for further studies assessing influences of hypoxia on cardiac regeneration in human beings.

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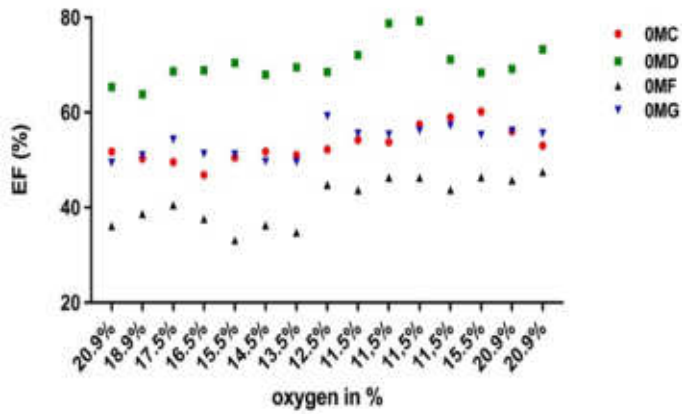


Fig. 2: Course of echocardiographically biplan measured left ventricular ejection fraction. Note the tendency to increase under hypoxia and the persistent improvement in LVEF in OMF.

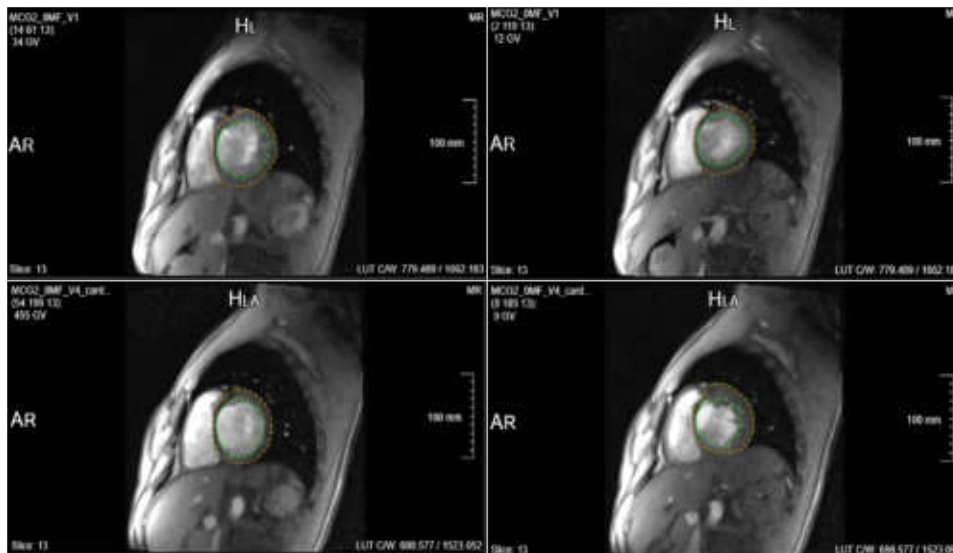


Fig. 3: Comparison of enddiastolic and endsystolic mid systolic anatomy left ventricle in short axis (MRI). Upper row presents baseline measurement, lower row measurements of follow-up two months after study. Improved lateral and inferior systolic functions led to an increased LVEF from 36% in baseline to 48% in follow up (MRI).

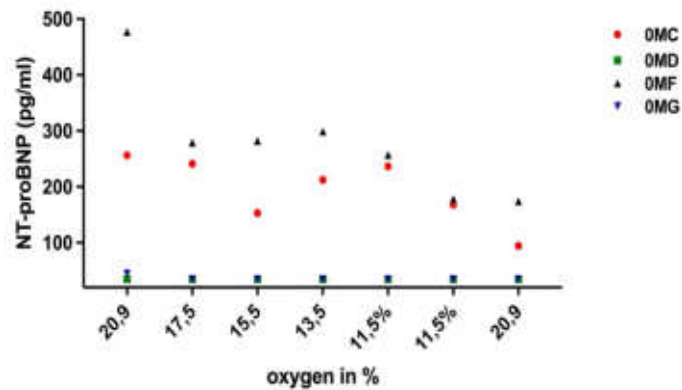


Fig. 4: Reduction of NTproBNP under hypoxia, lower detection limit 35 pg/ml; first measurement at 11.5% on day 1; 2nd on day 4.

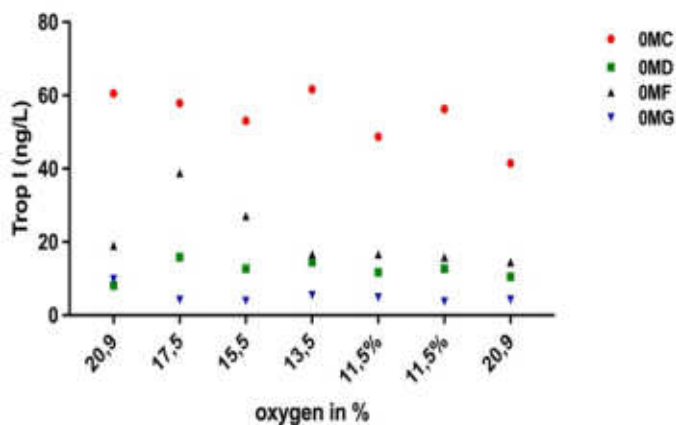


Fig. 5: No laboratory evidence of myocardial cell injury under hypoxia; first measurement at 11.5% on day 1; second on day 4.



## Sleep and Human Factors Research

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# 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. This research includes examining aeronautic protective equipment and emergency protocols for aviation industry. Digital health expertise provides medical support for patients and research through remote applications.

## *Working Group*

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

- Effects of sleep loss, adverse work hours and workload
- Neuromolecular mechanisms conveying individual (trait) vulnerabilities
- Developing individualized countermeasures

## *Teams*

### ***Baromedicine (Prof. Dr. Daniel Aeschbach)***

- Effects of breathing atmosphere on sleep, circadian phase shifting, performance and cardiometabolic disease
- Hypoxia and hypercapnia interactions guiding aircraft design
- Fit-for-air-travel testing in diseased individuals
- Human proof-of-concept studies (e.g., hypoxia as a potential chronobiotic intervention, cardiac regeneration)

### ***Digital Health (Dr. Markus Lindlar)***

- Developing and evaluating biomedical systems and care concepts

### ***Noise Effects Research (Prof. Dr. 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)

# Aircraft noise through the lens of social justice research

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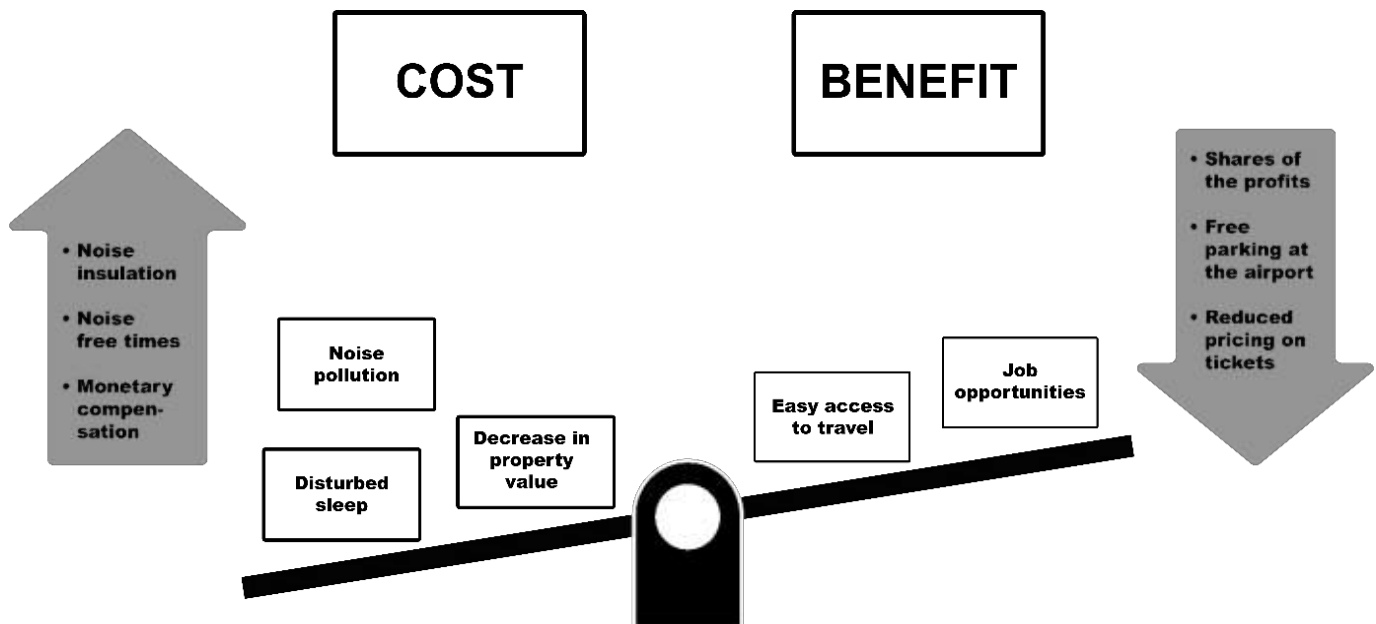


Fig. 1: Illustration of balancing the individual cost-benefit ratio (Hauptvogel et al., 2021).

Long-term exposure to aircraft noise is associated with a wide range of adverse effects including annoyance, sleep disturbance, impaired cognition, and negative impact on health [1,3,4,7]. Annoyance due to aircraft noise, seen as stress response, is not only a consequence of noise, but may also mediate adverse health effects. Therefore, measures aiming at reducing annoyance might also mitigate negative health effects. Perceived (un)fairness is seen as an important factor in the experience of annoyance [5].

## ***Why should aircraft noise exposure be considered from the perspective of fairness research?***

While some residents benefit from the airport in the region (easier access to travel, employment opportunities), a large number of residents living under the flight paths suffers from the negative effects of aircraft noise (see Fig. 1). Aircraft noise through the lens of fairness research reflects a new way to see the dispute of aircraft noise and offers novel approaches that could potentially be effective in mitigating the effects of aircraft noise. But how can fairness research help to deal this dilemma?

## **Distributive fairness**

From the point of view of distributive fairness, the distribution of advantages and disadvantages that the airport brings to the region is unfair (see Fig. 1). One way to mitigate the effect of this circumstance is achieving a balance between costs and benefits for residents (see Fig. 1).

## **Procedural Fairness**

Research has shown that the perception of fairness is not only impacted by the outcome, in this case the amount of noise, but in many ways by the process that leads to the noise level. People are more likely to accept and adopt outcomes that are unwanted, when the decisions were based on procedures that have been viewed as fair. Leventhal [6] developed a set of criteria that determine the perception of procedural fairness and Hauptvogel [5] newly applied them to the context of aircraft noise. Procedural aspects can have an enormous influence on how people perceive aviation, the airport, and the noise and to what extent they are annoyed by noise. Interventions that take these insights into account can therefore be very effective.



Representativeness	The concerns and opinions of all affected residents are represented. Involving independent and neutral bodies would be a way to applicate this.
Consistency Rule	The decision-making processes at the airport are consistent across all residents.
Bias Suppression Rule	Decisions at the airport, e.g. on night flights, should not only be made on the basis of self-interest, but should also be based on current scientific findings regarding health risks.
Accuracy Rule	Decisions affecting aircraft noise should be made on the basis of sufficient, correct and appropriate information.
Correctability Rule	Every affected group of people has the opportunity to question, adjust and reverse decisions that have been made.
Ethicality Rule	In general, all processes that have an impact on noise should be able to be reconciled with ethical and moral standards.

Table 1: Standards of procedural fairness applied to the context of aviation noise according to Hauptvogel et al. (2021).

Truthfulness	When the airport communicates with residents, it should always be honest and sincere, even if the message is unfavorable to the residents. Downplaying the impact of decisions made can be perceived as lying or deception by affected residents.
Justification	Decisions affecting aircraft noise will be perceived as fairer if they are thoroughly and comprehensively explained and adequate justification and reasoning is provided.
Respect	The airport should be respectful and courteous in its dealings with residents and take seriously every individual concern that is perceived as subjectively important.
Propriety	In dealing with residents, the airport should refrain from prejudice and inappropriate comments, even when residents are upset or angry. This is about recognizing the emotional situation of residents.

Table 2: Standards of procedural fairness applied to the context of aviation noise according to Hauptvogel et al. (2021).

### Interactional Fairness

From the perspective of fairness, informational and interpersonal aspects are important, in such a way that people may perceive unfairness, even though they consider the procedure and its results as fair, just because of improper treatment or a lack of justification. Bies & Moag [2] developed a set of criteria that constitute interactional fairness. When applied to the field of aircraft noise research, they would resemble as follows:

### Conclusion and Outlook

Fairness aspects are regarded as potentially important factors in dealing with the aircraft noise problem. At first glance, many of these measures and findings seem plausible and common knowledge, but in reality, they are rarely or insufficiently implemented. A full integration of fairness psychology findings into the process of aircraft noise impact mitigation can be very successful in reducing perceived annoyance and improving the quality of residents' life.

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# Synergetic effects of nocturnal road noise exposure and work-related stress on self-rated sleep quality

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Sleep disturbance may be caused by nocturnal transportation noise but also by other non-acoustic stressors, particularly by psychosocial factors such as work-related stress. However, few studies have focused on their synergetic effects on sleep. A survey among 3,460 Swedish working women aged 23-65 years investigated the effect of nocturnal road noise exposure, work-related stress and their potential synergetic effect on self-rated sleep quality. Self-rated sleep quality was assessed via five questions (general sleep quality, problems to fall asleep, early awakenings, and problems to fall asleep again, tiredness in the morning, and sleepiness during the subsequent day). Responses were condensed and dichotomized differentiating between “poor sleep” and “no poor sleep”.

In a subsample A with N = 2,192 respondents, the equivalent sound pressure level was modelled for the time between 22:00 to 06:00 and for the most exposed façade ( $L_{night}$ ), and its effect on the prevalence of poor sleep was examined. Exposure classes were < 45 dB(A), 45-50 dB(A), and > 50 dB(A). For a subsample B with N = 1,764 respondents, we examined the effect of the façade of the bedroom differentiating between facing either no street, a low-traffic street, or a medium/high-traffic street.

Work-related stress was operationalized by the construct Job Strain [1] that reflects the ratio between psychological job demands and job control. We differentiated between low, medium, and high Job Strain.

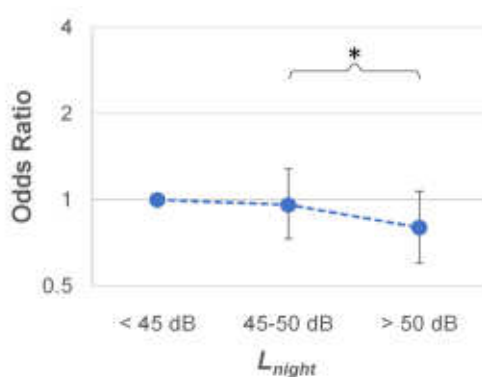


Fig. 1: Odds Ratios (OR) and 95 % Confidence Intervals for the effect of the  $L_{night}$  on the prevalence of poor sleep (Subsample A).



Fig. 2: Odds Ratios (OR) and 95 % Confidence Intervals for the effect of the bedroom façade on the prevalence of poor sleep (Subsample B).

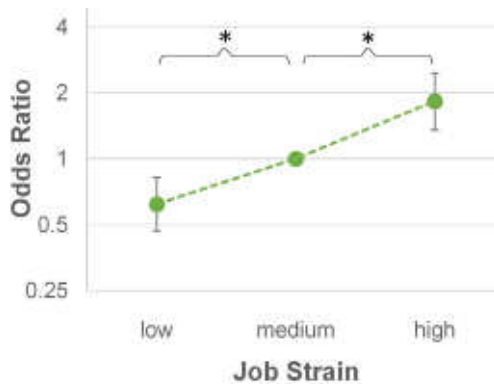


Fig. 3: Odds Ratios (OR) and 95 % Confidence Intervals for the effect of Job Strain on the prevalence of poor sleep (Subsample A).



Fig. 4: Odds Ratios (OR) and 95 % Confidence Intervals for the effect of several combinations of levels of Job Strain and different bedroom façades on the prevalence of poor sleep (Subsample B).

In order to examine the effect of the predictors on the prevalence of poor sleep, we applied multivariate logistic regression models including a noise exposure variable each, Job Strain and a broad range of a priori selected modifiers and cofounders, such as age, BMI, and general sensitivity to noise. Synergetic effects were examined via testing for additive interaction and applying the index Attributional Proportion [2].

The  $L_{\text{night}}$  was not positively associated with the prevalence of poor sleep as it would have been expected (Fig. 1). On the contrary, the prevalence of poor sleep was lowest in the highest noise exposure class. Possibly, the noise exposure was misclassified since information on the façade of the bedroom and further relevant variables (story, window opening behaviour) were not available for this subsample.

We found a non-significant increase in the prevalence of poor sleep in respondents with bedrooms facing medium or high-traffic streets compared to a quiet façade (Fig. 2). Future noise impact studies should consider the bedroom façade in the modelling of nocturnal exposure levels.

The prevalence of poor sleep significantly increased with increasing Job Strain (Fig. 3). Moreover, we found a trend for an additive interaction between the bedroom façade and Job Strain (Fig. 4). The Attributional Proportion (AP) that quantifies the extent of the additive interaction, however, was not significant (AP = 0.46, 95 % CI: -0.09 – 1.00).

Our results suggest that work-related stress and potential additive interactions with noise exposure can have relevance for self-rated sleep quality and should be considered more thoroughly in future (epidemiological) noise impact studies. Examinations on a population level including men is recommended to establish generalizability and to consider sex differences.

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# Impact of coffee on sleep and performance in sleep-restricted and caffeine-sensitive individuals

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Caffeine is commonly trusted to counteract the performance impairing effects of sleep loss and extended work shifts, conditions that are frequently encountered by operators in aviation and space missions. However, the knowledge on the day-to-day efficacy of caffeine in preserving optimal cognitive performance under conditions of chronic sleep restriction is scarce and complicated by the fact that caffeine also negatively impacts sleep. Especially deep sleep duration, a state which is important for nighttime recovery and consequently next-day performance, is reduced by caffeine.

To answer the question how caffeine consumption affects sleep and cognitive perfor-

mance under conditions of chronic sleep restriction, we investigated the efficacy of caffeine in individuals who carry the C/C-allele of the adenosine A2A receptor (ADORA2A c.1976), a genotype known to have a high caffeine-sensitivity. We chose a naturalistic caffeine administration of brewed coffee consumed twice a day – in the morning and in the early afternoon. Seventy-one healthy volunteers aged 20 to 40 years were examined in the sleep and simulation area of the DLR :envi-hab. 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), followed by 5 experimental nights (E1-E5) and

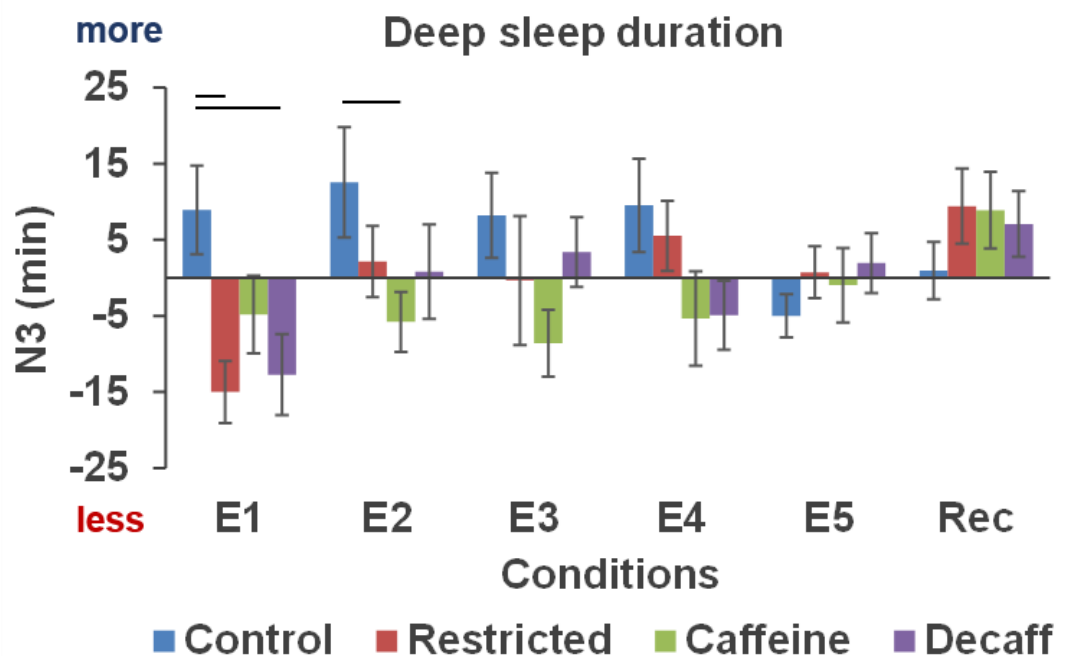


Fig. 1: Deep sleep duration (N3) measured with polysomnography. N3 duration under different experimental conditions is displayed as difference from rested baseline. Significant between-group differences are indicated with horizontal lines. Rested control group (Control, blue), sleep restriction group (Restricted, red), caffeine group (Caffeine, green), decaffeinated coffee group (Decaff, violet). Experimental night 1 to 5 (E1 to E5), recovery (Rec).

one final recovery night (Rec) with 8 h TIB. (1) The rested control group (mean age  $\pm$  SD  $28 \pm 6$  years,  $n=15$ , 5 female) was not sleep restricted and continued with 8h TIB through E1 to E5. (2) The restriction group ( $26 \pm 4$  years,  $n=21$ , 9 female) had 5 h TIB through E1 to E5. (3) The caffeine group ( $30 \pm 5$  years,  $n=19$ , 8 female) had the same schedule as the restriction group, but received standardized 600 ml coffee per day (in total  $\sim 300$  mg caffeine: morning dose 200 mg, early afternoon dose 100 mg) double-blind during E1 to E4 and 400 ml coffee ( $\sim 200$  mg caffeine, morning dose only) on E5. (4) The decaffeinated coffee group (Decaff,  $28 \pm 5$  years,  $n=16$ , 7 female) underwent the same schedule as the caffeine group, but consumed decaffeinated coffee. Participants of the caffeine (76% C/C) and Decaff (88% C/C) groups predominantly carried the caffeine-sensitive genotype. Polysomnography was recorded to quantify deep sleep (N3) duration. A 10-min Psychomotor Vigilance Task (PVT) was used to calculate participants' mean daytime (at 2h, 5h, 11h, and 15h awake) speed (1/reaction time). Differences between groups were examined using mixed ANOVAs with Bonferroni adjusted  $p < 0.016$ .

N3 duration was reduced on E1 in the restriction group and the Decaff group in compari-

son to the control group ( $p < 0.01$ ). The caffeine group had on trend niveau reduced N3 duration on E1 to E4 accumulating a N3 deficit during sleep restriction of on average  $-31$  min (n.s.). Speed was faster in the caffeine group compared to the restriction group during the daytime after E1 and E2 ( $p < 0.002$ ). While participants' performance in the restriction and Decaff groups was not different from the control group after Rec, speed in the caffeine group was still impaired.

Under conditions of chronic sleep restriction,  $\sim 300$  mg caffeine per day kept caffeine-sensitive individuals' cognitive performance at rested levels for two days. However, the use of caffeine delayed recovery. The caffeine-induced N3-deficit might be causal for the observed delay in recovery.

