Human Physiology Workshop

8th December 2023

Venue: DLR
:envihab
Forum
51147 Cologne
Germany
Planitzweg

Human Physiology Workshop 2023

We are pleased to welcome you to the 8th German Human Physiology Workshop 2023. The workshop shall provide a forum for researchers at all stages (student to professor) to meet and discuss their latest findings in human physiological research and space research and give room for mutual exchange and benefit between space and non-space scientists.

Organizers

Jörn Rittweger, Claudia Kaiser-Stolz, Alexandra Noll, Willi Pustowalow, Friederike Wütscher (German Aerospace Center (DLR), Institute of Aerospace Medicine, Cologne)
Katrin Stang, Michaela Girgenrath, Christian Rogon (German Space Agency at DLR, Bonn)

humanphysiologie-ws@dlr.de

Jury

Markus Braun	German Aerospace Center (DLR), Space Agency, Research and Exploration/Life Sciences, Bonn, Germany
Tadej Debevec	University of Ljubljana, Faculty of Sports, Slovenia
Peter zu Eulenburg	LMU Munich, Germany
Joachim Fandrey	University of Duisburg-Essen, Institute of Physiology, Germany
Nandu Goswami	Medical University of Graz, Institute of Physiology, Gravitational Physiology and Medicine, Graz, Austria
Bruno Grassi	University of Udine, Department of Medicine, Italy
Markus Gruber	University of Constance, Sensorimotor Performance Lab, Germany
Peter Hodkinson	King's College London, Centre for Human & Applied Physiological Sciences, UK
Ylva Hellsten	University of Copenhagen, Department of Nutrition Exercise and Sports, Denmark
Jens Jordan	German Aerospace Center (DLR), Institute of Aerospace Medicine, Cologne, Germany
Tobias Kammerer	University Hospital Cologne, Germany
Justin Lawley	University of Innsbruck, Department of Sport Medicine, Austria
Anja Niehoff	German Sport University, Institute of Biomechanics and Orthopaedics, Cologne, Germany
Oliver Opatz	Charité Medical University, Center for Space Medicine and Extreme Environments, Institute of Physiology, Berlin, Germany
Barbara Pospieszna	Poznan University of Physical Education, Department of Athletics, Strength and Conditioning, Poland
Jörn Rittweger	German Aerospace Center (DLR), Institute of Aerospace Medicine, Space Physiology, Cologne, Germany
Stefan Sammito	Oberfeldarzt, Zentrum für Luft- und Raumfahrtmedizin der Luftwaffe, Cologne, Germany
Tobias Weber	ESA, Cologne, Germany
Rob C. I. Wüst	Vrije Universiteit Amsterdam, Faculty of Behavioural and Movement Sciences, the Netherlands

Program

Friday, December 8, 2023

08:00 **Registration**

08:30 **Welcome (DLR)**

Session 1:

Chair: Reinhold Ewald & Alberto Minetti

08:45 **(1) Ebner, Ines:** Changes in physical activity levels and gait parameters after 60-days of 6°Head-Down-Tilt Bed Rest (HDT-BR) – a preliminary data analysis

09:00 **(2) Luciano, Francesco:** Runners inside an emulated Lunar 'Wall-of-Death' self-generate high enough artificial gravity to potentially fight muscle/bone/neurocontrol/cardiovascular deconditioning

09:15 **(3) Bothe, Tomas L.:** COOLFLY – cooling counters cardiovascular instability during parabolic flights: A first look at the final results

09:30 **(4) Henkel, Sara:** Influence of ambient temperature on resting energy expenditure in metabolically healthy women and men

09:45 **(5) Böcker, Jonas:** Quantification of acceptance and feasibility for implementation of a training algorithm in a nursing home environment

10:00–10:30 Coffee break

Session 2:

Chairs: Joachim Fandrey & Anja Niehoff

10:30 **(6) Burger, Nicole:** Assessing immune function in space: Validation of an in-vitro CR-assay setup for astronaut immune monitoring

10:45 **(7) Kowalski, Tomasz:** Respiratory muscle training induces additional stress and training load in well-trained athletes – randomized controlled trial

11:00 **(8) Son, Yuliya:** Investigating the immune status of cosmonauts after a long-term spaceflight: Implications for wound healing

11:15 **(9) Badalì, Constance:** SpaceBike – The influence of immobilisation on neuromuscular performance (preliminary data)

11:30 **(10) Tang, Ge:** Longitudinal brain-age predictions encompassing long-duration spaceflight missions

11:45–12:45 Lunch break

Session 3:

Chairs: Isabelle Mack & Stefan Schneider

12:45 **(11) Possnig, Carmen:** Low level lower body negative pressure attenuates the decrease in cerebral blood flow during bed rest

13:00 **(12) Fisher, Jason T.:** Haemodynamic and microvascular responses to Combined hypergravity, heat stress and hypoxia

13:15 (**13) Michno, Manuel:** Effect of acute hypoxia exposure on the availability of A1 adenosine receptors in the human brain measured with [F-18]CPFPX PET

13:30 **(14) Möller, Fabian:** Ground-based validation of transcutaneous PCO_2 measurements by blood gas analysis

13:45 **(15) Calà, Edoardo:** Influence of Muscle Architecture on Muscle Perfusion in Bed Rest

14:00–14:30 Coffee break

Session 4:

Chairs: Rob Wüst & Kirsten Albracht

14:30 **(16) Faivre-Rampant, Victorien:** The effect of reduced rostrocaudal gravitational load on cardiac function

14:45 **(17) Meinhold, Marius:** Exploring the role of the Hippo pathway member Yap in a model of Duchenne Muscular Dystrophy

15:00 **(18) Charlton, Braeden T.:** Physical inactivity does not explain exercise intolerance and skeletal muscle adaptations in long COVID

15:15 **(19) Klos, Bea:** The effects of a one-year antarctic sojourn at the Concordia Research Station on olfactory and gustatory functions

15:30 **(20) Jacko, Daniel:** Resistance exercise and training alters desmin phosphorylation in human skeletal muscle and makes it less prone to degradation

15.45–16:45 Andrea Casini:
How the LUNA facility enables research for a human presence on Moon

16.45–17.00 Awards

17:00 Adjourn

1

Changes in physical activity levels and gait parameters after 60-days of 6°Head-Down-Tilt Bed Rest (HDT-BR) – a preliminary data analysis

Ines Ebner[1,2], Birte Coppers[1,2], Elie-Tino Godonou[1,2], Maren Dreiner[3], Simon Herger[4,5,6], Annegret Mündermann[4,5,6], Georg Schett[1,2], Anja Niehoff[3,7], Anna-Maria Liphardt[1,2]

