Research Report
Institute of Aerospace Medicine 2017

DLR

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Preface

The Institute of Aerospace Medicine at the German Aerospace Center (DLR) comprises departments in Cologne and in Hamburg with an internationally unique research infrastructure. At DLR, the Institute serves as the interface between sophisticated technology and life sciences research comprising biology, medicine, and psychology. The research is conducted in close collaboration with leading national and international research institutions. 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 are conducted in dedicated simulation facilities and are complemented by successful investigations in space. Our overarching goal is to conduct research that improves the lives of human beings in space and on Earth.

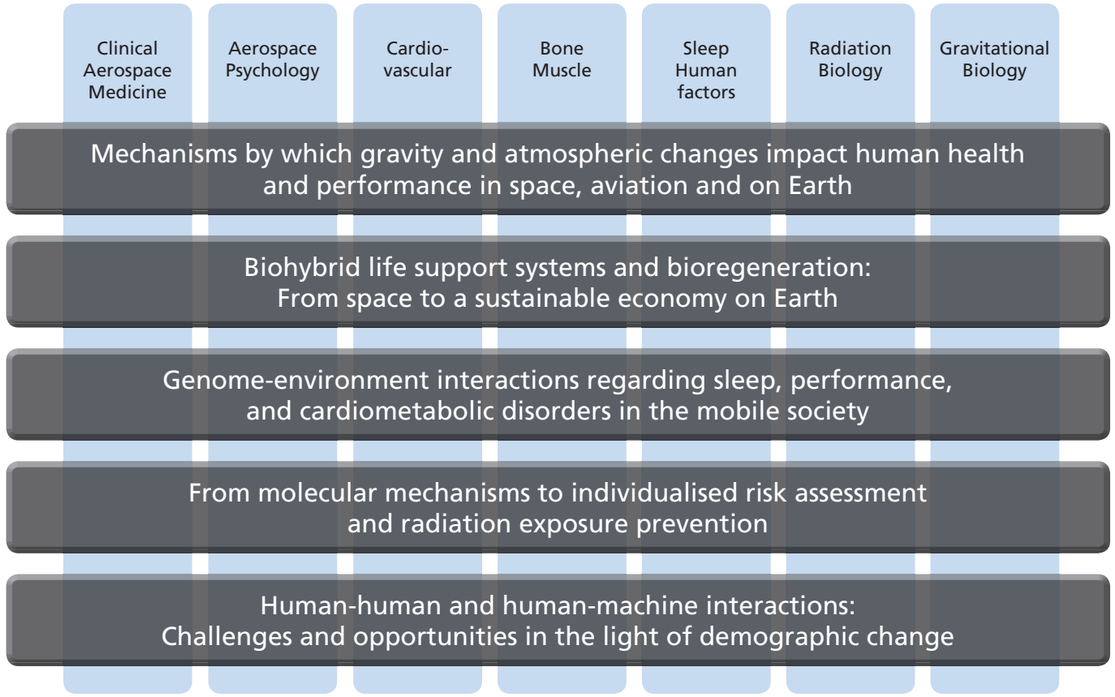
In 2017, we changed the structure of the Institute and defined major interdisciplinary research topics that address important societal challenges. Influences of environmental factors, such as atmosphere conditions, radiation, gravity, and noise, on human beings are in the focus of the research. Mechanistic understanding is the key to targeted preventive measures. Furthermore, we extended our efforts to elucidate man-man and man-machine interactions which will be increasingly relevant given the demographic change and digitalization thrush in years to come.

The present report provides an exemplary overview of our research activities in 2017 illustrating our interdisciplinary and translational research approach.

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

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

Institute of Aerospace Medicine – Research topics
Scientific integration and translation



1. Reports

1.1 Gravitational Biology

1.1.1 Combined Regenerative organic food Production – C.R.O.P.®. Treatment and utilization of organic wastes

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Bioregeneration is a vital part of life support systems development, because biological components are essential for nutrient recycling. Healthy and palatable food can only be produced by means of crop cultivation. In a closed system with minimized supply, fertilizer has to be produced from organic waste. As urine and feces contain a variety of nutrients, toilet sewage can be considered the raw material for fertilizer production in space. Within the framework of the C.R.O.P.® project, an aqueous fixed bed biofiltration system was developed, which can be used for the conversion of organic waste to plant-available inorganic matter (mineralization). In long-term experiments the capability of the C.R.O.P.® filters to mineralize the organically bonded nitrogen in urine was examined. Process optimization was obtained by changes in operation mode.

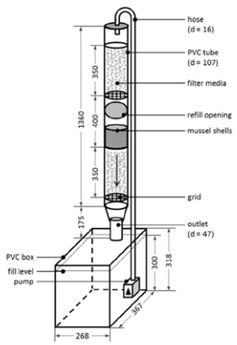

Fig. 1: The C.R.O.P.® filter. The liquid flow is cyclic. The filtrate passes repeatedly through the filter, until the process is finished. Internal dimensions are given in mm.

The C.R.O.P.® filter technology is based on the pumice, which is used as filter material providing a porous, rough surface and the micronutrients necessary for biofilm growth. Filter design is given in Fig.1.

In the C.R.O.P.® Biofiltration Lab the filters are constantly in operation. During the first two year experiment the filters were operated in batch mode (=after processing the batch was completely removed and replaced by a fresh one). Triplets of filters were fed with synthetic urine in differing concentrations. Here, the operation parameters of the filters fed with 80% urine [1] are presented in comparison to the parameters of filters run in fed batch operation (= filter tanks were filled stepwise, with 1l of synthetic urine per day until fill level was reached, then the batch was removed and the process started again) in the subsequent experiment. At the day of replacement, 9l of water and 1l of urine were added to the tanks to reach the volume needed for pump operation. The resulting batch reached a urine concentration of approximately 70 % at the end of the processing period.

The comparison of the different operation modes showed that fed batch operation led to higher nitrate production rates than batch operation (Figs. 2, 3, Tab. 1).

During batch mode operation white precipitates occurred and could be identified as calcium phosphate using the data from IC measurements. Fed batch operation led to red precipitates, which could not be identified on the basis of the available data. An X-ray diffraction analysis is implemented.

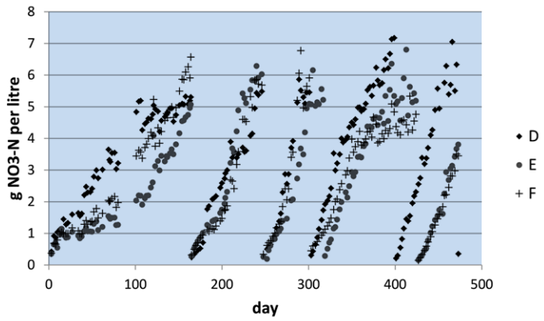

Fig. 2: Batch mode. Nitrate production of the filters D,E,F, which were fed with batches of 80% urine solution over a period of 475 days.

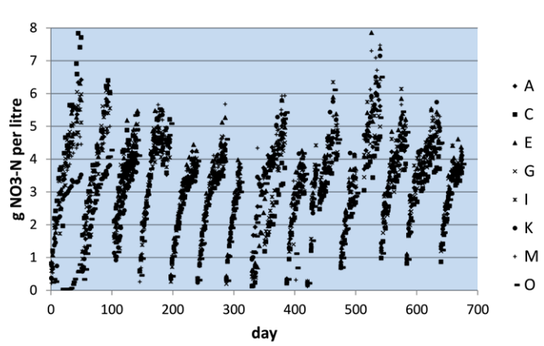

Fig. 3: Fed batch. Nitrate production of eight filters, which were fed with 1 l of synthetic urine per day over a period of 680 days.

Table 1: Batch mode. Nitrate production of the filters D,E,F, which were fed with batches of 80% urine solution over a period of 475 days.

	BATCH MODE	FED BATCH
PROCESSING TIME [D]	93	48
PROC. TIME [RANGE]	55–164	31–66
V [MG NO3-N/D]	1762	2801
V [RANGE]	865–3007	2417–3184
% N IN NO3-N	85	84
MG UREA DEGRADED/D	3847	6003

In summary the long-term experiments with the C.R.O.P.® filters showed that fed batch operation reaches higher nitrate production rates than batch operation. Precipitates also differ between operation modes.

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[1] Bornemann et al., Life Sci. Space Res. 18, 2018

1.1.2 Cardiomyocyte beating activity under altered gravity during parabolic flight

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Earlier studies showed that altered gravity influences the mouse embryonic stem cells differentiation. Human inducible pluripotent stem cells (hiPSCs) provide a good model to study human stem cell differentiation under space conditions and are promising in regard to personalized medicine. hiPS cells can be differentiated to beating cardiomyocytes which can then serve as a model system to study the effect on cardiomyogenesis and heart beating under altered gravity conditions. We used the parabolic flight mission to study the effect of gravity on the interactions of drugs which elevate or decrease the beating frequency of cardiomyocytes under 1 g ground conditions. By this experiment we were able to examine the effects of gravity (microgravity/hypergravity) on differentiation and beating frequency of hiPSCs-derived cardiomyocytes (CMs).

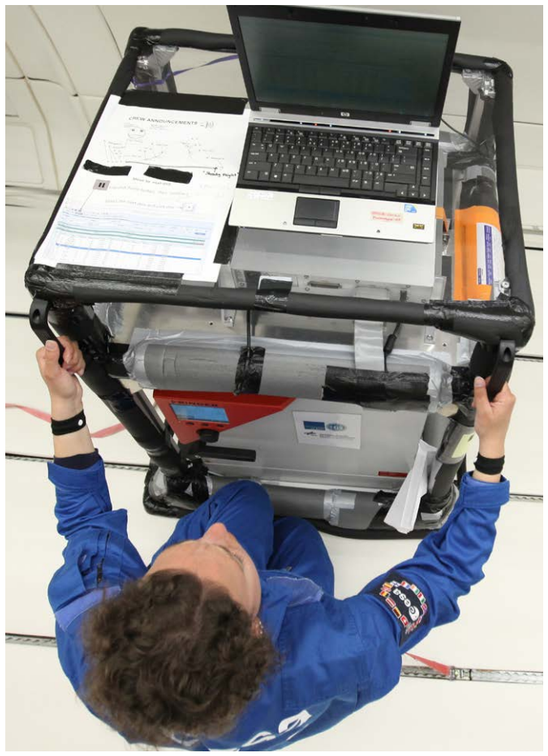

Fig. 1: Parabolic flight experimental set-up operated by Dr. Sonja Brungs during the flight.

The parabolic flight set-up (Fig. 1) included an incubator with the xCELLigence Cardio RTCA system to detect cardiomyocytes viability and monitor functional alterations of purified human cardiomyocytes by measuring the beating frequency under physiological conditions in altered gravity. The E-plate Cardio96 (Multi-well plates) were seeded with CMs and put into the measurement instrument in the presence and absence of various drugs (e.g., Isoproterenol). The beating activity was measured throughout 3 parabolic flights (67. ESA campaign) and compared to ground measurements. During all flight days, a full set of cells could be measured under 37 °C. The results show that individual parabolas – including hyper- and microgravity phases – did not immediately change beating rate, beating amplitude and cell index, compared to ground conditions. However, when comparing all data from the flight experiment with the ground controls, it became obvious, that the flight conditions increase the beating frequency (Fig. 2). These results open new insights in the early stage of human developmental biology and heart function with respect to the impact of environmental forces such as gravity and significantly contribute for testing of the effectivity of drugs on cardiomyocytes function under different gravity conditions.

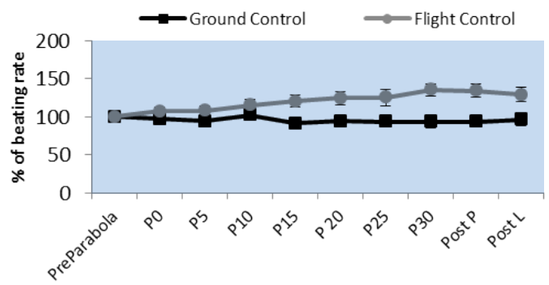

Fig. 2: Cardiomyocyte beating frequency throughout the entire parabolic flight compared to 1g ground control measurements.

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[1] Nuthmann et al., Psychol. Rev. 117, 2010

1.1.3 Artificial gravity training as a countermeasure for long duration space flight

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Current exercise countermeasures on the ISS are individually tailored for each astronaut and differ slightly between each member agency. Crewmembers train 6–7 days per week for around 2.5 h/day with a total of 6-7 resistance and 4–7 cardiovascular sessions per week [1]. Despite being successful in maintaining astronaut´s performance for mission durations of 4–6 months, current ISS countermeasures do not stop physical deconditioning in µG environment completely.

One explanation could be the lack of gravity during the training. Therefore a gravity-like environment (so called Artificial Gravity, AG) generated by short arm human centrifuges (SAHC) could be a beneficial countermeasure for long-term missions (> 300 days). Recent studies showed that passive rotation with short intervals of AG (e.g., 6x5 min) was more effective on cardiovascular deconditioning during 21-days bed rest than longer centrifugation [2]. Aerobic exercises during AG showed some advantages in maintaining cardiovascular and skeletal muscle functions during bed rest [3].

Compared to training concepts on Earth passive rotation or aerobic exercises under AG seem not enough to affect the whole body (e.g., cardiovascular system, muscle and bone). Kramer et al [4] showed that short but intense intervals of jump training were effective to prevent major cardiovascular and musculoskeletal deconditioning during 60 days bed rest.

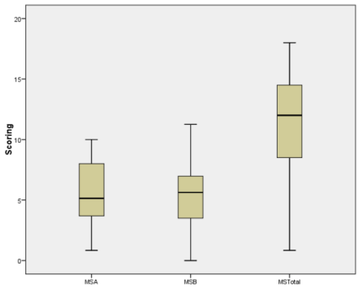

Fig. 1: Mean scores for Motion Sickness Susceptibility grouped for motion sickness symptoms from childhood experience (MSA), for motion sickness symptoms over the last 10 years (MSB) and total scoring (MSA+MSB). The median line is indicated in the boxplots.

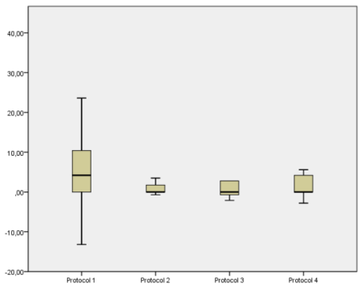

Fig. 2: Mean scores for differences of Motion Sickness Assessment Questionnaire (Post - Pre) for protocol 1 (SAHC at +1 Gz at CoM), protocol 2 (Vertical control), protocol 3 (Sledge jump system) and protocol 4 (SAHC at +0.5..1.5 Gz at CoM, vertical control and sledge jump system).

To test if jump training on a centrifuge could be beneficial and be tolerated by subjects 15 male subjects performed reactive jumps under AG. In a cross-over design each subject performed 15x15 reactive jumps in 4 different protocols in randomized order. 2 protocols included jumping exercises under AG with Gz-level either at constant 1Gz at CoM or Gz-level ranging from 0.5–1.5 Gz at CoM with 3x15 jumps at each Gz level. Jumping exercises without AG in vertical position as well as on a horizontal sledge were used as control. During all protocol no head strap was used to limit subjects head movements. To evaluate motion sickness different questionnaires (MSSQ, MSAQ, PANAS, ESS) were filled by the subjects directly pre/post centrifugation.

All subjects completed the protocols without drop-outs according to motion sickness symptoms. Preliminary results show that mean values for motion sickness susceptibility scoring (MSSQ) were 11.00 (SD = 4.51) that is lower than average scoring 12.90 (SD = 9.90). Motion Sickness Assessment Questionnaire (MSAQ) showed only for the first SAHC protocol a slightly higher scoring 2.42 (SD=7.65) after centrifugation. Interestingly the second SAHC protocol was not causing further motion sickness symptoms despite frequent changes of g-loads (0.5–1.5 +Gz).

As a conclusion these preliminary findings show that also complex exercises like jump training can be tolerated at moderate Gz-level. Future tests will evaluate subject tolerance to combined exercises including jumps, squats and bicycle ergometry.

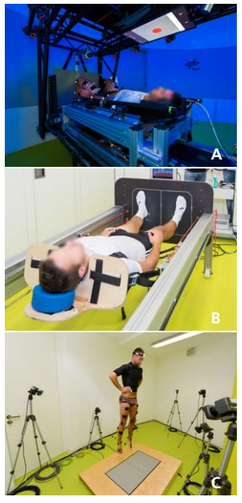

Fig. 3 (A): Subject position during centrifugation on the SAHC, on a horizontal sledge jump system (B) and in vertical position as control (C).

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[1] Petersen et al., Extreme Physiol. Med. 5, 2016
[2] Stenger et al., J. Appl. Physiol. 112, 2013
[3] Kaderka et al., Acta Astronautica 5, 2010
[4] Kramer et al., Sci. Rep. 7, 2017

1.1.4 MemEx and DinoDrop – Pharmacodynamics of hydrophobic and amphiphilic substances under microgravity and altered membrane fluidity

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By investigating the fluidity and transport mechanisms through artificial and biological membranes, we aimed to identify the impact of gravity on these fundamental processes. Alteration would impact the pharmaceutical protocols for astronauts and arises the general question of the role of the cell membrane in gravity perception.

Aim of the experiment **Mem-Ex** was to investigate the pharmacodynamics of lidocaine upon integration into artificial membrane vesicles, made from asolection, a lipid mixture derived from soy beans. The experiment hardware was developed to perform fluorescence polarization (FP) measurements under microgravity during the DLR MAPHEUS 6 sounding rocket campaign. By using FP measurements it is possible to examine changes in membrane fluidity. With the onset of microgravity, the FP signal was measured. After 100 seconds, lidocaine and vesicles were mixed and the FP signal was measured until reentry of the capsule and opening of the parachute.

Under 1g and microgravity, upon addition of 16 mM lidocaine (Fig. 1; start of mixing is indicated by an arrow; the mixing period is indicated by #; artifacts caused by moving air bubbles are marked by *), fluorescence polarization decreased. A reduced fluorescence polarization indicates a decrease in membrane viscosity, or an increase in membrane fluidity respectively.