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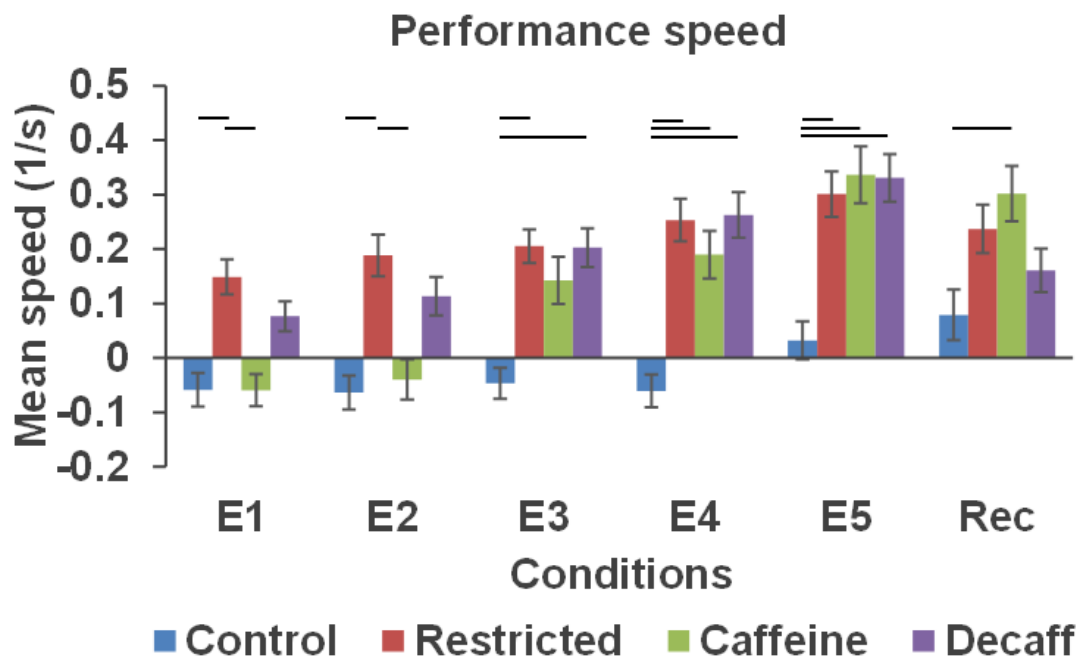


Fig. 2: Cognitive performance measured as speed on a 10-min psychomotor vigilance task. Mean daytime speed is displayed as difference from rested baseline. Significant between-group differences are indicated with horizontal lines. Rested control group (Control, blue), sleep restriction group (Restricted, red), caffeine group (Caffeine, green), decaffeinated coffee group (Decaff, violet). Experimental night 1 to 5 (E1 to E5), recovery (Rec).

# Effects of fatigue due to sleep loss and adverse time of day on team performance in control rooms

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Fig. 1: Example of a simulated control room in the lab.

Sleep deprivation impairs individual cognitive performance [1]. However, effects of fatigue on team performance and collaborative decision making are also affected by the social processes in the group [2,3] and their interaction is poorly understood [4]. We examined how sleep deprivation affects team performance in a simulated control room situation. We hypothesized that performance is less impaired by fatigue when operators work in a cooperative team than when they work alone.

Sixty-six healthy volunteers (32 females, mean age  $26 \pm 5$  years SD) were randomly assigned to groups of 3 members and underwent a sleep laboratory study for 5 consecutive days. Each participant performed a simulated control room task (ConCenT: Control Center Task Environment [5]) once following 19 h of wakefulness (sleep deprivation condition) during the circadian low (02:00 h - 07:00 h) and once between 08:00 h and 13:00 h following 8 h of

scheduled sleep and 1 h awake (baseline condition). Three different team conditions (solo, i.e. working alone, cooperative team condition pursuing the same goals, competitive team condition with conflicting goals) were applied. Subjective team cohesion was measured by questionnaire. Each team member completed the task on a separate computer (Fig. 1). The terminals were interconnected and team members communicated via intercom during the team conditions. We analyzed reaction times and accuracy of the responses in a monitoring task (monitoring for system failures requiring sustained attention) and in a diagnosis task (identifying the cause of system failures by logical reasoning) using linear mixed models. To investigate the effect of working in a team, interactions between sleep and team condition were calculated using data from the solo and cooperative team condition.

In the monitoring task, participants' reactions to system failures were slower under sleep

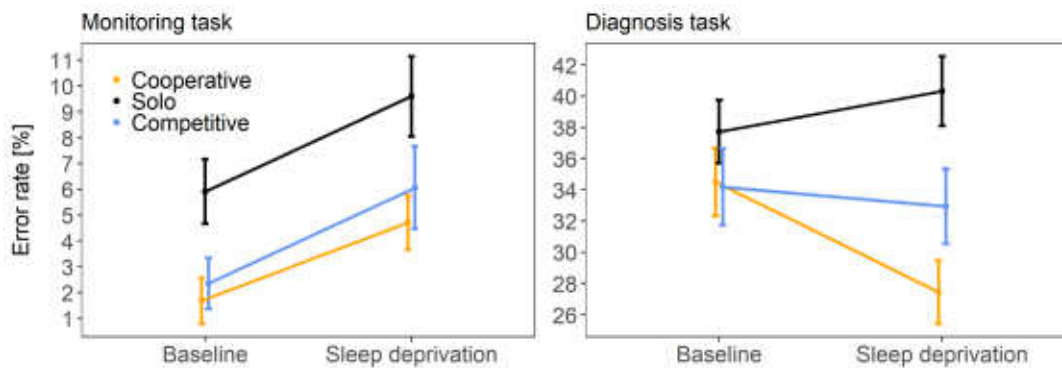


Fig. 2: Effects of sleep and team conditions on response accuracy in the monitoring task (left panel) and in the diagnosis task (right panel).

deprivation than during baseline ( $p < .001$ ), and faster in the solo condition than in both team conditions (both  $p < .001$ ). We found no interaction between sleep and team condition. Furthermore, individuals were less accurate (Fig. 2, left panel) under sleep deprivation than during baseline ( $p < .001$ ) and also less accurate in the solo condition than in both team conditions (both  $p < .001$ ). Again, we observed no interaction between sleep and team condition.

In the diagnosis task, participants took longer to solve the task when sleep deprived in comparison to baseline ( $p < .001$ ). We observed slower reactions in both team conditions compared to the solo condition (both,  $p < .001$ ), as well, but no interaction between sleep and team condition. We found no main effects of sleep and team condition on the accuracy in the diagnosis task (Fig. 2, right panel), but a significant interaction effect ( $p < .001$ ). Interestingly, in contrast to the solo condition participants in the cooperative team condition were even more accurate under sleep deprivation than in the baseline condition. Subjectively, team members reported higher team cohesion when sleep deprived than at baseline ( $p = .004$ ), and in the cooperative team condition compared to the competitive team condition ( $p < .001$ ).

Our findings demonstrate that not only individual performance is affected by sleep deprivation, but also team performance. Though team work had no general protective effect, it seemed to mitigate the effects of fatigue in one of the two tasks. As such, in the monitoring task, reaction time and accuracy were impaired by sleep loss in the solo as well as in the

team conditions. In the diagnosis task, however, working in a cooperative team in contrast to working alone resulted even in higher accuracy under conditions of sleep deprivation compared to baseline. The knowledge of the sleep loss induced performance decrements of the other team members may have motivated them to support each other. This idea is in line with the reported group cohesion in cooperative teams and under sleep deprivation.

In conclusion, sleep loss deteriorates group performance in a control room simulation, but during specific tasks (logical reasoning) and team contexts (cooperative teams) operators may be able to compensate fatigue effects.

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## Clinical Aerospace Medicine

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# 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.

## *Teams*

### ***Aeromedical Center (Dr. 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. 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)

*Photo: Application of electrodes during an electro-retinogram examination in the SANS CM study.*

# Training astronauts to conduct eye examinations in space

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Fig. 1: Training SpaceX Crew 3 for taking optic disc images by means of our eye diagnostics device. Image credit: ESA/NASA.

## Background

As part of an International Space Station (ISS) Technology Demonstration Experiment, planned for European Space Agency (ESA) Astronaut Matthias Maurer's Increment 66 Cosmic Kiss Mission, Space X Crew 3 was trained to conduct their own eye examinations in space using a small, lightweight mobile device (see Fig. 1).

Training on eye diagnostic devices is important to detect and mitigate against the eye pathologies that astronauts experience, collectively termed Spaceflight Associated Neuro-ocular Syndrome (SANS) (previously called Visual Impairment and Intracranial Pressure (VIIP) syndrome) [1]. Smaller footprint devices, like these, may eventually replace older eye diagnostics devices, which are currently

used in spaceflight, by offering multiple advantages in size, weight, and diagnostic capability.

This technology is currently at Technology Readiness Level (TRL) 6, as defined by the National Aeronautics and Space Administration (NASA). Parabolic flight testing to advance the TRL from 4 to 6 was conducted in 2021 (Fig. 2). Testing aboard the ISS is a necessary step for TRL advancement from 6 to 7. The technology demonstration experiment enables human-in-the-loop (HITL) testing of eye diagnostic devices during spaceflight, as the final step in TRL advancement. This TRL advancement would determine feasibility for long-term use in microgravity for potential use during the Artemis program, and for TRL advancement from 7 to 9 [2].



Fig. 2. Parabolic flight testing for space approval of our tablet-based eye diagnostic device. Image credit: Nicolas Courtioux/Novespace.

### Current status

Astronaut eye medical monitoring is currently done aboard the ISS using Optical Coherence Tomography (OCT) scanners (10+ kg, 140 VA). To monitor these changes during spaceflight, OCT scanners have been launched to the ISS. These machines are the gold standard in clinical ophthalmology, but they cost approximately \$100,000 USD, weigh over 10 kg, and have a power consumption of 140 VA. Assuming launch costs of \$10,000 USD per kg, launch alone costs \$100,000 USD per machine [3]. Previous activities related to this experiment conducted by DLR include comparison of retinal fundus image and video collection using several imaging devices, which occurred during medical monitoring in the most recent head-down tilt bed rest studies from 2019-2020. Anonymized images from both the left and right eyes of normal retinas and retinas with degrees of optic disc edema were collected. These and other retrospectively collected images are being used to develop machine learning models to detect SANS [4].

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# Space meets glaucoma

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Fig. 1: Eye-examination.

## Introduction

Glaucoma is among the most common causes for blindness worldwide. The prevalence of the condition in people >65 years of age is approximately 2-4%. In Germany, approximately 1,000 people are estimated to become legally blind secondary to glaucoma each year. Elevated intraocular pressure is crucial to the pathogenesis of glaucoma causing secondary optic disc atrophy and is the only risk factor amenable to therapy. Intraocular pressure follows circadian rhythms [1,2] and depends on body position with an increase in the supine position [3]. We showed that head down bedrest partly reproduces some of the changes of SANS (Spaceflight associated neuro-ocular syndrome), an unresolved challenge to human spaceflight characterized by optic nerve

head swelling, likely through volume shifts towards the head. Therefore, we reasoned that sleeping in the head up tilt position during the night could unload the eye and ameliorate intraocular pressure.

## Study design

We included 16 patients with ocular hypertension, primary open-angle glaucoma, or secondary open-angle glaucoma. In a cross-over fashion, patients slept in the supine or in a 10° head-up-tilt position at the DLR research ward. We conducted non-invasive intraocular pressure measurements during day and night. In addition, we assessed non-invasive blood pressure and non-invasive examinations of the optic nerve using Optical Coherence Tomography (OCT) (Table 1).

Table 1: Detailed eye examination protocol: OCT = Optical Coherence Tomography; IOP = IntraOcular Pressure.

Activity	Description	Duration [min]
Arrival/Anamnesis Day 1	<ul style="list-style-type: none"> <li>Briefly medical examination</li> <li>Slit lamp examination</li> <li>First IOP measurements with ICare and Goldmann, repetition every 4-6 hours</li> <li>Application of blood pressure cuff</li> <li>Randomization into Group A or B</li> </ul>	~45min
Before night 1	<ul style="list-style-type: none"> <li>OCT</li> </ul>	~30 min
Night 1	<ul style="list-style-type: none"> <li>Sleeping either in head tilted up 10° position (Group A) or supine (Group B)</li> <li>IOP with Icare at 3 and 6 o'clock</li> </ul>	~8 hours ~10min
After night 1	<ul style="list-style-type: none"> <li>OCT</li> </ul>	~30min
Day 2	<ul style="list-style-type: none"> <li>IOP measurements with Icare, repetition every 4-6 hours</li> </ul>	~10 min
Before night 2	<ul style="list-style-type: none"> <li>OCT</li> </ul>	~30 min
Night 2	<ul style="list-style-type: none"> <li>Cross-over: Sleeping in head tilted up 10° position (Group B) or supine (Group A)</li> <li>IOP measurements with Icare, repetition every 4-6 hours</li> </ul>	~8 hours ~20 min
After night 2	<ul style="list-style-type: none"> <li>OCT</li> </ul>	~30min
Day 3	<ul style="list-style-type: none"> <li>IOP measurements with Icare, repetition every 4-6 hours</li> </ul>	~20min
End of protocol	<ul style="list-style-type: none"> <li>Medical release</li> </ul>	5 min

## Conclusion

Observations and technologies generated in space medicine can be translated to applications in terrestrial medicine. The data of the study are still evaluated. In case intraocular pressure can simply be reduced by sleeping with the head tilted up, this would have implications for the management of glaucoma, particularly for patients not sufficiently responding to current therapies or living in medically underserved parts of the world.

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## Muscle and Bone Metabolism

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# 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 long-lasting 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 the prevention and rehabilitation of immobilization-related musculoskeletal disorders. To this purpose, we aim 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. 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 (Dr. Uwe Mittag)***

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

### ***Training and Countermeasures (PD Dr. Jochen Zange)***

- Exercise training studies, musculoskeletal imaging, exercise countermeasure development

*Photo: Investigation of internal muscle mechanics in the Democles study.*

# Lower limb bone geometry in adult individuals with X-linked hypophosphatemia

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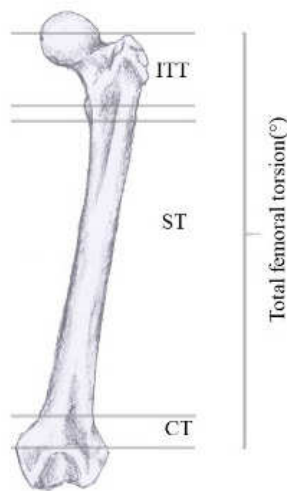


Fig. 1: On the left sections measured to assess the regional torsion.

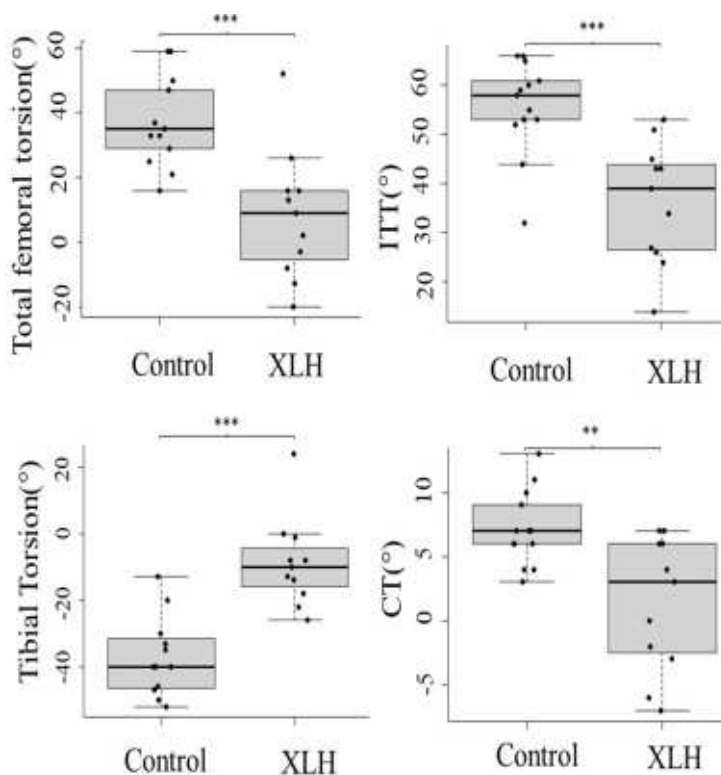


Fig. 2: Box plots of Total torsion (FNA) and the regional torsion.

## Introduction

X-linked hypophosphatemia (XLH) is a rare genetic condition that affects phosphate metabolism, resulting in osteomalacia. Individuals with XLH are also at risk of lower limb deformities and early onset of hip osteoarthritis. These two factors may be linked, as abnormal femoral torsion is a risk factor for hip osteoarthritis. The contributions of regional femoral torsion e.g. intertrochanteric torsion (ITT), shaft torsion (ST), and condylar torsion (CT) to total femoral torsion differ between clinical groups and are important when planning femoral osteotomies to correct femoral torsion. Other lower limb deformities such as bowing of femur and tibia and lower limb alignment, have to be considered as well. This study aimed to compare total and regional femoral torsion, lateral and frontal bowing of the femur and tibia, limb alignment and bone cross sectional area (CSA) between adults with XLH and controls.

## Methods

13 individuals with XLH (5 male, age 49±9y) and 12 age, sex, and weight-matched control participants (7 male, age 49±8y) were recruited following ethical approval and informed consent. Magnetic resonance imaging (MRI) scans of the left lower limb were obtained, from which lower limb bone geometry of the femur and tibia were measured. Data were normally distributed; therefore, group differences were assessed using t-tests.

## Results

Total femoral torsion was 29° lower in individuals with XLH than controls (p<0.005). This resulted mainly from lower ITT (p<0.001) and in part CT (p<0.05) whereas ST was similar in the two groups (Fig. 1). Femoral lateral bow-



ing was higher in individuals with XLH ( $13.1 \pm 7.0^\circ$ ) than controls ( $-1.0 \pm 2.5^\circ$ ,  $p < 0.001$ ), as was femoral frontal bowing ( $31.4 \pm 7.3^\circ$  XLH,  $17.8 \pm 1.4^\circ$  controls,  $p < 0.001$ ). There was a  $2.9^\circ$  difference in the mechanical axis between the XLH group ( $5.6 \pm 5.3^\circ$ ) and the control group ( $1.5 \pm 2.5^\circ$ ,  $p < 0.05$ ). and no difference in the average of the femoro-tibial angle. Acetabular version was significantly increased in individuals with XLH ( $23.6 \pm 8.4^\circ$ ) as compared to those in the control group ( $17.5 \pm 3.9^\circ$ ,  $p < 0.05$ ). Additionally, acetabular coverage was  $32.6^\circ$  higher in individuals with XLH ( $192.5 \pm 22.6^\circ$ ) than the control group ( $159.9 \pm 9.1^\circ$ ,  $p < 0.001$ ). The total CSA of the femoral shaft was 22% greater in individuals with XLH ( $p < 0.001$ ). The bone marrow cavity of the femoral shaft was  $\sim 64\%$  greater in individuals with XLH ( $p < 0.001$ ). In the tibia the total CSA was similar, but the marrow cavity was  $\sim 40\%$  greater in the XLH individuals.

### Conclusion

Adults with XLH have substantial differences and greater inter-individual variation in lower limb bone geometry, principally lower femoral torsion originating in the intertrochanteric region, and higher lateral and frontal femoral bowing, whilst differences detected between the groups in the mechanical axis and tibi-ofemoral angle are minimal. The observation of a significantly increased total cross-sectional area of the femur and proximal tibia is remarkable, considering the overall reduced body size of XLH patients as compared to controls. Looking at it more closely, the difference results from an enlarged marrow cavity on all height levels along the femoral axis and the proximal tibia while cortical cross-sectional area is not significantly different on these levels. One may speculate if this is a matter of childhood rickets with compromised bone quality and deficient mineralization leading to increased bone turnover with enhanced endosteal bone resorption and periosteal apposition.

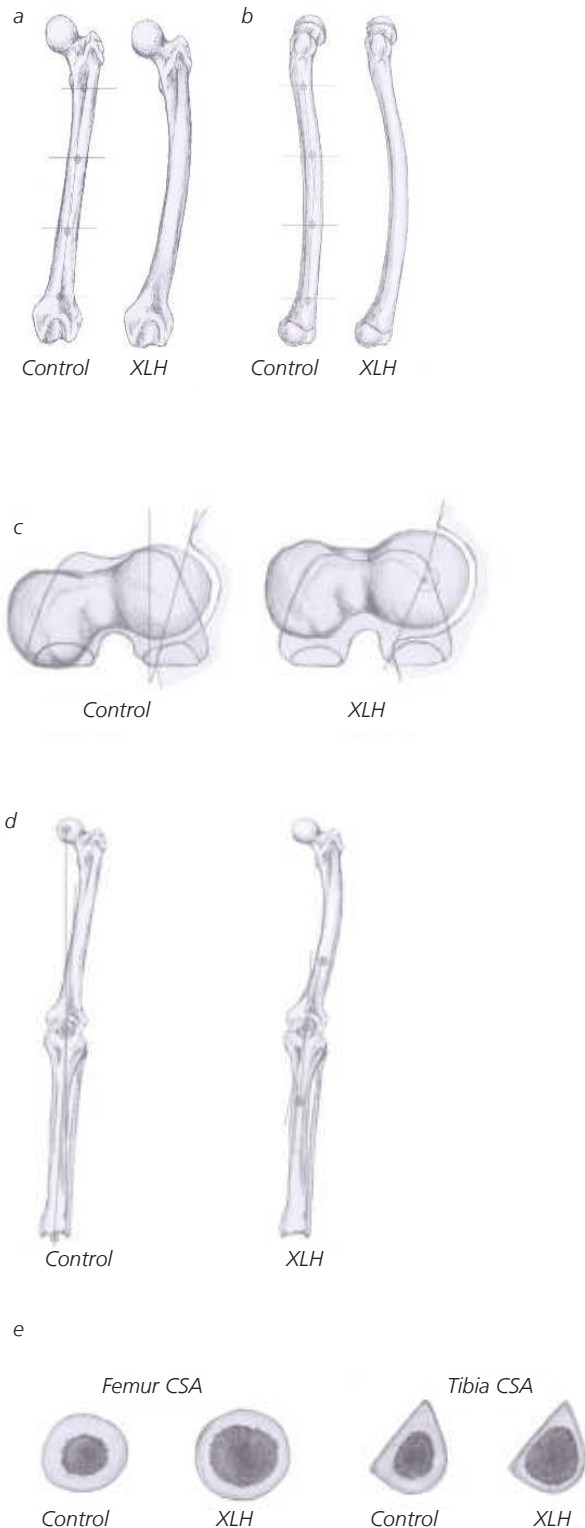


Fig. 3 a): visual representation of the average difference between the two groups from a frontal view. On the control panel the method of the bowing's measurement is drawn on. b): visual representation of the average difference from a lateral view. c): visual representation of the acetabular geometry, the femoro-acetabular relationship and total femoral torsion. On the control panel the acetabular version measurement is drawn on and on the XLH panel we can see the acetabular coverage measurement. d): visual representation of lower limb alignment. Also, the mechanical axis is drawn on the control limb and the femorotibial angle on the XLH limb. e): visual representation of average CSA of femur and tibia in the respective groups. Illustrations by X. O'Reilly-Berkeley.

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# Fascicle dynamics during sinusoidal perturbation in the human gastrocnemius medialis muscle before and after bed rest

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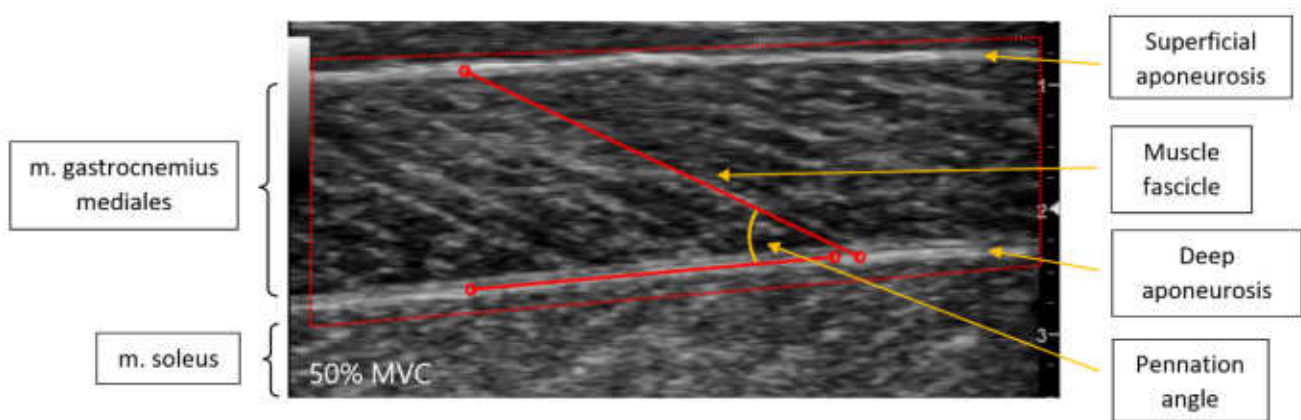


Fig. 1: Ultrasound image of gastrocnemius medialis muscle and UltraTrack tracking software inputs. Region of interest, fascicle and deep aponeurosis defined for processing fascicle length and pennation angle.