[1] Dept. of Internal Medicine 3 – Rheumatology & Immunology, Universitätsklinikum Erlangen & Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg, Germany
[2] Deutsches Zentrum Immuntherapie (DZI), Universitätsklinikum Erlangen & FAU Erlangen-Nürnberg, Germany
[3] Inst. of Biomechanics and Orthopaedics, German Sport University Cologne
[4] Dept. of Biomedical Engineering, University of Basel, Allschwil, Switzerland
[5] Dept. of Orthopeadics and Traumatology, University Hospital Basel, Switzerland
[6] Dept. of Spine surgery, University Hospital Basel, Switzerland
[7] Cologne Center for Musculoskeletal Biomechanics (CCMB), Medical Faculty, University of Cologne, Köln, Germany

Introduction: Disuse leads to deconditioning of the human body. Physical activity and gait parameters are important indicators of physical function and could serve as predictors of the rate of deterioration and responsiveness to countermeasures. The aim of this study is to investigate accelerometer-based physical activity and spatiotemporal gait parameters before, during and after 60 days of 6° head-downtilt bed rest (HDT) with and without artificial gravity and exercise countermeasures.

Methods: The data were collected during the European Space Agency (ESA)-funded "Bed Rest with Artificial gravity and Cycling Exercise (BRACE)" study, a randomized controlled trial with two campaigns (C1, C2) and three interventions (60 days of 6° head-down-tilt bed rest (HDT), HDT+cycling, and HDT+articifical gravity (AG)+cycling. HDT was preceded by 14 days of baseline data collection (BDC) and followed by 14 days of recovery (R). This is the preliminary analysis of twelve healthy male participants (age 30.3 ± 5.9 years; body mass index 23.3 ± 2.1 kg/m²) of C1. Physical activity (inactive (IN), light (LIG), moderate (MOD), and vigorous (VIG))[1] was collected by wrist-worn (non-dominant) accelerometry (GENEActiv, Activinsights Ltd, Kimbolton, UK) before C1 (preStudy (BDC-28 to BDC-14), during (HDT18 to HDT23) and after C1 (R+0 to R+13, R+14 to R+28) and analyzed with R-package GGIR[2]. Spatiotemporal gait parameters walking speed, total number of steps (SteN), cadence (Cd), stride time (StrT) and stride length (StrL) were collected on BDC-4, R+2 and R+29 with a seven-inertial-sensors system (RehaGait Analyzer Pro, Hasomed, Magdeburg, Germany) during a 30-minute treadmill walking protocol. Univariate and repeated measures ANOVAs were computed to detect changes in the physical activity parameters and spatiotemporal gait parameters over time and by intervention with Bonferroni corrected post-hoc tests.

Results: Time significantly affected IN (preStudy vs. HDT23: +26.8% ± 17.1; preStudy vs. R+28: - 4.5% ± 9.7; $F_{1.4,8.42}$=24.30; p=0.001), LIG (preStudy vs. HDT23: -53.8% ± 13.9; preStudy vs. R+28: +29.3% ± 33.6; $F_{1.51,9.05}$=27.12; p<0.001) and MOD (preStudy vs. HDT23: -69.3% ± 14.0; preStudy vs. R+28: +44.9% ± 54.7; $F_{4,24}$=15.66; p<0.001), but not VIG (preStudy vs. HDT23: -91.1% ± 11.9: preStudy vs. R+28: -19.8% ± 42.8; p=0.132). There was no intervention effect on any physical activity parameter (group: all p-values> 0.336; time*group: all p-values > 0.246). There were no time effect (all p-values > 0.083), and no time*group interactions (all p-values > 0.387) on any gait parameters. Control group participants had slower walking speed (HDT: 3.86 km/h ± 0.51; HDT+AG+cycling: 4.13 km/h ± 0.25; HDT+cycling: 4.08 km/h ± 0.10; $F_{2,9}$=4.388; p=0.047 and shorter StrL (HDT: 1.08 m ± 0.11; HDT+AG+cycling: 1.22 ± 0.06; HDT+cycling: 1.26 ± 0.05; $F_{2,9}$=5.995; p=0.022) at BDC compared with HDT+cycling and HDT+AG+cycling and the difference persisted at all time points.

Conclusions: Physical activity levels did not differ between the groups, but as expected, time spent in moderate and low activity changed over time and already between the preStudy and the ambulatory BDC period. Despite attempts to maintain preStudy physical activity levels during BDC, an increase in time spent inactive is evident. The intra-individual changes in physical activity from preStudy to HDT will allow to investigate the influence of habitual physical activity routines, and intra-individual differences should be considered when interpreting results on the response of the musculoskeletal system to immobilization. Walking speed and stride length during the gait experiment were lower in the control condition compared to the interventions, with no change over time.

References: [1]Hildebrand M et al. 2017, Scand J Med Sci Sports 27:1814-1823
[2]Migueles JH et al. 2019, J Meas Phys Behav. 2(3), 188-196

2

Runners inside an emulated Lunar 'Wall-of-Death' self-generate high enough artificial gravity to potentially fight muscle/bone/neurocontrol /cardiovascular deconditioning

Alberto E. Minetti, Gaspare Pavei, Valentina Natalucci, *Francesco Luciano*

University of Milano, Dept. of Pathophysiology and Transplants, Italy

Introduction: Despite the ongoing Artemis Space Program1, promising in a few years time Lunar and Martian permanent settlements, and the shared awareness that long-lasting exposition to low gravity elicits in humans an impairing combination of muscle hypotrophy, bone demineralization, and cardiovascular, neurocontrol deconditioning, no consensus has been reached so far on the simplest, sustainable, and shortest training regime to adopt as a countermeasure.
Gym machines often focus on selected muscle groups, while more ancestral, 'whole-body' activities such as locomotion are also impaired due to low gravity. Walking on the Moon suffers from the imbalance between kinetic and potential energy of the body centre of mass2: to re-establish that balance, the speed range must restrict to low values, nullifying training. Bouncing gaits as running3, skipping4 and hopping5 are faster than walking, while exhibiting some mechanical mismatch within the muscle-tendon complex6, in part preventing a terrestrial-like, high-impact training.

Methods: Here we firstly investigated running horizontally inside a passive 5 m radius, 4 m tall cylinder (WoD, Wall of Death, an amusement park attraction), at emulated Lunar gravity and speeds that prevented falling, as a viable countermeasure when on low gravity celestial bodies, through a much higher, selfgenerated (lateral) artificial gravity. Subjects, whose weight was 83% unloaded by programmatically pre-tensed 36 m high bungee jumping bands7, were videorecorded and motion analysis was performed.