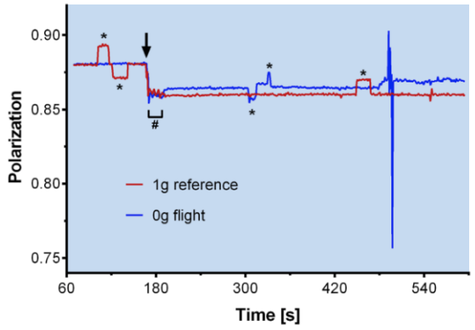

Fig. 1: Changes in fluorescence polarization of the microgravity experiment and 1 g reference. The red line indicates the ground control, the blue line the in-flight data.

The increase of membrane fluidity was less as compared to 1 g. The big spike was caused by the deployment of the parachute. During the reentry phase FP significantly increased again due to the general dependence of membrane fluidity itself, but it did not return to the previous level before the addition of lidocaine.

The **DinoDrop** experiment was focused on membrane fluidity changes under microgravity in living organisms. The dinoflagellate *Pyrocystis noctiluca,* responsible for the marine luminescence, is a highly sensitive reporter for membrane shearing in living cells [1]. This reporter system is one of the fastest luminescence assays. When the cells are deformed by external forces, blue light is emitted by flashing of scintillions, specialized caverns in the acidious vacuole membrane. Hence, the flashing of *Pyrocystis noctiluca* is an ideal reporter for the detection of membrane fluidity changes.

The DinoDrop experiment was carried out in the ZARM drop tower at Bremen. To prevent mechanical stimulation of *Pyrocystis noctiluca* during the release impact of the drop capsule, a floating hardware setup was choosen.

The DinoDrop experiment shows a direct increase of counted photons during the transition from 1 to 0 g (Fig. 2), which indicates an altered membrane fluidity. The bioluminescence signal decreased during the free fall. With the impact of the experiment, the cells were mechanically stimulated resulting in a constant bioluminescence signal for some minutes (data not shown).

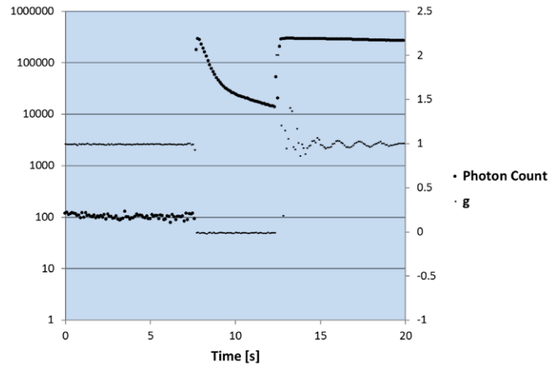

Fig. 2: DinoDrop experiment. The bioluminescence signal increases.

In conclusion, membrane fluidity increases at microgravity, influencing the integration of pharmaceuticals into a membrane and thus having an impact on space pharmacology.

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[1] Hauslage et al., NPJ Microgravity 3, 2017

1.1.5 NeuroSpace – Hypergravity selectively augments neuronal in vitro differentiation

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Disturbed neuronal connectivity is the ultimate cause of disability in individuals with neurological disease including spinal cord injury, head trauma, and stroke. Functional neurological recovery is limited through an unfavorable balance between neuronal regrowth and glia scar formation. Neuronal growth requires dynamic cytoskeletal protein rearrangements. Because hypergravity stabilizes microtubules, while de-stabilizing actin filaments, we hypothesized that experimental hypergravity would shift the balance between neuronal and astroglial growth in vitro.

We exposed murine primary hippocampal neurons during different developmental stages to 2 g using the DLR hypergravity platform. This inhouse-designed platform unlike commercial laboratory centrifuges models hypergravity in a physiological range and allows for cell cultivation and live-cell imaging. We assessed neuritogenesis, neuronal polarization and maturation processes including synaptogenesis and synaptic integration in mature neural networks. Moreover, we studied primary astrocytes to shed light on their role during glial scar formation at neural lesion sites.

Exposure of hippocampal neurons to 24 h of 2 g hypergravity increased initial neurite sprouting from the cell soma by app. 30 % and neurite projection length by app. 20 % compared to 1g. Neurite outgrowth was enhanced especially in leading neurites, i.e. the processes differentiating to the future axon. At later developmental stages, mature synaptic contacts were formed under hypergravity conditions. Interestingly specifically pre-synaptic terminals showed a minor trend towards a reduction in number, while post-synaptic spines were not affected. In contrast, astrocytes showed decreases in cell spreading and lamellipodial protrusions under hypergravity.

This effect could have important implications for astrocytic cell migration and glial scar formation, which could be inhibited in consequence to hypergravity exposure. The hypergravity-induced perturbation of the glial scar would have substantial impacts on neuronal regeneration, since the inhibition of axonal growth by astrocyte-secreted cytokines would be diminished.

We conclude that experimental hypergravity ameliorates neuronal cell growth and synaptic contacts while halting astrocyte spreading and migration in vivo. Given the importance of this balance for neuronal regeneration in human neurological disease, we will now study the underlying mechanisms in more detail under altered gravity conditions (hypergravity and simulated weightlessness) using the corresponding DLR ground-based facilities.

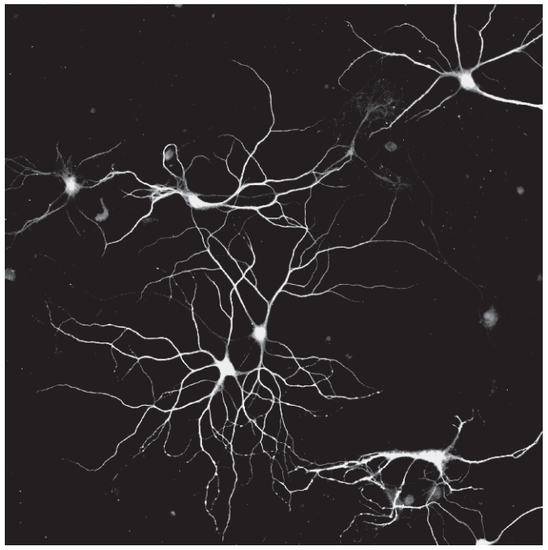

Fig. 1: Mature neuronal network of primary murine hippocampal neurons after 20 days in vitro (DIV 20). The cells formed functional synaptic contacts in a complex neuronal network very similar to neuronal networks in the mouse and human brain.

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1.2 Radiation Biology

1.2.1 NF-κB in the response to space-relevant radiation qualities

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One of the major limiting factors in human spaceflight is cosmic radiation. Exposure to space relevant radiation qualities (such as accelerated heavy ion nuclei) can have detrimental effects on human health. Investigation of the transcription factor Nuclear Factor B (NF-κB), as one of the major regulators of the immune system and stress responses such as the cellular radiation response, can improve risk assessment and might be a potential pharmacological target to prevent deleterious radiation effects.

In order to analyze the signaling pathway, reporter cell lines for NF-κB activation have been created (wildtype NF-κB: HEK-pNF-κB-d2EGFP/Neo L2, NF-κB knock-down: HEK shRNA RelA). The cell lines were stably transfected with a reporter plasmid carrying the destabilized Green Fluorescent Protein (d2EGFP) under control of a promoter containing four NF-κB binding sites.

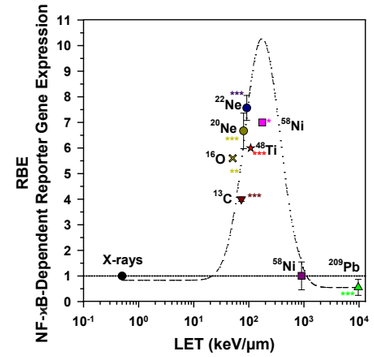

Fig. 1: The relative biological effectiveness (RBE) for NF-κB activation by heavy ions (LET 0.3-10'000 keV/µm) was assessed using the reporter cell line HEK-pNF-κB-d2EGFP/Neo L2 which indicates NF-κB activation by an increased green fluorescence.

The cells were exposed to radiation qualities of different linear energy transfer (LET), performed at the DLR and in cooperation with different workgroups at international particle accelerators (HIMAC, GSI, GANIL).

Gene expression analyses of wildtype NF-κB cells revealed that NF-κB target genes affecting intercellular communication are induced after exposure to radiation qualities of differing LET values. Additionally, exposure to radiation qualities of medium LET leads to a downregulation of anti-apoptotic genes [1].

In order to assess the role of NF-κB in the cellular radiation response, clonogenic survival after radiation exposure of cells with NF-κB knock-down was compared to wildtype cells.

Knock-down of the NF-κB subunit RelA increased the sensitivity towards low LET radiation qualities (X-rays, Fig. 2 left). The killing effect of moderate (carbon ions 100 MeV/n, Fig. 2 right) and high 1000 MeV/n nickel ions, Fig. 2 right LET radiation qualities was much higher compared to X-rays, and RelA knock-down did not further reduce the clonogenic survival.

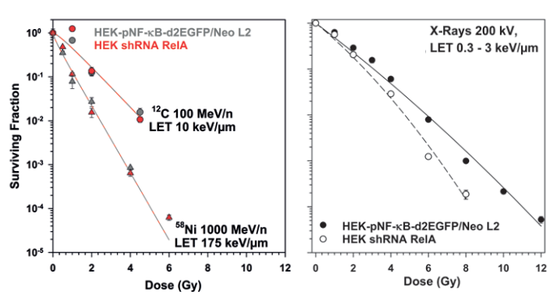

Fig. 2: Relative clonogenic survival in cells with normal NF-κB status (grey) and after NF-κB RelA knock-down (red) after exposure to X-rays (left, LET 0.3 3 keV/µm) and to 1000 MeV/n nickel ions (LET 175 keV/µm) and 100 MeV/n carbon ions (LET 10 keV/µm).

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[1] Chishti et al., Rad. Res. 189, 2019

1.2.2 Impact of galactic cosmic radiation on *Bacillus subtilis* biofilms grown under simulated microgravity conditions

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[2] Department of Basic Medical Sciences for Radiation Damages, NIRS/QST, Chiba, Japan

On spacecraft, like the ISS, material degradation by microbial biofilms, communities of microorganisms that attach to a surface by excreting a sticky, sugar-like substance that encompasses them in a matrix, can be a danger. So far, the effect of extraterrestrial conditions on biofilms is largely unknown. We investigated the impact of heavy ions as components of galactic cosmic radiation (GCR) in combination with simulated microgravity on the biofilms and spores, one of the most resistant forms of microbial life, formed by the bacterium *Bacillus subtilis*.

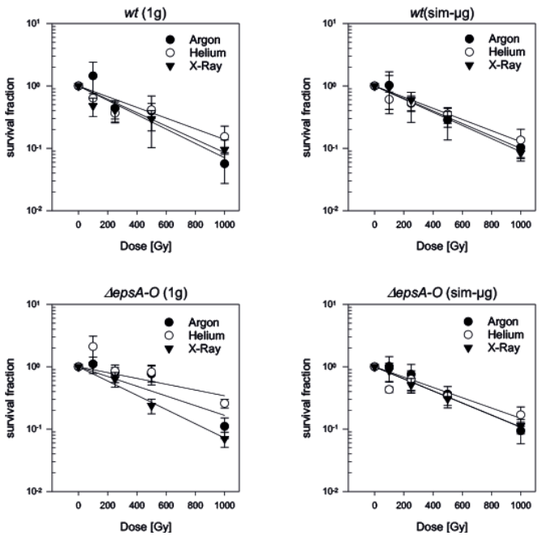

Fig. 1: Survival fractions of *B. subtilis* spores after irradiation with He and Ar ions and X-rays. Top row: Irradiated wild-type (wt) spores. Lower row: ΔepsA-O, a mutant strain unable to form biofilms. Left side: spores grown under normal gravity, right side: spores grown under sim-µg.

Here, filters were incubated with *B. subtilis* spores in MSgg, a minimal medium which promotes *B. subtilis* biofilm formation [1]. Controls (1g Earth samples) were incubated upside-down. Samples for simulating microgravity were mounted into a fast rotating 2D-clinostat (sim-µg). After incubation, biofilms were dried and irradiated. Biofilms and spore samples were irradiated with accelerated Helium ions (He, 150 MeV/n, LET 2.2 keV/µm) and Argon ions (Ar, 500 MeV/n, LET 90 keV/µm) doses (ranging from 0 to 1000 Gy), at the HIMAC facility at the NIRS/QST in Japan. Spores of several mutants have been tested towards their resistance to simulated GCR and ionizing radiation (X-rays). Most mutants had a deletion of important biofilm genes, i.e. ΔepsA-O (Fig. 1). Biofilms (consisting of both: spores and vegetative cells, embedded in a self-built matrix) grown under sim-µg conditions, showed 3.4 % survival (total colony forming units, 1000 Gy, Ar ions) and ~100 % survival after 1000 Gy Helium-ion treatment. The survival of samples grown under normal gravity conditions was 0.1 % after 1000 Gy Argon-ion treatment and 32.8 % after 1000 Gy Helium-ions exposure (Fig. 2).

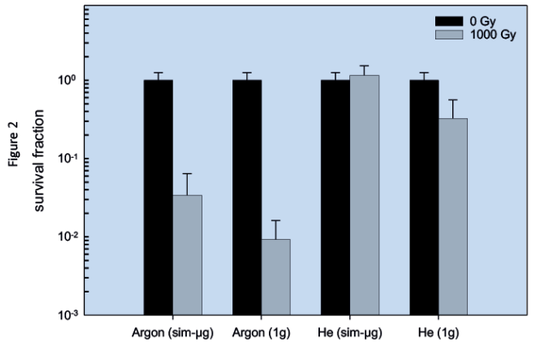

Fig. 2: Spore survival fractions (N/N0) of biofilms (1g and sim-µg) after treatment with 0 Gy and 1 kGy of Ar and He ions.

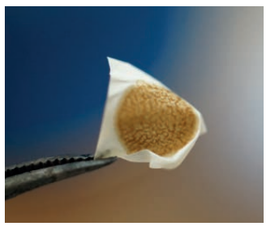

Fig. 3: *B. subtilis* (wt) biofilm, dried on a filter.

In summary, biofilms grown under simulated microgravity exhibited a better survival after exposure to heavy ions. The difference in survival when irradiated with He ions is significant (P=0.031, 1g versus sim-µg). Generally, spores which were irradiated with He ions tend to show a better survival (not significant), compared to Ar ions or X-rays (Fig. 1, 2). In total, 384 samples resulting in ~3200 dilutions were analyzed. Generally spores grown under simulated microgravity seem to be more resistant to heavy ions. *B. subtilis* spores lacking important biofilm genes showed a similar survival compared to the wildtype. The detrimental effects of Ar ions and X-rays were mainly indistinguishable in terms of survivability. Biofilms irradiated with 1000 Gy He ions, showed a significant difference in spore survival, indicating that spores grown in simulated microgravity are more resistant. These experiments help us to understand the influence of microgravity towards microbial resistance towards GCR.

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1.2.3 MSL-RAD: The radiation environment on a trip to Mars and on its surface – Numerical calculations and measurements

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Exposure to cosmic radiation poses a significant risk to humans travelling in space and can endanger mission success. Consequences of elevated radiation levels are twofold: long-term exposure at comparatively low dose rates increases the risk of stochastic effects such as cancer formation; short-term exposure at high dose rates can lead to immediate tissue reactions, for instance reddening of the skin, nausea and internal bleeding. The cosmic radiation which is encountered in space and on planetary surfaces mostly comprises omnipresent galactic cosmic radiation (GCR) and sporadic solar energetic particles (SEP). Due to their high energy, GCR are deeply penetrating and difficult to shield. SEP only occur during limited periods of time following eruptive events on the sun. They have significantly lower energies and are easier to shield but can expose humans to life threatening doses in lightly shielded environments. The radiation assessment detector (RAD) on the Mars Science Laboratory (MSL) is a collaboration of Southwest Research Institute (SwRI), German Aerospace Center (DLR) and Christian-Albrechts-Universität (CAU).

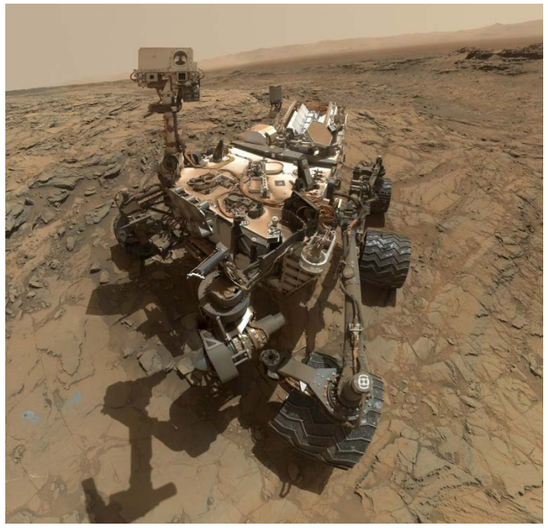

Fig. 1: Curiosity rover of the Mars Science Laboratory (MSL) on Mars containing the Radiation Assessment Detector (RAD).

RAD measures dose rate and charged particle spectra in a stack of silicon, plastic and caesium iodide detectors. Through coincident measurements in two silicon detector planes, the angle of incident charged particles can be limited, and the linear energy transfer and the corresponding biologically relevant quality factor Q of the radiation can be estimated. RAD measured the radiation exposure at moderate solar activity during its cruise to Mars between Dec 2011 and Aug 2012 (0.48±0.08 mGy/d; 1.84±0.33 mSv/d; Q=3.82±0.25). The combined contribution of measured SEPs was 24.7 mSv [1]. Since August 2012, RAD has measured dose rates (0.21±0.04 mGy/d; 0.64±0.12 mSv/d) [2] and particle spectra on the Martian surface.

Numerical simulations at DLR are performed with GEANT4, a Monte-Carlo toolkit calculating the transport of particles through matter. A combination of GEANT4 and PLANETOCOSMICS, a framework providing descriptions of planetary atmospheres, is used to calculate the radiation environment in low Earth orbit, in interplanetary space and planetary atmospheres. The GCR model developed at DLR [3] provides the description of the primary spectra.