## Background

Vibration exposure has been used more and more frequently in recent years in sports, health, research, preventive medicine, and rehabilitation. It has been proven to be a useful training and examination method in a variety of contexts. In the body, periodic stretching and shortening cycles of the muscle-tendon complex occur during vibration, accompanied by periodic changes in fascicle length (FL) and pennation angle (PEN). However, little is known about the extent to which stretching and shortening depends on muscular preload and frequency. In the present study, SP was used to determine the dynamics of fascicles in human gastrocnemius medialis (GM) muscle. Therefore, the primary aim was to investigate the response of FL and PEN in GM to vibrations at different frequencies and contraction levels. In addition, the influence of long-term bed rest on FL and PEN deflectability was evaluated as well as the change of fascicle architecture under static conditions due to different levels of contraction.

## Methods

24 subjects performed the SP protocol before and after 60 days of bed rest (artificial gravity bed rest study AGBRESA). Subjects were grouped into three countermeasure groups: iAG (6 x 5 min centrifuge drive per day), cAG (1 x 30 min centrifuge drive per day) and control group (only bed rest). Ultrasound videos of GM were recorded during vibration exposure at ten different frequencies (4 -16 Hz) and four levels of contraction (isometric plantar flexion at 0, 25, 50 and 75% MVC). Muscle architecture and deflection of FL and PEN during vibration were evaluated using a semi-automated tracking software (UltraTrack, Fig. 1) and custom-made R-scripts. The peak-to-peak amplitude values ( $A_{p2p}$ ) were determined by means of peri-event averaging technique (Fig. 2) and referred as relative values ( $relA_{p2p}$ ) to the initial FL or PEN value. Linear mixed effects models with all possible interaction terms were constructed and stepwise simplified. Significant effects observed in the ANOVA were followed up by a-priori defined treatment contrasts with 4 Hz, 0% MVC, control group and baseline data as reference level of contrasts.

**Results**

The  $relA_{P2P}$  for reference level of contrasts was 1.94 (0.82) % for FL and 1.30 (0.99) % for PEN. The  $relA_{P2P}$  of FL and PEN was statistically significant smaller when muscle was contracted (FL:  $P < 0.001$  for 25 and 50% MVC,  $P < 0.01$  for 75% MVC; PEN:  $P < 0.001$  for 25% MVC and  $P < 0.01$  for 50% MVC). From 7 to 10 Hz there was a significant increase in  $relA_{P2P}$  for pre-tensioned muscle, especially in FL. After bed rest,  $relA_{P2P}$  was significantly greater at 9 and 10 Hz ( $P < 0.05$ ) for FL and at 8 Hz, 10 Hz ( $P < 0.01$ ) and 9 Hz ( $P < 0.05$ ) for PEN, respectively (Fig. 3).

**Conclusions**

Fascicle deflection decreases as the muscle contracts. However, no further correlation between level of contraction and decrease in  $relA_{P2P}$  could be found. The main finding of this study was a significant resonance effect at 7 – 10 Hz vibration in contracted muscle. Resonance was even more evident after bed rest. There was no alteration of resonance frequencies across the levels of contraction, potentially due to an equivalent increase in damping properties and stiffness as muscle activity elevates. It is furthermore conceivable that the increase in  $relA_{P2P}$  at vibration frequencies ranging from 7 – 10 Hz is a consequence of resonance within the natural tremor frequency, i.e. the induced vibration causes the physiological tremor to resonate. However, the exact cause of this resonance effect requires further investigation.

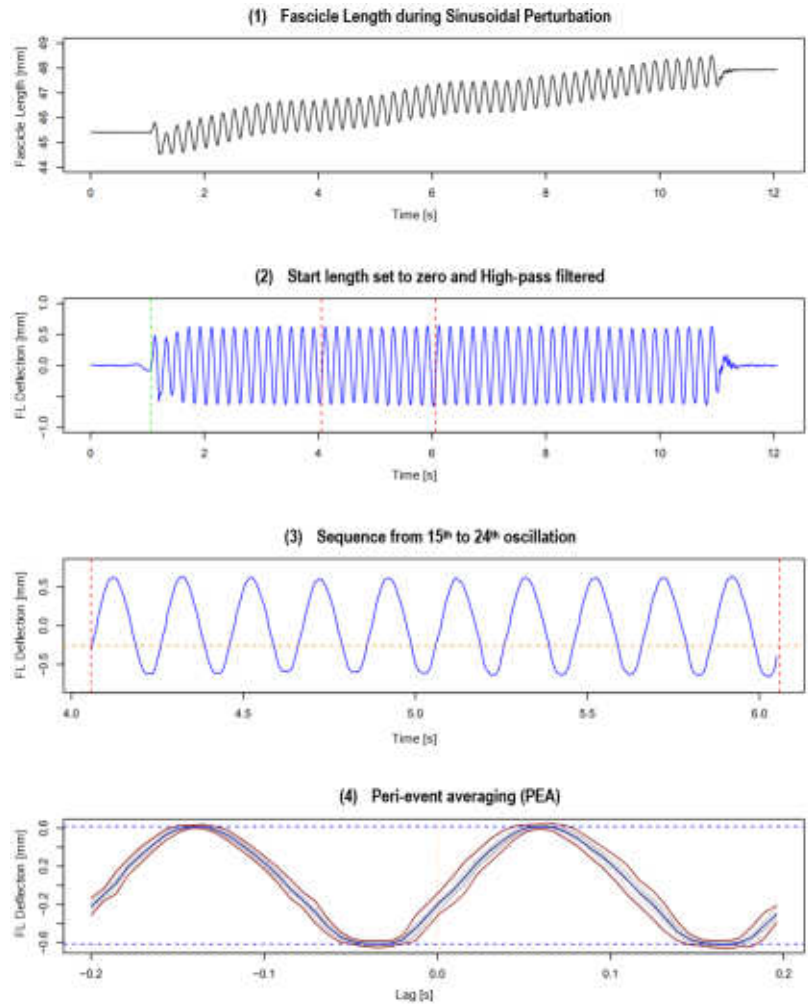


Fig. 2: Development process of peri-event averaging technique. (1) FL processed by tracking software. (2) Initial length set to zero and high-pass filtered. Start of perturbation (green dotted), start and end of sequence to be analyzed (red dotted). (3) Sequence of ten oscillation cycles and threshold value (orange dotted). (4) Peri-event averaging plot. Overlaid oscillations (grey), mean oscillation (blue), maximum and minimum value (blue dotted).

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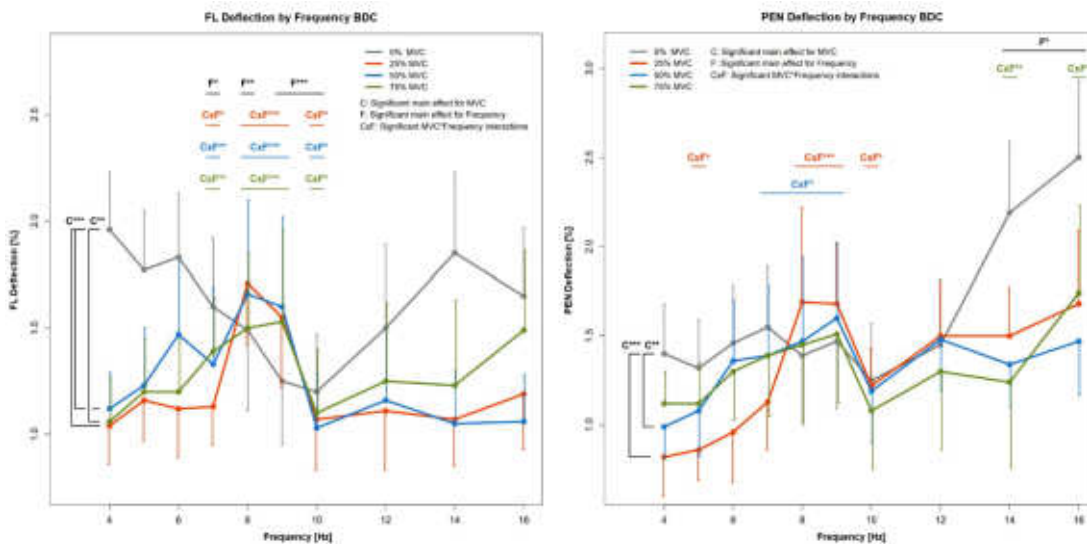


Fig. 3: Mean (and 95% confidence level) relative peak-to-peak amplitude of FL and PEN at baseline data collection by contraction level and frequency. F and C denote significant main effects for frequency and MVC level, respectively. CxF denotes significant MVC x frequency interactions, with 0% MVC x 4 Hz as reference level of contrast. Color represents MVC level. (\*\*\*)  $P < 0.001$ , (\*\*)  $P < 0.01$ , (\*)  $P < 0.05$ .

# Definition of a combined training protocol for application on short-arm centrifuges

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## Background

Despite daily training, long term exposure to zero gravity impairs muscle health, bone mineral density, the neurovestibular and cardiovascular system as well as ocular health, known as spaceflight-associated neuro-ocular syndrome (SANS) [1]. Short-arm centrifugation is a promising option to simulate an Earth-like (1 g) gravity and hence prevent physical deconditioning and reduce orthostatic intolerance and cardiac atrophy.

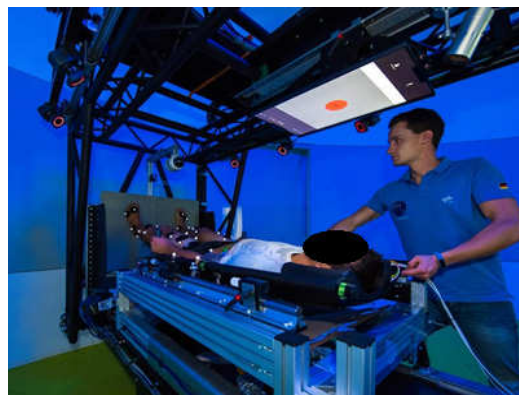


Fig. 1: Jumping exercises using a supine sledge (study: JUMP).

Only a few ground-based studies investigated tolerability of exercising during centrifugation. Intensive cycle training on a short-arm centrifuge was effective to preserve thigh muscle volume [2] and peak oxygen uptake [3] after 20 day bed rest. Squat exercises were well tolerated even at relatively high rotation of 20-30 rpm [4]. Furthermore, our group could show tolerability of jumping exercises (Fig. 1) at different gravity levels [5, 6]. In the present study, we evaluated the tolerability and feasibility of abdominal and back muscle exercise performance during 1 g centrifugation at the participants center of mass (CoM).

## Methods

Fifteen (8 male:  $33.8 \pm 7$  years,  $178.4 \pm 8.2$  cm,  $72.1 \pm 9.6$  kg) recreationally active participants performed two isometric ("contralateral" and "trunk exercise") and one functional ("wood chopper") abdominal and back muscle exercise in 3 sessions in a randomized order in a cross-over design (Fig.2). The exercises were performed upright with 1 g at CoM and in two SAHC sessions with clockwise and counter clockwise rotation. Cardiovascular loading (ECG, blood pressure), motion sickness, rating of perceived exertion (BORG), and surface trunk muscle activity (Mm. rectus abdominis, ext. obliques and multifidii) were compared between each session, with mean center of pressure (CoP) evaluated between SAHC sessions.

## Results

No sessions were terminated and no significant increase in heart rate (Fig. 3) or motion sickness (Fig. 4) were reported in either SAHC session compared to exercises in upright position. No differences in exertion scores (Fig. 5) were observed between sessions although the iso-

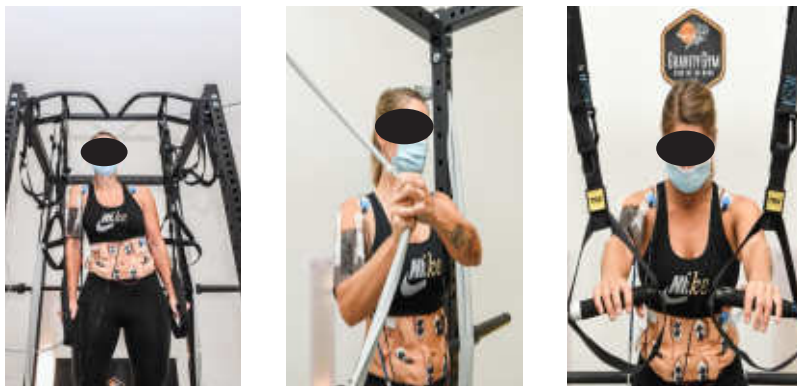


Fig. 2: Contralateral (left), trunk rotation (centre) and abdominal isometric exercises (right) performed in upright condition at 1g.

metric exercises induced the highest scores (for "contralateral": SAHC  $10.5 \pm 3$ , Control  $11.0 \pm 2.9$ , for "trunk exercise": SAHC  $11.1 \pm 3.4$ , Control  $11.5 \pm 2.7$ ). A higher systolic blood pressure (clockwise:  $+13$  mmHg ( $p = 0.022$ ), counter clockwise:  $+21.4$  mmHg ( $p = 0.001$ ) was found only initially while exercising in supine position during centrifugation. Trunk muscle activity was comparable between all 3 sessions. However, innervation levels of targeted muscle groups for each exercise showed that only the isometric "trunk exercise" provided an intensity level of 40-60% for straight abdominal muscles that would lead to an increase in strength after longer-term application.

**Conclusion and Outlook**

Trunk muscle exercises during centrifugation appear tolerable and generate comparable physiological loading and muscle activity compared to upright training on Earth. However, effectivity of ground-based centrifuge training is limited by safety aspects. Optimization of muscular innervation could be expected by a familiarization phase prior to training on the centrifuge.

As a next step, an integrated centrifuge training protocol will be evaluated. In parallel to current training protocols and systems on the International Space Station different endurance and resistive exercises (i.e. for rowing, running and strength training) will be tested.

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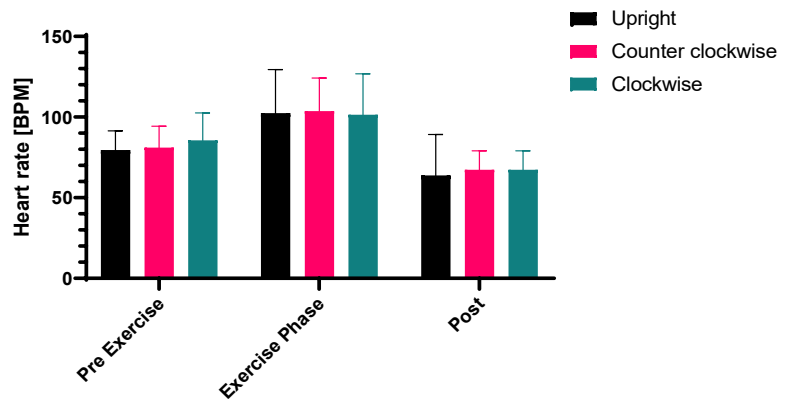


Fig. 3: Heart rate when standing upright in natural gravity and during short-arm human centrifugation when rotated clockwise and counter-clockwise with 1g at the participants center of mass in supine position before (Baseline), during passive SAHC (Pre-Exercise), during training (Exercise phase) and after exercises (Post). Data are shown as mean  $\pm$  (SEM); BPM=beats per minute.

**Motion Sickness**

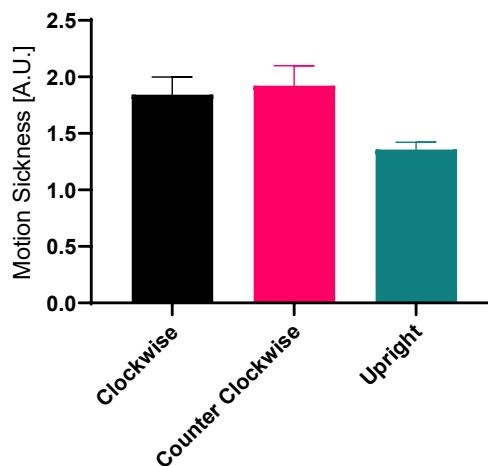


Fig. 4: Motion sickness scoring when standing upright in natural gravity and during short-arm human centrifugation when rotated clockwise and counter-clockwise with 1g at the participants center of mass in supine position. Data are shown as mean  $\pm$  (SEM).

**Exertion scoring**

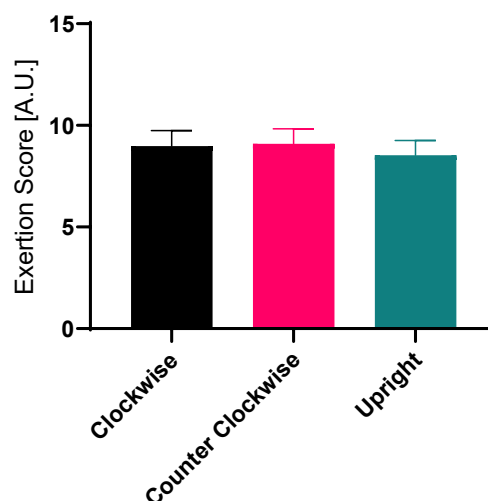


Fig. 5: Perceived exertion rating (RPE) when standing upright in natural gravity and during short-arm human centrifugation when rotated clockwise and counter-clockwise with 1g at the participants center of mass in supine position. Data are shown as mean  $\pm$  (SEM).



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# Aerospace Psychology

*Dr. phil. Peter Maschke (Head)*

*Dr. phil. Hinnerk Eißfeldt, Prof. Dr. phil. Dirk Stelling (Deputies)*

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 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 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. Hinnerk Eißfeldt; Dr. Y. 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. 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. Peter Maschke)***

- Selection of astronauts
- Psychological inflight support of astronauts

# Exploring possible effects of cognitive training on robotic-assisted surgery – A pilot study

V. Oubaid

Department of Aerospace Psychology, Institute of Aerospace Medicine, German Aerospace Center (DLR), Hamburg, Germany

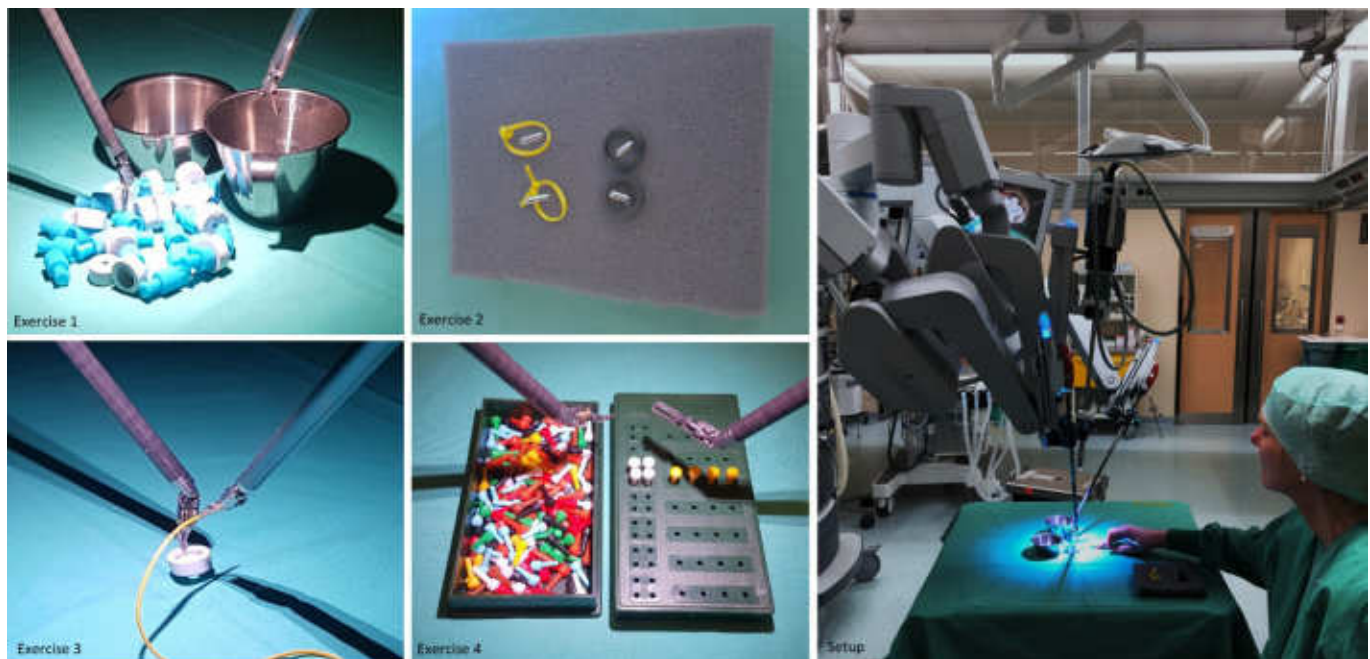


Fig. 1: Exercises 1-4 and experimental setup in the operation room at T1 and T2. Exercise 1: Sort as much blue and gray connectors as possible within 60 seconds. Exercise 2: Lift two yellow and two black rings onto the respective screw. Exercise 3: Thread a yellow rubber loop through a gray connector and tie and tighten the loop. Exercise 4: Arrange 4 plastic connectors of the same color in a square and one row behind.

Robotic-assisted surgery (RAS) is a rising technology and operation technique with many potential advantages. RAS necessitates a specialized, efficient and standardized training, but nearly all RAS training techniques need to be carried out on an expensive virtual RAS simulation [2] or on the RAS device itself in the operation room. Therefore, a concept should be designed to reduce time in the operation room and costs in accessing RAS simulation training. The resulting aim for this pilot study was to provide a frame design for a cost-effective RAS training curriculum with a first proof of concept: will cognitive training be able to substitute RAS training, and do personality characteristics contribute to explain training gains?

For the current pilot study possible outcomes of training and acquisition of cognitive skills are inferred from two areas of research: psychometric research regarding practice and re-test effects [7], and research concerning the acquisition of cognitive skills [1]. The scientific psychological literature reveals a strong effect of basic cognitive training patterns on skill ac-

quisition and performance in various areas, such as occupations and sports, music etc. And skill acquisition is partly dependent on personality traits, e.g. level of conscientiousness and motivation. A cognitive training of the underlying mental abilities, like memory capacity, concentration etc., should therefore result in significant improvements in surgical skills and a lean support of regular RAS-training.

For this study, the validated DLR-cognitive training modules for pilot & ESA-astronaut selection were used (see [2]). They were assembled following published job requirement analysis on surgery: spatial orientation and concentration (see [5]). The sample of participants included 25 medical student volunteers, randomly assigned to three groups: (1) Training at the da Vinci RAS (N=7), (2) cognitive training (N=7), and (3) no training (N=10). The experimental design included an initial baseline measure on the da Vinci simulator (T1), see fig. 1. This measure was then repeated (T2) after the completion of training/non-training phase. A semi-structured psychological interview (SPI) to self-evaluate performance and



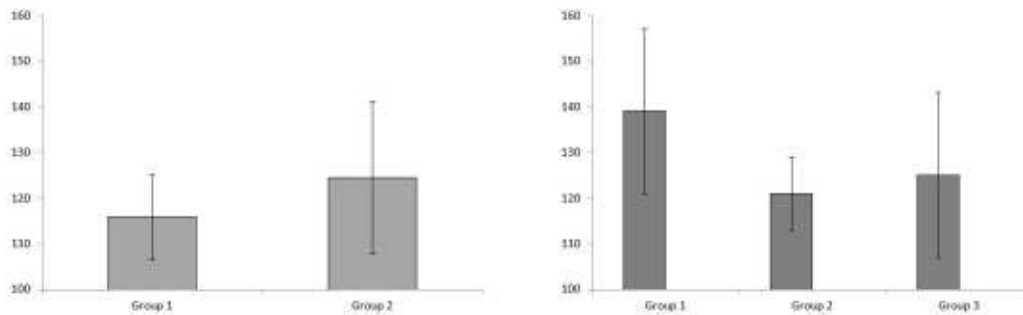


Fig. 2: Left Training success - Mean (%) and Standard deviations for da Vinci training (N=7, group 1, RAS) and cognitive training (N=7, group 2, CT); baseline = 100%  
Right: Performance gain T1>T2 - Mean (%) and Standard deviations for da Vinci performance gain from T1 to T2; T1 = 100%

mental workload was conducted after T1 and T2 (see [6] Schoenburg et al., 2021). As a personality measure the reduced version of the NEO PI-R questionnaire [4] was administered. During the training phase group 1 passed through a set of da Vinci tasks: EndoWrist manipulation 1 & 2, needle control and needle driving. The total training time was 6 hours. Group 2 passed through a set of DLR-CT-modules, namely spatial orientation and concentration. The total training time was 6 hours. The results showed that there was a general performance gain between T1 and T2. The resulting average training gain of group 1 was significantly higher than those of group 2&3 (see fig. 3), whereas group 2&3 showed no significant mean differences. The NEO conscientiousness scale showed a moderate positive correlation ( $r=.26$ ) with the mean RAS performance score in T1, in line with existing research. The SPI measures revealed significant correlations between RAS measures and both self-evaluated performance ( $r=.92$ ,  $P<.01$ ) and mental workload scores ( $r=.90$ ,  $p<.01$ ). A conclusive explanation for the higher training gains of group 1 is that this group has worked eight times on the device as part of the training. An unexpected result was that no differences were found between group 1 and 2 in T2 performance. One possible explanation is the low number (5 trials) of training trials in group 2. Similarly, [2] observed that successful cognitive training requires a larger number of repetitions. Limitations of this pilot study include the small sample size and the low number of training

trials. Further research should address these limitations and extend the training design (e.g., a group 4 with combined cognitive training and RAS training). Nevertheless, our findings may help using training capacities in the operating room more efficiently.