Results: While on Earth only fast motorized vehicles can move in WoDs, our subjects unprecedentedly managed to initiate and maintain horizontal running at Lunar emulated gravity. The chosen speeds were 40-80% higher than the theoretical minimum (to prevent falling), with average contact forces corresponding to 50-73% of Earth gravity, and intense metabolism (estimated8 as 40-45 mlO2/kg/min). Motion analysis showed high enough impacts at landings to inhibit, via Piezo Channel stimulation9, bone calcium resorption10.

Conclusions: We anticipate our findings will promote passive, low-gravity WoDs, optimally designed for running, where astronauts could (have fun and quickly) preserve their overall locomotion fitness when on the Moon, during further space exploration and in preparation for the return back home.

References:
1) www.nasa.gov/specials/artemis-accords/index.html
2) Minetti A. E. Nature 409: 467-469, 2001.
3) Margaria, R. & Cavagna, G. Aerospace Med. 35, 1140–1146, 1964.
4) Minetti A. E. Proc. R. Soc. B 265: 1227-1235, 1998.
5) Pavei G. & A. E. Minetti. J. Appl. Physiol. 120(10): 1223-9, DOI:
10.1152/japplphysiol.00839.2015, 2015.
6) Waldvogel J. et al. Front. Physiol. 12:614060. doi: 10.3389/fphys.2021.614060, 2021.
7) LOOP Facility in Milan:
www.esa.int/Science_Exploration/Human_and_Robotic_Exploration/The_science_of_Moon_hopping
8) Pavei G., Biancardi C. M. and A. E. Minetti. J. Appl. Physiol. 119(1): 93-100, doi:
10.1152/japplphysiol.01021.2014, 2015
9) Xu X. et al. Int. J. Mol. Sci. 22, 6429. https://doi.org/10.3390/ijms22126429, 2021.
10) Kramer A., et al. Sci Rep. 7(1):13177. doi:10.1038/s41598-017-13659-8, 2017.

3

COOLFLY – cooling counters cardiovascular instability during parabolic flights: A first look at the final results

Tomas L. Bothe[1], Niklas Pilz[1,2], Oliver Opatz[1]

[1] Charité Universitätsmedizin Berlin, Institute of Physiology, Center for Space Medicine and Extreme Environments, Berlin, Germany
[2] Charité Universitätsmedizin Berlin, Institute of Translational Physiology, Berlin, Germany

Introduction: The study focuses on maintaining cardiovascular stability, essential for the success of human spaceflight. Astronauts and military pilots face dynamic acceleration conditions that cause peripheral blood pooling and cardiovascular instability, including sudden or prolonged drops in blood pressure and risk of loss of consciousness. We investigated the use of peripheral cooling to reduce this blood pooling during parabolic flights. Our hypothesis was that peripheral cooling would mitigate the effects of peripheral blood pooling in hyper-gravity conditions. The outcomes of this study are aimed at informing the design of new countermeasure systems for human spaceflight.

Methods: Over the course of the 39th to 41st DLR parabolic flight campaigns, 17 healthy participants were recruited for the study. During the first 15 parabolas, one subject was equipped with a peripheral cooling system targeting the legs, thighs, and waist, while maintaining an upright standing position. A different participant was similarly instrumented for the subsequent set of 15 parabolic trajectories. In a cross-over design, where each participant served as their own control, each subject flew twice, being under physiological measurement once cooled and once uncooled (control) for 15 parabolas.
The study aimed to investigate the effects of peripheral cooling on venous blood pooling and cardiovascular stability. To this end, a suite of non-invasive diagnostic tools was employed. Continuous blood pressure and pulse wave velocity were monitored, along with peripheral perfusion metrics, gathered via both laser Doppler and near-infrared spectroscopy techniques. The laser Doppler and near-infrared sensors were strategically positioned on the lower extremities and forehead (near-infrared, brain perfusion), while continuous blood pressure data were collected from the left arm using pulse transit time analysis.

Results: Our findings demonstrate the advantageous impact of peripheral cooling on hemodynamic stability, particularly in blood pressure and perfusion, under conditions of hyper-gravitational stress. The most marked cardiovascular responses were observed during the transitional phases into hyper-gravity— specifically, during the pull-up maneuvers preceding and following the micro-gravitational state. These transitions were characterized by substantive reductions in blood pressure, attenuations in peripheral and microvascular perfusion, and an elongation of both peripheral and central pulse wave velocities. The peripheral cooling system effectively ameliorated these perturbations, both by dampening the magnitude of fluctuation between micro/normo- and hyper-gravitational states and by elevating the baseline levels of perfusion and, critically, blood pressure.
Notably, the variations in blood pressure during gravitational transitions were attenuated by over 50%, alongside elevated mean arterial pressure levels. Perfusion indices also indicated enhanced stability and continuity in tissue perfusion during the cooling intervention. Moreover, subjective evaluations from all participants revealed a strong preference for the cooled state, along with reports of a perceptible beneficial effect.

Conclusions: The study substantiates the practicality of employing a peripheral cooling system as an effective countermeasure in parabolic flight scenarios. This has implications not only for astronautics and military aviation but also for clinical populations subjected to extended periods of bed rest or patients with acute cardiovascular decompensation is states of shock. Owing to its non-pharmacological basis, the cooling intervention presents a minimized risk profile in terms of potential side effects and an easily applicable, low inhibition threshold countermeasure.

4

Influence of ambient temperature on resting energy expenditure in metabolically healthy women and men

Sara Henkel[1], Petra Frings-Meuthen[2], Christina Diekmann[1], Martin Coenen[3], Birgit Stoffel-Wagner[3], Robert Németh[4], Dominik Pesta[2], Sarah Egert[1]

[1] University of Bonn, Institute of Nutritional and Food Sciences, Bonn, Germany
[2] German Aerospace Center, Institute of Aerospace Medicine, Cologne, Germany
[3] University Hospital Bonn, Institute of Clinical Chemistry and Pharmacology, Bonn, Germany
[4] University Hospital Bonn, Institute of Medical Biometry, Informatics and Epidemiology (IMBIE), Bonn, Germany

Introduction: The determination of resting energy expenditure (REE) forms the basis for the calculation of the total energy expenditure (TEE) of an individual per day. The REE makes up the largest part of TEE with approx. 50-70 % and can be determined by a respiratory gas analysis according to the principle of indirect calorimetry, e.g. by canopy method. REE mainly depends on the amount of lean body mass, as well as age, sex and total body mass. Another influencing factor is the maintenance of core body temperature. Both the regulatory mechanisms for heat production and heat release increase the REE. Current studies provide evidence for changes in REE with various temperature exposures over a prolonged period of time. However, it is not yet clear to what extent the physiological regulatory mechanisms for maintaining core body temperature are reflected by changes in REE even after short exposures to different ambient temperatures.