In an international collaboration, the radiation environment on the surface of Mars in terms of particle spectra and dose rates has been calculated with a number of models and compared to RAD measurements [4,5,6]. Measured dose rates, charged and neutral particle spectra provide an excellent basis for the benchmark and improvement of numerical models. These models can be used to estimate quantities that are experimentally inaccessible, for instance dose rates to human organs. Through the development of shielding strategies and adapting the exposure time in lightly shielded environments, the models developed at DLR can be used to mitigate negative effects endangering the health of astronauts and mission success. Organizing a series of workshops helps to harmonize model development worldwide. The first workshop organized by SwRI, DLR, CAU and NASA took place in June 2016 and resulted in the publication of a special issue in Life Sciences in Space Research (LSSR).

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[6] Matthiä et al., Life Sci. Space Res. 14, 2017

1.2.4 EXPOSE-R2: The BOSS experiment. Biofilms of *Deinococcus geothermalis* survive 16 month residence in space

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Biofilms, where bacteria live within matrix-embedded communities, are now and presumably have always been the dominant life forms and so far the oldest known evidence of life on Earth. The nearly universal existence over such a lengthy period of time implies that living in this "lifestyle" carries significant advantages compared to a life as isolated individual. The fact that biofilms can become fossilized and the discovery of putative aqueous environments on other planetary bodies such as Mars motivates an interest in understanding their potential role as the first life forms also on other planets and moons of the solar system. Through the realization of the BOSS experiment (Biofilm Organisms Surfing Space) carried out within the ESA EXPOSE-R2 facility aboard the International Space Station from July 24, 2014, to July 5, 2016, an international consortium of scientists took the opportunity of a comparative study on the survivability of biofilms or planktonic cells exposed to space and Mars-like conditions. In several mission preparatory and complementary tests performed in the Planetary and Space Simulation Facilities at DLR, Cologne, suitable strains or microorganism species and a suitable exposure material and set up were defined for the mission [1]. As a result a variety of biofilm producers like *Deinococcus geothermalis DSM 11300* [2], *Bacillus horneckiae BH+*, *Halococcus morrhuae* und *Halomonas muralis),* the cyanobacteria *Gloeocapsa OU_20* and *Chroococidiopsis sp.* *CCME 029* were investigated. In focus was their survivability in this unique mixture of stress factors including desiccation, temperature oscillations, vacuum or a Mars-like gas atmosphere and pressure either individually or in combination with extra-terrestrial UV radiation residing during this long-term space mission. Here the outcome of the flight and mission ground reference analysis of *Deinococcus geothermalis* as one of the BOSS "space travellers" investigated by the authors are presented. The culturability results demonstrated that an exposure to space vacuum and Mars gas atmosphere in combination with extraterrestrial UV radiation in LEO for almost 16 months had a high impact. Still part of the *Deinococcus geothermalis* biofilm and planktonic cell samples were able to remain viable. Here the culturability was preserved in biofilm cells at a significantly higher level than in planktonic cells. In contrast, cultivation independent parameters such as membrane integrity, ATP content and enzyme activity remained nearly unaffected. The unaltered culture-independent parameters suggest that the cells had switched to the viable but not countable (VBNC) state which can be considered as a stress response. The findings contribute to the understanding of the opportunities and limitations of life under extreme environmental conditions and gives answers to the question whether in harsh places including space and Mars once more cooperation is the key to survival.

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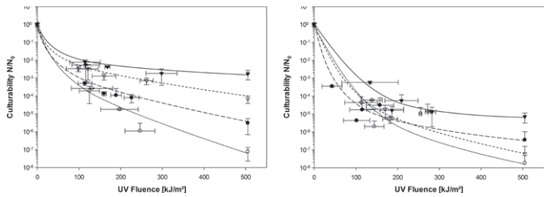

Fig. 1: Fluence effect of extraterrestrial UV radiation (left side) and UV irradiation (corresponding mission based calculations by Redshift) (right side) under space (circles) and Mars like conditions (triangles) on the culturability of biofilms (closed symbols) and planktonic cells (open symbols) of *D. geothermalis*. n=3.

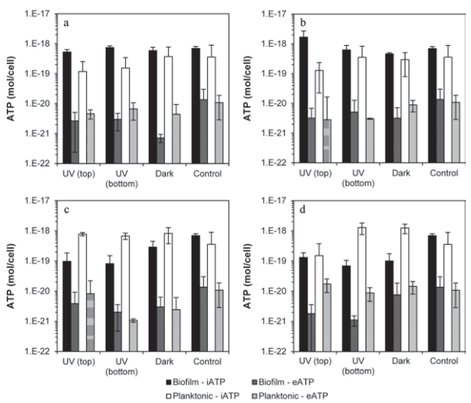

Fig. 2: Intracellular ATP (iATP) and extracellular ATP (e-ATP) of biofilms and planktonic cells of *D. geothermalis* under space (a,c) and Mars like (b,d) conditions in the EXPOSE-R2 mission (a, b) and the MGR experiment (c, d). n =3.

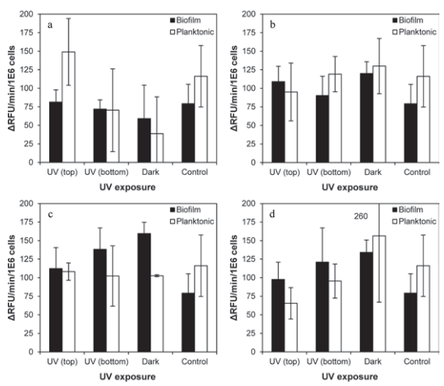

Fig. 3: Esterase activity of biofilms and planktonic cells of *D. geothermalis* under space (a, c) and Mars like (b, d) conditions in the EXPOSE-R2 mission (a, b) and the MGR experiment (c, d). n = 3.

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[2] Frösler et al., Astrobiol. 17, 2017
[3] Panitz et al., accepted for Astrobiology, special collection BOSS experiments, 2019

1.2.5 Radiation measurements in Low Earth Orbit (LEO) and in preparation for exploration missions

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The space radiation environment and the related higher radiation exposure to humans in space has been recognized as one of the main health detriments for long duration human space missions. The Biophysics Group of the Radiation Biology Department works on the development and characterization of new radiation detectors for applications in LEO and also for exploration mission. Further on the work includes simulations and benchmarking of radiation data with relevant radiation transport codes.

Onboard the ISS (inside the Columbus Laboratory) the group carries out the DOSIS 3D project (2012). Its aim is to measure the spatial and temporal variation of the radiation environment with active and passive radiation detectors. Eleven passive detector packages are therefore distributed in Columbus and two active radiation detectors, developed in cooperation with CAU, Kiel, are positioned beneath the EPM Module.

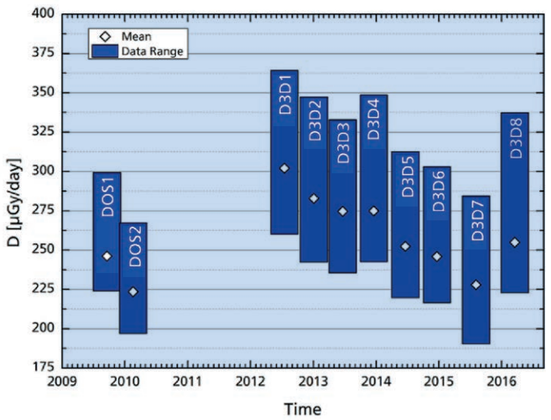

Fig. 1: Variation of the absorbed dose measured with passive radiation detectors inside Columbus for 2009–2017 [1,2].

In addition to the long-term dose monitoring inside the Columbus Laboratory of the ISS the Biophysics Group also developed within an international collaboration the EAD (ESA Active Dosimeter) system which provided the first TechDemo proof of active personal dosimetry for astronauts in the years 2016–2017.

For upcoming future exploration missions it is crucial to provide active radiation detectors with the possibility to determine relevant radiation field parameters in real time. For this application and for the coming MARE experiment on board the NASA ORION EM-1 mission to the Moon the Biophysics Group developed the M-42 radiation detector.

Fig. 2: European Astronaut Thomas Pesquet with the EAD system in the Columbus Laboratory of the ISS.

Fig. 3: The prototype of the DLR developed M-42 active radiation detector.

M-42 is a battery powered active radiation detector for applications in space, at aircraft altitudes and for terrestrial radiation protection purposes and was already successfully tested in free space on board MAPHEUS.

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[1] Berger et al., J. Space Weather Space Clim. 6, 2016
[2] Berger et al., J. Space Weather Space Clim. 7, 2017

1.3 Muscle and Bone Metabolism

1.3.1 Effects of head down tilt on cognitive performance

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Head-down tilt (HDT) is a ground-based simulation of microgravity. Cranial perfusion decreases at -12° HDT while venous congestion increases [1], with concomitant increase in intracranial pressure (Fig.1). It is unclear whether this is also associated with a decline in cognitive performance [3].

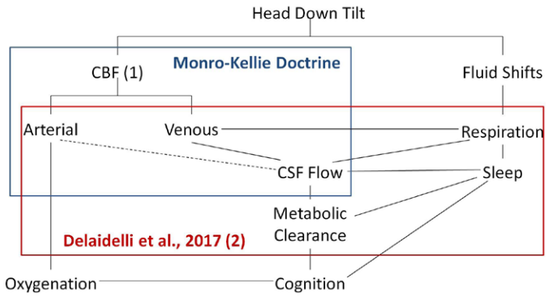

Fig.1: Effects of HDT on the intracranial fluid system.

We assessed cranial perfusion in combination with measures of cognition and sleep during -12° HDT. Eleven healthy male subjects participated in a randomized, cross-over designed study with two conditions – staying in horizontal position -12° HDT. Each campaign tested one condition and lasted for three days (Fig. 2) The interventional phase started on the morning of the second day and included one night in the respective position. The tilting procedure was integrated in the first interventional measurement block to assess acute changes in near infrared spectroscopy (NIRS) signals. During the interventional night objective sleep parameters were assessed.

Linear mixed models were used for the statistical analysis. The level of significance was set at P = 0.050.

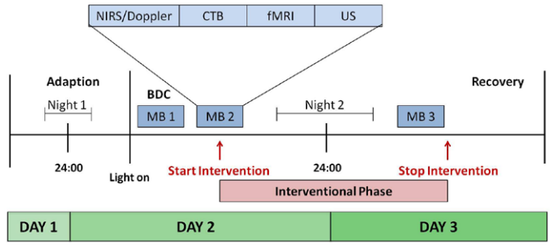

Fig. 2: Campaign Overview [BDC: Baseline data collection, MB: Measurement block, NIRS: Near-infrared spectroscopy, CTB: Cognitive test battery, fMRI: (functional) magnetic resonance imaging, US: Ultrasound of the jugular vein].

In the first minutes the NIRS showed acute effects of the tilting process with a significant decrease in total haemoglobin (P < 0.001). The tissue saturation index dropped with tilting (P = 0.007) and stayed lower with HDT during the total 20 minutes of the measurement (P = 0.050, g = -0.056). These effects diminished over time with no significant difference on the second interventional day. The Manometer test – a means to assess information processing – yielded longer response times with -12° HDT on the second interventional day (P = 0.016, g = 0.307) as compared to horizontal position. Deep sleep (P = 0.002, g = -0.898) and REM sleep (P = 0.035, g = -0.634) were significantly reduced at -12° HDT, while light sleep was elevated (P = 0.002, g = 1.078). Subjective sleep quality was lower at -12° HDT (P = 0.047, g = -0.968).

Changes in oxygenation and content of haemoglobin were short-lived, which hints at quick compensation. One possible mechanism is respiration as it is a major driving mechanism for cerebrospinal fluid circulation [2]. Impaired sleep might be one of the factors responsible for the significant cognitive changes aty -12° HDT. Fluid shifts towards the head might have resulted in obstruction of the upper respiratory tract. That could explain the observed sleep impairment. Yet, an important confounding variable is sliding of the subjects towards the head-end of the bed.

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[1] Marshall-Goebel et al., J. Appl. Physiol. 120, 2016
[2] Delaidelli & Moiraghi, J. Neurosci. 37, 2017
[3] Lipricki & Gunga, Eur. J. Appl. Physiol. 105, 2009

1.3.2 What happens to our tibia when we exercise? A 3D *in vivo* study

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Objectives: Understanding the tissue mechanics of bones during exercises is important in order to determine effective countermeasures against bone loss in Space.

Methods: The MUST study (MUscle induced Strains in the Tibia) utilized an optical system to measure the displacements marker-clusters while the subjects performed common physical exercises like walking, running or hopping [1].

Results: Peak strains were greatest during hopping, followed by running and walking, and they were lowest for static exercises. However, within given exercises the strain distribution varied in time and space within the tibia.

Conclusions: Jumping and other plyometric exercises have greatest countermeasure potential. Additional exercise elements may help to address all anatomical bone areas.

Finite element modeling (FEM), based on densitometric data of the individual subjects' tibia, were constructed to calculate bone strains with an inverse algorithm. Hitherto, all acting forces were reconstructed tibia, and the *in vivo* displacements were fed into an optimization algorithm that balances the applied force values (fmp) in order to mimic the measured displacement of the marker cluster ($\mathbf{U}_{meas}$).

In a final step, the calculated forces were applied to the FE tibia to gain the strain values for the whole model. This process was repeated for all repetitions of all activities the subjects performed.

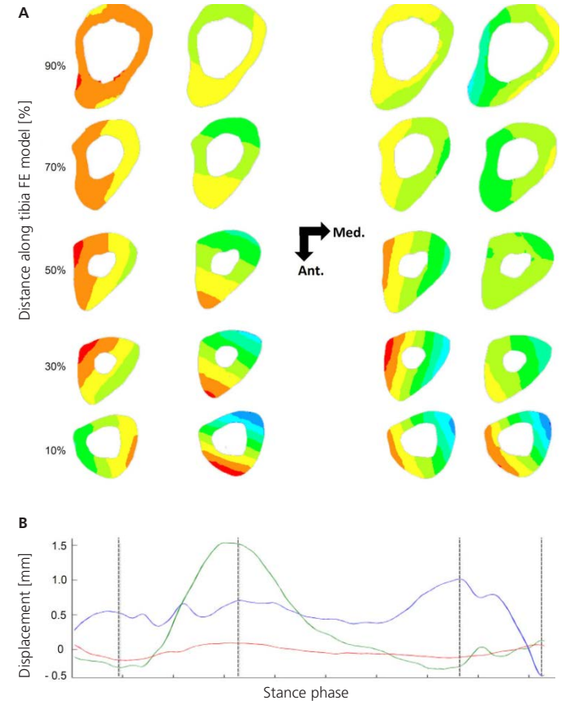

Fig. 2: A) Exemplary strain distribution at 10%, 30%, 50%, 70% and 90% of the tibia's length during the stance phase of walking. B) posterior-anterior (green), medial-lateral (blue) and cranial-caudal (red) cluster displacements.

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1.3.3 Lower body negative pressure enhances muscle oxygen supply and AMPK phosphorylation during intense resistive exercise

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Objectives: We compared the physiological and molecular adaptations of exercising leg muscles to intense resistive training in supine position with and without the use of lower body negative pressure (LBNP), which simulates the blood shift to the lower body similar to the effects of gravity in upright position [1] without affecting mechanical properties of the exercise. We hypothesized that the gravity-simulating properties of LBNP would enhance the blood supply to the working leg muscles detectable through changes in both total hemoglobin (tHb) and the tissue oxygenation index (TSI) [2, 3]. We expected this to result in an enhancement of oxidative metabolism reflected by an overall increase in respiratory oxygen uptake ($V'O_2$), as well as local reactions of energy-sensing molecules such as the adenosine monophosphate activated kinase (AMPK) [4] in the muscle tissue.

Methods: In supine position, two groups of subjects performed 15 repetitions of 8 s resistive concentric-eccentric exercise targeting their knee extensor muscles at 60% of their individual one repetition maximum (1-RM). The LBNP group (n=9) performed the exercise at lower body negative pressure (-40 mbar), the control group (n=9) at ambient pressure. Exercise was performed on an robotically controlled leg press with a force-distance profile starting at 10 % of the target force at knee flexion and linearly increasing to full target force at half of the range of motion, then remaining constant into knee extension. Low force periods facilitated blood perfusion in the contracting muscle. TSI and tHb were measured on the right vastus lateralis muscle using near infrared spectroscopy (NIRS). The levels of AMPK and its activated form P-AMPK were measured via western blot in a series of biopsies taken from the vastus lateralis (at baseline, 10 min, 30 min and 60 min after exercise). All variables were tested by a linear mixed effects model (LME) using group (control, LBNP) as a fixed factor.

Results: During exercise, the tHb content was elevated with LBNP, accompanied by a gradual reduction in TSI and increased $V'O_2$. Levels of total and phosphorylated AMPK were elevated in the LBNP group at 10 and 30 min after exercise. These protein levels eventually recovered, with no significant difference between control and LBNP 60 min after exercise.

Conclusions: During slow intense resistive exercise, the gravity dependent blood shift simulated by LBNP increased the oxygen availability in the working musculature, elevating the level of oxidative metabolism and affecting signaling pathways controlling muscle growth and differentiation.

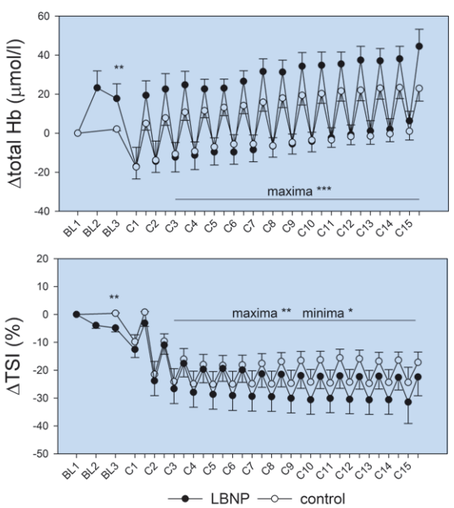

Fig. 1: Changes in total hemoglobin (tHb) content and tissue oxygen saturation index (TSI). BL1: initial baseline, BL2: LBNP at rest, BL3: after 2 sets of warm-up exercise, C: contraction cycle (minima at high force, maxima at low force); mean ± SEM, * P<0.05, ** P<0.01.