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# Insights on civil multicopter drone pilot competencies and training needs

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Fig. 1: Multicopter drone mission at the DLR National Experimental Test Center for Unmanned Aircraft System in Cochstedt.

## Objectives

Civil use of remotely piloted aircraft (RPA) is continuously growing, in quantity, application, and type and has become increasingly complex, e.g. operations beyond visual line of sight. RPA are used for inspection, filming, agricultural spraying, emergency activities and are also supposed to be used for transport in the future. This growth of RPA operations underlines the need of qualification and training concepts for civil remote pilots, instead of individual in-house training-by-doing. Under the direction of the Institute for Flight Guidance, the urban air mobility project City-ATM aims at developing a concept for future air traffic management (ATM) in urban airspace, which will enable safe and efficient integration of unmanned aircraft systems. Being part of this interdisciplinary project of the German Aerospace Center, this study for the first-time evaluated competencies and training needs of professional remote pilots in Germany.

## Approach

Based on workshops with 19 subject matter experts (drone pilots from public emergency or commercial services, and representatives of public authorities in the field of unmanned aviation) task-based requirements for remote pilots have been explored. The resulting list of competencies was narrowed down to 38 key Remote Pilot Competencies (RPCs), including knowledge, flight skills, cognitive abilities, interpersonal skills and personality aspects. In a second step those RPCs were evaluated in an online survey for multicopter drone pilots (N = 88), predominantly working for public authorities and organizations with security tasks and commercial services. Following participants' assessment, the competencies were assigned to either initial or recurrent training, based on the DIF (Difficulty, Importance, Frequency) model [1] [2].

**Results & implications**

Overall, the results add to previous remote pilot training concepts by highlighting the importance of interpersonal skills and personality aspects. Table 1 summarizes the competencies that should be part of initial remote pilot training as well as those competencies that should be additionally trained in repeated refresher trainings. Whereas the initial training section shows a slight accumulation of knowledge and cognitive abilities, refresher training competencies involve a comparably higher ratio of flight skills and personality aspects. On the one hand, the findings endorse previous training concepts regarding initial remote pilot training [3] [4], and on the other hand spotlight skills that need to be trained repeatedly in order to perform well as remote pilot. The content of the refresher training section in Table 1 signalizes that especially competencies that involve the handling of critical and unforeseen events need to be trained more frequently compared to the basic RPCs in the initial training section. Further-

more, the results highlight that regular job performance alone is not sufficient to maintain remote pilot competencies, but rather recurrent training is necessary to continuously ensure safe performance – especially when dealing with critical events.

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Table 1: Remote Pilot Competencies in initial and refresher training.

Categories of Remote Pilot Competencies	Initial training	Refresher training
<b>Flight skills</b> (n=11)	1 out of 11: <ul style="list-style-type: none"> <li>Establishing routine procedures</li> </ul>	1 out of 11: <ul style="list-style-type: none"> <li>Flying under poor visibility</li> <li>Flying under poor weather conditions</li> <li>Flying beyond visual line of sight (BVLOS)</li> <li>Reacting to operational threats (e.g. birds)</li> <li>Taking over manual control of the drone</li> <li>Re-planning during flight</li> <li>Flying in narrow surroundings of building structures</li> <li>Flying in narrow surroundings of other drones</li> <li>Utilization of the “kill switch”</li> <li>Flying without GPS</li> </ul>
<b>Knowledge</b> (n=10)	6 out of 10: <ul style="list-style-type: none"> <li>Application of equipment knowledge</li> <li>Abiding by aviation law</li> <li>Task allocation among team members</li> <li>Utilization of distinct phraseologie</li> <li>Paying regard to battery constraints</li> <li>Paying regard to air space restrictions</li> </ul>	3 out of 10: <ul style="list-style-type: none"> <li>Paying regards to system’s performances envelope</li> <li>Technical emergency behavior</li> <li>Utilisation of emergency landing site</li> </ul>
<b>Cognitive abilities</b> (n=6)	5 out of 6: <ul style="list-style-type: none"> <li>Three-dimensional perception</li> <li>Spatial orientation</li> <li>Range perception</li> <li>Instrument monitoring</li> <li>Ability to respond quickly</li> </ul>	1 out of 6: <ul style="list-style-type: none"> <li>Awareness for potential safety hazards</li> </ul>
<b>Personality aspects</b> (n=6)	2 out of 6: <ul style="list-style-type: none"> <li>Preventive risk management</li> <li>Accepting responsibility for own errors</li> </ul>	4 out of 6: <ul style="list-style-type: none"> <li>Handling of human performance limitations (e.g. fatigue)</li> <li>Operating responsibly</li> <li>Stress management in emergency situations</li> <li>Risk-taking behavior</li> </ul>
<b>Interpersonal skills</b> (n=5)	5 out of 5: <ul style="list-style-type: none"> <li>Team communication and information flow</li> <li>Inter-team communication (e.g. with other drone pilots)</li> </ul>	3 out of 5: <ul style="list-style-type: none"> <li>Handling of distractions</li> <li>Team work</li> <li>Handling of customer expectations</li> </ul>

# Selecting air traffic controller trainees during COVID 19 – candidates' acceptance

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The COVID 19 pandemic posed great challenges when resuming the multi-stage selection procedure for air traffic controller trainees for the German Air Navigation Service Provider DFS Deutsche Flugsicherung after an initial lockdown in 2020. However, the procedure could successfully be resumed by implementing a strict hygiene concept. This concept comprised, among others, reducing the number of candidates per event, wearing a face mask at all times (with the exception of the interview, where a spit guard was used), keeping appropriate distance to others, and using spit guards during the group exercises (see Fig. 1). A selection procedure is an applicant's first contact with the involved organization(s). This

Fig. 1: Sneeze guard used during the group exercise.



first impression influences not only how candidates, regardless of their success in the selection procedure, perceive the respective organization but also how they convey it to their friends and family. Furthermore, it can even affect their future behavior like accepting a job offer or later job performance [1]. On top of this, a candidate's evaluation of the selection procedure is an important aspect of social validity [2], i.e. an applicant's acceptance of and satisfaction with the selection procedure. During the COVID 19 pandemic, it was thus especially important to assess the candidates' view on the selection procedure, as they faced special circumstances.

A total of 191 applicants were surveyed in three different selection stages (cognitive aptitude tests, assessment center, psychological interview). The assessment took place from May to June 2021 and was administered contact-free and time-efficiently either over test computers, or candidates could use a QR Code to access the online questionnaire. Applicants received statements regarding their view on the selection procedure (e.g. "I was treated friendly and respectfully.") and rated these on a 5-point Likert scale from 1 (completely disagree) to 5 (completely agree). The questionnaire comprised items regarding the view on the selection procedure (atmosphere, transparency, treatment by test administrators), and the hygiene measures.

Acceptance of treatment by the test administrators, task transparency, and atmosphere in general and among the candidates were all high, as all ratings regarding these aspects reached at least a mean of 4 ("agree") or higher. More variance occurred for the perceived level of demand and stress. While demand was rated somewhat medium with means ranging between 3 ("partly") and 4,

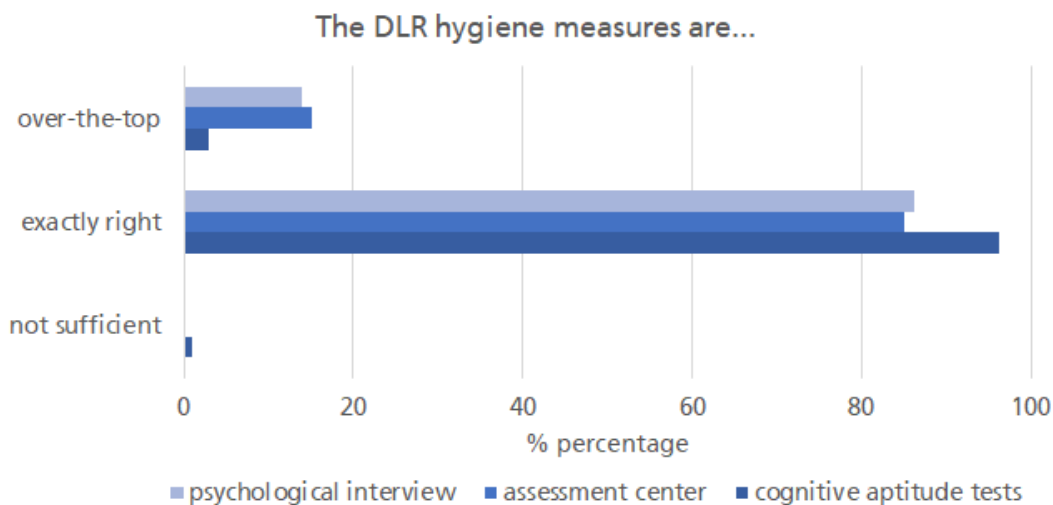


Fig. 2: Candidates' perceived adequacy of the hygiene measures for all three selection stages in percent.

stress received the lowest ratings with means below 3, i.e. while participants perceived the selection procedure as demanding, they did not perceive it as stressful.

Acceptance of hygiene measures was high (see Fig. 2): a majority of candidates in all three selection stages rated the hygiene concept as "exactly right". Only 1 person of all 191 rated the measures as "not sufficient" and a minority (ranging between 3% and 15%) of the candidates viewed the measures as "over-the-top". The candidates agreed that they felt safe due to the measures in all three selection stages, with average ratings reaching means above 4.

In conclusion, even though a strict hygiene concept had to be implemented in the selection procedure, candidates' acceptance of the procedure was high and the hygiene measures were perceived as adequate. The results of the current study proved high acceptance of our hygiene concept in place. It is thus supposed to be equally well accepted by candi-

dates in the psychological selection of astronaut candidates for the European Space Agency (ESA), carried out at our DLR test facility in Hamburg in 2021, where comparable measures were also planned and strictly implemented.

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# Display latencies in artificial cabin windows

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Fig. 1: Passenger cabin of the full-flight Air Vehicle Simulator (AVES).

One part of the LuFo 2 project EFFKAB was research on the impact of artificial windows on flight sickness. Artificial cabin windows offer exciting opportunities for future aviation industry for cost and design reasons. However, little is known about how displays replacing real windows in an airplane influence passenger comfort. Research here mainly focusses on pilots in flight simulators or not flight-related laboratory virtual environments but not on passengers. One result in these studies is that display latencies may cause flight sickness symptoms which can diminish comfort. Therefore, the purpose of our study was to evaluate the impact of latency on passengers' comfort. 104 participants were recruited as passengers in a full-motion cabin simulator. The DLR Air Vehicle Simulator (AVES) consists of a dome, which is mounted on an electro-mechanically driven motion system. For our study, we used a passenger cabin (l 4.2m; w 3.3m; h 2.4m) with four seat rows in a 2+2 layout providing space for 16 passengers which can be rolled into the

dome (Fig 1). As cabin windows we used high-resolution digital displays (Fig. 2). In three flights, the delay between actual motion of the cabin and windows' outside view was varied (0/ 0.5/ 10 seconds) and four flight segments (take-off, cruise, turbulence and approach) were compared. Inflight and post-flight sickness measures and realness estimates were analyzed. The Simulator Sickness Questionnaire (SSQ) (measured in the post-flight phase of the three flights) showed that under all three conditions, most participants showed no or just minimal flight sickness symptoms, with 41% – 51% showing no symptoms at all (Fig. 3). A close monitoring of sickness symptoms during each flight indicated that low latency has no additional impact on passengers' well-being. Long latency, in our study 10 seconds, had an impact on the severity of sickness symptoms in some passengers (Fig 3, SSQ > 15), mainly characterized by an increase of oculomotor symptoms. Remarkably, about one third of the participants reported sickness symptoms with-

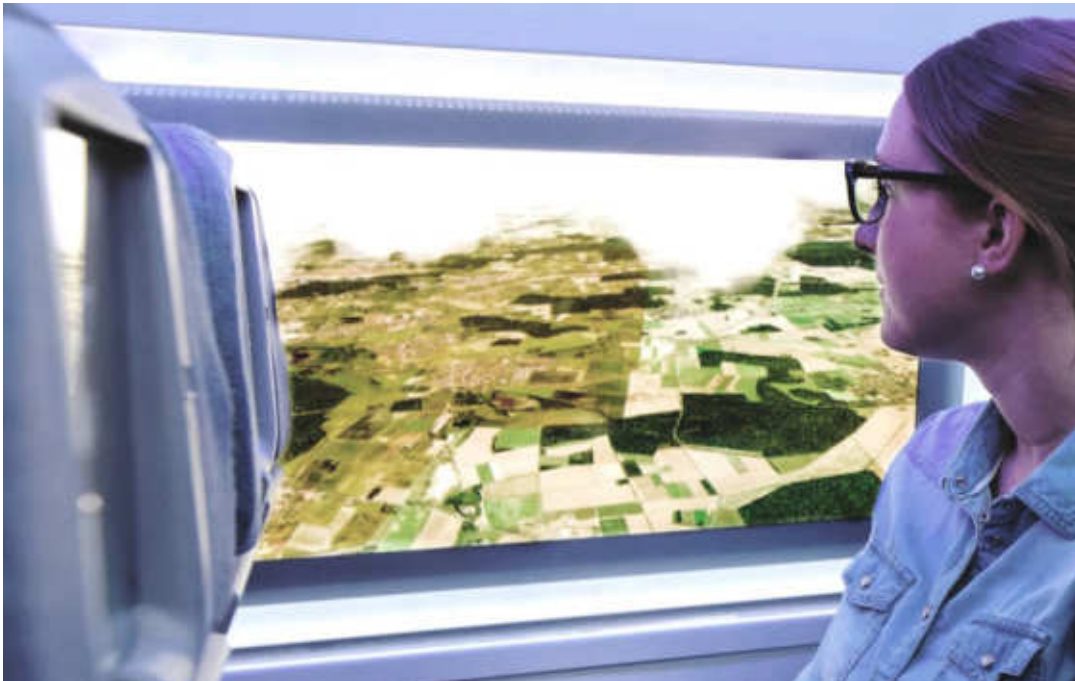


Fig. 2: Passengers' view of cabin window presenting the virtual outside view. Shown is the photo-realistic display of clouds and terrain during the flight.

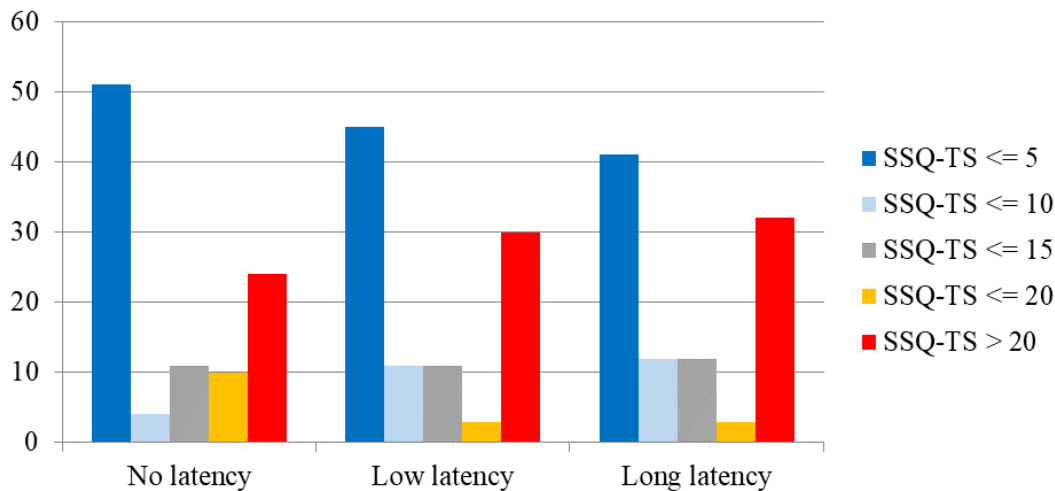


Fig. 3. Severity of sickness in percentage based on the total scores of the Simulator Sickness Questionnaire (SSQ-TS) by condition of latency.

out latency. Passengers who suffered from sickness reported more symptoms in the late flight sequences (Turbulence, Approach), especially under long latency conditions, suggesting that long latency interacts with certain phases of a flight. We also found that the subjective evaluation of realness is correlated with the severity of sickness in the sense that people who describe the situation as “less real” suffer more from sickness. Seating, however, had no effect on severity of sickness under different latency conditions in our cabin.

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# Effects of personal control for thermal comfort in long-distance trains

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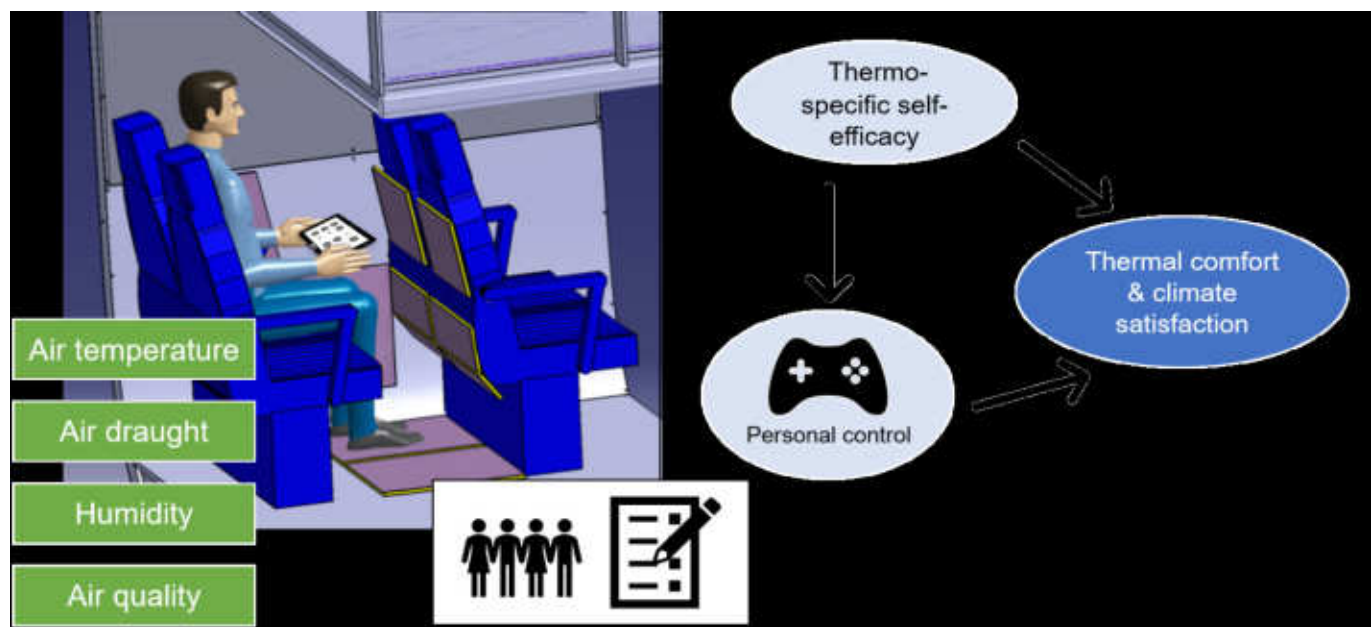


Fig. 1: Individually controllable heating options and thermo-specific self-efficacy as influencing factors for climate satisfaction.

In the White Paper on Transport (2011) the EU defined the goal to shift 50% of passenger transport from road to other transport modes by 2050. To achieve this goal, passenger rail transport has to become more attractive. One important step to enhance attractiveness of a rail trip is thermal comfort. It is generally assumed that individual control over indoor climate settings contributes to the passengers' thermal comfort. The two studies presented here examine this assumption by considering the concept "thermo-specific self-efficacy" (specSE) as psychological construct in the context of thermal comfort in a railway car. Furthermore, the effect of personally controllable infrared panels on thermal comfort was investigated. The studies were performed in a passenger rail car mock up (see Fig. 1) in cooperation with the DLR Institute of Aerodynamics and Flow Technology at Göttingen.

## Study 1

In the first study, the psychological construct of "thermo-specific self-efficacy" (specSE) was explored. SpecSE describes peoples' expectations towards their competence to execute effective operations to improve thermal conditions in their environment successfully [1]. The construct includes knowledge about

identifying and controlling thermal parameters, and the subject's level of acceptance for suboptimal thermal conditions. N = 160 subjects participated in 8 test runs. Half of the subjects were female (N = 79), half male (N = 81). The subjects' age ranged between 18 and 63 years (M = 34 years, SD = 12 years). The experimental conditions included three different ventilation systems and temperatures between 21 and 29°C. After each condition the test subjects rated the comfort level of four indoor climate parameters, namely air temperature, air velocity, humidity and air quality and their general indoor climate satisfaction. For the assessment of thermo-specific self-efficacy in long-distance trains, a new 10-item-questionnaire was developed. Sample items are: "On the train, I always have the option of creating a comfortable temperature" or "My well-being on the train depends to a large extent on the quality of the air conditioning".

## Results

Significant correlations were observed between all thermal comfort ratings and climate satisfaction. The highest correlations with climate satisfaction were found for temperature evaluation ( $r = .76^{**}$ ), and air draught





Fig. 2: Test subjects in the passenger rail car mock-up.

evaluation ( $r = .61^{**}$ ). Also, specSE correlated with the climate satisfaction with  $r = .21^{**}$ . The higher the subjects' thermo-specific self-efficacy, the more satisfied they were. In a regression analysis with climate satisfaction as criterion and the climate parameters as predictors, specSE as a further predictor added a significant amount of explained variance to the regression ( $p_{change} < .01$ ). That means specSE was a relevant construct for the prediction of climate satisfaction in the train passenger cabin mock-up adding to the predictive power of the thermal comfort ratings.

## Study 2

In contrast to Study 1, individual control over climate settings was possible in one experimental condition: Four seats were equipped with remotely controllable infrared (IR) heating panels (see Fig. 1 left side). Twelve subjects (6 female, 6 male,  $M = 35$  years,  $SD = 11$  years) in 3 test runs could individually manage the heating level by a control device. In the other experimental condition, the climate settings including IR panels were centrally managed. The effects of individual control and specSE were analyzed.

## Results

The main effects of both independent factors on climate satisfaction were not significant. However, the interaction of specSE and available control had a significant effect on climate satisfaction: The interaction was significant with  $p < .01$  and an effect size of  $\eta^2 p = 0.58$  (see Fig. 3). When subjects were given control, those who were predominantly low in specSE profited significantly more. This is in line with earlier results showing that subjects with low specSE preferred having more control than subjects with high specSE [1].