Methods: The present study investigated the influence of a 1-hour exposure of 18 °C (cool room temperature), 22 °C (room temperature), 28 °C (thermoneutral zone) and 38 °C (heat) on REE derived from assessing VO_2 and VCO_2 from indirect calorimetry. Interventions were performed on four consecutive days in a randomized order. Based on *a priori* sample size calculation, a total of 32 metabolically healthy participants (16 m, 16 f, age: 25 ± 3 years, BMI: 22,4 ± 1,6 kg/m²) were included in the study after a screening examination. Statistical analysis included determination of main REE determinants via multiple linear regression models. Subsequently, linearly mixed models were calculated to determine the effects of the different ambient temperatures and predefined REE determinants on the outcome measures.

Results: Multiple linear regression revealed that lean body mass, ambient temperature and heart rate were the most important REE determinants (all $p<0.001$), which could explain 61.3 % of the variance in REE. Due to the correlation between heart rate and core temperature ($r=0.426$, $p<0.001$), heart rate was excluded as an influencing factor in the main linear mixed model. The main linear mixed model (without heart rate) revealed lean mass ($p<0.001$) and ambient temperature ($p=0.001$) to have a significant influence on REE. The following regression formula can be formulated for REE determination at 38 °C: REE (kcal/24 h) = 780.761 + 15.87 * lean mass – 61.382 (female sex) + 57.302 (18 °C) + 33.873 (22 °C) – 38.703 (28 °C). Furthermore, there were significant differences in REE between 18:28 °C ($p<0.001$), 18:38 °C ($p=0.016$) and 22:28 °C ($p=0.003$).

Conclusions: In addition to the lean body mass, the REE is significantly influenced by the ambient temperature, which is already detectable after a short 1-hour exposure. According to the thermoneutral zone of humans, the REE is lowest at 28 °C, as less energy has to be converted to maintain the core body temperature compared to the cooler temperatures of 18 °C and 22 °C.

5

Quantification of Acceptance and Feasibility for Implementation of a Training Algorithm in a Nursing Home Environment

Jonas Böcker[1], Ludwig Sachs[1,2], Michael Drey[3], Claudia Kaiser-Stolz[1], Anja Dekant[4], Wilhelm Bloch[5], Jörn Rittweger[1,6]

[1] Department of Muscle and Bone Metabolism, Institute of Aerospace Medicine, German Aerospace Center, Cologne, Germany
[2] Specialist in psychosomatic medicine and psychotherapy, Bad Endorf, Bavaria, Germany
[3] Department of Internal Medicine IV, Ludwig-Maximilians-University of Munich, Munich, Germany
[4] Medical Director Cluster, Orpea Germany GmbH, Frankfurt am Main, Hessen, Germany
[5] Section Molecular and Cellular Sports Medicine, German Sport University Cologne, Cologne, Germany
[6] Department of Pediatrics and Adolescent Medicine, University of Cologne, Cologne, Germany

Introduction: Age-related muscle wasting (sarcopenia) and weakness is a growing problem in society. The loss of muscle strength results in a loss of autonomy, social participation and therefore quality of life. Resistance training is the only effective therapy that is known, and its efficacy has been repeatedly demonstrated. Even though training concepts exist even for nursing homes, these concepts are often difficult and costly to be implemented. In other words, their roll-out is probably hindered by poor feasibility or poor acceptance. Therefore, this study aimed to investigate a new training algorithm regarding acceptance and feasibility in a nursing home setting. Furthermore, the reliability of endpoint measurements to quantify the effects of the training intervention should be measured.

Methods: A 4-week training intervention (5 sessions per week from Monday to Friday) was implemented in five nursing homes, the purpose of which was to quantify the acceptability and feasibility of the training algorithm. Quantitative information was assessed by means of training documentation by the nursing staff who instructed the training sessions after briefing. To determine the reliability as well as the efficacy of the training algorithm, measurements of physical performance, which are also used for the diagnosis of muscle weakness, were performed both before and after the intervention.

Results: Quantification of acceptability and feasibility turned out to be more difficult than anticipated, despite a generally high motivation of staff and nursing home residents to participate in the study. Thus, the Corona pandemic led to unavailability of staff, thereby to cancellation of an unknown number of training sessions, and to incomplete documentation. In total, 275 documentations of training sessions of the participants were present. Compared to the initial planned 560 training sessions (28 included participants with intended 20 training sessions), it corresponds to a rate of 49%. 7% of these documented training sessions were carried out, among the study protocol, during the weekend. The results of physical performance showed that both female and male participants were mostly below the threshold for sarcopenia in the results of grip strength (male: 64%, female: 60%) as well as gait speed (male: 73%, female: 60%). Only for the fat-free mass just a lower number of participants was below the cutoff for sarcopenia (male: 27%, female: 36%). However, the power achieved in the jump test was also below the cutoff for sarcopenia. The reliability of the performed measurements all showed an intraclass correlation coefficient >=0.84, so that a good to excellent reliability was present. After four weeks of intervention, a decrease in percent body fat could be determined (p=0.046), no other parameters showed a difference from PRE to POST.

Conclusions: In principle, the acceptance and feasibility of the new training algorithm is given, although the present study failed to provide full documentation of this. The measurements performed are reliable, i.e. they can demonstrate training-related differences. A first adaptation due to the training could be measured. Based on this information, we are now able to power a longer-lasting intervention study to test the training algorithm for efficacy.

6

Assessing immune function in space: Validation of an in-vitro CR-assay setup for astronaut immune monitoring

Nicole Burger[1], *Alexander Choukér*[1], *Judith-Irina Buchheim*[1], *and the Immunity Assay Study Group*[#]

[1] Laboratory for Translational Research "Stress & Immunity", Dpt. of Anesthesiology, LMU University Hospital, LMU Munich, Germany
[#] Immunity Assay Study Group: M. Feuerecker, R. Quintens, B. Baselet, R. Vermeesen, B. Crucian

Introduction: Space is an extreme environment for humans. Space travel affects immunity and results in immune dysregulation. These effects, such as hypersensitivity rashes, cold sores and prolonged congestion have been shown to occur during and immediately after flight. Inflight data on immune function remains scarce due to the limited ability to analyze human samples on board. The cytokine release assay (CRA) assesses the immune response after stimulation with antigens *ex vivo* and allows quantification of cell-mediated immunity in form of pro- and anti-inflammatory cytokine concentrations. So far, the CRA has been applied in space studies on ground only.
The focus of this study was to systematically assess the reliability of a novel reaction tube (RT) hardware designed by Kayser Italia (Livorno, Italy) for inflight implementation of the CRA on board.