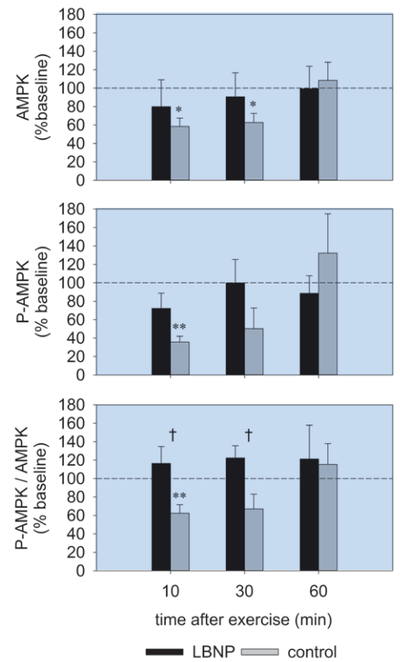

Fig. 2: Alteration of AMPK content and phosphorylation after exercise. Western-blots are shown on the right side. Time effect: *P<0.05, **P<0.01; group effect: †P<0.05.

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[1] Baisch et al., Eur. J. Clin. Invest. 30, 2000
[2] Zange et al., Pflügers Archiv 455, 2008
[3] Egaña & Green, J. Appl. Physiol. 98, 2005
[4] Richter et al., Biochem J. 418, 2009

1.3.4 Exercise performance with the body mass accelerated by rotation compared with the acceleration by the terrestrial gravitational field

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Long-duration space missions require countermeasures against the muscular wasting and cardiovascular deconditioning associated with microgravity [1]. Replacing gravitational acceleration by means of centrifugation is a promising alternative as it challenges all physiological systems at once. Furthermore, a short arm centrifuge like the one used in this study is simultaneously small to fit into current launch vehicles. Centrifugation in combination with exercise, either resistive [2] or cardiovascular [3], was shown to improve the effects against deconditioning.

The aim of the present study was to examine the metabolic energy costs of squatting on a centrifuge in comparison with squatting in an upright standing posture under natural gravity.

Twenty-four subjects (11 male, 13 female) performed continuous squatting exercise for 9 minutes with increasing cadence (10, 12, 15 squats/min). This was done in three conditions: Upright under natural gravity and lying supine on a centrifuge at two radii (2.5 and 3.5 m) at 1 g of centrifugal acceleration. A mobile spirometer was used alongside 4 EMG electrodes on the left leg and 2 NIRS sensors on the right leg. Two foot reaction force plates were used on both the centrifuge as well as during upright squats.

The g level was set by altering the RPM of the centrifuge while the subject was at the mid-point of the squat until the force at the foot plates equalled the subject's weight. A custom made positional feedback system was used to guide the subject's movement.

Generally, subjects did not suffer from motion sickness. Exercise under natural gravity led to a higher excess VO2/body mass (7.1±2.0, ml/min*kg, mean ± SD,) compared with training on the centrifuge (6.1 ±1.6). VO2/power (ml/min*W) was also higher under natural gravity (5.1±0.9) than on the centrifuge (3.8±0.6). As expected, oxygen consumption increased with increasing cadences. The Coriolis-effect had a negligible impact as there was no significant difference in VO2 between the two radii. However, during centrifugation and upwards movement the right leg was loaded more than the leg left and vice versa during downwards movement. The EMG data supported this, but would ideally have been measured on both legs. The NIRS data showed increased blood pooling in the legs prior to squatting on the centrifuge. The lower VO2 on the centrifuge may be attributed to the improved stabilization of the torso which had to be provided by the subjects themselves while in the upright condition. Subjects tolerated high rotational rates combined with exercise very well.

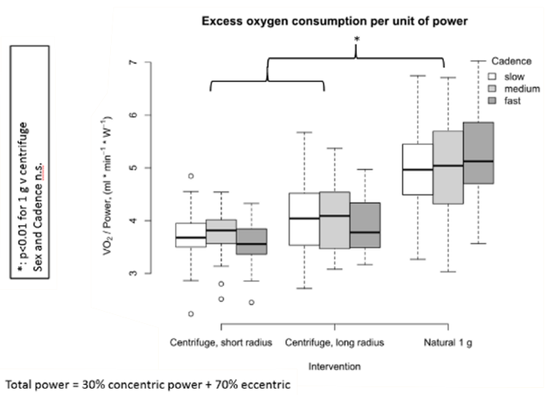

Fig. 1: Excess oxygen consumption per unit of power as a measure of efficiency, showing mean +- SE. * = p < .05 for g-condition.

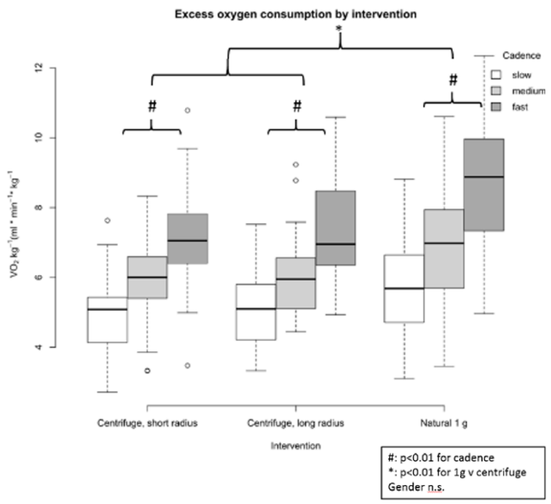

Fig. 2: Excess oxygen consumption normalized to body weight showing mean ± SE. * = p < .05 for g-condition. † = p < .05 for cadence.

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[2] Yang et al., J. Appl. Physiol. 103, 2007
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1.3.5 Neuromuscular adaptations on 6 weeks of high intense, progressive resistive vibration training

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Objectives: Whole-body vibration (WBV) added to resistive exercise results in increased activity of motor units in the working musculature and in an elevation of respiratory oxygen uptake ($V'O_2$) in comparison with the corresponding exercise without WBV [1, 2]. However, when WBV was applied at a constant frequency over 5 training days, the elevation in motor unit activity declined to not significant levels [3]. In this study, we tested the hypothesis that during progressive resistive exercise on a Smith-machine a progressive increase of the WBV frequency conserves the additional stimulation of whole-body vibration on the motor unit activity and on $V'O_2$.

Methods: Two groups of healthy male subjects performed 6 weeks of either Resistive Exercise (RE, n=13, Smith machine, 2 to 3 sessions per week with squats, 3 sets with 8 repetitions, and heel raises, 3 sets with 12 repetitions, load corresponded to 80% of the one repetition maximum for squats) or Resistive Vibration Exercise (RVE, n=13, RE+WBV, 20 to 40 Hz). During the first and the last training session we recorded $V'O_2$ and the motor unit activity in terms of the electromyogram (EMG) from rectus femoris (squats) and gastrocnemius lateralis (heel raises) muscles. $V'O_2$ and EMG were normalized on the total training weight (ttw, body weight plus training load). Using liner mixed effect models for repeated measurements, the fixed factors session (before, after), group (RVE, RE) and time x intervention were analyzed.

Results: During 6 weeks of training, the progression of ttw was significantly lower (P<0.05) under RVE (25 %) than under RE (33 %) [4]. At RVE, EMG/ttw during squats was marginally (P=0.08) higher than RE values before training and lower (P<0.05) after training (s. figure 1). In both groups, EMG/ttw were decreased after training (P<0.05). During heel raises EMG/ttw decreased after training in both groups (P<0.05), whereas group effects between RVE and RE didn't reach significance. Before and after 6 weeks training, $V'O_2$/ttw during RVE was higher than during RE (P<0.05). In both groups, $V'O_2$/ttw were lower after training than before (P<0.05).

Conclusions: In both groups, 6 weeks of progressive training increased efficiency of exercise shown by decreases in whole body energy turn-over ($V'O_2$/ttw) and motor unit activation (EMG/ttw). After 6 weeks of training, RVE with progressively increasing frequencies and training load could conserve the elevation of $V'O_2$/ttw, despite lower values compared to the first session. The more specific effect of RVE on the working musculature in terms of an elevation in EMG/ttw could not be found anymore after 6 weeks training.

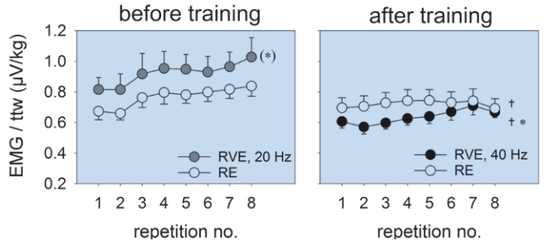

Fig. 1: EMG amplitudes of rectus femoris muscle during squats normalized to total training weights (ttw) measured before and after 6 weeks of RVE and RE training (mean±SEM), *P<0.05, (*) P=0.08 for group (RVE, RE) per session (before, after), †P<0.05 for session per group.

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[1] Rittweger et al., Eur. J. Appl. Physiol. 86, 2001
[2] Ritzmann et al., Eur. J. Appl. Physiol. 113, 2013
[3] Rosenberger et al., PLoS One 9, 2014
[4] Beijer et al., Musculoskelet. Neuronal Interact. 13, 2013

1.4 Cardiovascular Aerospace Medicine

1.4.1 Neurogenic blood pressure control traced through functional brainstem imaging

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Baroreflexes are important for-short and long-term blood pressure (BP) regulation. BP increases activate stretch-sensitive baroreceptors in the carotid artery and aortic wall, increase parasympathetic activity and reduce heart rate, which stabilizes BP. Vagal baroreflex function decreases with aging. Impaired vagal baroreflex function has significant prognostic value in patients after myocardial infarction. Knowledge about central integration of baroreceptor afferences is mainly based on animal experiments. Data on brainstem nuclei involved in cardiovascular regulation in humans are rare. The aim of our study was to detect BP regulating nuclei in individual subjects using baroreflex sensitivity (BRS) testing combined with novel functional magnetic resonance imaging (fMRI). The continuous blood pressure and electrocardiogram is registrated during multiband fMRI brain acquisitions. This allows the detection of baroreflex activity during the following interventions: Pharmacological baroreflex testing with phenylephrine and nitroprusside boluses, lower body negative pressure (LBNP) and peripheral chemoreflex testing with hypoxia. fMRI images of the brainstem and hypothalamus were cropped to remove adjacent areas with high physiological noise [1]. Blood pressure and RR interval changes were correlated with blood-oxygen-level dependent contrast (BOLD) by mixed-effects general linear model and Masked independent component analysis (mICA) is utilized for connectivity estimation [2]. The image analysis reveals human cardiovascular reflex control at the brainstem level. Furthermore this pilot study shows the feasibility of beat to beat BP recording during fMRI and the automated bolus administration as an intervention unconfounded by subject movement or active participation. A larger subject number is needed to support the preliminary results.

Fig. 1: Experimental fMRI setting to test baroreflex function with LBNP and pharmacological testing.

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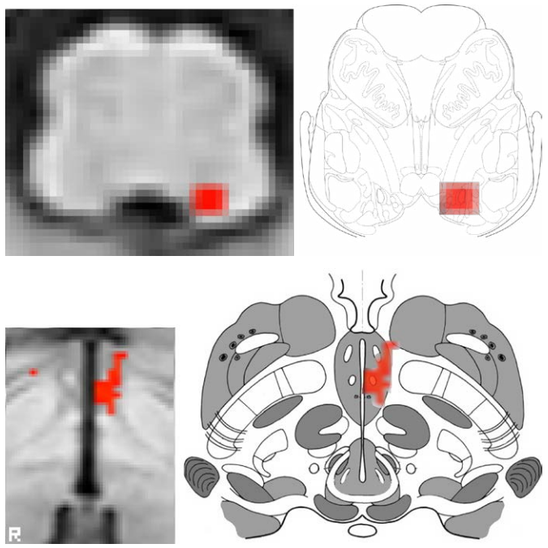

Fig. 2: upper image: Lateral activation of nucleus tractus solitarius in the lower brainstem [3]. Lower image: Lateral activation of the hypothalamic paraventricular nucleus [4].

[1] Beissner et al., Neuroimage 86, 2014
[2] Alsady et al., Hum. Brain Mapp. 37, 2016
[3] Mai et al., Atlas of the Human Brain, Academic Press, 2008
[4] Naidich et al., Duvernoy´s Atlas of the Human Brain Stem and Cerebellum, Springer, 2008

1.4.2 Battle of reflexes: Chemoreflex vs baroreflex

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Electrical carotid sinus stimulation is a non-pharmacologic treatment option in refractory hypertension. The stimulation is expected to activate the arterial baroreflex and, thereby, to lower blood pressure. Unfortunately, not all patients respond to the therapy. It has been claimed that the peripheral chemoreflex may be tonically activated which could inhibit the arterial baroreflex.

In this project, we tested the following hypothesis:
The antihypertensive effect of electrical carotid sinus stimulation is reduced under peripheral chemoreflex activation.

We assessed responses to electrical baroreflex stimulation in 11 hypertensive patients with an implanted electrical carotid sinus stimulator during isocapnic hypoxia (SpO_2~80%) vs hyperoxia in randomized order by recording ECG, systolic blood pressure (SBP), ventilation, SpO_2, end-tidal CO_2 and O_2 fractions, and vasoconstrictor muscle sympathetic nerve activity (MSNA, Fig. 1).

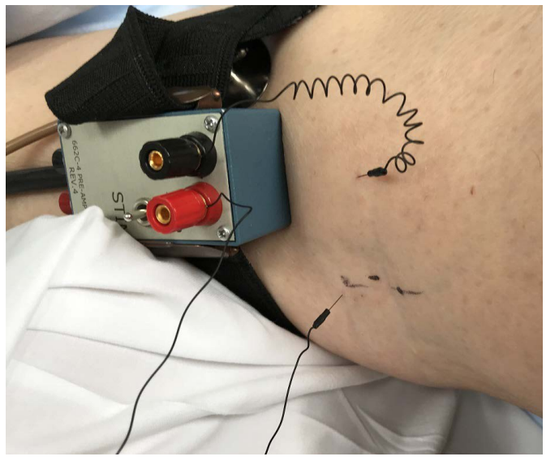

Fig. 1: Microneurography of the right peroneal nerve. Marks in the popliteal space indicate the nerve's course as detected by external electrical stimulation.

Fig. 2 shows that electrical carotid sinus stimulation reduces blood pressure, heart rate, and vasoconstrictor sympathetic activity. However, the responses were not blunted during hypoxia.

We conclude that peripheral chemoreflex activation does not diminish the efficacy of electrical baroreflex stimulation. Thus, tonically active peripheral chemoreflexes are less likely to explain the failure rate of baroreflex activation therapy (BAT) in hypertensive patients.

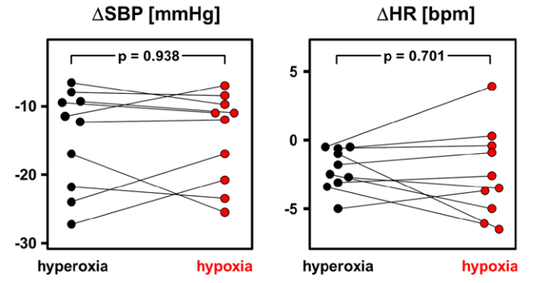

Fig. 2: Comparison of hemodynamic (upper) and sympathetic (lower) responses to electrical carotid sinus stimulation under hyperoxic and hypoxic conditions.

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[1] Somers et al., J. Clin. Invest. 87, 1991

1.4.3 Effect of hypoxia on baroreflex function in humans

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Baroreflexes and peripheral chemoreflexes have a powerful effect on efferent cardiovascular autonomic activity making them attractive targets for hypertension management. Whether or not activation of the peripheral chemoreflex restrains arterial baroreflex function is still debated [1]. A possible reason for the conflicting findings may be the intraindividual variability in baroreflex sensitivity assessments. We conjectured that a large number of repeated measurements in each single subject would yield more reliable data. We hypothesized that activation of the peripheral chemoreflex would reduce cardiac baroreflex sensitivity and baroreflex buffering capacity.

We planned to enrol 10 healthy men. By now, data from 8 men (18-40 years) are available. During supine rest, participants were subjected to normoxic and normocapnic hypoxic (80 % SpO_2) breathing gases in randomized order for 90 mins per condition with a 30-min break in between. We determined cardiac parasympathetic baroreflex sensitivity (BRS) and baroreflex buffering function using repeated phenylephrine bolus injections every 4 mins (20 repetitions per subject and condition). The individual phenylephrine dose of 75 or 100 µg was predetermined to raise blood pressure by no more than 30 mmHg.

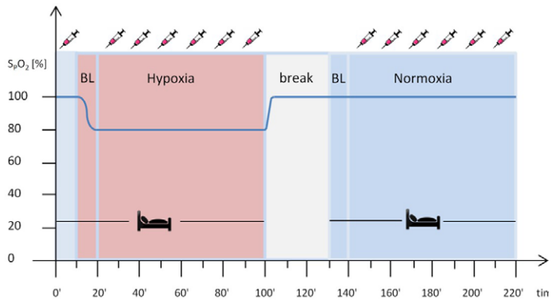
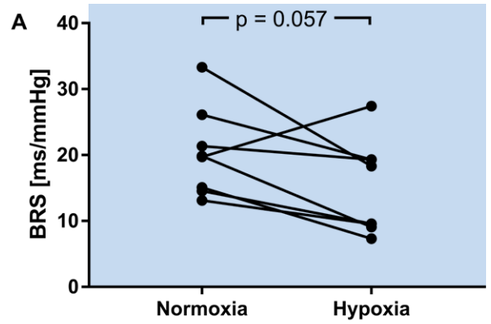


Fig. 1: Schematic figure of the study protocol. Hypoxia and normoxia were applied in randomized order.

Hypoxia decreased BRS by 5.4 ms/mmHg ± 6.7 (20.4 ± 6.7 vs 15.0 ± 7.1 ms/mmHg, p = 0.057) but did not change the blood pressure increase on phenylephrine (23.3 ± 5.5 vs 22.8 ± 6.5 mmHg, p = 0.832).

In healthy men, moderate hypoxia does not impair arterial baroreflex buffering which contrasts with lowered cardiac baroreflex sensitivity. Several explanations may account for the discrepancy. In the short-term, blood pressure is regulated by different interrelated effectors, e.g., SA node, myocardium, and vasculature. Hypoxia may shift the balanced contributions between these effectors. Individual analysis could help explain different findings in different labs.