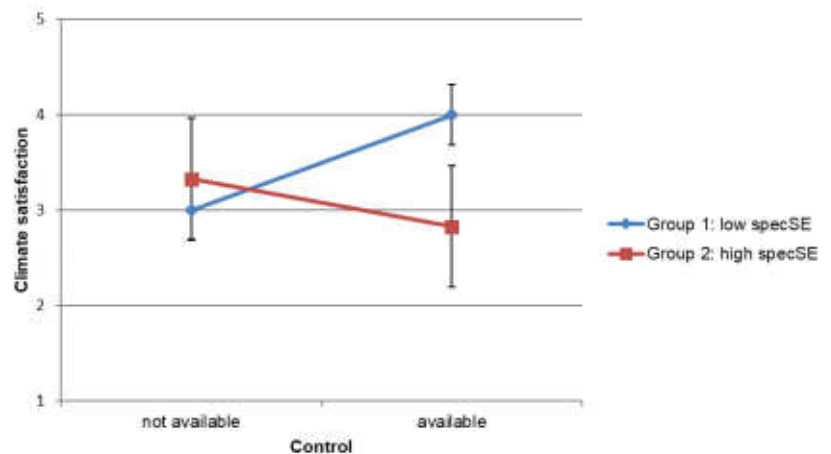


Fig. 3: Effects of control and specSE on climate satisfaction.

## Conclusions

Study 1 indicated that additionally to thermic conditions, psychological expectations have an effect on climate satisfaction. The influence of the psychological construct "specSE" on climate satisfaction is as high – that means as relevant – as the effect of the thermal comfort ratings for air draught and humidity. According to Study 2, specSE can act as a moderator for the relation between thermal conditions, available control and climate satisfaction [2].

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## Radiation Biology

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# 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. Ralf Möller)***

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

### ***Astrobiology (Dr. Petra Rettberg)***

- Life in extreme environments and microbiome of confined habitats

### ***Biodiagnostics (PD Dr. Christine E. Hellweg)***

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

### ***Biophysics (Dr. Thomas Berger)***

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

### ***Genome Maintenance Mechanisms in Health and Disease (Prof. Dr. 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 (Dr. Matthias M. Meier)***

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

# Questioning the radiation limits of life – *Ignicoccus hospitalis* between replication and VBNC (viable but not cultivable)

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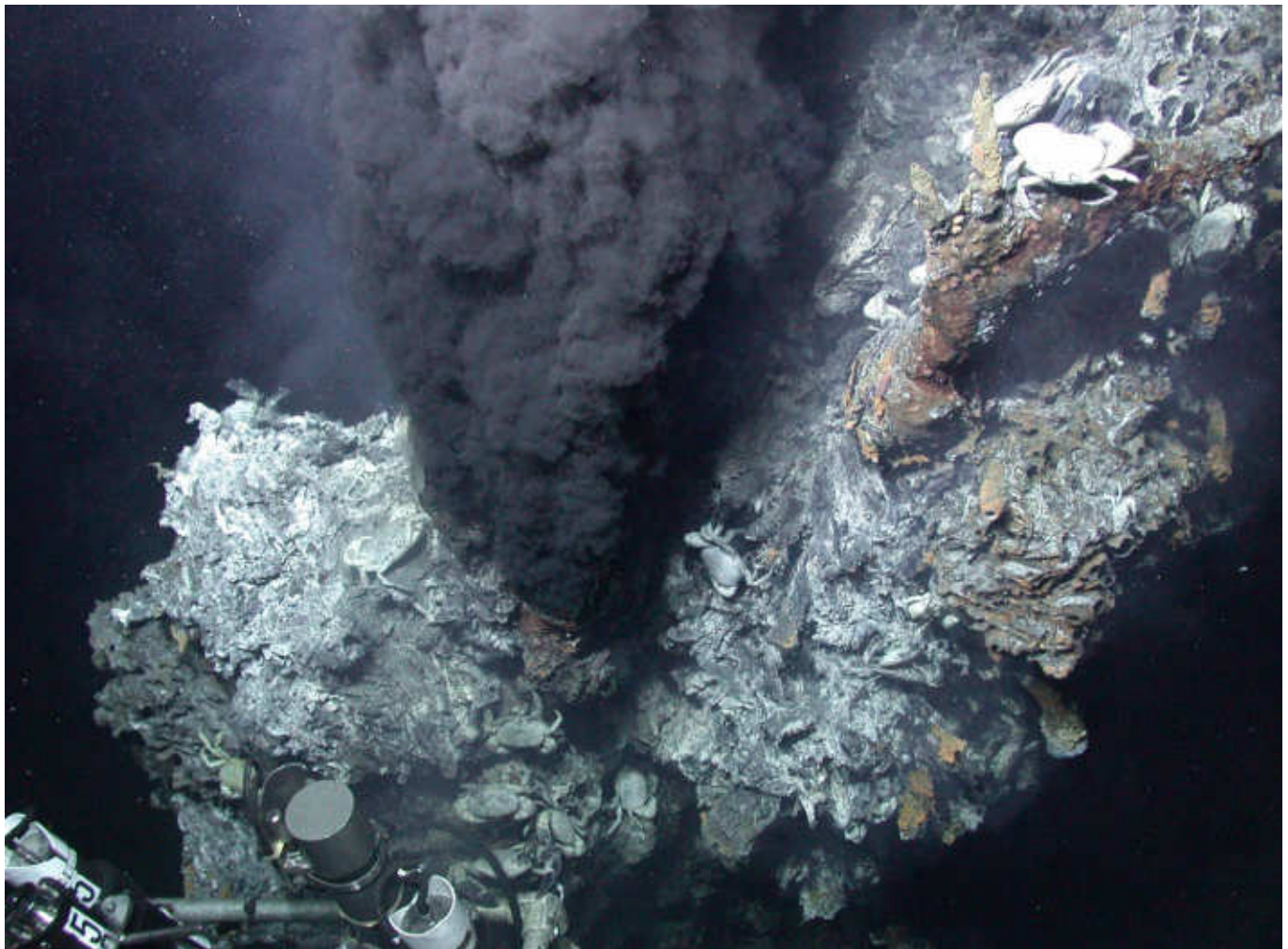


Fig. 1: Black smokers (here in the East Pacific Ridge) are the natural environments of chemolithoautotrophic hyperthermophilic Bacteria and Archaea including *Ignicoccus* strains © Kristina Beblo-Vranesevic, DLR.

Radiation of ionizing or non-ionizing nature has harmful effects on cellular components including lipids, proteins, and DNA. Radiation-induced DNA damages can result in potentially harmful mutations, cell death, or, in higher organisms, in cancer. Nevertheless, radiation tolerance based on several complementary fast and efficient repair mechanisms can be found in all three domains of life (Bacteria, Archaea, Eukarya). Extreme radiation tolerance, however, occurs more frequently in the prokaryotic lineage, and can be found in the domain Bacteria as well as Archaea. For an efficient genome maintenance and for the protection of the proteome, distinct molecular

mechanisms exist in these microorganisms to resist radiation of non- and ionizing nature and other genotoxic agents. One prominent bacterial example for an extremely radiation tolerant microorganism is *Deinococcus radiodurans*. This representative is the most radioreistant bacterium known so far with a  $D_{10}$ -value of 10 kGy. The  $D_{10}$ -value is giving the dose where 90 % of the irradiated population is killed. Several other Bacteria and Archaea, including extremophilic ones, like the *hyperthermophilic* Archaea *Archaeoglobus fulgidus* or *Pyrococcus furiosus* have been investigated in respect to their radiotolerance as well. Both showed a comparable high  $D_{10}$ -value of

around 1 kGy in comparison to the mesophilic bacterium *Escherichia coli* ( $D_{10}$ -value 0.25 kGy). The analysis of the ionizing radiation tolerance of the chemolithoautotrophic (producing  $H_2S$  by consuming elemental  $S^0$ ), obligate anaerobic, hyperthermophilic (optimal growth temperature 90 °C; originating from a black smoker in the Kolbeinsey Ridge) archaeon *Ignicoccus hospitalis* showed a  $D_{10}$ -value of ~3.5 kGy, threefold exceeding the doses previously determined for other extremophilic Archaea.

Bacterial viability but non-culturability (VBNC) and the reversal of this status has already been known since three decades from pathogenic and other bacteria; however, nothing is known in terms of Archaea. Our results showed the remarkable radiation tolerance of *I. hospitalis*, and its ongoing metabolic activity (visualized by the detection of produced  $H_2S$  with a lead acetate test). The genome integrity of *I. hospitalis* after exposure to ionizing radiation in relation to its survival was assessed by RAPD and qPCR and we were able to discriminate between the survival in terms of reproduction and metabolic activity after exposure to extremely high doses of ionizing radiation exceeding 100 kGy. This phenomenon allowed, for the first time, the postulation of a potential VBNC state in the domain of hyperthermophilic Archaea.

We hypothesize that an extraordinary fast and efficient repair system exists in *I. hospitalis*. In

less than an hour, the highly fragmented genome is repaired. Nevertheless, it is unclear how *I. hospitalis* manages this exceptional tolerance intracellularly. In other radiation tolerant microorganisms, diverse intracellular protective mechanisms and features are known, such as polyploidy, the presence of salt-induced compatible solutes, and a specific Mn/Fe ratio. All these properties do not seem to play a role in *I. hospitalis*. Additionally, only a few known repair genes are annotated in the sequenced genome. Therefore, the next step is to decipher molecular processes during repair by transcriptomics and metabolomics.

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Adapted from:  
Koschnitzki, D. et al. (2021) Questioning the radiation limits of life: *Ignicoccus hospitalis* between replication and VBNC. Archives of Microbiology, 203(4), 1299-1308

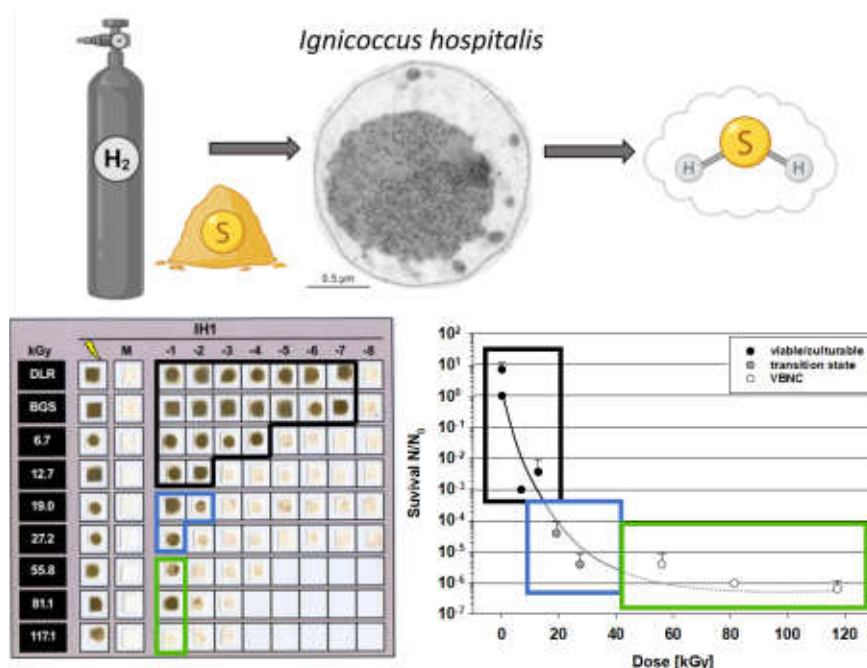


Fig. 2: *Ignicoccus hospitalis* is metabolizing  $H_2$  and elemental sulfur by producing  $H_2S$ . Produced  $H_2S$  can be visualized by a lead acetate test. The presence of  $H_2S$  is thereby detectable by brown color on the lead acetate paper stripes. Active metabolism can be detected until high doses of ionizing radiation exceeding 100 kGy.

# Effect of hypoxia on radiation-induced cell killing and cell cycle redistribution in A549 lung cancer cells

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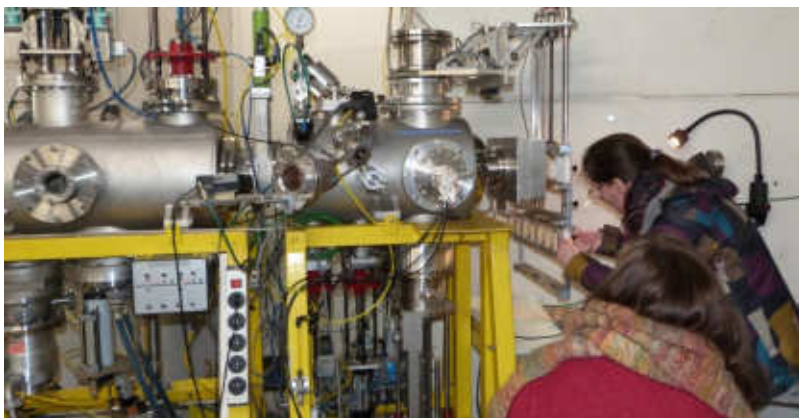


Fig. 1: Cell culture samples being positioned in front of the beam exit window at the heavy ion accelerator „Grand Accélérateur National de Ions Lourds” (GANIL), Caen, France.



Fig. 2: Work with A549 lung cancer cells in the InVivO2 Hypoxia Workstation.

The effectiveness of tumor radiotherapy can be limited by hypoxic areas in the tumor as they are usually more radio-resistant. The phenomenon is well-established in radiobiology as ‘Oxygen Effect’ whereby the presence of molecular oxygen during irradiation (normoxia) reduces the radiation dose needed to produce an effect in comparison to anoxia or hypoxia. However, the effect of hypoxia on cell survival in the period after irradiation largely unknown. Hypoxia tends to pool cells in the G1 phase of the cell cycle due to slower proliferation while irradiation is a known cause of G2 arrest which allows cells time to repair. Also, data on the combined effect of hypoxia and irradiation on cell cycle progression are sparse.

We selected the A549 cell line to characterize hypoxia-induced radio-resistance in lung adenocarcinoma cells in terms of cell survival and cell cycle progression by using two hypoxia protocols based on the presence or absence of hypoxia after low (X-rays) and high linear energy transfer (LET) radiation (carbon ions). We maintained cells in normoxic (20% O<sub>2</sub>) or hypoxic (1% O<sub>2</sub>; InvivoO2, Baker Ruskinn, USA, Fig. 2) conditions and exposed them to doses of 0-8 Gy at a dose rate of 1 Gy/min using either 200 kV X-rays (Gulmay RS225, Surrey, GB) or 95 MeV/n carbon ions (GANIL, Caen, France; Fig. 1). After irradiation, we either returned hypoxic cells to hypoxia (continuous hypoxia) or transferred them to normoxia (transient hypoxia). We then determined radiation-induced cell killing and cell cycle progression under normoxic and hypoxic conditions by performing Puck’s colony formation assay (CFA) and by flow cytometry (Cytoflex S, Beckman Coulter, USA), respectively. For CFA, we seeded cells either immediately (immediate plating) or 24 h after irradiation (late plating). Late plating allows time for DNA repair. For flow cytometry, we

stained cells with 5 µg/ml 4',6-diamidino-2-phenylindole (DAPI) after fixing them with 3.5 % formaldehyde at various time intervals up to 24 hours following irradiation.

After exposure to X-rays and immediate plating of cells (Fig. 3), the relative cell survival was lower for continuous hypoxia compared to normoxia. After irradiation with transient hypoxia conditions, the shoulder in the survival curve disappears, indicating diminished repair capacity possibly due to reoxygenation. Interestingly, for late plating experiments, relative cell survival under continuous and transient hypoxia was higher than under normoxia.

For carbon ions (Fig. 3), relative cell survival was higher for normoxia compared to both continuous and transient hypoxia in case of immediate plating but for late plating was highest for continuous hypoxia compared to normoxia or transient hypoxia.

These results raise the hypotheses that shorter intervals between radiation fractions may be more effective in killing hypoxic lung cancer cells and that carbon beam therapy may be more effective than X-rays.

Cell cycle studies showed that the G2 cell population 12 h after X-ray irradiation (Fig. 4) was highest in normoxia (62 %) vs continuous (27 %) or transient (25 %) hypoxia. The G2 population 12 h after carbon ion irradiation (Fig. 4) was also highest in normoxia (56 %) but the difference was less remarkable compared to continuous (46 %) and transient (46 %) hypoxia. These results are interesting because the G2 arrest is known to provide cells time to repair particularly through the relatively error-free Homologous Recombination (HR) pathway. However, the higher relative survival seen in hypoxia late plating experiments compared to normoxia does not seem to be associated with a more pronounced G2 arrest. Furthermore, the G2 arrest persists one day after carbon ion exposure and might result in a permanent cell cycle arrest and thereby contribute to the lower colony forming ability.

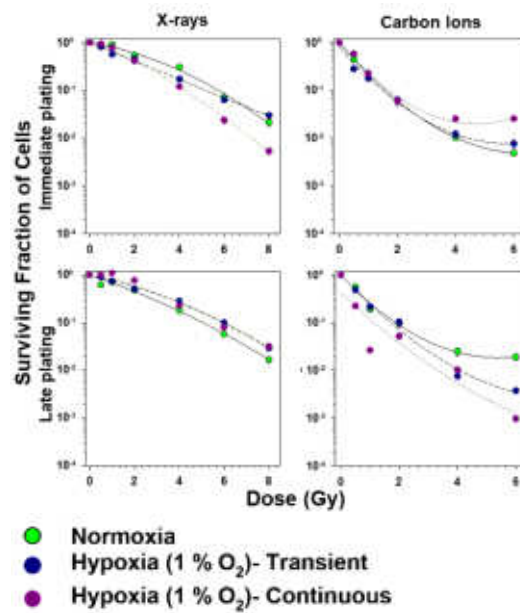


Fig. 3: Cell survival after exposure to X-rays (left) and carbon ions (right).

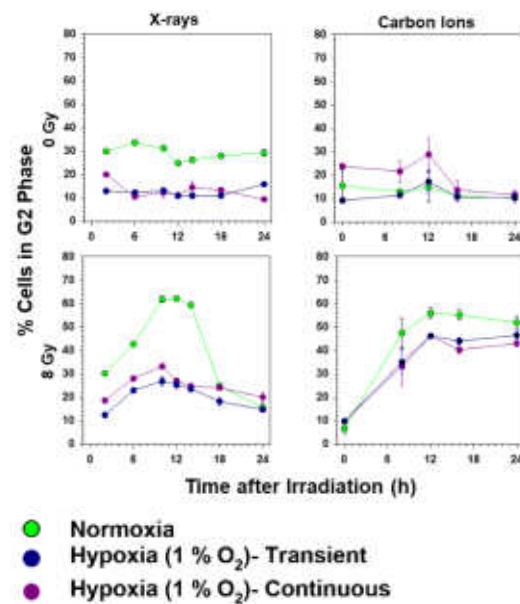


Fig. 4: G2 cell cycle phase distribution after exposure to X-rays (left) and carbon ions (right).

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# 1000 days of RAMIS science data

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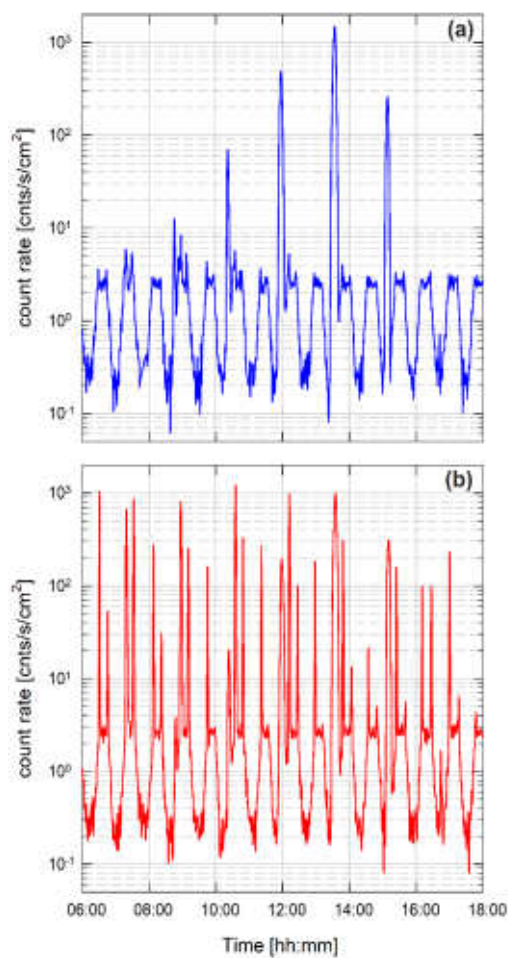


Fig. 1: The count rate (cnts/s/cm<sup>2</sup>) for a twelve-hour time interval for (a) 1 January 2019 and (b) 9 September 2019. Time in UTC.

The RAMIS instrument is a detector for ionizing radiation operated on the DLR Eu:CROPIS satellite mission. RAMIS uses an arrangement of two silicon detectors in telescope geometry and maps the radiation environment in the course of the mission providing baseline data as count rate in the silicon detectors, but also dosimetric quantities as absorbed dose and dose equivalent rate. The Eu:CROPIS satellite launched on 3 December 2018 into a polar orbit circling around Earth at an average altitude of around 600 km. RAMIS is located on the outside of the satellite and was activated on 5 December 2018 and has continuously provided data. Due to the polar orbit of the satellite RAMIS enables to measure: a) the variation of galactic cosmic radiation (GCR) in dependence on the orbit location showing the influence of the shielding of the Earth magnetic field; b) the contributions of protons in the inner Earth radiation belts in the South Atlantic Anomaly (SAA) and c) variations of the trapped electron intensity during crossings of the outer radiation belt at high latitudes.

Typical variations in the radiation environment are exemplarily shown in Fig. 1 in snapshots of RAMIS data for twelve-hour time periods on 1 January 2019 (Fig. 1a) and on 9 September 2019 (Fig. 1b). Fig. 1a shows at first the variation of the GCR environment caused by changes of the geomagnetic shielding along the orbit with minimum count rates at the geomagnetic equator and maxima with more than 2 cnts/s/cm<sup>2</sup> at the geomagnetic poles. In addition, we observed five crossings of the SAA with count rates reaching close to 2000 cnts/s/cm<sup>2</sup> shortly before 14:00 UTC on 1 January 2019. Fig. 1b provides the data for the same time of the day but 9 months later. At that time the influence of a geomagnetic storm increased the number of electrons in the outer radiation belts. These electrons are



seen as additional horns during the crossings of the North- and South pole. Just this snapshot of data shows, that the radiation environment at these high altitudes can change drastically over time.

The highlights of the mission so far are that on 30 September 2021 (day 1034 of the mission) we reached an amount of science data equivalent to 1000 days of measurements, corresponding to an average data coverage of 97% over the whole mission. The summary of this data averaged over these 1000 days and correlated with the location of the measurement for the Eu:CROPIS orbit is provided in Fig. 2. Fig. 2a shows the count rates and Fig. 2b the relevant absorbed dose rates in  $\mu\text{Gy}/\text{min}$ . Both count rates and dose rates vary by over four orders of magnitude in dependence on the location of the satellite. The figures show distinct features of the radiation environment in low Earth orbit (LEO): the extremely high dose and count rates in the SAA centered above the east-coast of South America, the contribution from the outer radiation belt visible as bands in the high latitude regions, and the underlying omni-present GCR background. The comparison of the average dose rates ( $\sim 4.5 \text{ mGy}/\text{day}$ ) with data measured on-board the International Space Station (ISS) ( $\sim 0.4 \text{ mGy}/\text{day}$ )

reveals that the dose at the 600 km orbit behind very low shielding is around 10 times higher than on-board the ISS. This increase is almost exclusively caused by the radiation belt particles.

With RAMIS, we have a radiation detector in a polar orbit which has been working flawlessly in the last three years. The mission started towards the end of the previous solar cycle, the measurements covered the solar activity minimum and corresponding GCR intensity maximum, which happened in early 2020, and we are now slowly progressing towards the solar maximum of the current solar cycle. In addition, two very small Solar Particle Events (SPEs) could be observed in late 2020 and early 2021 which were also seen by the CRaTER instrument flying in lunar orbit. More SPEs are expected to occur when the solar activity increases along the evolution of the solar cycle. With this we now have perfect data for long-term comparison with similar radiation detectors as flying on-board the ISS (DOSIS 3D DOSTEL), on other satellites (SATRAM) but also with instruments in lunar orbit (CRaTER) and on the surface of the Moon (LND) and for model validation.