Methods: We conducted two separate sets of experiments. In the first set, we filled the RTs with eight different stimulants, comprising negative and positive controls, and froze them for prolonged time intervals inside the RT to observe storage effects of stimulants. These intervals simulate the duration between filling and upload of RTs to the International Space Station (ISS) and their usage onboard. After storage, whole blood was transferred into the RTs and the CRA executed and analyzed according to the standard protocol.
In the second set, we wanted to investigate the effect of storage time on samples which already underwent stimulation until download to Earth and final cytokine analysis in the Lab. We stimulated whole blood from three healthy donors with five different conditions and froze the stimulated samples again for prolonged time intervals inside the RTs. The cytokine concentrations after storage were compared with cytokine concentrations measured immediately. Cytokine measurements were executed using the Multiplex system by MagPix (Luminex Corporation, Austin, Texas). We assessed the accuracy of filling the reaction tubes by weight, which served as a surrogate parameter for handleability.

Results: The reaction tubes were filled consistently and almost perfectly with a 0.5 ml target volume, as shown by a minimal standard deviation of 0.01 ml, a critical prerequisite for the cytokine measurements. Proinflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), Interferon gamma (IFN-γ), and interleukin-10 (IL-10) were measured. Stimulation of whole blood in the reaction tube with a positive control (Pokeweed mitogen) resulted in a significant increase in cytokine levels of IL6, TNF-α, IFN-γ, and IL-10 ($p = 0.05$).
Additional examination revealed important results: (1) In set-up 1, measurement of cytokines at different time points after prolonged freezing exhibited a persistent cytokine response at every time point. (2) Parallel trends were observed in cytokine levels between subjects after receiving stimulation with the same antigens in set-up 2.
These results demonstrate the reliability of the novel CRA set-up and its capability in studying cytokine responses with precise experimentation handling on board the ISS.

Conclusions: In summary, the new hardware configuration has proven effective for the execution of the *in vitro* CRA meeting the operational requirements of a spaceflight experiment. Handling of the reaction tubes can be easily executed by non-medically trained personnel. The results are reliable, even after prolonged freezing and storage of stimulants and allows monitoring the astronauts' immune system dynamically in response to varying stimuli. Notably, this setup has recently been successfully applied for the first time on the ISS in the frame of the ESA IMMUNITY ASSAY project.

7

Respiratory muscle training induces additional stress and training load in well-trained athletes – randomized controlled trial

Tomasz Kowalski[1], *Kinga Rebis*[1], *Przemysław Seweryn Kasiak*[2], *Andrzej Klusiewicz*[3], Dominika Granda[4], Szczepan Wiecha[3]

[1] Department of Physiology, Institute of Sport, National Research Institute, Warsaw, Poland
[2] 3rd Department of Internal Medicine and Cardiology, Medical University of Warsaw, Warsaw, Poland
[3] Department of Physical Education and Health in Biala Podlaska, Faculty in Biala Podlaska, Jozef Pilsudski University of Physical Education in Warsaw, Biala Podlaska, Poland
[4] Department of Nutrition Physiology and Dietetics, Institute of Sport, National Research Institute, Warsaw, Poland

Introduction: Respiratory muscle training (RMT) has been investigated in the context of improved athletic performance and pulmonary function. However, psychophysiological costs of RMT remain understudied. Voluntary isocapnic hyperpnoea (VIH) and inspiratory pressure threshold loading (IPTL) are widely applied RMT methods. The main purposes of this study were to assess whether RMT induces additional load on athletes and determine differences in RMT-induced load between sexes and applied methods.

Methods: 16 well-trained triathletes (n = 16, 56% males) underwent 6 weeks of VIH or IPTL program with progressive overload. Blood markers, subjective measures, cardiac indices, near-infrared spectroscopy indices, inspiratory muscle fatigue, and RMT-induced training load were monitored pre-, in and post-sessions. We used multiple ANOVA to investigate effects of sex, training method, and time on measured parameters.

Results: There were significant interactions for acid-base balance ($p = 0.04$ for sex, $p < 0.001$ for method), partial carbon dioxide pressure ($p = 0.03$ for sex, $p < 0.001$ for method), bicarbonate ($p = 0.01$ for method), lactate ($p < 0.001$ for method), RMT-induced training load ($p = 0.001$ for method for single session, $p = 0.03$ for method per week), average heart rate ($p = 0.03$ for sex), maximum heart rate ($p = 0.02$ for sex), intercostales muscle oxygenation ($p = 0.007$ for testing week), and intercostales muscle oxygenation recovery ($p = 0.003$ for testing week and $p = 0.007$ for method).

Conclusions: We found that RMT induced additional load in well-trained athletes. Elicited changes in monitored variables depend on sex and training method. VIH significantly increased subjective training load measures. IPTL was associated with disbalance in blood gasometry, increase in lactate, and reports of headaches and dizziness. Both methods should be applied with consideration in high performance settings.

More to come: We plan to expand the aforementioned experiment with measuring acute effects of RMT on blood gasometry and hormonal secretion in active population. We are confident that we will be able to present our findings in December. Preliminary results suggest that RMT significantly influences both with noteworthy method- and sex-related differences.

8

Investigating the immune status of cosmonauts after a long-term spaceflight: Implications for wound healing

Yuliya Son[1], Alexander Choukér[1], Judith-Irina Buchheim[1] for the #IMMUNO-2/WHISPER-study group

[1] Laboratory of Translational Research "Stress and Immunity", Department of Anesthesiology, LMU University Hospital, LMU Munich, Germany
[#] IMMUNO-2/ WHISPER-study group: S. Matzel, K. Biere, M. Hoerl, M. Feuerecker, M. Rykova, G. Vassieleva, S. Ponomarev, D. Moser, M. Monici

Introduction: The hostile conditions of space, characterized by microgravity and hazardous environments, exert significant psychological and physiological challenges for the human body. Among the numerous physiological concerns, the occurrence of wounds poses a significant risk during space missions. Wound healing is a pivotal physiological process, marked by an acute and targeted inflammatory response, vital for regeneration and recovery. Cosmonauts aboard the International Space Station (ISS) operate within a demanding environment, facing elevated workloads and daily stressors, which can compromise immune function. As a result, the conventional wound healing process can be disrupted, resulting in delayed wound closure.