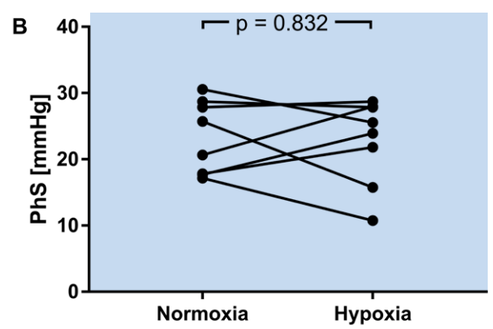


Fig. 2: A) Cardiac baroreflex sensitivity. B) Phenylephrine sensitivity, i.e., baroreflex buffering capacity.

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[1] Hallwill & Minson, J. Appl. Physiol. 93, 2002

1.4.4 Cardiovascular health monitoring in space – Cardiovector

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Crew health monitoring is one of the major research areas since the first manned space flight. Non-invasive, simple to use, reliable and cheap techniques have been used in space medicine including impedance cardiography (ICG), seismocardiography (SCG), and ballistocardiography (BCG). Autonomic cardiovascular control has been assessed using heart rate variability (HRV) analysis. New developments over the last decades in sensor technology and in biosignal analysis allow new approaches with small wearable devices. Since 2014 the space experiment Cardiovector combines HRV analysis, SCG, ICG, and 3D-BCG in one device for crew cardiovascular health monitoring [1, 2].

Eleven cosmonauts have been studied during six-month and one cosmonaut during a year-long ISS mission. The sessions were scheduled every month during the mission and conducted twice prior to launch and twice post landing. Measurements are performed under resting conditions and during standardized breathing maneuvers.

1) Classification based on HRV parameters showed in all cosmonauts a moderate shift from a normal regulatory type to a prenosological state with large inter individual differences (Fig. 1).

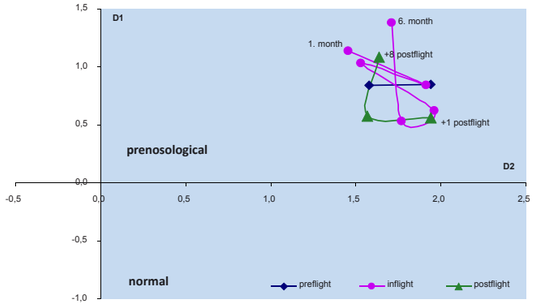

Fig. 1: HRV changes during 6 month space flight in one cosmonaut.

2) Stroke volume estimated by transthoracic impedance cardiography remained stable during space flight and was comparable with preflight supine values (Fig. 2, top).

3) Cardiac mechanical force measured by 3D-BCG is increased compared to preflight supine measurements and remains stable over 6 and 12 month in space (Fig. 2, bottom).

Our results demonstrate that wearable devices combining classical non-invasive techniques can be used to screen for individual changes in cardiovascular control and function. These findings encourage the use in terrestrial medicine for home monitoring or screening.

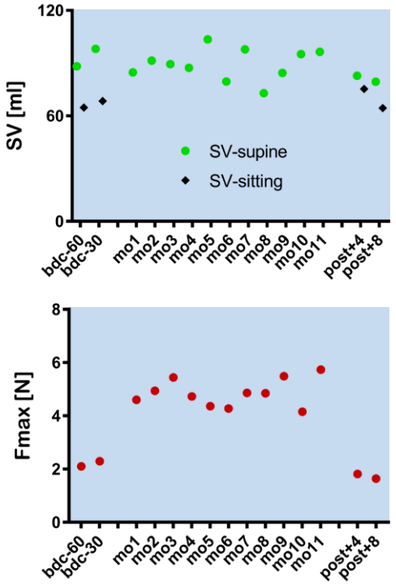

Fig. 2: Stroke volume (SV) estimated from transthoracic impedance cardiography (top) and maximum ballistic cardiac force (Fmax, bottom) during 12 month space flight.

Corresponding author: jens.tank@dlr.de

[1] Tank et al., J. Physiol. 595, 2015
[2] Baevsky et al., J. Appl. Physiol. 103, 2007
[3] Chernikova et al., J. Appl, Physiol. 103, 2017

1.5 Sleep and Human Factors Research

1.5.1 ASYSTED – an advanced system for tele-guidance in diagnostics imaging

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The aim of the project was to develop a software application that combines conventional voice-guided teleultrasonography with visual instructions presented to the examiner.

Experts in ultrasonography often are not present when needed at the Point of Care (PoC). This can lead to poor quality examination results when performed by inexperienced examiners. How can quality of examinations be increased?

Remote guidance of the examiner at the PoC can be realized by using video communication systems in combination with assistive technology. Tele-ultrasonography systems in combination with examiner guidance can deliver both, examination support for inexperienced examiners and high quality data for diagnostics [1].

The scenario
An ultrasound examination is performed and the video signal is transferred to a remote medical expert via an IP-communication line. The expert assists the examiner by sending optical and acoustic signals. DICOM images of relevant findings are produced by the ultrasound device and transferred to SCOTTY's examiner system. DICOM files are sent to the expert's system and diagnosis can be made (Fig. 2).

Fig. 1 Left: Expert using input device while watching live ultrasound video. Right: Examination and video grabbing by the SCP. © T. Banneyer.

The teleultrasonography system SCP (SCOTTY Communication Platform) is optimized for high quality video streaming at low bandwidths over any IP-network, primarily over satellite networks. The SCP transfers real time ultrasound video to an expert. In addition the system provides the transfer of files. Using serial channels in the SCP-Teleporter software the commands of an input device can be transferred in real time between expert and examiner.

Fig. 2: Expert site: Presets can be selected and be opened remotely on the examiner's site. Instructions can be sent using software buttons or the multiaxis "Space mouse" (a DLR development).

ASYSTED consists of 2 applications, one on the expert's site (RemoteControl Expert (Fig. 1) and one on the examiner's site (RemoteControl Examiner)).

Presets can be sent to the examiner to indicate the starting point of the examination. Instructions on how to move the ultrasound probe can be given using software buttons or a multiaxis joystick. Once the probe is in correct position DICOM images are produced with the ultrasound device and transferred to the expert for diagnosis.

The quality of diagnostics in teleultrasonography can be increased when a less or not experienced examiner is supported in positioning the ultrasound probe by visual instructions in addition to audio guidance.

ASYSTED can support examiners
- Telesonography is a reliable tool to support examiners with a minor experience in performing examinations.
- Visual teleguidance can improve telesonography to enhance precision in sound probe positioning.
- ASYSTED is a communication tool to support examinations, not a medical product2 (BfArM 2018).
- Diagnostics is made on the basis of DICOM files.

Outlook
- Signing of a License Agreement with Scottygroup
- Validation in the medical environment of the German Armed Forces – Bundeswehr
- Technology transfer completed
- Commercial exploitation by Scottygroup

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[1] Walcher et al., British J. Surg. 93, 2006
[2] Council Directive 93/42/EEC 14/06/1993

1.5.2 Trading accuracy for speed in selective attention tasks during sleep deprivation

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Selective attention is a critical cognitive function in tasks that require careful monitoring of visual information. An increasing amount of night work on jobs that meet such requirements motivates the study of the effects of sleep deprivation (SD) on selective attention. Monitoring tasks in occupational settings can be operationalized for study in the laboratory by visual search tasks, in which the subject has to identify rare target items among distractor items. Visual search under SD leads to a decrease of overall response speed and accuracy. However, an increase of response speed per item with increasing number of items was also found under SD. This might indicate an unfavorable speed-accuracy trade-off: decision speed per item increases, while accuracy decreases in turn. Eye gaze tracking may provide additional indications for the duration of individual decisions during the search process.

We recorded gaze behavior during two standard visual search tasks to explore if SD leads to faster and sloppier decisions per item (shorter fixation durations). Visual search performance (response time and sensitivity d') in the conjunction (CST) and spatial configuration (SST) search task and the associated gaze behavior were tested in two groups of subjects. While sleep deprived participants (N=24, age: 25 ± 5 STD; 12 women) were kept awake during a 24 hour period, participants of a control group (N=24, age: 26 ± 4 STD; 10 women) were allowed to sleep (time in bed: 8 hours).

We found an increase of response time under SD compared to the control group (CST: $p = 0.019$; SST: $p < 0.001$) and a decrease in sensitivity d' (CST: $p = 0.03$; SST: $p < 0.001$). For gaze behavior (see Fig. 1), we found slower saccade velocities for the SD group compared to the control group (CST: $p < 0.001$; SST: $p < 0.001$). In contrast, fixation durations decreased in the SD group relative to the control group (CST: $p = 0.018$; SST: $p = 0.008$). Moreover, the change in fixation duration was positively correlated with the change in task accuracy (CST: $r = 0.29$, $p = 0.048$; SST: $r = 0.33$, $p = 0.022$), suggesting that subjects that showed the strongest decrease in fixation duration exhibited also the strongest decrease in search accuracy. Further analysis showed that the general decrease of fixation duration was mainly associated with a steep increase of the frequency of very brief fixation durations, so called 'express fixations' with durations shorter than 120 ms.

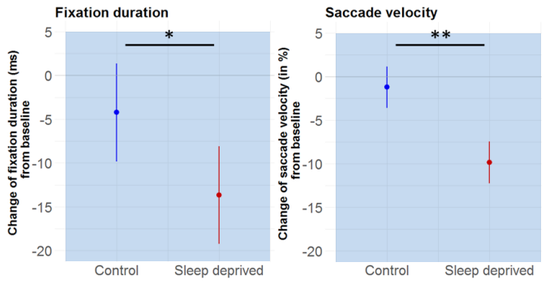

Fig. 1: Estimated effects and confidence intervals of 24 hours SD on oculomotoric parameters for SD and control group (* p<0.05, ** p<0.01).

The decrease in fixation duration under SD is further evidence for a shifted speed-accuracy trade-off as indicated by earlier search studies. SD seemingly leads to an increase of decision speed at the cost of reduced accuracy. Consequently, SD not only results in overall cognitive slowing but also in an impairment of adequate resource allocation in selective attention, potentially due to the absence of prefrontal inhibitory control.

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[1] Horowitz et al., Psychol. Sci 14, 2003
[2] Santhi et al. PloS One 2, 2007

1.5.3 Psychological effects of a night flight curfew: Comparison of aircraft noise-induced short-term annoyance in the NORAH and STRAIN sleep studies

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In October 2011, a new runway was opened at Frankfurt Airport and an associated night flight curfew between 11:00 pm and 5:00 am was introduced. This temporal redistribution of nocturnal overflights caused a "high-rate-of-change" (HRC) in aircraft noise exposure in the surrounding community [1]. The DLR examined in the NORAH* sleep study the psychological effects of the new night flight curfew on short-term annoyance of exposed residents in the Rhine-Main area around Frankfurt Airport [2].

In 2001/2002 the DLR carried out the methodolically similar sleep study STRAIN (N=64) in the vicinity of Cologne-Bonn Airport, one of the airports with the highest traffic densities at night. The Cologne-Bonn Airport can be classified as steady-state or "low-rate-of-change" (LRC) airport, i.e., no distinct change in operations or noise exposure occurred during the STRAIN sleep study. Significant differences for nocturnal annoyance reactions between both sleep studies were expected.

In the NORAH sleep study a total of 187 healthy adult airport residents (aged 18-78 years, 107 female) was studied in 2013 approximately 2 years after the introduction of the night flight curfew. The study took place at home under real-life conditions for three consecutive nights. Participants evaluated their aircraft noise-induced short-term annoyance retrospectively on a five-point scale ("1 = not" to "5 ="very" annoyed) in the morning. Further information on non-acoustical parameters of noise annoyance (e.g., noise sensitivity, adaptation to chronic aircraft noise exposure, long-term annoyance due to aircraft noise) was inquired after the study. The A-weighted energy equivalent sound pressure level related to subject`s time in bed (LASeq) and number of nocturnal overflights were determined based on acoustical measurements inside the bedroom.

Data of the NORAH and STRAIN sleep studies were cross-sectionally compared in terms of exposure-response curves for aircraft noise-induced short-term annoyance. Random effects logistic regression analysis was used to estimate the probability to be highly and moderately annoyed (categories > 3) by aircraft noise as a function of acoustical, i.e., number of overflights per night (Fig. 1) and LASeq (Fig. 2), as well as non-acoustical factors.

The differences in short-term annoyance between both sleep studies were statistically significant (model 1, number of overflights: $p<0.001$, OR=0.084, 95% CI 0.035-0.180; model 2, LASeq: $p<0.001$, OR=0.148, 95% CI 0.065-0.307), indicating a higher annoyance probability at Frankfurt Airport than at Cologne-Bonn Airport. Subjective adaptation to chronic aircraft noise exposure and long-term aircraft noise annoyance were significant non-acoustical variables affecting short-term annoyance response.

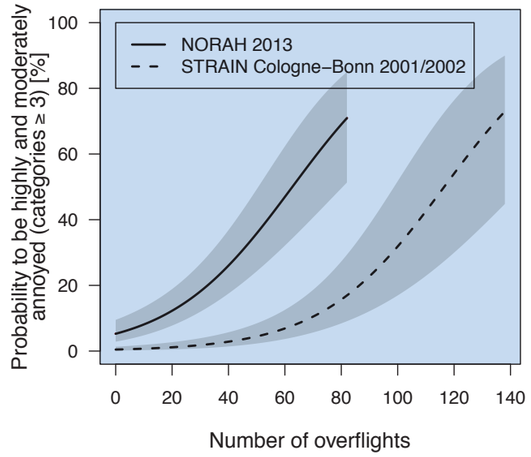

Fig. 1: Probability to be highly and moderately annoyed by aircraft noise of the previous night predicted by model 1. The grey areas show the 95% confidence intervals.

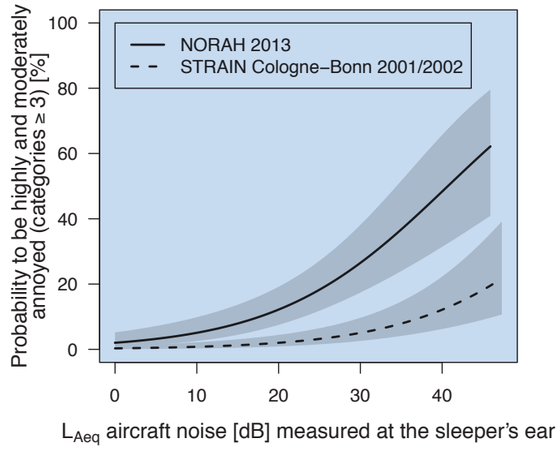

Fig. 2: Probability to be highly and moderately annoyed by aircraft noise of the previous night predicted by model 2. The grey areas show the 95% confidence intervals.

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*NORAH (Noise-Related Annoyance, Cognition, and Health) is the most extensive study on transportation noise impact in Germany so far. The NORAH sleep study was performed on behalf of the Gemeinnützige Umwelthaus GmbH (UNH) in the forum airport and region (FFR).

[1] Guski et al., Proc. Internoise 2016
[2] Quehl et al., Int. Arch. Occup. Environ. Health 90, 2017

1.5.4 Fitness for air travel assessment in obese individuals with and without chronic obstructive pulmonary disease (COPD)

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Lifestyle diseases are on the rise and the airplane as a common mode of travel is starting to pose a serious health risk for a growing number of people. Due to the reduced atmospheric pressure in an airliner cabin, up to an altitude-equivalent of 8000 ft (2438 m), individuals with obesity and chronic obstructive pulmonary disease (COPD) are at elevated risk for medical complications during flight. Physicians increasingly need to evaluate a person's ability to fly safely, but since numerous studies dismiss the diagnostic nature of this question evidence on accuracy of available tests is inconclusive or even contradictory.

This study assessed diagnostic accuracy of three index tests for air travel fitness in obese individuals with and without COPD, 50 meter (50mWT) and six minutes (6MWT) of walking and normobaric hypoxic challenge testing (HCT):

- **50mWT:** Participants walked 50 meter as fast as possible and the time required was measured.
- **6MWT:** Participants walked for six minutes as far as possible, distance covered was recorded.
- **HCT:** Participants breathed 15.1% O_2 in N_2, simulating the oxygen partial pressure in an aircraft at cruising altitude. Outcome measure was equilibrium SpO_2.

The secondary goal was to explore whether perceived dyspnoea could be diagnostically useful:

- **Borg scale:** Participants scored perceived dyspnoea at rest and subsequent to each diagnostic test on a 0–10 scale ranging from "nothing at all" to "very, very severe".

Of the 21 (10 female) participants included in the study 11 (4 female) had a diagnosis of COPD. Mean±SD of BMI was 36±5kg/m² and average age was 51±15 years.

Fitness for air travel was defined as a person's ability to maintain SpO_2 greater or equal 90% when exposed to flight conditions. This reference standard was established in an altitude chamber. We identified 13 individuals with in-flight hypoxia, of which 9 had COPD. Mean SpO_2 was 88±1% in those not fit to fly and 92±2% in those fit to fly.

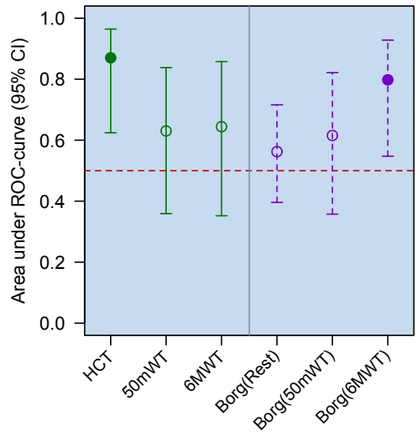

Fig. 1: AUC estimators and 95% confidence intervals.

Test Performance was estimated by the area under the receiver operating characteristic (ROC) curve (AUC) as shown in Fig. 1. While both walking tests were in good agreement with each other (Pearson's r=-0.83) only the predictions of HCT and dyspnoea after 6MWT can be distinguished from chance level. For the latter it apears that the excercise imposed by 6 minutes of walking was sufficient to trigger dyspnoea symptoms in susceptible individuals while walking 50 meters did not provide the required stimulus to evoke this.