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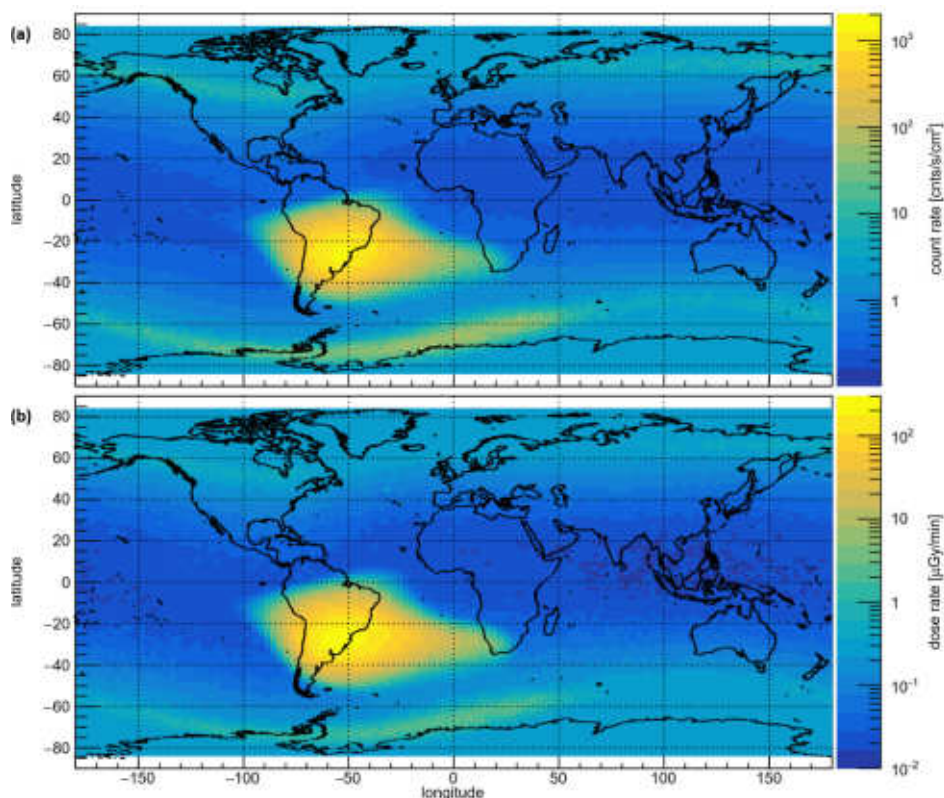
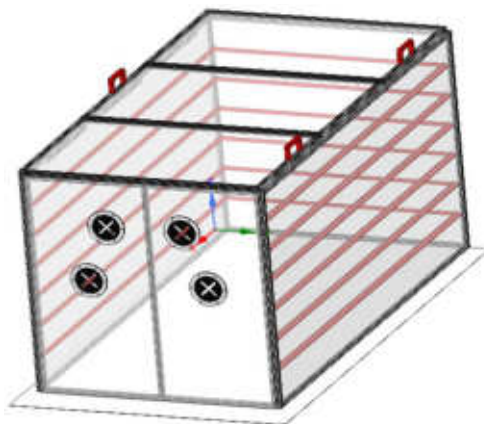


Fig. 2: (a) The count rate ( $\text{cnts}/\text{s}\cdot\text{cm}^2$ ) and (b) the absorbed dose rate ( $\mu\text{Gy}/\text{min}$ ) measured with the RAMIS radiation detector between 5 December 2018 and 30 September 2021.

# DICE Decontamination Chamber: Testing innovative decontamination systems with common and novel microbiological indicators (defined bioaerosols)

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To prevent the transmission of viral, bacterial, and fungal disease patterns, there is a need for innovative decontamination methods. Such methods should be environmentally and economically friendly and work in a targeted manner. Targeted in the sense that the decontamination method should be efficiently adapted to relevant bioindicator organisms. To contribute to methods that are effective against a broad spectrum of microorganisms, the **D**econtamination **C**hamb**E**r (DICE) was designed, built and tested. DICE enables the testing of decontamination methods to be nebulized within a closed environment, where test organisms are exposed.

The chamber consists of three plexiglass walls with fixtures to hold samples, a plexiglass front door, a bottom plate and a ceiling made of polycarbonate. In the front door there were four cavities covered with rubber, which was cut crosswise to allow a possibility of interaction with the interior. With the help of the decontamination chamber, the effect of nebulized „Atmosphäre8“ (kindly provided by Centerline Design GmbH), a hydrogen peroxide solution, was tested on bacteria, bacterial, and fungal spores. Hydrogen peroxide has an oxidizing effect and can therefore be used as a topical antiseptic (3 % solution) or sterilant, disinfectant and sanitizer, depending on its concentration, exposure time and form of use [1]. For example, in addition to its use as a liquid, it can also be nebulized. Hydrogen peroxide has a disinfecting effect due to its oxidative action and radical formation (hydroxyl free radicals) and, thus, damages essential cell compartments, including lipids, proteins, and DNA [2]. An advantage of hydrogen peroxide nebulization is that no residues remain after a sufficient aeration, so there is no need for subsequent cleaning. For the experiment, dried organisms were applied on glass slides

Fig. 1: 3D representation and image, setup of the hydrogen peroxide treatment, of the Decontamination Chamber (DICE). Dried biological samples were placed with different distances from the aerosol generator (front) within the DICE.

Width	1.10 m
Length	2.05 m
Height	1.02 m
Tolerance	3.0 % H <sub>2</sub> O <sub>2</sub>
Accessibility	Doors above, Cavities at front
Additional features	Sample holders at six different heights

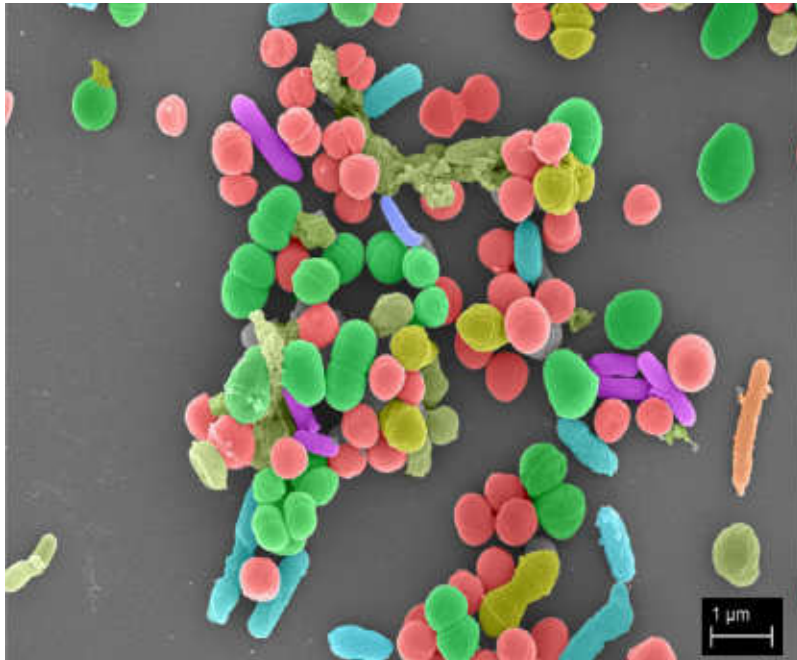


Fig. 2: Scanning electron microscopy of microbial mock-up community. 20.000-fold magnification. (Images: RKI, Berlin, 2021)

### Characteristics of the MOB:

- |   |
|---|
| <ul style="list-style-type: none"> <li>• Set of nine bacterial species abundant in public transportation</li> <li>• Microbial enriched bioaerosol</li> </ul>  |
| <ul style="list-style-type: none"> <li>• Standardized composition</li> <li>• Embedded in artificial saliva, mimicking a natural setting</li> <li>• Tool for safety assessment</li> <li>• Application in aerosol, aviation and traffic research</li> </ul> |

at different distances from the aerosol generator. After the decontamination process, organisms were recultivated and the colony forming units per ml were determined by cultivation. The distribution of hydrogen peroxide in the DICE could be detected with the help of hydrogen peroxide test strips and the leakage of hydrogen peroxide from the chamber could be refuted. In contrast to the liquid Atmosphäre8 solution, the nebulized substance did not reduce viable cells. Since a strong disinfecting effect of the liquid substance on viruses was observed, while no or only a weak effect was observed in other organisms, Atmosphäre8 could be a suitable method to reduce the viral load within a room by nebulization without destroying the useful skin flora.

A defined **MicroBial Bioaerosol (MOB)** consisting of a microbial community out of biosafety level 1 bacteria that are most commonly found in aircraft cabins [3] was designed and developed, contributing a tool used to evaluate decontamination methods in course of the fight against pandemic threats. It can be laid out on glass slides in the DICE and gassed with various decontaminating substances such as hydrogen peroxide. From this, the effectiveness of the agents used can then be evaluated via cultivation. Further, the DNA can be extracted before and after the treatment, followed by sequencing to detect possible

changes at the metagenomic level. However, the DICE can also be used for other purposes, e.g. as an enclosed space for experiments in which the microbial mock-up community is aerosolized, which is important with regard to aerosol research. For instance, the distribution of the bioaerosol in the room can be measured, detecting the microbial load on different positions of the DICE, also in combination with a dummy from which the bioaerosol is aerosolized to embody a realistic scenario of a human breathing and distributing its aerosol to an enclosed environment. The setup for the production of the microbial mock-up community is ready for implementation.

*Acknowledgement: We would like to thank Lucas Labendsch for his help with the DICE construction and the creation of its technical sketch.*

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## Gravitational Biology

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# 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.<sup>®</sup> (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. 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)

### ***Cell and Molecular Neuromuscular Research (Prof. Dr. 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

# Astrocyte reactivity under altered gravity – A path towards neuronal regeneration?

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Neural regeneration following injuries to the central nervous system (CNS) in mammals is inhibited by several factors. One important mechanism preventing axonal regrowth and, thus, healing of CNS injuries is glial scar formation. Key players in glial scar formation are reactive astrocytes that migrate into the region of the injury and produce an inhibitory extracellular environment, rich in chondroitin sulfate proteoglycans (CSPGs) and other signaling molecules. These, in turn, have an inhibiting effect on axon growth and actively induce axon dystrophy. We observed that exposure to altered gravity directly affects primary astrocytes and that hypergravity in particular might mitigate glial reactivity.

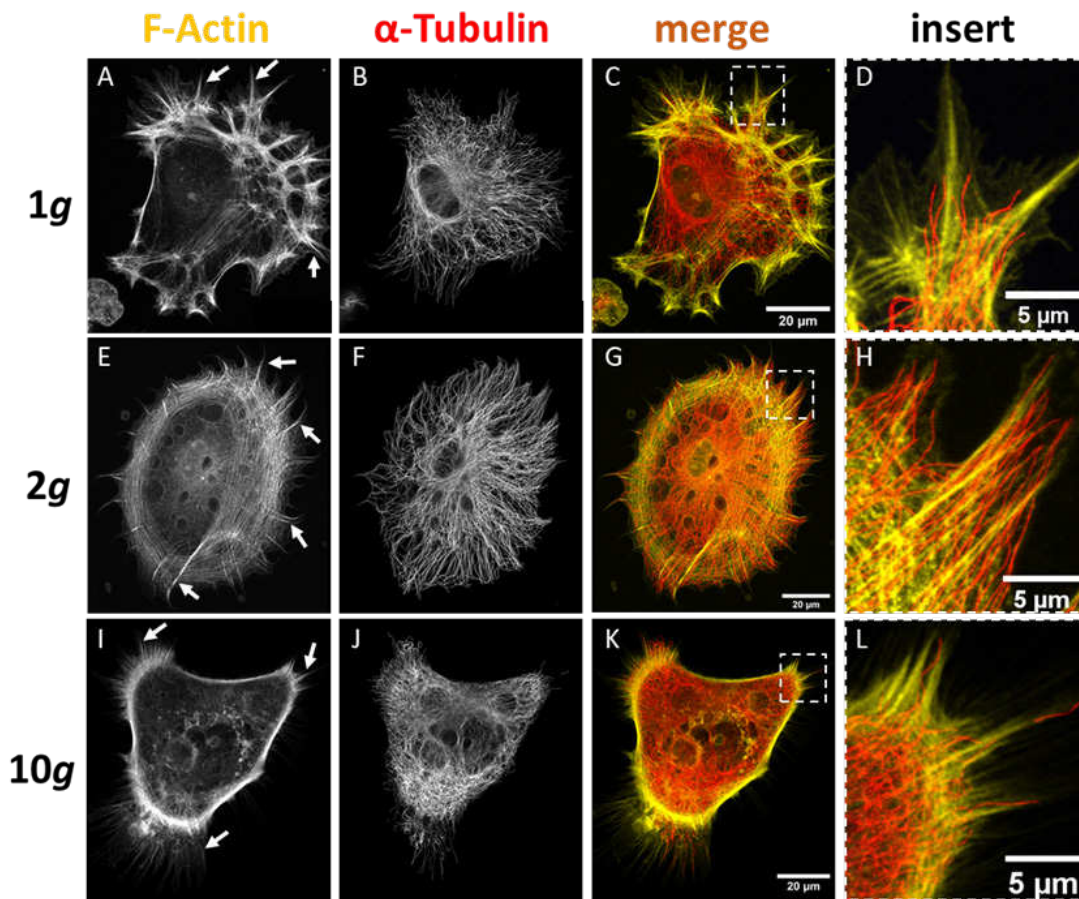
We exposed primary murine cortical astrocytes to altered gravity on our custom-designed experimental platforms. Performing experiments under altered gravity conditions requires meticulous controls, as gravity is a weak environmental factor that needs to be investigated with vigilance, controlling for other environmental stimuli that otherwise might disturb the measurements. Our custom-built devices to expose cells to defined gravity conditions were designed to precisely control gravity levels without generating vibrations, temperature fluctuations or osmotic changes due to media evaporation during rotation. To investigate cellular dynamics and migration speed live under hypergravity, we employed our Hyperscope platform at DLR, a fully automated fluorescent live-cell imaging microscope installed on the :envihab human short-arm centrifuge (SAHC).

We aimed to decipher the role of gravity in astrocyte reactivity induction. Astrogliosis *in vivo* occurs in line with induction of reactivity, a phenotypic change with characteristic features, such as hypertrophy, increased cell migration, hyperproliferation, increased cellular

maintenance (decreased apoptosis), gene expression profile changes, chromatin remodeling and cytokine secretion. Investigation of these aspects revealed that astrocytes do not become reactive upon exposure to hypergravity. On the contrary, several phenotypes could be efficiently inhibited under hypergravity conditions, which might lead to future identifications of underlying pathways and signaling molecules that ultimately shall be employed as targets for novel therapies promoting neuronal regeneration by inhibiting astrocyte reactivity.

Astrocytes under the influence of hypergravity in the physiologically relevant range of 2g could be identified as gravity-sensitive cells. Astrocyte spreading, a well-known response of 2D cultures, is significantly reduced by about 20% in hypergravity (2g), while cell proliferation and apoptosis rates are unchanged. Diminished astrocyte spreading in combination with morphological alterations indicates an impact of altered gravity conditions on the cytoskeleton. Since cellular migration depends on a dynamically rearranging actin and tubulin cytoskeleton, we expected an impact of hypergravity on astrocyte migration. To test this hypothesis, we performed *in vitro* wound-healing assays (scratch-assays) on cells exposed to hypergravity enabling an assessment of the migrational behavior of astrocytes live for the first 24h and on fixed samples for longer durations. As a result, astrocyte migration diminished by about 33% during an initial phase followed by cell adaptation with a less substantial but prolonged reduced cell speed of about 10 % compared to the 1g control.

We investigated further changes in the cytoskeleton via live-cell imaging and STED super-resolution microscopy. For live assessment of actin rearrangements, we employed



*Fig. 1: STED (STimulated Emission Depletion) microscopy images of a primary murine astrocyte cultured under 1g, 2g, and 10g hypergravity conditions immunostained for F-actin using Phalloidin conjugated to an Atto542 dye and for  $\alpha$ -tubulin using a specific antibody and a secondary anti-body conjugated to an Abberior STAR RED dye. Astrocytes were exposed to normal 1g gravity conditions (A-D), 2g hypergravity (E-H) and 10g hypergravity (I-L) in the MuSIC incubator-centrifuge. The arrows mark several lamellipodia with additional filopodia extruded from the cell membrane at various points. Shown are single channels of F-actin (yellow) and  $\alpha$ -tubulin (red) and a merged image. Marked with a box is a magnified protrusive element. The images are maximum intensity projections of 5 optical sections acquired by a z-stack of 200 nm step size.*

LifeAct-GFP expressing astrocytes that feature a fluorescently labelled dynamic actin network under hypergravity on the Hyperscope platform. Actin cytoskeleton remodeling was less dynamic for fast network rearrangements, e.g. in filopodial protrusions, but stress-bearing structures, such as stress fibers remained largely unchanged. Only through STED super-resolution microscopy, fine architectural changes in both actin filaments and microtubules could be visualized. Especially actin filaments were pronounced in cortical cell regions. Central or perinuclear actin stress fibers could be observed less frequently under hypergravity conditions. Microtubules became denser but were still well-structured under hypergravity conditions with their density depending on the gravitational load. Microtubules innervated the lamellipodial pro-

trusions to the edge of the cells under hypergravity rather than on the basis of the protrusion as under control conditions. Larger, force-bearing elements, such as actin stress fibers or microtubules in the cells center remained unchanged, as only dynamic areas with high turnover showed changes in response to hypergravity.

Our further steps are the identification of the underlying mechanisms on a deeper biochemical level employing proteomic approaches to generate an advanced model of astrocyte responses to altered gravity. For the fine cytoskeletal adaptations, we are currently testing KI-based image analysis to facilitate the microscopic image evaluation process.

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# Enhancing synaptic plasticity in vitro using novel ketamine derivatives

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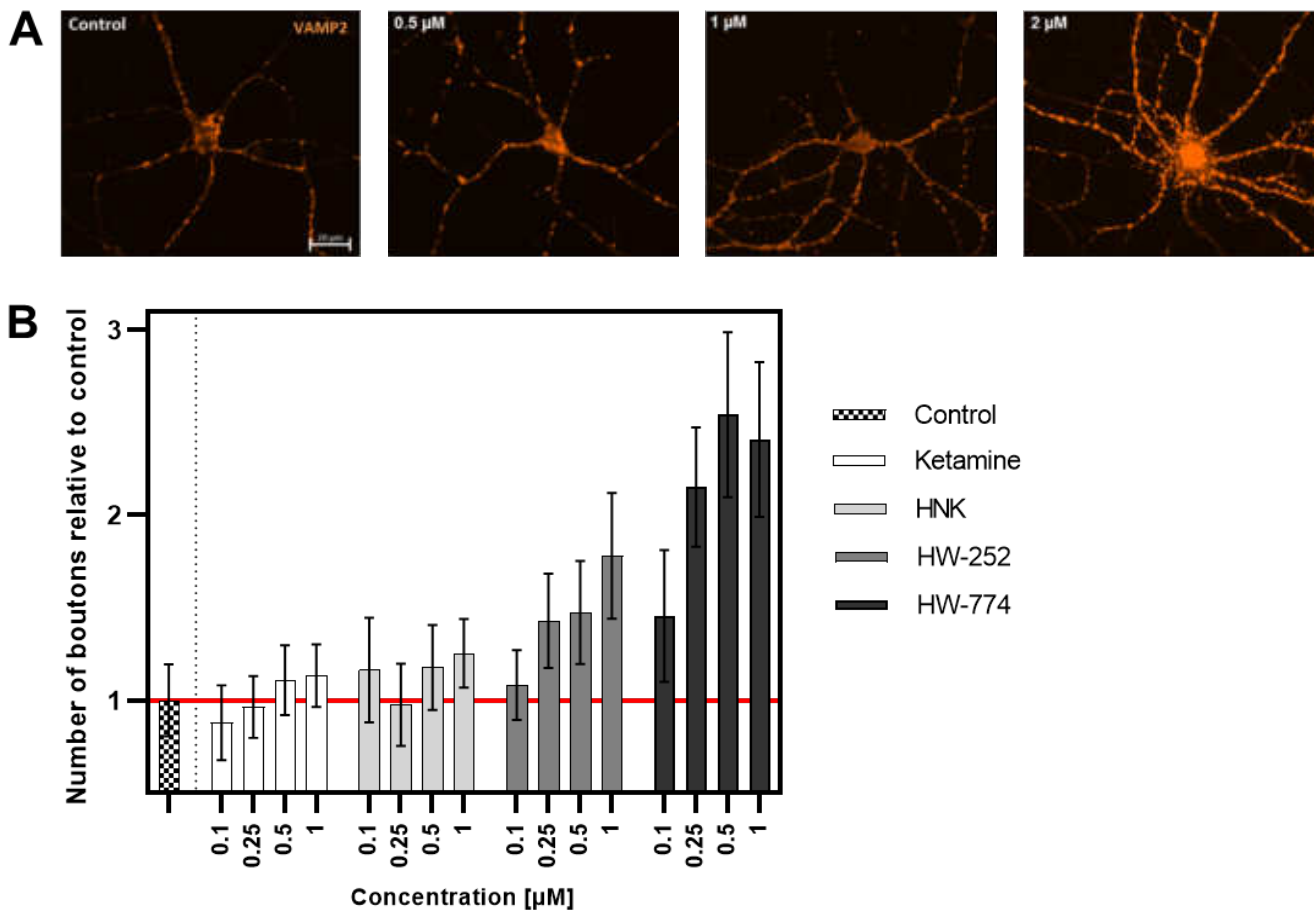


Fig. 1: (A) VAMP-2 immunostaining of untreated (Control) and cells treated with the novel Ketamine derivative at increasing concentrations. Scale bar: 20  $\mu\text{m}$ . (B) Number of pre-synaptic boutons of neuronal cells treated with Ketamine, the active metabolite hydroxynorketamine (HNK) as well as the novel derivatives HW-252 and HW-774 for 48h at different concentrations. Higher concentrations of the HW-252 and HW-774 compounds correlate with higher pre-synapse counts. Values shown as mean  $\pm$  SD. The analyzed cells were derived from 3 individual neuron cultures isolated from 3 gravid mice.

Loss of synaptic plasticity in the brain has been linked to aging-associated cognitive decline and neurodegeneration, thus providing a promising target for therapeutic interventions. Ketamine, a drug applied for analgesia in emergency medicine and in treatment-resistant depression, and some of its metabolites rapidly induce synaptic plasticity. However, ketamine cannot be reasonably applied as a neuroprotective agent given its side-effect

profile. With the aim to dissociate pro-neuroplastic actions from NMDA receptor-mediated psychotropic side effects we studied novel ketamine derivatives in vitro. We applied ketamine and different ketamine derivatives at various concentrations and incubation durations to primary hippocampal neurons cultivated until maturity of synaptic development. VAMP-2 immunostaining served as a measure for pre-synaptic density (Fig. 1A). For



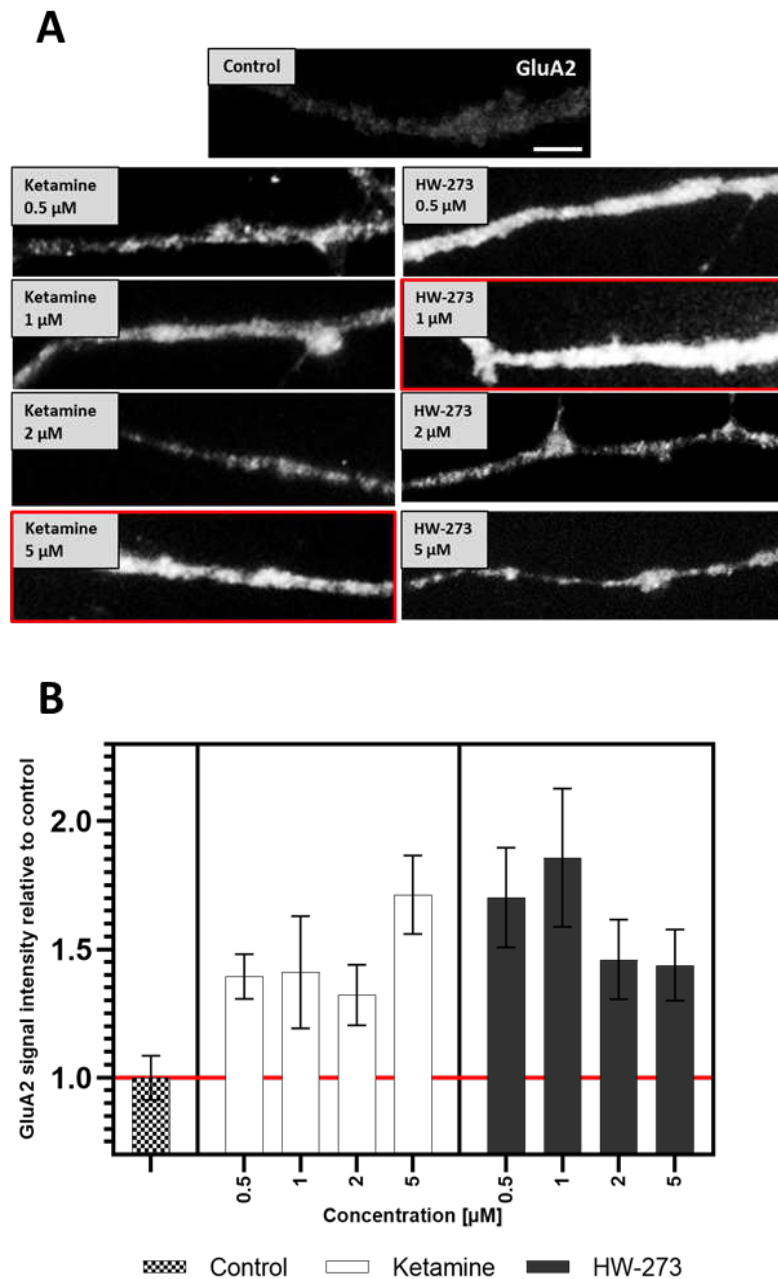


Fig. 2: (A) GluA2 immunostaining of untreated controls and cells treated with Ketamine and HW-273 for 48h at different concentrations. Scale bar: 5  $\mu$ m. (B) Relative fluorescence intensity for GluA2 immunostaining of treated versus control cells (Mean  $\pm$  SD, n=12 cells, n>1000 synapses).

treatment with several candidates, e.g. compound HW-273, pre-synapse number was enhanced in a concentration-dependent manner (Fig. 1B). Furthermore, enhanced intensity measures of post-synapse immunostaining for GluA2 (AMPA subunit) in compound-treated cells indicated elevated AMPA receptor activation at low doses (0.5-1  $\mu$ M), whereas for ketamine a higher dose was required for comparable effects (Fig. 2). In addition, treatment with high compound concentrations showed no obvious cytotoxic effects, opposite to treatment with ketamine.