Methods: This study (Funding numbers: WHISPER: 4000130928/20/NL/PG/pt; IMMUNO-2: ELIPS 3 and 4 and SciSpaceE programs and 50WB0919, 50WB1319 and 50WB1622) investigates the immune status and wound healing processes of seven cosmonauts, each enduring a minimum of five months on the ISS during long-term missions. Extensive measurements and surveys were conducted from pre-flight to post-flight, including three critical in-flight time points. Wound healing surveys provided subjective insights, while a multidimensional approach integrated various questionnaires to evaluate psychological factors that may influence wound healing outcomes. Stress levels were assessed via the State Trait Anxiety Inventory (STAI), Profile of Mood States (POMS), and Current Stress Test (CST). Complementing this, we evaluated stress levels through objective measures, including endocannabinoid concentrations and the cortisone level in the hair samples. Additionally, we conducted assessments to determine blood count parameters and investigated T-cell subsets (phenotypic profiles) using flow cytometry. Furthermore, the whole blood samples were in-vitro stimulated with lipopolysaccharide (LPS) for 24h and 48h, respectively. Cytokine concentrations, among others, pro-inflammatory IL-1β, were measured utilizing the magnetic bead cytokine assay and evaluated using the MAGPIX multiplex system. We plotted the obtained data in a descriptive way to show the individual variations.

Results: We observed the responses to the wound healing surveys to diverge within our study group, leading to classification into three groups: expedited, decelerated, and unaltered healing. Despite the demanding conditions of space travel, stress level tests consistently indicated a moderate perception of stress among the cosmonauts during their missions. However, elevated endocannabinoid and cortisone levels in hair samples were measured after landing, indicating a somatic stress response. Blood cell count results corroborated previous findings. Notably, we observed a relative shift from $CD8^+CD28^-$ effector to $CD8^+CD45RA^-$ memory immune cell populations. The IL-1β levels after LPS stimulation revealed two cohorts: cosmonauts with slower wound healing experienced reduced IL-1β production, whereas IL-1β production of those with expedited wound healing was not impaired.

Conclusions: Prolonged exposure to space can cause stress despite rigorous cosmonaut preparations. This stress can lead to individual immune system variations, which affect core processes in the body, such as wound healing. Extended space exposure may induce stress-related immune cell shifts, leading to a less responsive immune system and delayed immune responses, also impacting wound healing. Additionally, disruptions in cytokine production of cosmonauts reporting slower wound healing suggest impaired T-cell responses. This study underscores significant heterogeneity in wound healing responses among cosmonauts during spaceflight, emphasizing a profound variability in individual reactions to the space environment.

9

SpaceBike – The influence of immobilisation on neuromuscular performance (preliminary data)

Constance Badalì, Petra Wollseiffen, Stefan Schneider

German Sport University Cologne, Institute of Movement and Neurosciences, Cologne, Germany

Introduction: Throughout evolution, human movement has always been a key factor for manned space exploration. Regarding the current plans of lunar and Martian exploration, the significance of the human motor system resurfaces. This system relies on well-established neuronal networks called motor engrams. These motor engrams are responsible for automated movements like running, walking, and cycling and are generally stable; however external parameters can affect them. An increased intracranial pressure (ICP) can impact their functionality as observed in astronauts who experience a fluid redistribution in microgravity. In addition, astronauts report limitations in their visual, vestibular and motor systems after living in a non-gravitational environment for six months. Research has already demonstrated that reduced gravity alters neural communication [1]. By using a stable, automated movement pattern, like cycling, it is possible to assess the impact of environmental changes, e.g. a permanently increased ICP, on neuronal activation patterns. Previous studies showed the ability to localise cortical activity during cycling through electroencephalography (EEG) and combine it with electromyography (EMG), where EEG and EMG revealed stable oscillations and a strong correlation [2]. The SpaceBike project aims to enhance knowledge of the interaction between mechanical factors of muscle physiology and the corresponding neuromuscular regulation in evolving environmental conditions and their impact on the human body. It is hypothesised that the engrams responsible for controlling cycling undergo changes or instability. The findings will be relevant in establishing appropriate countermeasures for astronauts and for rehabilitation strategies in neurological recovery.

Methods: Data presented here were recorded on a recumbent bike at baseline (BDC-3) and the recovery phase (R+3) during a 60-day head-down tilt bed rest study in Toulouse, France. The participants (n=12) were subdivided into three groups with training interventions six times per week: Cycling with artificial gravity (AG+EX), only cycling (EX) and control group (CON) with no countermeasure. In our experiment every participant performed a submaximal incremental cycling task, starting with a load of 1 W/kg body weight and increasing by 1 W/kg body weight every two minutes until maximal exhaustion. During exercise, brain activity was recorded with a 64-channel EEG cap and averaged cortical density was calculated for the lower limbs' representation in the motor cortex (MNI coordinates 0/0/60). Muscle activity of 14 muscles with wireless EMG electrodes was continuously recorded to define and differentiate the central and peripheral adaptation processes. The data are currently descriptive, as the number of participants for each group is too small for adequate statistical analysis.

Results: Pre bed rest oscillations in the motor cortex were overall less stable than expected. The participants who cycled and experienced artificial gravity displayed more pronounced and stable oscillations in the motor cortex post bed rest. Participants who cycled during the bed rest demonstrated greater but less consistent amplitudes in the motor cortex after bed rest compared to the AG+EX group. The CON group depicted no oscillation in the motor cortex after bed rest. Muscle activity did not change in the AG+EX and EX group between before and after the bed rest period. The CON group revealed lower values for EMG after 60-days of bed rest.

Conclusion: The presented data are descriptive as the limited number of participants in each group allows no statistical approach. However, first data let us assume, that AG+EX leads to a possible development of a motor engram, as the use of a recumbent bike was new for the participants, which is reflected in more pronounced oscillations in the AG+EX group, whereas the EX group results in less significant formation. The EX group experienced a permanently increased ICP during the whole period of bed rest. The nonexistent oscillations in the CON group lead to the assumption, that no engram was developed and the less muscle activity could be due to fewer recruited motor units owing to muscle loss. If the formation has indeed transpired in the AG+EX group, it would be of great importance in the context of neurorehabilitation strategies.