Given the demographic and public health challenges in modern societies it is necessary to refine the diagnostic instruments for pre-flight assessment. To leverage research efforts in this direction we need a better understanding of how we define and measure fitness for air travel. In this study HCT performed as expected, but in contrast to a widely held opinion walking tests did not proof informative in regard to in-flight hypoxia. However, the current study indicates that exercise triggered symptoms, such as dyspnoea, could be of substantial prognostic value.

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1.5.5 Effects of nocturnal road traffic noise on residents' sleep

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Nocturnal traffic noise causes sleep disturbances in residents. Thus, knowledge about noise effects is important to help protect residents' sleep and maintain health, well-being, and performance. In recent years, DLR has established exposure-response curves regarding the effects of aircraft and railway noise on the awakening probability of residents [1]. However, such a curve has not yet been established for road traffic noise.

We conducted a field study in residential areas where road traffic was the dominant noise source and noises were attributable to separate events. Forty healthy participants (mean age = 29.1, SD = 11.7; 26 females) that were free of sleep disorders were polysomnographically examined for five consecutive nights. Acoustic measurements were undertaken at the sleepers' ears. The synchronous collection of electrophysiological and acoustic data allowed for an event-related analysis of noise events and associated awakenings.

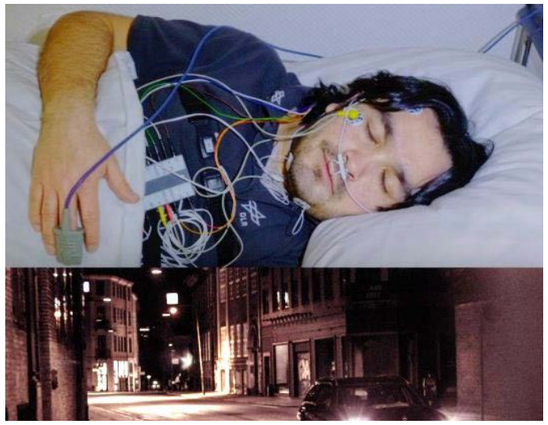

Fig. 1: Detection of awakening reactions due to road traffic noise via polysomnography, the gold standard to examine sleep quality.

The present analysis included 152 nocturnal recordings with a total of 11265 road traffic noise events within the participants' sleep period. Participants were exposed to a median of 107 road traffic noise events per night. A random effects logistic regression model, including acoustic, sleep-related and participant-related (e.g., age) variables, revealed a significant increase in the awakening probability with increasing maximum sound pressure level of a noise event ($p < 0.001$). When holding all confounding variables constant at their respective sample median, the awakening probability per single noise event ranged from 0.5 % at 24.2 dB(A) to 3.8 % at 70 dB(A) maximum sound pressure level. Assuming an exposure of 107 noise events per night with maximum sound pressure level of 39.4 dB(A) (median) the model estimates on average one noise-induced awakening per night.

The present study is of high ecological validity and provides for the first time an exposure-response curve regarding the effect of separate road traffic noise events on the awakening probability. Our study focussed on residential areas with moderate traffic density at night. Further investigations of urban areas with dense traffic are still needed, which, however, will require a novel methodological approach as an event-related analysis is no longer feasible. The ultimate goal will be to establish physiologically based noise protection measures.

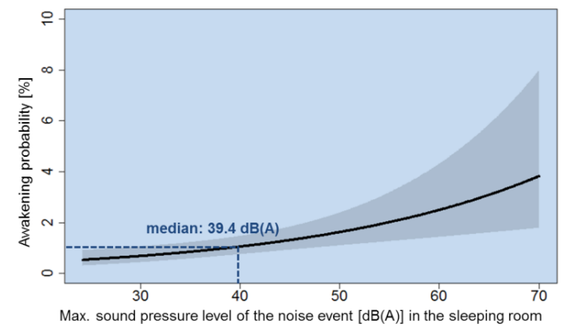

Fig. 2: Exposure-response curve for road traffic noise; assumptions (median): 1-min background LAeq: 24.2 dB(A), duration of the noise event: 21.4 sec., number of aggregated vehicles: 1, age: 25 years, elapsed sleep time: 3.6 hours; awakening from sleep stage S2. Maximum sound pressure level (median): 39.4 dB(A).

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[1] Elmenhorst et al., Sci. Total Environ. 424, 2012

1.6 Study Team

1.6.1 Implementation of the VaPER bed rest study in :envihab

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Aim of Bed Rest Studies
Comparable effects of microgravity and 6° Head Down Tilt-Bed Rest
- Decrease of muscle and bone mass
- Fluid shift (negative effects on cardiovascular system)
- SANS (Spaceflight Associated Neuro-ocular Syndrome, formerly VIIP syndrome)
  – > **Development of countermeasures**

Study Design – Study Protocol
Different duration depending on the objective:
- Short-term bed rest (e.g. cardiovascular system)
- Medium-term bed rest (e.g. muscle)
- Long-term bed rest (e.g. bone)

BDC: Baseline Data Collection (5–14 days)
HDT : Head Down Tilt (6°) Bed rest (5–60 days)
R: Recovery (5-14 days)
(+Follow up: R+14, R+28, R+90, R+180, R+360, R+720)

The recent "Medium-term Bed Rest Study - VIIP and Psychological :envihab Research Study (VaPER)" was conducted in 2017 as a joint project between NASA and DLR in Cologne, Germany. The primary aim of this comprehensive study was to test influences of the novel paradigm for microgravity simulation combining -6° head down tilt (HDT) with increased ambient CO_2 (0.5 %) on cerebral and ocular anatomy and physiology. The study focused on the Spaceflight Associated Neuro-ocular Syndrome (SANS, formerly visual impairment and intracranial pressure, or VIIP syndrome).

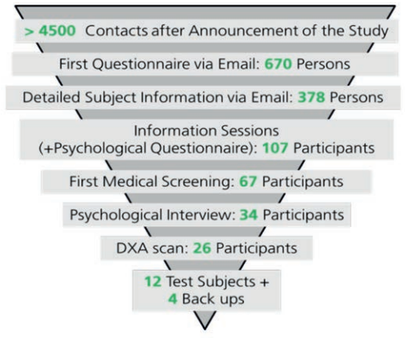
Hypercapnia (like on the ISS) potently augments cerebral blood flow which may acutely increase intracranial blood volume [1, 2] and intracranial pressure (3). When added to the cephalad fluid shifts in space, hypercapnia may further raise intracranial pressure and hence SANS risk.

HDT has proven its effectivity as ground-based microgravity analogue for space medicine research. However, unlike in microgravity where all hydrostatic gradients are abolished, a gravitation vector is still present in HDT bed rest which may elicit different physiological responses. Indeed, -6° HDT studies have not reproduced cerebral or ophthalmic findings observed in astronauts affected by SANS. Possibly, -6° HDT alone may not create head-ward fluid shifts mimicking true microgravity conditions. Steeper HDT tilt angles are unrealistic for long-duration bed rest studies. On the other hand, all experimental bed rest studies thus far had provided pillows. Consequently, we sought to establish whether the bed rest model for SANS-related research could be improved by mimicking hypercapnia on board the ISS and stricter controlled -6° HDT bed rest position.

During the VaPER Study no pillows were permitted except for a thin pillow when subjects were lying on the side. Subjects were camera-monitored 24 h per day and feedback on head position was provided during waking hours whenever needed. Test subjects showed an excellent adherence and maintained strict -6° HDT throughout the study.

Adherence is of central importance for successful completion of bed rest studies. One prerequisite is careful screening before study inclusion with emphasis on psychological aspects.

Fig. 1: Subject in 6° Head Down Tilt position during Bed Rest Study (VaPER study).



Test Subjects – Recruitment Steps Subject Care
- Daily ward round (physician, nutrition expert, study assistant)
- Physiotherapy and reconditioning
- Psychological support

The :envihab facility and the experienced staff at the DLR-Institute of Aerospace Medicine create an atmosphere of best possible well-being during confinement.

Future studies will determine whether strict -6° HDT bed rest, hypercapnia, or both combined are required to model SANS-like findings.

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[1] Artru, J. Cereb. Blood Flow Metab. 7, 1987
[2] Fortune et al., J. Trauma 39, 1995
[3] Lawely et al., J. Physiol. 595, 2017

1.6.2 Nutrition standardization in the VaPER bed rest study

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Introduction
Bed rest studies, in which healthy volunteers are confined to bed in a -6° head-down tilt position, are a well-established model for some of the adaptations experienced by astronauts during spaceflight. They are therefore a very valuable tool both for investigating possible mechanisms and for testing measures to counter these adaptations. Further, the results obtained in these studies have obvious relevance and applications in terrestrial clinical contexts which make them even more valuable.
In order to achieve better standardization of bed rest studies in the spaceflight context, an International Academy of Astronauts (IAA) study group was initiated, including members from most of the entities that are actively pursuing this type of activity.

Development of Master Menu Plans for the VaPER-Study
To avoid any impact of irregular nutrient supply to the human organism, adequate nutrient intake levels have been defined. These recom-mended values should be regarded either as an adequate range, if a range is mentioned, or as a minimum intake level. For some of these nu-trients these recommended intakes should be achieved on an average per week. For all other nutrients the recommended intake should be achieved every day.

Table 1: Recommended nutrient Intake levels to be achieved.

Nutrient	Adequate intake
Energy and Macronutrients (per day)	
Energy (total energy expenditure, TEE)	WHO equation for Resting Meta-bolic Rate (RMR) x 1,1 (bed rest: HDT) or x 1,4 (ambulatory: BDC, Recovery)
Total fat (%TEE)	30 to 35
Protein (g)	1,2 g/kg BW
Carbohydrates (%TEE)	50 to 60
Total Fibre (g)	≥ 30g
Elektrolytes & Water (per day)	
Sodium (g)	2.5 to 3
Potassium (g)	3,5 to 5,0
Calcium (mg)	1000 to 1200
Water (ml)	50 ml/kg BW
Vitamins (average per week)	
Biotin 30 µg/d	Vitamin B6 2 mg/d
Folate 400 µg/d	Vitamin B12 2 µg/d
Niacin 20 mg/d	Vitamin C 100 mg/d
Panthothenic Acid 5 mg/d	Vitamin D 1000 IE/d
Vitamin A 1000 µg/d	Vitamin E 15 mg/d
Thiamin (Vit.B1) 1,5 mg/d	Vitamin K 80 @g/d
Riboflavin (Vit.B2) 1,5 mg/d	
Elements (average per week)	
Iron (male) 10 mg/d	Copper 1,5 to 3 mg/d
Iron (female) 10 mg/d	Magnesium 300 mg/d
Fluoride 1,5 to 4 mg/d	Phosphorus 0,7 to 1,7 g/d
Iodine 200 µg/d	Zinc 12 to 15 mg/d

Besides matching the nutrient intake levels, some other dietary restrictions are mandatory:
- No methylxanthine derivates (coffee, black/ green tea, energy drinks, chocolate, coke)
- No alcohol intake
- No flavor enhancer
- No sweat inducing spices (chili, hot curry)

For the VaPER-Study we developed 14 Master Menu Plans. The following restrictions had to be considered:

RESTRICTIONS FROM GUIDELINES OF STANDARDIZATION
- Adequate and standardized nutrient value
- Dietary restrictions

RESTRICTIONS FROM TEST SUBJECT
- Body weight, total energy expenditure
- Preferences
- Diversified meals
- Food for "sweet tooth"
- Intolerances, allergies, religious constraints

RESTRICTIONS FROM FOODS
- Constant composition and quality (e.g. NaCl)
- Not too many different foods
- Foods with only one nutrient to adjust plan
- Easy in preparation, long-lasting
- Permanently available (no seasonal goods)

Adaptation of Daily Menues to Subjects' Characteristics
The above-mentioned 14 master menu plans had to be adapted with respect to individual body weight and total energy expenditure (TEE), resulting in 720 daily plans for the duration of the study (12 test subjects x 60 study days).

Metabolic Kitchen: Menu Preparation
"Metabolic kitchen" describes a kitchen where metabolic meals are prepared in accordance with specific requirements. The metabolic kitchen personnel must observe and follow the regulations of German law according to industrial hygiene. The metabolic kitchen staff is responsible that the food items on the menu are provided to the test subject in exactly the defined amount. They shall also ensure that all food items/beverages needed on the respective next study day are available in the required amount, defrosted and ready to use. The weight of each food item/beverage to be offered to the test subject should be exactly the weight foreseen on the menu (max. deviation of 0.01g and 1g depending on study design and food item).

Documentation of Daily Nutrient Intake
The actual amount/time of meal consumption will be taken down first on the individual hard-copies of the daily menus and then evaluated by nutrition software regarding nutrient content.

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[1] Anonymous. Guidelines for Standardization of Bed Rest Studies in the Space-flight Context, International Academy of Astronautics (IAA), June 2014.
[2] Anonymous, Standardization of bed rest study conditions, 5th of August 2009

1.6.3 Artificial gravity: the 2nd National Centrifuge Program

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Artificial gravity induced by a human centrifuge is considered as a promising countermeasure for negative physiological effects of weightlessness during long-term space flight. In contrast to actual training equipment e.g., on the ISS, centrifugation has the ability to provide gravity loading across the entire body.

However, there is a need to understand the effects of the centrifuge-induced gravity gradient on physiological responses in more detail. Our Institute provides two short arm human centrifuges (SAHC), one belongs to ESA, the other one is the worldwide unique DLR-SAHC with multifunctional exercise and research opportunities during centrifugation.

In order to improve the effectiveness of Artificial gravity as a countermeasure, the DLR Space Agency established a scientific program called the National Centrifuge Program (NZP). In 2016/2017 two projects were conducted in the frame of the current 2nd NZP.

SelfOG (Hochschule Bonn-Rhein-Sieg)
Investigation of Self-Orientation under Varying Gravity States
In one study the aim was to identify a threshold of the influence of gravity for perceptual upright. This helps to understand what happens with the self-orientation during different g-levels. Therefore 16 participants (8 male, 8 female) were tested while lying on the centrifuge (Fig. 1).

Fig. 1: Position of lying on the ESA-SAHC during the SelfOG-study.

24 logarithmically spaced g-levels were provided between 0.04 and 0.5 g. Baseline was performed lying on the centrifuge without rotation and in upright position.

The perceptual upright was measured with the OCHART (Oriented Character Recognition Test). The OCHART uses the ambiguous symbol whose identity ("p" or "d") depends on its perceived orientation. First results indicate that a gravitational field of at least 0.15 g is necessary to provide effective orientation information for the perception of upright, which is close to the gravitational force found on the Moon of 0.17 g. For whole body linear acceleration, the vestibular threshold is around 0.1m/s².

JUMP (University of Konstanz and DSHS Köln)
Reactive Jump Training under Hypergravity – comparability of movement and effects on the metabolism of articular cartilage
A second study was performed in cooperation with the University of Konstanz and the German Sports University Cologne. Long-term stay in weightlessness leads to extensive physiological deconditioning processes (including cardiovascular, muscle mass and bone density, cartilage mass). Therefore maintaining physical fitness for future space mission is critical. In a cross-over design we tested a special training with reactive jumps on a sledge system mounted on a short-arm centrifuge and compared the effects with jumps in vertical position and on the SJS (Sledge Jump System. The SJS was successfully used as countermeasure in a recent long-term bed rest study (RSL).

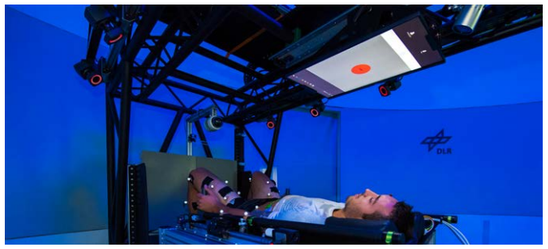

Fig. 2: Subject position on the jumping sledge at the DLR-SAHC during the JUMP-study.

We hypothesized an increase in cartilage metabolism (including COMP, collagen II) after reactive jumps under hypergravity compared to control conditions.
15 male healthy subjects between the ages of 20 and 35 with a Body Mass Index (BMI) of 19-26 kg /m² were examined.

First results indicate that jumps on the SAHC under hypergravity lead to lower ground reaction forces but no significant increase of motion sickness due to Coriolis forces.

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[1] Kramer et al., Sci. Rep. 7, 2017
[2] Harris et al., PLoS One 9, 2014

1.7 Clinical Aerospace Medicine

1.7.1 Medical selection of the first German commercial female astronaut

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In Europe the number of professional female astronauts is very low. There are only two professional European women that had been into space so far: Claudie Haignere (France, in 1996 and in 2001) and Samantha Christoforetti (Italy, in 2014). There are 11 German male astronauts, but not a single female astronaut.

That was the reason for a CEO of a commercial company to publish a job advertisment for a female German astronaut. The minimum requirement was a bachelor or master's degree in engineering or science or an equivalent in the military field. In addition to that the applicants needed to submit an EASA class 2 medical certificate for private pilots.

More than 400 women applied. 81 of them were invited to the psychological selection of which 8 women were identified to be psychologically suitable.

These eight women were examined in January 2017 according to the medical standards for space flight participants of the International Space Station program and its space agencies of Europe, Russia, Japan, the U.S.A. and Canada.

The examinations included, but were not limited to, internal medicine, cardiology, ophthalmology, neurology, psychiatry, orthopaedics, ENT, dentistry, gynecology, anthropometry and MRI of the brain.

Finally six women were identified of being medically qualified.
These women were presented to the public at Airbus Bremen.

The six finalists in Bremen in March 2017.

Out of these six finalists two commercial astronaut candidates were selected by a commission which was led by the astronaut Professor Ulrich Walter.

Drs. Suzanna Randall (left) and Insa Thiele-Eich (right).

Dr. Insa Thiele-Eich, a meteorologist of the University of Bonn and the Eurofighter pilot Nicola Baumann were chosen. These two women started their part-time training with a visit in Star City, centrifuge runs and parabolic flights. The main focus is on teaching role models, especially for girls, in order to interest them in science. The other important aspect is PR to contribute to the fund raising campaign. As this is a private and commercial call the whole amount of 40–50 million Euros must be procured by crowd funding and other activities.

After about six months the Eurofighter pilot Nicola Baumann quit and a successor was nominated. It is Dr. Suzanna Randall, an astrophysicist.