We conclude that novel ketamine derivatives potentially augment neuronal plasticity in a concentration-dependent fashion. Our study provides preliminary evidence that the potentially beneficial effect on neuronal plasticity can be dissociated from NMDA receptor engagement, which could pave the way for development of new neuroprotective therapies with less unwanted side-effects.

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# C.R.O.P.<sup>®</sup> medic: First success in xenobiotics removal

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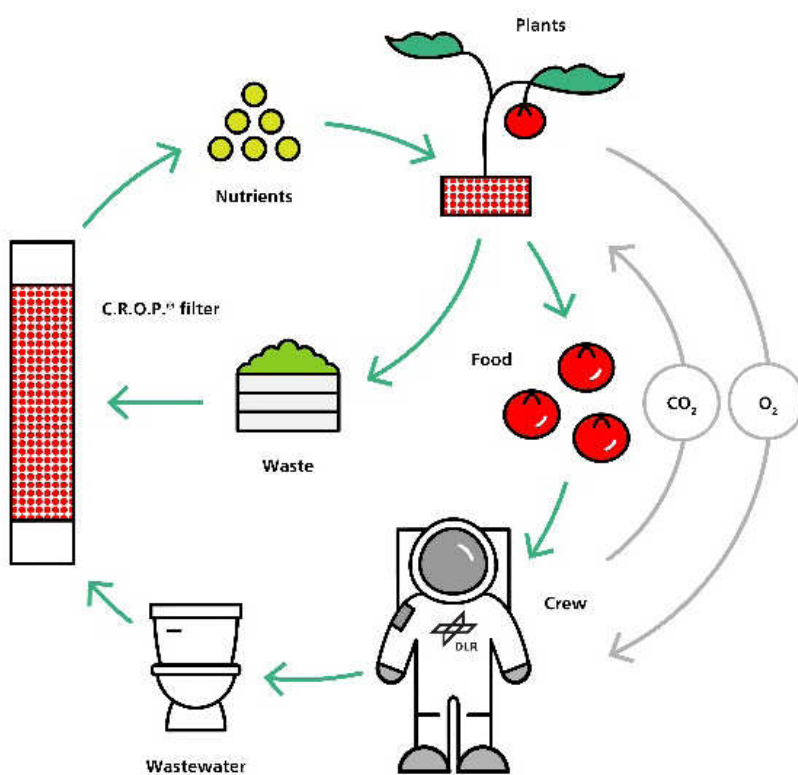


Fig. 1: Bioregenerative Life Support. Pathways for material cycling in space include urine as a nitrogen source.

A significant problem in recent years is the increase of xenobiotics concentration in ground- and tap-water. Xenobiotics are mainly drug or solvent residuals and their degradation products that enter the environment via wastewater. Pain killers, tranquilizers and hormones are the most abundant representatives of drug residuals present in water bodies. Due to high dilution, they are usually only detectable in trace amounts, but these concentrations are sufficient to change animal behavior or to impair fertility of individuals. In contrast to the impact on natural ecosystems, the highly diluted contaminants often pass through the biological stages of wastewater treatment without being removed. Presumably because the concentrations are not sufficient to select for microbes able to degrade them in the diverse microbial populations typical for wastewater treatment. As a consequence, human wastes containing large amounts of drug residues, e.g. from toilets in hospitals or nursing homes, should be collected and treated separately.

## Xenobiotics removal by the C.R.O.P.<sup>®</sup>-filter

In the DLR C.R.O.P.<sup>®</sup>-project (Combined Regenerative Organic food Production), biofilters for fertilizer production from urine were developed. In the filters, the urea contained in urine is converted to nitrate, which is a readily available nitrogen source for plants. The filter is envisioned to be a part of a Bioregenerative Life Support System in which the urine of a space crew is recycled as fertilizer for the production of fresh food (Fig. 1). We studied the capability of the C.R.O.P.<sup>®</sup>-biofilters to biologically remove drug residues from a synthetic urine spiked with high concentrations of the common drugs Diclofenac ( $17 \pm 9$  ng/L), Ibuprofen ( $496 \pm 254$  ng/L) and Sulfamethoxazol ( $697 \pm 73$  ng/L). The experiment involved

three differing types of filter units. The first was completely sterilized and filled with demineralized water instead of C.R.O.P.<sup>®</sup>-solution from processed urine. The second was sterilized and filled with sterilized C.R.O.P.<sup>®</sup>-solution from normally operated urine processing filters. The third was a normal filter with an active biofilm which was filled with unsterilized C.R.O.P.<sup>®</sup>-solution. Each type was present in triplicate and spiked with a mixture of the drugs once. Samples were taken on the first and the ninth day. In the sterile filter with water, removal rates were low for all tested drugs (Fig. 2). This shows that the drugs are not removed from the solution by adsorption to the filter media consisting of porous lava rock. In the sterile filter with the sterilized C.R.O.P.<sup>®</sup>-solution, removal rates were higher and Ibuprofen was even degraded to 80 %. Since the system was sterile, removal cannot be attributed to microorganisms.

It can be assumed that the properties of the C.R.O.P.<sup>®</sup>-urine solution led to partial chemical degradation of the drugs. Due to the nitrification process that converts the urea in the urine into nitrate, the solution is acidic (pH 3 – 4) and highly corrosive. This reactive environment is likely to support chemical degradation. Highest removal rates were observed in the unsterilized filter unit. This shows that the microorganisms in the C.R.O.P.<sup>®</sup>-filter also contributed to the removal of the drugs from the urine solution.

### Implications for future wastewater treatment

The results imply that a separate collection and treatment of urine would help to solve the problem of water contamination with drug residuals on Earth. As the C.R.O.P.<sup>®</sup>-filter is technically simple, consisting mainly of a filter tube, a tank and a pump (Fig. 3), it is suitable for the implementation of a decentralized wastewater treatment system in which the separation of different waste streams is realized.

Furthermore, the processed urine can be utilized as a fertilizer for local food production. This would be a contribution to the closure of regional material cycles which helps reducing mineral fertilizer consumption - a step towards a climate-friendly bioeconomy.

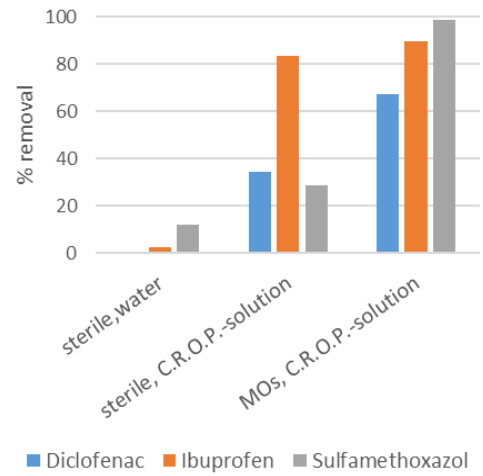


Fig. 2: Mean degradation rates [%] of Diclofenac, Ibuprofen and Sulfamethoxazol in the filters assigned to different experimental set-ups.  $N = 3$ . MOs = microorganisms.



Fig. 3: The C.R.O.P.<sup>®</sup>-biofilter for urine treatment. The blue barrel contains the urine which is processed by the microorganisms growing on the lava rock in the red tubes. A pump in the barrel circulates the urine through the tube bringing it in repeated contact with the microorganisms.

# C.R.O.P.<sup>®</sup> agrar: Road to scale-up – prepare for a future with green slurry

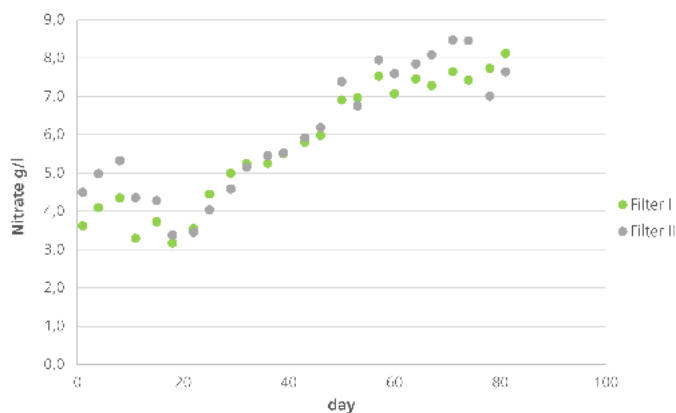
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Over the past two years we showed that the C.R.O.P.<sup>®</sup>-biofilter can be applied to process cattle slurry to a high-quality green fertilizer. The filter produces nitrate from the ammonia present in the slurry, thus mitigating problems with gas emissions and nutrient wash-out (Fig. 1). The technology initially developed for closed nutrient cycles in Lunar and Martian habitats could be successfully transferred to an application on Earth. For use in agriculture, the technology must be very robust and resistant to the impacts of weather. Also, cattle slurry is a challenging substrate being an inhomogeneous material with high solids content. For this reason, a measurement and control system were developed to handle these difficult conditions and to operate the plant in a fully automated way.

Technology transfer is carried out in cooperation with DLR Technology Marketing. In the project, a scale-up of a C.R.O.P.<sup>®</sup>-biofilter plant to an industrial scale is planned and will be built during the year. The goal is to develop and operate a plant able to process 1 m<sup>3</sup> of cattle slurry per day. This plant size is suitable for small farms with less than 50 cattle. A first pilot plant for the treatment of 100 l of slurry per day has been set up at the DLR site in Cologne (Fig. 2).

Fig. 1: Nitrate concentration of two independent C.R.O.P.<sup>®</sup>-biofilters in Lab-Scale over 81 days, indicating constant biological nitrate production; nitrate is a direct plant available nutrient.



## Interest generated in the agricultural sector

The C.R.O.P.<sup>®</sup>-biofilter is a novel processing technology based on a very simple process compared to other technologies. Initial marketing activities raised considerable interest from farmers, scientists and decision-makers in German agriculture. Over the first project phase, a network was established involving various universities, research institutions and farmers.

The network enabled an informal exchange with experts from different fields and potential users in order to achieve the best possible product fitting accurately the requirements of farmers and environmental protection. In early 2022, large-scale C.R.O.P.<sup>®</sup>-systems will be put into operation on farms for field tests.

A greenhouse experiment testing the fertilizing effect of a C.R.O.P.<sup>®</sup> fertilizer solution produced from cattle slurry in corn cultivation was conducted this summer.

We showed that the fertilizer solution generated by C.R.O.P.<sup>®</sup> had 97 % of the effectiveness of an industrial fertilizer and produced 30 % more yield compared to untreated cattle manure. In cooperation with the North Rhine Westphalia Chamber of Agriculture, a larger field study starting in spring 2022 will evaluate the effects of the C.R.O.P.<sup>®</sup>-fertilizer when applied to arable soils.

## Value proposition for farmers and society

Processing cattle slurry with the C.R.O.P.<sup>®</sup>-technology enables farmers to fertilize more efficiently with the resources available on the farm. The development strengthens the farmers' independence from fertilizer prices on the world market, which are directly linked to the increasing energy prices due to energy-intensive production processes. The environment is protected by the more efficient use of manure



*Fig. 2: First scale-up of a C.R.O.<sup>®</sup>-biofilter in outdoor operation for the treatment of 100 l of cattle slurry per day.*

preventing nutrient washout into surrounding surface or groundwater. Faster absorption of nutrients in the plants also leads to reduced gas emissions from the fields. This includes the greenhouse gas nitrous oxide as well as ammonia, which triggers the formation of fine dust in the atmosphere. The society benefits from minimized nitrate contamination in ground- and tap water, which eliminates health risks and the need for cost-intensive water treatment. In summary, a space technology for survival on other planets can significantly improve life on Earth by making a major contribution to climate and environmental protection

# Muscle wasting in disease and space – Analyses of mouse and cell models

*P. Lau, C. Clemen*

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## **Musculoskeletal deconditioning under space conditions**

Despite vigorous daily exercise routines, astronauts in space develop substantial muscle and bone loss. During long-term missions, microgravity-induced muscle loss can therefore account e.g., for up to fifteen percent of calf muscle mass. As a consequence, there is a need to optimize the currently applied exercise-based countermeasures. At this point, Earth-bound analogue studies like head-down tilt bed rest has provided unique insights into the physiology of deconditioning of the musculoskeletal system. To further investigate cellular adaptation and muscle wasting processes, mouse models and immortalized myoblast cultures are employed.

## **Muscle degeneration in genetically determined protein aggregate myopathies**

Autosomal-dominantly and recessively inherited cardiomyopathies and myopathies caused by mutations in the desmin gene are another focus of our research on muscle wasting. In most patients suffering from desminopathy, a so far non-treatable rare disease, cardiac involvement comprising cardiomyopathy, conduction defects, and arrhythmias determines prognosis. Skeletal muscle weakness and pathology may result in distal, limb-girdle, scapulo-peroneal, and generalized myopathy phenotypes. To further delineate the disease pathophysiology inflicted by either the absence of desmin or the presence of mutated desmin, mouse and cell models reflecting the human disease are of importance.

## **Determination of common denominators in muscle deconditioning and degeneration**

There is sustained need to optimize the currently applied and only partially effective exercise-based countermeasures as well as to develop novel treatment concepts for desminopathies and related myopathies and cardiomyopathies. With regard to both issues, muscle deconditioning and muscle degeneration, we are conducting corresponding multi-level analyses comprising clinical, morphological, biochemical, transcriptomic, proteomic, and microscopic methods [1-5]. Obtained results will broaden our understanding of the molecular mechanisms underlying musculoskeletal deconditioning and muscle degeneration in desminopathies. Moreover, we aim to identify relevant factors that may be targeted by chronic low-strenuous physical exercise, physiological hypoxia, altered gravity (mechanical loading), and drug application. At this point, we have already completed pilot experiments by using the chemical chaperone 4-phenyl butyrate in our mouse models and derived myoblasts (Fig. 1). Further exploiting our mouse and cell models, we investigate effects of acute, strenuous versus chronic, low intensity exercising and of additional drugs that were already approved for the use in humans. For example, we subject desminopathy mice and wild-type siblings that were kept under standard housing conditions, i.e., living in a sedentary way, to acute, strenuous treadmill running. This strenuous exercise is performed without or with a prior, two-week period of 4-phenyl butyrate administration. After exercising to their maximal possible indi-

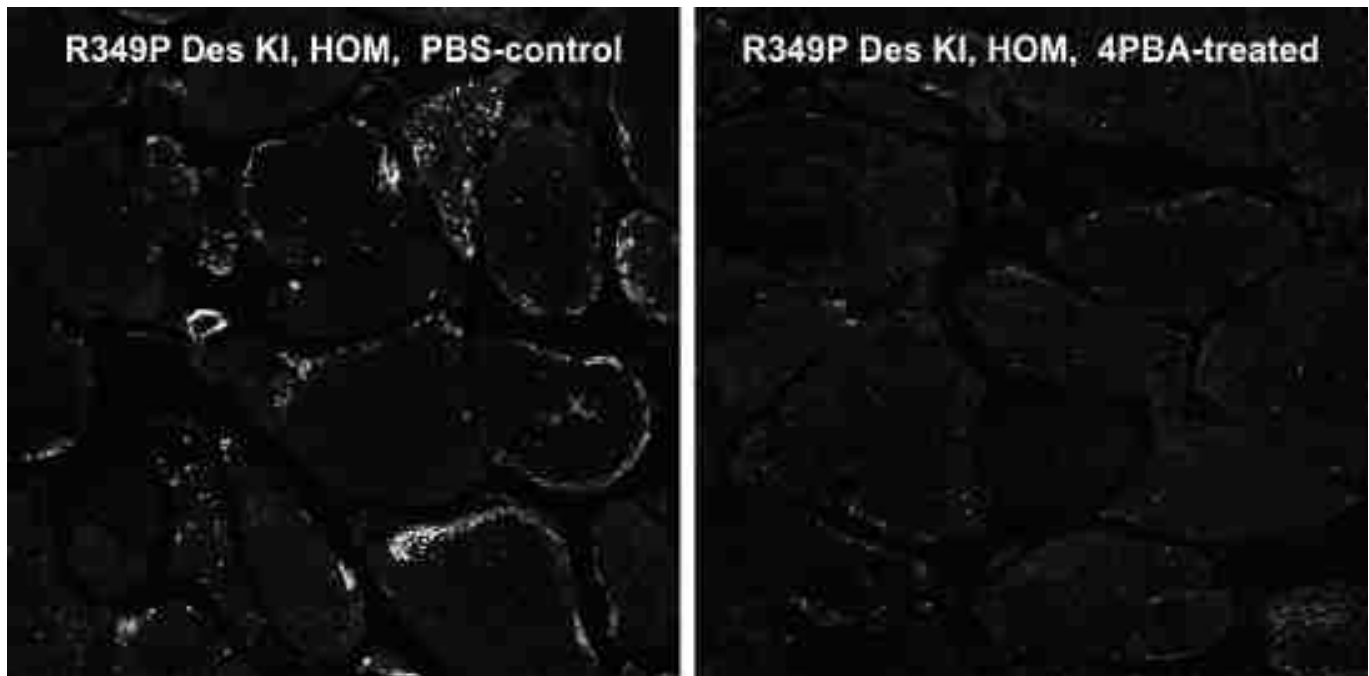


Fig. 1: Xin immunofluorescence signal pattern in sections of soleus muscle derived from homozygous R349P desmin knock-in mice treated with 4-phenylbutyrate (4PBA, right image) recorded by confocal microscopy in comparison to vehicle-treated animals (PBS, left image). Note the marked reduction of the number of Xin-positive spots indicating a possible sarcomer-protective effect of 4-phenylbutyrate that may stabilize or even improve the contractile function in the desminopathy disease context. The therapeutic potential of this drug on striated muscle tissue will be analyzed in a more detailed way.

vidual performance, their dissected skeletal and cardiac muscle tissue specimens are, in a first step, analyzed for the extent of sarcomeric micro-lesions (unpublished work). Such work is accompanied by in vitro studies employing our immortalized desminopathy myoblasts. Here, mass spectrometry analyses of differentiated myotubes with and without drug treatment as well as electrostimulation of the cultured myotubes will help to identify disease-related biomarkers which can monitor effects of drug treatment and mechanical strain on the muscle cells (unpublished work). In the context of our cell models, we further assess putative combined beneficial effects of altered gravity (hypergravity as well as simulated microgravity) and reduced oxygen levels. In all scenarios, we aim at analyzing the effects of these interventions on muscle strength, muscle wasting, muscle cell degeneration, protein aggregate and sarcomeric lesion formation, mitochondrial pathology, autophagy induction, and heat shock protein response (unpublished work). Beyond its high relevance for spaceflight medicine research, our work has the potential to pave the way on Earth for novel treatment approaches of human musculoskeletal diseases.

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## Study Team

Ewald, A. et al.: **Effects of short-term hypercaloric nutrition on orthostatic tolerance in healthy individuals**



# Study Team

*Dr. rer. nat. Melanie von der Wiesche (Head)*

*Alexandra Noppe (Deputy)*

The major objective of DLR's research facility :envihab is to explore the effects of different environmental conditions on human beings in long-term studies (e.g. at varying pressure or atmosphere conditions) and the development of appropriate countermeasures and life support systems for long-term space missions, for aeronautics, and for patients on Earth. To guarantee a consistent high quality of all different types of human studies the Institute uses a functional, interdivisional working group, the Study Team. This Team is an essential unit of the Central Management of the Institute of Aerospace Medicine. Here, internal and external human studies are centrally coordinated. With more than 13 years of experience the Study Team plans, prepares and implements various biomedical as well as clinical studies. The overall aim is to ensure rigorous standardization and high quality of the study-management, with all relevant laws and regulations being adhered to, at the same time providing the required medical care and monitoring. The main focus is on complex, highly standardized in-patient studies, e.g., head-down tilt bed rest studies (lasting several months) as well as clinical studies. Additionally the Study Team plans and realizes ambulant studies, focused on tests with the Short-Arm Human Centrifuge (SAHC) at :envihab inducing artificial gravity.

## ***Main features of the Working Group***

- Application procedure (ethical protocol, insurance of subjects)
- Management of subject-recruitment
- Management of highly standardized nutrition
- Project-Management
- Preparation of study documents such as protocol, case report forms, and informed consent documents
- On-site management, with GCP-trained key personnel
- Comprehensive internal reporting and communication to ensure high quality
- Central Management for scheduling studies in :envihab
- General counselling

# Effects of short-term hypercaloric nutrition on orthostatic tolerance in healthy individuals (HyNu-OT-Study)

A. C. Ewald<sup>1</sup>, R. De Gioannis<sup>2</sup>, D. Gerlach<sup>3</sup>, K. Heußer<sup>3</sup>, F. Hoffmann<sup>3</sup>, A. Noppe<sup>1</sup>, P. Frings-Meuthen<sup>4</sup>, M. Heer<sup>5</sup>, J. Tank<sup>3</sup>, J. Jordan<sup>6,7</sup>

<sup>1</sup>Study Team, Institute of Aerospace Medicine, German Aerospace Center (DLR), Cologne, Germany; <sup>2</sup>Department of Sleep and Human Factors Research, Institute of Aerospace Medicine, German Aerospace Center (DLR), Cologne, Germany; <sup>3</sup>Department of Cardiovascular Aerospace Medicine, Institute of Aerospace Medicine, German Aerospace Center (DLR), Cologne, Germany; <sup>4</sup>Department of Muscle and Bone Metabolism, Institute of Aerospace Medicine, German Aerospace Center (DLR), Cologne, Germany; <sup>5</sup>Human Nutrition, Institute of Nutrition and Food Sciences (IEL), University of Bonn, Germany; <sup>6</sup>Head of Institute of Aerospace Medicine, German Aerospace Center (DLR), Cologne, Germany; <sup>7</sup>Chair of Aerospace Medicine, University Hospital Cologne, Germany

Reduced caloric intake lowers blood pressure through sympathetic inhibition and worsens orthostatic tolerance within days. Conversely, hypercaloric nutrition augments sympathetic activity and blood pressure. Because dietary interventions could be applied in patients with orthostatic intolerance we tested the hypothesis that short-term hypercaloric dieting could improve orthostatic tolerance.