References: [1] Kohn et al. (2018). Gravity and neuronal adaptation, in vitro and in vivo-from neuronal cells up to neuromuscular responses: A first model. European Biophysics Journal. DOI: 10.1007/s00249-017-1233-7
[2] Schneider et al. (2013): Cortical current density oscillations in the motor cortex are correlated with muscular activity during pedalling exercise. Neuroscience. DOI: 10.1016/j.neuroscience.2012.10.037

10

Longitudinal Brain-age predictions encompassing long-duration spaceflight missions

Ge Tang[1,2], Kaustubh R. Patil[3], Felix Hoffstaedter[3], Shammi More[3], Simon B. Eickhoff[3], Steven Jillings[4], Ben Jeurissen[5], Elena Tomilovskaya[6], Darius Gerlach[7], Liudmila Litvinova[8], Inna Nosikova[6], Ekaterina Pechenkova[9], Victor Petrovichev[8], Ilya Rukavishnikov[6], Stefan Sunaert[10], Paul Parizel[11], Valentin Sinitsyn[12], Jan Sijbers[5], Jitka Annen[13], Steven Laureys[13], Angelique Van Ombergen[4], Floris Wuyts[4], and Peter zu Eulenburg[1,2]

[1]Institute for Neuroradiology, LMU Hospital Munich, Germany; [2]Graduate School of Systemic Neurosciences, LMU Munich, Germany; [3]Institute of Neuroscience and Medicine, INM-7: Brain & Behaviour, Forschungszentrum Jülich, Germany; [4]Lab for Equilibrium Investigations and Aerospace, University of Antwerp, Belgium; [5]Imec-Vision Lab, University of Antwerp, Belgium; [6]Institute of Biomedical Problem, Russian Academy of Sciences, Moscow, Russia; [7]Institute of Aerospace Medicine, DLR, Cologne, Germany; [8]Department of Radiology, National Medical Research Treatment and Rehabilitation Centre of the Ministry of Health of Russia, Moscow, Russia; [9]Laboratory for Cognitive Research, HSE University, Moscow, Russia; [10]Department of Imaging and Pathology, Katholieke Universiteit Leuven, Belgium; [11]Department of Radiology, Royal Perth Hospital, Australia; [12]Department of Radiology, Lomonosov Moscow State University, Russia; [13]Coma Science Group, University of Liège, Belgium

Introduction: Time dilation aboard the International Space Station (ISS) from a physics perspective should theoretically slow down human aging including the brain. Voxel-based morphometry findings from our group have recently shown that long-duration exposure (6 months) to microgravity onboard the ISS may have adverse effects on brain-structural integrity in the early days after return to Earth and does not fully normalize at follow-up 6-7 months later (Van Ombergen et al. 2018). Unmatched brainageing with chronological ageing can predict the risk for accelerated brain-tissue decay. Large datasetbased machine learning models have recently allowed for predicting this from structural MRI, mostly T1- weighted images, alone (Dartora et al., 2023; Hahn et al., 2022; More et al., 2022).

Methods: T1-weighted images from 14 long-duration ROSCOSMOS cosmonauts (44.7±6 yrs) and 5 ESA astronauts (43.4±4.6 yrs) measured at two sites for three time points each half a year apart (preflight, postflight, follow-up). For each timepoint, two identical T1w-images were acquired about 30 minutes apart. 23 age-, gender- and education-matched subjects with identical data acquisition schemes were added as controls. Extracted grey matter maps were then fed into three state-of-the-art brain-age prediction models. One is an uncertainty-aware Monte Carlo dropout composite quantile regression Neural Network, MCCQRNN (Hahn et al., 2022), the second is a highly refined regression model, S4_R4+GPR (More et al., 2022) and the third is a convolutional neuro network, CNN3, with minimally processed T1 images (Dartora et al., 2023).

Results: The sanity check of the model prediction shows that the Mean absolute error (MAE) and brain age delta were within the expected range from the literature for models MCCQRNN (MAE = 3.33±3.47 yrs) and S4_R4+GPR (MAE = 6.12±3.37 yrs) in our cohorts, but unacceptably large for model CNN3 (MAE = 11.0±4.73 yrs). The degree of brain-age replicability was very good for all models (MCCQRNN: 0.1±1.9 yrs; S4_R4+GPR: -0.08±1.95 yrs; CNN3: 0.24±1.14 yrs). The MAE for the different age groups in the data set revealed a clear age-driven bias (overestimation of brain age for younger subjects) for model CNN3. Astronauts give a u-shaped course with a postflight dip, no significant postflight effect directly due to the long-duration exposure to microgravity was detectable in a within-subject approach. Furthermore, we also fit linear mixed models to track the longitudinal brain-aging trajectories of all cohorts for the two selected models. According to the seminal paper by Bethlehem et al. grey matter structure for subjects 35-55 yrs should be almost unchanged (flat line), but we found significantly accelerated brain-ageing in all spacefarers.

Conclusions: We found that the three machine learning models showed a reliable prediction accuracy from the literature. Both models gave very good session stability. The postflight brain-age delta differs slightly from the preflight from the MCCQRNN predictions arguing for a mission effect upon return to Earth. We observed accelerated brain-ageing trajectories for spacefarers (cosmonauts>astronauts) in our unique longitudinal approach. To our surprise, one control cohort (ROS) also showed a similarly accelerated ageing trajectory.

References: 1. Van Ombergen (2018). Brain Tissue-Volume Changes in Cosmonauts. NEJM 379 (1678-80) 2. Hahn, T. (2022). An uncertainty-aware, shareable, and transparent neural network architecture for brain- age modeling. Sci Adv 8(1): eabg9471 3. More, S. (2022). Brain-age prediction: a systematic comparison of machine learning workflows. bioRxiv: 2022.2011.2016.515405 4. Dartora, C. (2023). A Deep Learning Model for Brain Age Prediction Using Minimally Pre-processed T1w-images as Input. medRxiv, 2022.2009.2006.22279594. 5. Bethlehem, R. A. I. (2022). "Brain charts for the human lifespan." Nature 604(7906): 525-533

11

Low level lower body negative pressure attenuates the decrease in cerebral blood flow during bed rest

Carmen Possnig[1], Kyohei Marume[1], Gautam Babu[2], Sylvan L. J. E. Janssen[3], Christopher M. Hearon Jr[2], Katrin A. Dias[2], Satyam Sarma[2], Justin S. Lawley[1], Benjamin D. Levine[2]

[1] University of Innsbruck, Innsbruck, Austria
[2] Texas Health Presbyterian Dallas, Dallas, TX
[3] Radboud University, Nijmegen, Netherlands

Introduction: Cerebral blood flow (CBF) decreases during spaceflight and bed rest, and may present a risk to long-distance spaceflight missions, where success and safety will depend on astronauts being autonomous. We hypothesised that lower body negative pressure (LBNP) can be used as a countermeasure to attenuate the decline in CBF, as it simulates the effects of gravity by pulling fluids away from (i.e., unloading) cardiac and cranial compartments.

Methods: Study 1: Ten men and seven women were subjected to strict bed rest for three days. Study 2: Of these, five men and two women subsequently underwent three days of bed rest with -20 mmHg LBNP for 8 hours each day. We assessed blood flow via duplex ultrasonography in the internal carotid (ICA) and vertebral arteries (VA), and via transcranial Doppler of the middle cerebral artery (MCA) before and after bed rest.