DLR advises the project because it has a vested interest in medical research on women in space and because the European data on this topic are very limited.

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1.7.2 Direct Return: Medical care for European astronauts

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Until 2014 European astronauts used to stay in Star City or were brought to the NASA Johnson Space Center after their Soyuz landing in Kazakhstan. Prior to the first mission of the German astronaut Alexander Gerst, a feasibility study of the European Astronaut Center and the Institute of Aerospace Medicine was performed to find out whether it is possible to bring European astronauts directly after their landing back to the European Astronaut Center and DLR in Cologne and cover the needs of postflight science examinations, clinical data collection, medical monitoring and rehabilitation issues. NASA examination protocols needed to be implemented and new instruments needed to be obtained. Direct returns include the preflight examinations as base lines and the postflight examinations following the exact same protocols.

As a result of that Alexander Gerst was the first European astronaut to profit from the so called "Direct Return" (Fig. 1).

Fig. 1: Nocturnal arrival of Alexander Gerst to the :envihab 14 hours after his landing in Kazakhstan.

In June 2017 the European astronaut Thomas Pesquet returned after a 197 day stay on board the International Space Station to the Institute of Aerospace Medicine´s research facility :envihab.
Following the agreed postflight examination protocol of the participating space agencies, we performed a blood draw and an electrocardiogram immediately after his arrival in the :envihab. During the first three postflight weeks the following examinations were performed:

- Several blood draws
- Exercise stress tests (cycle and treadmill)
- Eye examinations (including OCT and Ultrasound)
- Audiogram
- Dual-energy X-ray absorptiometry (DXA)
- Brain MRI
- Dermatological assessment
- Fitness assessment

The astronaut received also two hours of reconditioning every day in the European Astronaut Center.

Fig. 2: The European astronaut Andreas Mogensen receives his first electrocardiogram minutes after his arrival in the :envihab.

A main focus lays on the examinations of the eye as more than 60% of long-term astronauts show changes in the anatomical structure of the eye. These changes may include globe flattening with hyperopic shift, optic disc edema, cotton wool spots and choroideal folds.

We perform the medical examinations in the scope of medical monitoring to learn more about the impact of their stay on the International Space Station on the astronauts' health. But we also conduct medical examinations for scientific studies which address special fields of interest to research the long-term effect of microgravity on the human body for more knowledge and experience to prepare the astronauts better for Moon and Mars missions. When astronauts land in Kazakhstan, there is a huge armada of people helping them to leave the Soyuz capsule and to recover one´s legs – in the true sense of the word. This support will not be available on Moon and Mars and therefore the crew must stay in proper body condition during their long missions, reducing muscle and bone loss, as well as other microgravity side effects as much as possible.

With these examinations we contribute to the fast recovery of the astronauts as well as for science.

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1.8 Aviation and Space Psychology

1.8.1 Eye movement parameters as indicators of cognitive performance?

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Pilots and air traffic controllers work in a highly safety-critical environment. Therefore, pilot and air traffic controller applicants pass through a multiple-stage selection process with several tests, including cognitive ability and work sample tests. Their test performance is usually assessed based on the number of correct answers, incorrect answers, and reaction times. These variables, however, provide only an indirect measure for visual attention, whereas eye movements give an insight into underlying cognitive processes [1].

So far, little research on eye movements and interindividual differences in cognitive performance exists. Investigations on eye tracking in the context of personnel selection are thus of major interest. The current study addresses two research questions:

- Are eye movement data related to cognitive performance differences?
- Can eye movements make an additional contribution to current performance variables in personnel selection?

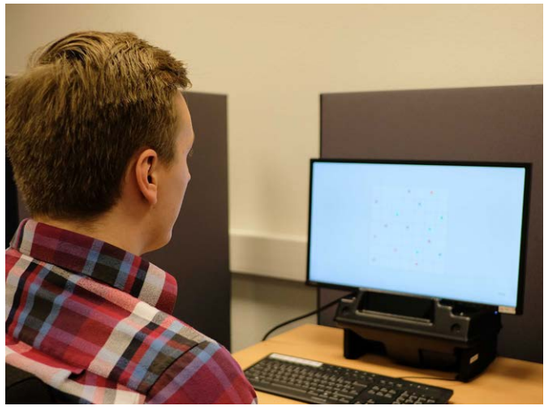

Fig. 1: Participant's work station with eye tracking setup.

The computer-based Eye Movement Conflict Detection Test contains tasks from an aviation context (Fig. 2). It was designed to investigate the relation between test performance and eye movement data. First results from 101 participants (applicants for air traffic control training, university students) are presented. Eye movements were tracked by the EyeFollower™ of LC Technologies (Fig.1).

In a first step, Areas of Interests (AOIs) were defined and aggregated to content-related AOI-groups. In a second step, transition matrices for each participant were compiled to analyze the (relative) count of transitions within and between AOI-groups. In a third step, the scanning behavior for each participant was measured using Shannon's entropy coefficient [2] based on relative transition frequencies. The higher the coefficient, the more randomly transitions are distributed. The lower the value, the more deterministic the transitions are distributed. It was hypothesized that lower entropy in the test would lead to a better test performance.

Fig. 2: Cutoff of a test task.

Entropy-based statistical analysis of eye movement transitions derived from individual transition matrices showed differences in entropy values. Furthermore, the entropy value was significantly related to the participants' individual performance in the test. The size of correlation between test performance and entropy showed a medium effect, suggesting that more random scanning behavior resulted in a lower test performance.

First results indicate that eye movement data can be treated as a measure to make visual attention distribution transparent and to quantify decision-making processes more directly. Furthermore, it can capture differences between participants and is related to test performance. In a next step, eye movement parameters will be validated using multiple selection tests for air traffic control applicants.

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[1] Nuthmann et al., Psychological Reviews 117, 2010
[2] Shannon, in Shannon & Weaver (eds), The Mathematical Theory of Communication. The University of Illinois Press 1964.

1.8.2 Thermal comfort in the aircraft cabin – new ventilation concepts

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Of current interest is the question whether ordinary mixing ventilation (MV) systems in an aircraft can be replaced by or combined with ceiling-based displacement ventilation (CCDV) systems. A reduction of energy consumption without risking a decrease in thermal comfort would be a valuable gain.

On this basis, the effects of four different ventilation systems on aircraft passengers' well-being were tested in four human subject tests by matching displacement ventilation (DV) from beneath the passenger seats with CCDV. The Do 728 cabin test facility of the German Aerospace Center (Fig. 1) was used with 45 subjects in each test.

Fig. 1: Subjects and Thermal Passenger Dummies in the Do 728.

Based on an empirical study [1] in the same test facility, the following settings for supply air volumes were selected: 50 % CCDV / 50 % DV; 70 % CCDV / 30 % DV; 100 % CCDV; 100 % MV. In each test, two of these settings were presented twice. Each run lasted 30 min, the whole test lasted about 3 ½ h. The average cabin temperature throughout the tests was 23.5 °C with 610 l/s of supply air and approximately 25 % relative humidity.

Objective and subjective data (via sensors and psychological questionnaires) were gathered to gain a differentiated image of the climate situation and the thermal comfort that arose for the passengers. All in all, 180 subjects were tested. All samples were stratified by gender, age, height and weight. Clothing was standardized beforehand.

Comfort evaluations did not differ between the four ventilation scenarios ($F_{(12;\ 458)} = 1.03$, n. s.). The overall satisfaction rating for all settings was close to the scale middle of "3" which means "neutral". To examine if the climate parameters were perceived to be spatially homogeneous, the subjects' ratings for temperature and air draught were analyzed per seat row lengthwise. Passengers in the aisle seats evaluated the comfort regarding temperature as being significantly lower than the other passengers in the 70 %/30 %, 100 %/0 %, and MV scenarios ($F_{(4,\ 160)} = 3.11$, $p < .05$, $\eta^2p = .07$), while in the 50 %/50 % scenario, comfort evaluations were comparable for all seat rows along the aircraft (Fig. 2).

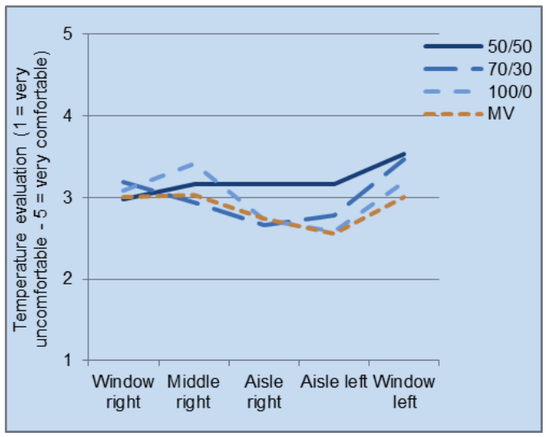

Fig. 2: Means for temperature evaluations (SD ranged between 0.27 and 1.30) per seat row lengthwise.

The value pattern for air draught was very similar: Comfort was evaluated as being lower in the aisle seats in the 70 %/30 %, 100 %/0 %, and MV scenarios ($F(4, 160) = 4.91$, $p < .01$, $\eta^2p = .11$). However, in the 50 %/50 % scenario, comfort was comparably high in all seat rows along the aircraft.

Generally, CCDV and DV systems can be used to provide comfortable climate in aircraft cabins. However, the smallest proportion of dissatisfied passengers was found in the 50 %/50 % CCDV/DV condition. Here, aisle seats were rated as being about 10 % higher in comfort regarding temperature and air draught compared to MV. Pure CCDV did not lead to an improvement in thermal comfort for the passengers.

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1.8.3 Virtual Bike – Cybersickness depending on display type and motion control

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Cybersickness is defined as the experience of motion sickness-like symptoms, caused by the presentation of virtual environments on different displays like HMDs or screens, but with the absence of vestibular motion [1]. It was suggested [2] that a more natural, dynamic motion control mitigates the degree of cybersickness as users of a treadmill showed fewer sickness symptoms than users that navigated statically by pressing a mouse button. Therefore, devices that more closely resemble real-world navigation in Virtual Reality, like a bike ergometer for a virtual bike ride, may induce less cybersickness than the same scenario controlled with a less intuitive device (e.g., a gamepad).

We tested 60 volunteers (40 female, 20 male) with a mean age of 25.62 years (SD = 9.34 years). They were randomly assigned to one of three conditions: twenty participants to the Bike/HMD condition, Gamepad/HMD condition and Bike/Screen condition, respectively. Participants completed three sessions. Each session included navigation from a starting point to a pre-specified target on a virtual island. The experimental setup can be seen in Fig. 1. Prior, within and after the VR immersion, participants filled in the Simulator Sickness Questionnaire [SSQ; 3].

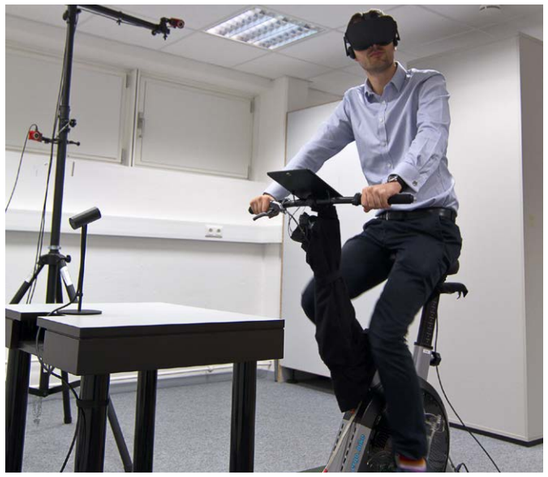

Fig. 1: Experimental setup with bike ergometer and HMD.

Due to severe nauseogenic symptoms 4 of the 60 participants prematurely terminated the immersion. Two of them were in the Bike/HMD and the other two were in the Gamepad/HMD condition. SSQ Total Scores before, during and after the VR immersion are presented in Fig. 2.

Significant differences between times of measurement were observed for all pairwise comparisons except the difference between Ses1 and Ses2 ($t(220) = .40$, $p = .995$) and between Ses3 and the post-immersion measurement ($t(220) = 1.53$, $p = .547$). Furthermore, significant differences between the Bike/Screen condition and both HMD conditions (with Bike/HMD: $t(57) = 2.56$, $p = .034$; with Gamepad/HMD: $t(57) = 2.66$, $p = .027$) were observed.

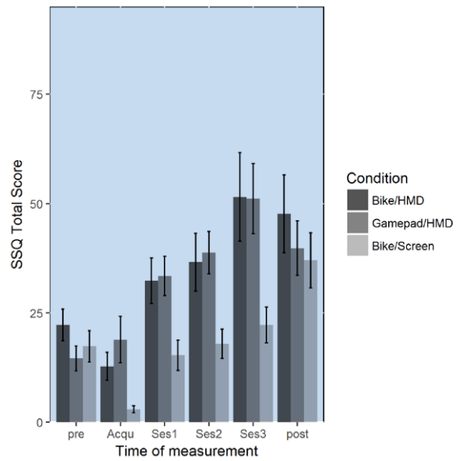

Fig. 2: Mean SSQ Total Scores for all times of measurements broken down by condition. Error bars indicate the standard error. pre = before the VR immersion; Acqu = familiarization phase inside VR (without motion); Ses1–Ses3 = three consecutive navigation sessions; post = after the VR immersion.

As for the interaction effect, Fig. 2 shows that there were no significant differences between conditions in the pre or the post-immersion measurements while there were significant differences in ratings given within the VR.

Levels of sickness increased with duration in all three conditions. What is worth noting is that the level of sickness did not substantially decline after the end of the immersion. On the contrary, in the Bike/Screen condition, sickness scores continued to increase after the immersion so that post-scores were at the same level as the other two conditions. These results suggest that sickness assessments within VR and post-immersion assessments by using paper-pencil versions yield slightly different ratings.

The present study confirmes results suggesting HMDs to be more sickness inducing than presentation displays such as large screens [4]. However, we were not able to confirm that a more realistic motion control (bike ergometer) induces less cybersickness than more generic means of motion control (gamepad) as has been previously found with walking [2].

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1.8.4 Relating gaze patterns to assess coordination within small groups

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Small working groups can be conceptualized as cognitive systems with behavioral couplings emerging between elements [1]. Coordination behavior is impaired when recurrent interactions are prohibited or when there is dissonance in the cognitive system [2]. Recurrent interactions are reflected in patterns of coupled visual attention [3]. It was tested if an integrated gaze-measure for N=3 generated by bivariate cross-recurrence analyses [4] is sensitive to established treatment effects, and thus can provide objective assessment of coordination processes within small groups.

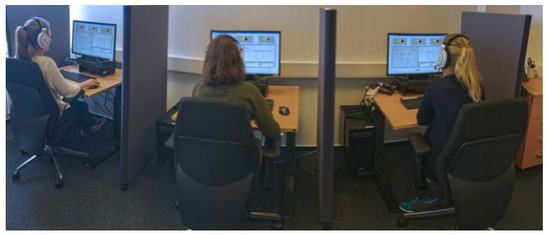

Fig. 1: Experimental setup with STE on display and three Eye-Follower® systems (120 Hz) below screens.

A 2 Communication [R/T on vs. off; within] x 2 social context [dissonant vs. non-dissonant; between] mixed design was chosen. In a Synthetic Task Environment (STE) [5] comprising detection and decision tasks, small groups have to react to critical events and decide about investments for remedy. During the detection task a group can draw simple inferences based on disjunctive information to reduce uncertainty. In the R/T-off condition the communication channel is deactivated during the signal detection task. For a dissonant social context a social dilemma plus competitive priming (by role description and incentive structure) is induced into the decision task. Gaze behavior of each participant is measured with an Eye-Follower® remote system (120 Hz). The coordination indicator 'percentage of integrated cross recurrence rate' (%iCRR) is calculated based on the synchronized gaze-data utilizing [6]. Only measurements during signal detection are reported. 144 participants (age: M=23.01; SD=5.03; gender: 51.4 % female, 48.6 % male) were grouped into 48 teams (15 ab-initio ATCo candidates, 33 students). During a 3.5 h session 2 scenarios are performed, each comprising 48 signal-detection trials with 3 malfunctions forcing a collective decision. Experimental conditions were balanced.

A Mixed-Model Analysis of the %iCRR values produced a main effect for R/T [$F(1, 679.2)= 92{,}21$, $p> .05$, $\eta p^2= .0841$]. The magnitude of %iCRR was higher when the communication channel was open (cf. Fig. 2). A main effect for social context [$F(1, 679.2)= 6{,}69$, $p> .05$, $\eta p^2= .006$] indicates lower behavioral couplings for groups performing under dissonant conditions (Fig. 2).

A significant interaction [$F(1, 679.2)= 4{,}47$, $p> .05$, $\eta p^2= .004$] indicates a mediation of the social context effect by communication (Fig. 2). Indication is provided that with focal goals in conflict (dissonant social context) behavioral coupling decreases. We assume the metric of integrated gaze cross-recurrence to be a sensitive objective measure for the assessment of the macrocognitive process of coordination within small groups. In a next step this metric will be empirically validated by external construct criteria.

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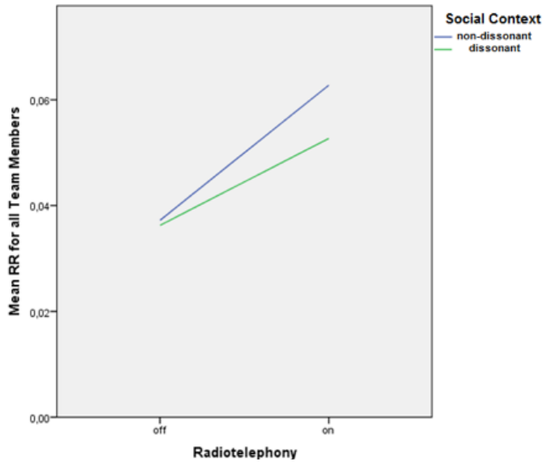

Fig. 2: Plotted main effects and interaction effect of experimental treatments on %iCRR metric.

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Hoermann, H.-J., Tsang, P.S., Vidulich, M.A., Alexander, A.L. (2017) *Researcher role in aviation operations.* In: Advances in Aviation Psychology, Volume 2 – Using Scientific Methods to Address Practical Human Factors Needs Advances in Aviation Psychology, 2. Routledge. Seiten 57–73. ISBN 1472481412.