The study was conducted at :envihab in a randomized crossover design. The study was divided into two phases. Both phases followed

the exact same study protocol except for the nutritional intervention. 20 healthy participants started with either a strict hypercaloric or normocaloric nutritional plan for four days. After a break of at least 23 days in-between both phases (washout period), the subjects switched the respective nutritional plan.

For the dietary intervention we determined individual total energy expenditure based on measured resting metabolic rate and estimated physical activity level. We assessed resting metabolic rate as well as substrate oxidation through indirect calorimetry (Fig. 3). Caloric content of the normocaloric diet corresponded to individual total energy expenditure. Caloric intake was increased by 25% above total energy expenditure during the hypercaloric diet. We increased energy content by raising fat intake while carbohydrate, fiber and protein were kept constant. Fluid as well as dietary sodium and potassium intake did not differ in both dietary phases. Additionally, we measured body composition via BodPod (Fig. 2) and bioelectrical impedance analysis (BIA). To assess the orthostatic tolerance, we performed head-up tilt table testing with incre-

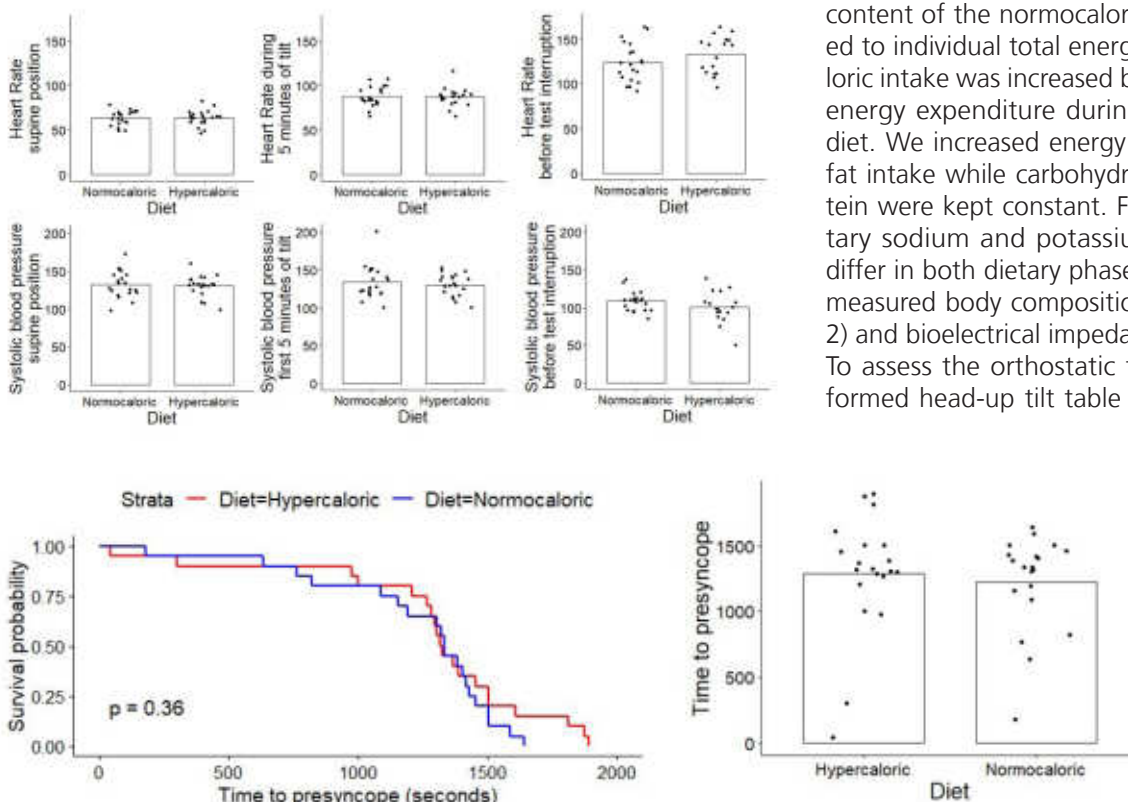


Fig. 1: Heart rate, systolic blood pressure and time to presyncope.



*Fig. 2: Body composition measurement.*



*Fig. 3: Resting metabolic rate via indirect calorimetry for nutritional intervention.*

mental lower body negative pressure while recording beat-by-beat blood pressure and heart rate. We conducted the test in the morning hours after an overnight fast. We collected blood samples 30 minutes before orthostatic testing. During the experiment we measured continuous finger blood pressure, brachial blood pressure, and electrocardiogram. Subjects rested in supine position for 15 minutes and were then tilted head up to a 60° position for 20 minutes. Subsequently, we applied incremental lower body negative pressure steps (-20, -40 and -60 mmHg), each lasting 10 minutes. The test was terminated when systolic blood pressure decreased below 80 mmHg (or <90 mmHg and rapidly decreasing), when participants reported presyncopal symptoms, when syncope occurred, or when subjects requested to abort the test. The primary endpoint of the study was the change in time to presyncope. Exploratory endpoints included blood pressure, heart rate,

heart rate variability and baroreflex sensitivity before and during orthostatic testing.

The results (Fig. 1) showed, that time differences to presyncope during combined head-up tilt and lower body negative pressure were not significant between hypercaloric and normocaloric dieting. Moreover, neither in heart rate nor in blood pressure, heart rate variability, or blood pressure variability in the supine position and during orthostatic testing we found any significant differences between both caloric conditions.

We conclude that four days moderate hypercaloric nutrition does not significantly improve orthostatic tolerance in healthy individuals. Nevertheless, given the important interaction between energy balance and cardiovascular autonomic control in the brain, caloric intake deserves more attention as potential contributor and treatment target for orthostatic intolerance.

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# Annex

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# Scientific activities

## *Teaching activities*

<b>Name</b>	<b>University</b>	<b>Subject</b>
Aeschbach, Daniel	Harvard Medical School	Sleep Medicine
Anken, Ralf	Universität Hohenheim	Zoology
Berger, Thomas	ISU Strasbourg	Radiation Physics
Berger, Thomas	FH Aachen	Radiation Physics
Berger, Thomas	Universität Stuttgart	Radiation Physics
Berger, Thomas	Hochschule Bonn-Rhein-Sieg	Radiation Physics
Clemen, Christoph	Universität Köln	Biochemistry & Molecular Genetics
Clemen, Christoph	Ruhr-Universität Bochum	Translational Myology
Elmenhorst, Eva-Maria	RWTH Aachen	Aviation and Travel Medicine
Elmenhorst, Eva-Maria	RWTH Aachen	Space Medicine
Gerlach, Darius	Universität Köln	Cardiovascular Physiology for midwife bachelor students
Gerlach, Darius	Universität Köln	Physiology practical training for medical students
Goerke, Panja	FH Wedel	Soft Skills
Hauslage, Jens	Tiermedizinische Hochschule Hannover	Gravitational Biology
Hauslage, Jens	Hochschule Bonn-Rhein-Sieg	Gravitational Biology, Botany
Hauslage, Jens	ISU Strasbourg	Gravitational Biology and Biological Life Support
Hauslage, Jens	IPEN Sao Paulo	Gravitational Biology and Biological Life Support
Hellweg, Christine	Universität Bonn	Radiation Biology
Hellweg, Christine	Freie Universität Berlin	Immunology
Hellweg, Christine	Freie Universität Berlin	Pathology
Hellweg, Christine	Universität Bonn	Radiation Biology
Hemmersbach, Ruth	Universität Bonn	Zoology & Gravitational Biology
Herzog, Merle	Universität Hamburg	Psychology
Heusser, Karsten	Universität Köln	Physiology
Kölzer, Ana	FH Wedel	Soft Skills
Liemersdorf, Christian	Universität Bonn	Molecular Genetics

Lindlar, Markus	Hochschule Bonn-Rhein-Sieg	Health Telematics
Lindlar, Markus	Hochschule Bonn-Rhein-Sieg	Literature seminar Digital Health
Mittelstädt, Justin	Universität Hamburg	Psychology
Möller, Ralf	Hochschule Bonn-Rhein-Sieg	Microbiology
Rittweger, Jörn	Universität Köln	Seminar paediatrics
Schudlik, Kevin	Int. School of Management (ISM), Hamburg	Psychology & Management
Schulze Kissing, Dirk	Hochschule Fresenius	Psychology
Stelling, Dirk	Hochschule Fresenius	Psychology
Stern, Claudia	Technische Universität Braunschweig	Luft- und Raumfahrtmedizin
Stern, Claudia	ISU Strasbourg	Human Visual System
Stern, Claudia	Universität der Bundeswehr München	Raumfahrtmedizin
Stern, Claudia	School of Aviation Medicine	Ophthalmology
Tank, Jens	Medizinische Hochschule Hannover	Propaedeutics
Zinn, Frank	Universität Hamburg	Psychology

# Graduations

## *Supervised Doctoral Students*

University	Space	Aviation	Traffic
Universität Bern	1		
Universität Bonn	3		
Medizinische Hochschule Hannover	3		
University of Hamburg	3		
Georg-August-Universität Göttingen	1		
RWTH Aachen	5	3	
Universität Salzburg		1	
University Leiden		1	
Universität Köln	5		
Universität Düsseldorf		2	
Justus-Liebig-Universität Gießen	1	2	1
Ruhr-Universität Bochum	1		
Universität Duisburg-Essen	2		
Technische Universität Braunschweig	1	1	
Universität Oldenburg	1		
Radboud University	1		

## *Bachelor Degrees*

University	Space	Aviation	Traffic
Hochschule Albstadt-Sigmaringen	1	1	1
Universität Bonn	2		
Hochschule Bonn-Rhein-Sieg	2	1	1
Universität Düsseldorf		1	
FH Aachen	1		
Universität Bochum	1		

## *Diploma Theses/Master Degrees*

University	Space	Aviation	Traffic
Goethe Universität Frankfurt	1		
FH Aachen	1		
OTH Regensburg	1		
Universität Bonn	2	1	1
University of Zagreb	1		
Universität Bonn	1		
Radboud University	1		

## *Doctorates*

University	Space	Aviation	Traffic
Medizinische Hochschule Hannover	2		
Darmstadt	1		
GAU Göttingen	1		



*Scientific exchange*

Collura, Salvatore	University of Bologna
Ferre, Elisa	Birkbeck University
Green, David	King's College
Harris, Laurence	York University
Herperts, Rainer	Hochschule Bonn Rhein Sieg
Hoffmann, Fabian	University Hospital of Cologne, Germany; Department of Cardiology, Pneumology, Angiology and Intensive Care
Hönemann, Jan-Niklas	University Hospital of Cologne, Germany; Department of Cardiology, Pneumology, Angiology and Intensive Care
Jenkin, Michael	York University
Kramer, Tilmann	University Hospital of Cologne, Germany; Department of Cardiology, Pneumology, Angiology and Intensive Care
Limper, Ulrich	Hospital of Cologne Merheim, Germany; Clinic for Anesthesiology and Intensive Care Medicine
Sánchez Trigo, Francisco Horacio	University of Seville
Scorcelletti, Matteo	Manchester Metropolitan University
Uy, May LI	International Space University
Weis, Henning	University Hospital of Cologne, Germany; Clinic and Polyclinic for Nuclear Medicine

# Awards

## **Beblo-Vranesevic, Kristina**

Best Presentation Award, European Astrobiology Network Association (EANA) Virtual Conference 2021

## **Cortesao, Marta**

Add-on Fellowship for Interdisciplinary Life Science 2021 der Joachim Herz-Stiftung

## **Gerlach, Darius A.; Manuel, Jorge; Hoff, Alex; Heusser, Karsten; Jordan, Jens; Tank, Jens**

High Impact Paper for Summer 2021 in the category of basic science of the journal "Hypertension": "Medullary And Hypothalamic Functional Magnetic Imaging during Acute Hypoxia in Tracing Human Peripheral Chemoreflex Responses"

## **Magliulo, Maria**

Three Minute Thesis competition, University of Essex

## **Palomeque Dominguez, Hector Hugo**

4<sup>th</sup> place of the Space Factor Contest, EANA 2021

## **Rettberg, Petra**

International Astronautical Federation Distinguished Service Award

## **Weber, Laura; Paulke, Tim; Stock, Johannes**

3rd place business plan competition KUER.NRW

# Events, lectures, workshops at the Institute

## 26.1.2021

Institute Seminar: Dr. Renata L.S. Goncalves, Site-specific mitochondrial ROS production underlies alterations in liver glucose homeostasis in obesity (online)

## 5./5.3.2021

Kompetenznetzwerk Immobilisationsbedingte Muskelstörungen KNIMS (online)

## 9.3.2021

Institute Seminar: Hans Kleine-Brüggeney, From Single-Cell Multi-Omics Technologies to Functional Phenomics (online)

## 13.3.2021

Ernährung – nur gesund oder macht sie auch glücklich? VBiO, DPG, DLR Workshop (online)

## 27.4.2021

Seminar: Initiative Lärmwirkungsforschung (online)

## 11.5.2021

Institute Seminar: Dr. rer. nat. Frank Duschek, Grundlagen und Laseranwendungen für die Biostoff-Detektion (online)

## 12.6.2021

DLR Fliegerarzttag (online)

## 28.9.2021

Institute Seminar: Prof. Dr. Ben Fabry, Single and collective cell forces in 3-D hydrogels (online)

## 26.–27.10.2021

Lehrgang zum Erwerb der Fachkunde im Strahlenschutz im Zusammenhang mit dem Betrieb von Luftfahrzeugen

## 29.–30.10.2021

4<sup>th</sup> International WAVex Workshop: Whole Body Vibration as an intervention in physical and mental health (online)

## 26.10.202

Special Colloquium Maurer Mission, Institute of Material Physics and Institute of Aerospace Medicine

## 2.11.2021

Institute Seminar: Carolin Reichert, PhD, Caffeine and human sleep-wake regulation (online)

## 4.11.2021

GANDALF – Graduierten Schule „Fighting Pandemic Threats“ – Virtuelles Science Kick-off Meeting

## 9.-19.11.2021

Direct Return Thomas Pesquet

## 10.–11.11.2021

InnoHealth USA 2021, German R&D Tour (online)

## 16.11.2021

Institute Seminar: Prof. Dr. Boris Pfander, The cellular decision of how to repair DNA breaks (online)

## 30.11.2021

Institute Seminar: Dr. Marta Cortesão, Adaptation of the black fungus *Aspergillus niger* to simulated spaceflight and Mars-like conditions (online)

## 4.12.2021

6<sup>th</sup> Human Physiology Workshop (online)

# Publications

## Publications with an impact factor above 10

Bashir, A.K., Wink, L., Duller, S., Schwendner, P., Cockell, C., **Rettberg, P.**, Mahnert, A., **Beblo-Vranesevic, K.**, **Bohmeier, M.**, **Rabbow, E.**, Gaboyer, F., Westall, F., Walter, N., Cabezas, P., Garcia-Descalzo, L., Gomez, F., Malki, M., Amils, R., Ehrenfreund, P., Monaghan, E., Vannier, P., Marteinson, V., Erlacher, A., Tanski, G., Strauss, J., Bashir, M., Riedo, A., Moissl-Eichinger, C. *Taxonomic and functional analyses of intact microbial communities thriving in extreme, astrobiology-relevant, anoxic sites.* Microbiome. 2021;9(1):50. BioMed Central. DOI: 10.1186/s40168-020-00989-5 ISSN 2049-2618.

Chellappa, S.L., Qian, J., Vujovic, N., Morris, Ch.J., Nedeltcheva, A., Nguyen, H., Rahman, N., Heng, S.W., Kelly, L., Kerlin-Monteiro, K., Srivastav, S., Wang, W., **Aeschbach, D.**, Czeisler, C.A., Shea, S.A., Adler, G.K., Garaulet, M., Scheer, F.A.J.L. *Daytime eating prevents internal circadian misalignment and glucose intolerance in night work.* Science Advances. 2021;7(49):eabg9910. American Association for the Advancement of Science (AAAS). DOI: 10.1126/sciadv.abg9910. ISSN 2375-2548.

Gerlach, D.A., Manuel, J., **Hoff, A.**, **Kronsbein, H.**, **Hoffmann, F.**, **Heusser, Karsten, Ehmke, H.**, **Jordan, J.**, **Tank, J.**, Beissner, F. *Medullary and hypothalamic functional magnetic imaging during acute hypoxia in tracing human peripheral chemoreflex responses.* Hypertension. 2021;77(4):1372-1382. American Heart Association, Inc.. DOI: 10.1161/HYPERTENSIONAHA.120.16385. ISSN 0194-911X.

**Heusser, K.**, Wittkoepper, J., Bara, C., Haverich, A., Diedrich, A., Levine, B., Schmitto, J., **Jordan, J.**, **Tank, J.** *Sympathetic vasoconstrictor activity before and after left ventricular assist device implantation in patients with end-stage heart failure.* European Journal of Heart Failure. 2021;23(11):1955-1959. Wiley. DOI: 10.1002/ejhf.2344. ISSN 1388-9842.

**Lecheler, L.**, **Hoffmann, F.**, **Tank, J.**, **Jordan, J.** *Run Vagus Run: Cardiovagal baroreflex function and the postural tachycardia syndrome.* Hypertension. 2021;77(4):1245-1247. American Heart Association, Inc.. DOI: 10.1161/HYPERTENSIONAHA.121.16578. ISSN 0194-911X.

**Limper, U.**, **Tank, J.**, Ahnert, T., Maegele, M., Grottko, O., Hein, M., **Jordan, J.** *The thrombotic risk of spaceflight – Has a serious problem been overlooked for more than half of a century?* European Heart Journal. 2020; 42(1): 97-100. Oxford University Press. DOI: 10.1093/eurheartj/ehaa359 ISSN 0195-668X.

Sujana, C., Salomaa, V., Kee, F., Costanzo, S., Söderberg, S., **Jordan, J.**, Jousilahti, P., Neville, C., Iacoviello, L., Oskarsson, V., Westermann, D., Koenig, W., Kuulasmaa, K., Reinikainen, J., Blankenberg, S., Zeller, T., Herder, C., Mansmann, U., Peters, A., Thorand, B. *Natriuretic peptides and risk of type 2 diabetes: Results from the biomarkers for cardiovascular risk assessment in Europe (BiomarCaRE) consortium.* Diabetes Care. 2021;44(11):2527-2535. American Diabetes Association. DOI: 10.2337/dc21-0811. ISSN 1935-5548.

## Further publications 2021

### Publications (peer-reviewed)

Alvero-Cruz, J.R., Brikis, M., Chilibeck, P., **Frings-Meuthen, P.**, Guzmán, J.F., **Mittag, U.**, **Michély, S.**, **Mulder, E.**, Tanaka, H., **Tank, J.**, **Rittweger, J.** *Age-Related decline in vertical jumping performance in masters track and field athletes: Concomitant influence of body composition.* Frontiers in Physiology. 2021;12:643649. Frontiers Media S.A. DOI: 10.3389/fphys.2021.643649. ISSN 1664-042X.

**Bartels, S.**, Ögren, M., Kim, J.-L., Fredriksson, S., Persson Waye, K. *The impact of nocturnal road traffic noise, bedroom window orientation, and work-related stress on subjective sleep quality – Results of a cross-sectional study among working women.* International Archives of Occupational and Environmental Health. 2021;94:1523-1536. Springer. DOI: 10.1007/s00420-021-01696-w. ISSN 0340-0131.

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## Publications in an anthology

**Maier, J.** *Kreativität messen: Ein trimodaler Ansatz*. In: Praxis der Wirtschaftspsychologie - Auswahl und Entwicklung von Fach- und Führungskräften Praxis der Wirtschaftspsychologie, 1. Pabst Publishers. 2021:50-63. ISBN 978-3-95853-683-8.

## Theses

- Arndt, F.** (2021) *The impact of environmental and space-flight-relevant conditions on the vancomycin resistance of *Enterococcus faecium**. Masterarbeit, Rheinische Friedrich-Wilhelms-Universität Bonn, Germany.
- Cortese, M.** (2021) *Morphological and molecular adaptation of *Aspergillus niger* to simulated spaceflight and Mars-like conditions*. Dissertation, Georg-August-University Göttingen, Germany.
- Dyck, B.** (2021) *Analysis of the buffer system of the C.R.O.P.<sup>®</sup>-process*. Bachelorarbeit, Ruhr-Universität Bochum (RUB), Bochum, Germany.
- Fesseler, A.** (2021) *Untersuchung zur Wirksamkeit von niederenergetischer Elektronenstrahlung auf die Inaktivierung von *Aspergillus niger* Sporen*. Bachelorarbeit, Hochschule Albstadt-Sigmaringen, Germany.
- Hoffmann, S.** (2021) *Astrocyte reactivity as a novel biomarker for combined effects of ionizing radiation and simulated microgravity*. Bachelorarbeit, Rheinische Friedrich-Wilhelms-Universität Bonn, Germany.
- Holbeck, I.M.** (2021) *Development of a closed, modular gas characterization environment for the C.R.O.P.<sup>®</sup>-filter*. Masterarbeit, FH Aachen, University of Applied Science, Aachen, Germany.
- Iannicelli Caiaffa, M.** (2021) *Evaluation of state-of-the-art decontamination techniques and innovative prevention methods on the astrobio logical model organism *Aspergillus niger**. Bachelorarbeit, University of Applied Sciences Bonn-Rhein-Sieg.
- Ly, Y.-T.** (2021) *Development and characterization of a standardized microbiome for aerospace research*. Masterarbeit, Rheinische Friedrich-Wilhelms-Universität Bonn, Germany.
- Mayat, N.** (2021) *Classification of Not-Worn Phases and Inactivity Phases in Accelerometry Data using Machine Learning*. Bachelorarbeit, University of Applied Sciences, RheinAhr-Campus, Koblenz, Germany.
- McAlpin, K.** (2021) *Bacillus subtilis spore resistance to simulated lunar conditions and the potential of thermocycling*. Bachelorarbeit, University of Applied Sciences Bonn-Rhein-Sieg, Germany.
- Meerholz, Z.** (2021) *Altered gravity exposure triggers autophagy-dependent morphological alterations of C2C12 murine muscle cells*. Bachelorarbeit, Rheinische Friedrich-Wilhelms-Universität Bonn, Germany.
- Müller, C.** (2021) *Radioresistance and metabolic profile of human lung carcinoma cells under extreme hypoxia*. Bachelorarbeit, Heinrich Heine University Düsseldorf, Germany.
- Nataniel, M.** (2021) *Development of a 3D printable clinostat for generating simulated microgravity under radiation*. Bachelorarbeit, FH Aachen, University of Applied Science, Aachen, Germany.
- Parganlija, D.** (2021) *Impact of altered muscle perfusion through lower body negative pressure on acute cardiovascular, physiological and molecular responses to resistive leg press exercise*. Dissertation, Deutsche Sporthochschule Köln, Germany.
- Pavletić, B.** (2021) *Impact of physical conditions of deep space on the infectivity of coliphage MS2*. Masterarbeit, University of Zagreb, Croatia.
- Pereira de Almeida, P.** (2021) *Radiation response of different phenotypes of primary murine astrocytes after X-ray exposure*. Masterarbeit, University Duisburg-Essen, Essen.
- Roggan, M.D.** (2021) *Reactivity of primary astrocytes after exposure to ionizing radiation*. Projektarbeit, South-Westphalia University of Applied Sciences, Iserlohn, Germany.
- Runzheimer, K.** (2021) *Intercomparison study of different biological indicators and their pigmentation to a selection of decontamination methods*. Masterarbeit, Rheinische Friedrich-Wilhelms-Universität Bonn, Germany.
- Sanchidrián González, P.M.** (2021) *Comparison of cytokine expression of different lung cancer cells in response to cellular stressors: a literature study*. Projektarbeit, Rheinische Friedrich-Wilhelms-Universität Bonn, Germany.
- Stöckmann, P.** (2021) *Cytoskeletal and mitochondrial pathology in immortalized R349P desmin knock-in myoblasts*. Bachelorarbeit, Fachhochschule Aachen, Campus Jülich.
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- Wallau, S.** (2021) *Design und Entwicklung einer neuartigen Fußballhalterung für das MARES-System Vergleich mit der herkömmlichen Halterung hinsichtlich Steifigkeit, Trägheit, Zuverlässigkeit/Handhabbarkeit und Komfort*. Bachelorarbeit, Hochschule Koblenz.
- Zaccaria, T.** (2021) *Assessment of the adaptability of nonfastidious pathogenic bacteria to the Martian environment*. Masterarbeit, Radboud University, Nijmegen, Netherlands.





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