Theses

Barzantny, C. (2017) *Investigating the Effects of Expectancy-Driven Monitoring in Control Room Operations by Eye Movement Measurements.* Masterarbeit, TU Dresden.

Heinze, T. (2017) *Eule oder Lerche : Hat der Chronotyp einen Einfluss auf die Leistung nach Schlafentzug?* Masterarbeit, Rheinischen Friedrich-Wilhelms-Universität Bonn.

Hoef-Emden, M. (2017) *Determination of the survivability of spaceflight relevant microorganisms on different copper-containing surfaces – a precursor study for ESA space experiment „no biofilm".* Bachelorarbeit, University of Cologne.

Mantas, M.J.Q. (2017) *The effects of heavy ion and X-ray exposure on SH-SY5Y cell differentiation.* Masterarbeit, King's College London.

Mauser, J. (2017) *Microalgae Cultivation at Spaceship EAC for Advanced Life Support Systems.* Masterarbeit, University of Stuttgart.

Schweizer, P. (2017) *Lipid-Anreicherung in Mikroalgen durch Kultivierung in C.R.O.P.® Nährlösung.* Masterarbeit, Universität Hohenheim.

Schüler, O. (2017) *A Molecular Characterization of the Response of Arabidopsis thaliana to a Simulated Microgravity Stimulus Using a Newly Constructed Hardware for Ground-Based Facilities.* Dissertation, Westfälische Wilhelms-Universität Münster.

Simon, D. (2017) *Entwicklung und Verifizierung einer Software zur Vermessung von murinen und humanen Nervenzellen des Hippocampus.* Bachelorarbeit, Hochschule Emden Leer.

Sjöström, S. (2017) *Microbial Life on Mars: The Response of Halophilic Archaea to Simulated Martian Conditions.* Masterarbeit, Royal Institute of Technology (KTH) in Stockholm, Sweden.

Vogelpohl, V. (2017) *Emotionale und motivationale Dynamiken bei der Entscheidungsfindung in Arbeitsgruppen.* Diplomarbeit, Christian-Albrechts-Universität zu Kiel.

Wermann, B. (2017) *Structural Design Concepts for Cell Culture Experiments on Sounding Rockets.* Masterarbeit, FH Aachen University of Applied Sciences.

Other Publications

Feles, S., Overath, C., Reichardt, S. (2017) *Die Etablierung der Neuroblastomzelllinie SY5Y als Modellsystem zur Abschätzung strahleninduzierter Schäden neuronaler Zellen bei einer bemannten Marsmission,* Fachschule für Technik am Kartäuserwall, Köln.

3. Events, Presentations and Talks

3.1 Institute Lectures

17.01.2017
Dr. Thomas Berger, Head Biophysics Group, Radiation Biology Department, Institute of Aerospace Medicine, German Aerospace Center, Cologne, Germany: **"Radiation measurements in space – Past and present experiments and new developments of the Radiation Biology Department"**

20.01.2017
Dr. Francesco Sartor, Research Scientist, Personal Health Department, Philips Research, Eindhoven, The Netherlands: **"Wearable sensing to facilitate mobile personal Health"**

07.02.2017
Dr. Michael Caspers, Clinic for Orthopaedics, Trauma Surgery and Sports Traumatology, Cologne Merheim, Germany: **"Risk factors for Venous Thromboembolism"**

21.02.2017
Dr. Matthias M. Meier, Radiation Biology Department, Institute of Aerospace Medicine, German Aerospace Center (DLR), Cologne, Germany: **"The Radiation Field at Aviation Altitudes"**

07.03.2017
Univ.-Prof. Dr. phil. nat. Florian Beißner, Endowment Professorship for Somatosensory and Vegetative Therapy Research, Hannover Medical School, Institute for Diagnostic and Interventional Neuroradiology, Hannover, Germany: **"Functional MRI of autonomic nuclei in the brainstem and hypothalamus"**

08.03.2017
Dr. Natalie Leys, Head of the Microbiology Research Unit at the Belgian Nuclear Research Center SCKCEN, Belgium: **"The use of microbes for oxygen, water and food production in space"**

09.05.2017
Prof. Dr. Hans-Peter Landolt, Institute of Pharmacology and Toxicology, University of Zürich, Zürich, Switzerland: **"Elucidating mechanisms of sleep-wake regulation in humans with pharmaco-genetic tools"**

16.05.2017
Prof. Dr. Gary R. Lewin, Head of the Group Molecular Physiology of Somatic Sensation, Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany: **"Molecular exploitation of an extremophile mammal: No oxygen, no problem"**

23.05.2017
Prof. Dr. Timothy Arnett, Professor of Mineralised Tissue Biology, Department of Cell & Developmental Biology, University College London (UCL), London, UK: **"The effects of hypoxia and acidosis on bone cells"**

13.06.2017
Prof. Dr. Thomas Illig, Managing Director and Scientific Director, Hannover Unified Biobank (HUB), Hannover Medical School (MHH), Hannover, Germany: **"Big data in medical research"**

29.08.2017
Dr. Peter Maschke, Head Department Aviation and Space Psychology, German Aerospace Center (DLR), Institute of Aerospace Medicine, Hamburg, Germany: **"Germanwings-Flug 9525: Der Absturz und die Konsequenzen"**

05.09.2017
Ass. iur. Yvonne Richter, Maître en droits français et allemand, German Aerospace Center (DLR), Legal Department, Cologne, Germany: **"Wissenschaft und Datenschutz. Umsetzung der Vorgaben des Datenschutzes in wissenschaftlichen Projekten des Instituts ME"**

11.10.2017
Boris Hespeels, Ph.D, Department of Biology (URBE), Laboratory of Evolutionary Genetics and Ecology (LEGE), Namur, Belgium: **"Bdelloid rotifers: new eukaryotic extremophile model organisms to study the impact of radiation and micro-gravity on biological processes?"**

17.10.2017
Miriam Capri, Ph.D, Assistant Professor, DIMES-Department of Experimental, Diagnostic and Specialty Medicine, CSR-Centro di Studio e Ricerca sull'Invecchiamento, CIG- Interdepartmental Centre "L. Galvani" for Bioinformatics, Biophysics and Biocomplexity, ALMA MATER STUDIORUM, University of Bologna, Bologna, Italy: **"Human ageing and microRNAs: the contribution of muscle tissue"**

25.10.2017
Prof. Dr. med. Walter E. Haefeli, University Hospital Heidelberg, Medical Clinic, Medical Director, Division of Clinical Pharmacology & Pharmacoepidemiology, Heidelberg, Germany: **"Ultrasensitive Massenspektrometrie von Arzneimitteln im Menschen: Von der Mikrodosierung zur Expositionsmessung in Bevölkerungen"**

26.10.2017
FLA Prof. Dr. med. Andreas Koch, Section of Maritime Medicine at the Institute for Experimental Medicine of the UKSH, Christian-Albrechts-Universität zu Kiel, c/o Marine Medical Institute of the Navy, Kronshagen, Germany: **"Risks and Adaptive Processes to Hyperoxia in Diving and Hyperbaric Oxygenation Therapy (HBO)"**

21.11.2017
Prof. Dr. Adam Cohen, Director, Centre for Human Drug Research (www.chdr.nl), Leiden, The Netherlands: **"Clinical Pharmacology ready for lift-off into method space"**

13.12.2017
Dr. Hélène Bœuf, Research Director, CNRS, INSERM U1026 BioTis, Université de Bordeaux, FRANCE: **"Hypoxia/ Physioxia regulates embryonic stem cell physiology"**

14.12.2017
Prof. Dr. med. Wolfgang Kummer, Institute of Anatomy and Cell Biology, Justus-Liebig-University, Gießen, Germany: **"The taste of infection"**

3.2 Workshops, Events, Seminars at the Institute

9.1.2017
Visit: "Research Track", Medical students, Cologne University

18.1.2017
Visit: Students Biomedical Engineering, RWTH Aachen

18.1.2017
Visit: DGLR

23.–25.1.2017
PPOSS Workshops
Workshops EU project "Planetary Protection of Outer Solar System" (PPOSS)

24.1.2017
Ministry of Defence Visitors Group

27._28.1.2017
51. Atmungs- und Leistungsphysiologische Arbeitstagung

7.2.2017
Visit: Students RWTH Aachen

9.2.2017
Visit: DJV Cologne

16.2.2017
Delegation of the Austrian Ministry of Transport, Innovation and Technology and School Group (winner of "Born to Explore" competition)

21.2.2017
Visit: Students Stuttgart University

1.3.2017
Visit: Students University of Bonn (Radiopharmacy)

10.3.2017
Visit: NEREUS delegation

14.3.2017
Visit: Free University of Berlin, John-F. Kennedy Institute of North American Studies

20.3.2017
Visit: Institute for Frontier Medical Sciences, Kyoto University

24.3.2017
Visit: Air Force

27.3.2017
Visit: KTH Royal Institute of Technology, Stockholm

27.4.2017
Girls Day

27.4.2017
Visit: Colloquium Humanum

27.4.2017
Visit: Participants Aircraft Noise Commissions

10.5.2017
Visit: Clinic for Anaesthesiology and Operative Intensive Care Medicine, University Hospital Bonn

16.5.2017
Visit: Ethical committee Cologne University

23.5.2017
Visit: "Research Track", Medical students, Cologne University

2.6.2017
Visit: Aeromedical Association of Belgium

14.6.2017
Visit: National Contact Points Space, Horizon 2020

28.6.2017
Visit: Physicians, course social medicine

3.7.2018
Visit: Deutsche Meteorologische Gesellschaft

11.7.2017
Visit: Representatives Federal Ministry of Education and Research

18.7.2017
Internal Lecture: Altitude Physiology

28.7.2017
Visit: Foundation Kinderherz

7.8.2017
Visit: Constituency representative Martin Dörmann with his constituency office

10.8.2017
Visit: Bonn University, Department of Human Nutrition

19.9.2017
Visit: DLR Graduate Program

20.9.2017
Visit: Military attachés

20.9.2017
Visit: Architects, Kölner Architekturpreis

25.9.2017
Visit: Representatives JAXA

20.10.2017
Association for General and Applied Microbiology (VAAM): First Topical Team Meeting "Space Microbiology"

27.10.2017
Visit: Minister Hendrik Wüst, Ministry of Transport of the State of North Rhine-Westphalia

2.11.2017
Visit: Representatives Bundeswehr

10.11.2017
Visit: Saxon Ministry of Economics

27.11.2017
Visit: Kölner Wissenschaftsrunde with Lord Mayor Henriette Reker

28.11.2017
Visit: Foundation Deutsche Sporthilfe with competitive athletes

29.11.2017
Visit: Participants workshop "Simulator Skill Acquisition, Maintenance and Evaluation Tool"

30.11.2017
Visit: Representatives ESA Houston Office

30.11.2017
Visit: Diplomats in the German Foreign Service

7.12.2017
Visit: Deutsche Akademie für Flug- und Reisemedizin

7.12.2017
Visit: Students RWTH and FH Aachen

8.12.2017
Visit: Participants "Adventure Day Space"

8.12.2017
Visit: Representatives Federal Ministry of Economics and Technology and Central Association of German Craft Trades

9.12.2017
2nd Human Physiology Workshop

11.12.2017
Visit: Students FH Aachen

14.12.2017
Visit: Research Field Officer Aeronautics, Space and Transport, Helmholtz Association

15.12.2017
Visit: Representatives Office for Environmental Protection, Rheinisch-Bergischer Kreis

15.12.2017
Visit: Chinese Manned Space Agency Delegation

18.12.2017
Visit: Students Bonn University

19.12.2017
Visit: China Astronaut Center

3.3 Teaching Activities

Name	University	Subject
Aeschbach, Daniel	Harvard Medical School	Sleep Medicine
Anken, Ralf	Universität Hohenheim	Zoologie
Baumstark-Khan, Christa	Hochschule Bonn-Rhein-Sieg	Strahlenbiologie
Berger, Thomas	Hochschule Bonn-Rhein-Sieg	Strahlenbiologie
Berger, Thomas	ISU Strasbourg	Radiation Physics & Biology
Elmenhorst, Eva-Maria	RWTH Aachen	Flug- und Reisemedizin
Elmenhorst, Eva-Maria	RWTH Aachen	Raumfahrtmedizin
Hauslage, Jens	ISU Strasbourg	Gravitationsbiologie
Goerke, Panja	FH Wedel	Communication Skills Group
Goerke, Panja	Universität Lüneburg	Vertiefungsseminar differentielle Psychologie
Goerke, Panja	FH Wedel	Communication Skills Group
Hemmersbach, Ruth	Universität Bonn	Zoologie
Hellweg, Christine	Hochschule Bonn-Rhein-Sieg	Strahlenbiologie
Hellweg, Christine	FU Berlin	Pathologie
Hellweg, Christine	FU Berlin	Immunologie
Hellweg, Christine	ISU Strasbourg	Radiation Physics & Biology
Hellweg, Christine	Universität Bonn	Strahlenbiologie

Name	University	Subject
Hellweg, Christine	Universität Köln	Weltraumphysiologie
Keye-Ehing, Doris	Universität Ulm	Angewandte Diagnostik in Luft- und Raumfahrt
Kölzer, Anna-Magdalena	FH Wedel	Communication Skills Group
Lindlar, Markus	Hochschule Bonn-Rhein-Sieg	Medizinische Informations-Systeme
Lindlar, Markus	Hochschule Bonn-Rhein-Sieg	Medizinische Businesssysteme
Lindlar, Markus	Hochschule Bonn-Rhein-Sieg	Health Telematics
Maier, Julia	ISM Hamburg	Einführung i. d. empirische Sozialforschung
Maschke, Peter	TU Hamburg Harburg	Faktor Mensch i. d. Luft- u. Seefahrt
Melcher, Wiebke	Leuphana-Universität Lüneburg	Einführung in die Psychologie
Melcher, Wiebke	Leuphana-Universität Lüneburg	Übung Interferenzstatistik II
Melcher, Wiebke	Leuphana-Universität Lüneburg	Computergesteuerte Datenanalyse
Mittelstädt, Justin	Universität Hamburg	Praktische Übungen zu diagnostischen Verfahren
Mittelstädt, Justin	Universität Hamburg	Psychodiagnostische Testverfahren
Pecena, Yvonne	ISU Strasbourg	Cognitive and personality testing
Pecena, Yvonne	ISU Cork	Space Psychology
Rittweger, Jörn/Jordan, Jens	Universität Köln	Humanmedizin
Stelling, Dirk	Hochschule Fresenius Hamburg	Differentielle Psychologie
Stern, Claudia	TU Braunschweig	Luft- und Raumfahrtmedizin
Tank, Jens	Medizinische Hochschule Hannover	Propädeutik
Zange, Jochen	Universität Köln	Physiologie
Zinn, Frank	Universität Köln	Diagnostik interaktiver Kompetenzen

4. Graduations

Supervised Doctoral Students

University	Space	Traffic	Aviation
RWTH Aachen	1	1	
Universität Bayreuth	2		
FU Berlin			1
Universität Bonn	1		
Universität Bremen	2		
Sporthochschule Cologne	4		
Universität Cologne	3		
TU Darmstadt	1		
Universität Dresden			2
Universität Duisburg-Essen	2		
Universität Erlangen-Nuremberg	2		
Universität Göttingen	2		
Universität Hamburg			3
Universität Hannover	1		
Universität Heidelberg	3		
Universität Konstanz	1		
King's College London, Great Britain	1		
Universität Lüneburg			1
Universität Magdeburg	1		
Universität Münster	1		
Universität Saarland, Homburg	2		

Doctorates

University	Space
Universität Cologne	1
Universität Eindhoven, Netherlands	1
King's College London, Great Britain	1
Universität Münster	1

Diploma Thesis/Master Degrees

University	Space	Aviation
FH Aachen	1	
Universität Bamberg		1
Universität Bonn		1
TU Dresden		1
Universität Stuttgart	1	
Universität Stuttgart-Hohenheim	1	
Universität Kiel		1
King's College London, Great Britain	1	
Universität Stockholm, Schweden	1	

Bachelor Degrees

University	Space
Hochschule Bonn-Rhein-Sieg	1
Universität Cologne	1
Universität Emden-Leer	1
Universität Magdeburg	1
Universität Osnabrück	1

5. Awards

Christian Liemersdorf, Timo Frett
ELGRA Research Prize 2017 für Live-cell Imaging of Neuronal Activity Changes under Altered Gravity

Denise Lange
Travel Grant der Nordrhein-Westfälischen Gesellschaft für Schlafmedizin

Denise Lange
Promotionsstipendium der Studienstiftung des Deutschen Volkes

Dajana Parganlija
Best Talk Award, Tagung Junge Physiologen

Karina Marshall Bowman
Nominierung Forbes 30 under 30 Science and Healthcare

Felix Fuchs
VAAM-Jahrestagung 2017 gemeinsam mit DGHM

6. Patents

Department Radiation Biology
United States Patent, 9.5.2017: **Method for providing a warning of radiation-dose-relevant space-weather events at cruising altitudes** (Patent No. 9,645,263 B2)

Department Muscle and Bone Metabolism
European Patent Office, 6.12.2017: **Unterschenkelorthese mit einer Schiene zur Ruhigstellung der Unterschenkelmuskulatur** (Patent No. 2755610)

Research Report Institute of Aerospace Medicine 2017_GB_02/2019

DLR at a glance

The German Aerospace Center (DLR) is the national aeronautics and space research centre of the Federal Republic of Germany. Its extensive research and development work in aeronautics, space, energy, transport, security and digitalisation is integrated into national and international cooperative ventures. In addition to its own research, as Germany's space agency, DLR has been given responsibility by the federal government for the planning and implementation of the German space programme. DLR is also the umbrella organisation for the nation's largest project management agency.

DLR has approximately 8000 employees at 20 locations in Germany: Cologne (headquarters), Augsburg, Berlin, Bonn, Braunschweig, Bremen, Bremerhaven, Dresden, Goettingen, Hamburg, Jena, Juelich, Lampoldshausen, Neustrelitz, Oberpfaffenhofen, Oldenburg, Stade, Stuttgart, Trauen, and Weilheim. DLR also has offices in Brussels, Paris, Tokyo and Washington D.C.

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