Results: Compared to the baseline in a supine position, three days of bed rest resulted in a decrease in total cerebral blood flow (1078±302 to 853±245 ml·min^{-1}, $P < 0.0001$), ICA blood flow (427±146 to 337±118 ml·min^{-1}, $P < 0.0001$), VA blood flow (112±59 to 90±45 ml·min^{-1}, $P < 0.001$), and MCA velocity (61±15 to 49±12 ml·min^{-1}, $P < 0.0001$). In the seven participants that spent 8 hours per day under - 20mmHg LBNP, the decrease in cerebral blood flow was attenuated by ~50% in the ICA (LBNP, -55±64 vs. control, -113±71 ml·min^{-1}; $P = 0.068$) and the MCA (LBNP, -6±7 vs. control, -13±5 cm·s^{-1}; $P = 0.026$), but not significantly changed in the VA (LBNP, -10±15 vs. control, -29±25 ml·min^{-1}; p=0.123).

Conclusion: These findings indicate that there is an overall reduction in CBF during bed rest compared to the supine posture, which can be attenuated by low-level (-20 mmHg) LBNP for 8 hours daily. LBNP therefore seems to be a promising countermeasure for the decline in CBF during spaceflight..

12

Haemodynamic and microvascular responses to combined hypergravity, heat stress and hypoxia

Jason T. Fisher[1], Urša Ciuha[1], Adam C. McDonnell[1], Hervé Normand[2], Pierre Denise[2], Igor B. Mekjavic[1]

[1] Department of Automatics, Biocybernetics and Robotics, Jozef Stefan Institute, Slovenia
[2] INSERM COMETE, Université de Caen Normandie, France

Introduction: The use of artificial gravity (AG) has been discussed as a suitable method of reducing microgravityinduced cardiovascular deconditioning, by producing a gravitational pressure gradient and initiating greater strain on the cardiovascular system. However, the extent to which hypergravity and hypoxia, at different temperatures, experienced during AG effect the cardiovascular system should also be evaluated. Previous research has considered the effect of differing levels of AG on cardiovascular and cerebrovascular responses, indicating a relationship between standing and 1G exposure at the level of the heart (Goswami et al., 2015; Verma et al., 2018). However, these studies did not measure regional microvascular responses, or the impact of differing ambient conditions. Therefore, the present study assessed the impact of AG in the head-to-foot direction and hypoxia, at different ambient temperatures, on haemodynamic responses and microvascular blood flow. It is hypothesised that both haemodynamic and microvascular responses to normal gravity (NG) and 1G will be comparable whereas higher G-loads will alter this response. Additionally, it is hypothesised that the combination of all stressors will cause conflict in autonomic cardiovascular control, possibly initiating pre-syncopal or heat stress symptoms.

Methods: 10 male participants (age: 27.9 ± 6.3 years, height: 179.8 ± 6.1 cm, weight: 78.2 ± 10.3 kg) completed four sessions where haemodynamic responses (heart rate, stroke volume, cardiac output, systemic vascular resistance, blood pressure), and microvascular blood flow measured at the forearm (armBF) and calf (legBF), were recorded; also, skin (T_{skin}) and core (T_{core}) temperature were measured. Three positions were used; standing normal gravity (NG), supine 1GRF (1GRF), supine 2GRF (2GRF). In addition, recovery from each condition was recorded for 10 minutes. Cardiovascular responses were measured using the model flow algorithm (Wesseling, Jansen, Settels, & Schreuder, 1993), and a 5- lead electrocardiogram (ECG). Cutaneous blood flow was measured by laser doppler flowmetry, T_{skin} via measured by four thermistors (chest, bicep, thigh, calf), and T_{core} via ingestible telemetric pills. The four sessions were: cool normoxia (18.4 ± 0.8 °C, 21%), cool hypoxia (18.4 ± 0.8 °C, 14%), hot normoxia (29.1 ± 0.8 °C, 21%), and hot hypoxia (29.1 ± 0.8 °C, 14%). 3-way ANOVAs assessed the main effects of temperature (TEMP), oxygen availability (OXY), and gravity (GRAV).

Results: Microvascular blood flow responses to ambient conditions of the forearm and calf were assessed. The analysis identified that hypoxia had no significant effect on the microvascular response, the ambient temperature and hypergravity did. ArmBF was significantly affected by both TEMP ($p<0.001$) and GRAV ($p<0.001$), observing a significant decrease in blood flow with increasing gravitational stimuli; particularly in hot conditions. LegBF observed a similar response to the increase in gravitational stimuli, regardless of ambient temperature, and thus was only significantly affected by GRAV ($p<0.001$).
In both ambient conditions, the cardiovascular responses to NG and 1GRF did not significantly differ from each other in any of the measured variables ($p>0.05$). Significant main effects of TEMP were observed in heart rate ($p=0.006$), systemic vascular resistance ($p=0.001$), and systolic blood pressure ($p<0.001$). The main effect of GRAV caused significant variations in heart rate ($p<0.001$), stroke volume ($p<0.001$), systemic vascular resistance ($p=0.003$), and systolic and diastolic blood pressures ($p<001$). OXY significantly affected heart rate only ($p=0.02$). There were no significant interaction effects between any of the main effects. Multiple comparisons analysis identified the source of these main effects originated solely from the 2GRF condition.

Conclusions: The microvascular blood flow results agree with our previous work, that identified a significant baroreceptor drive in the legs whilst the arm blood flow is modulated by multiple vascular mechanisms. It is clear that this thermoregulatory modulation in the arm is observed even in the presence of hypergravity. Additionally, the extra strains produced by differing ambient conditions and hypergravity appear to be well mediated by haemodynamic and vascular responses.

13

Effect of acute hypoxia exposure on the availability of A1 adenosine receptors in the human brain measured with [F-18]CPFPX PET

Manuel Michno[1], Henning Weis[2,3], Jan Schmitz[2,4], Anna L. Foerges[1], Simone Beer[1], Bernd Neumaier[5], Alexander Drzezga[1,3], Daniel Aeschbach[2,6,7,8], Andreas Bauer[1], Jens Tank[2], Eva-Maria Elmenhorst[2], David Elmenhorst[1,3]

[1] Forschungszentrum Jülich, Institute of Neuroscience and Medicine (INM-2), Germany
[2] German Aerospace Center, Institute of Aerospace Medicine, Germany
[3] Department of Nuclear Medicine, University Hospital Cologne, Germany
[4] Department of Anaesthesiology, University Hospital Cologne, Germany
[5] Forschungszentrum Jülich, Institute of Neuroscience and Medicine (INM-5), Germany
[6] Harvard Medical School, Division of Sleep Medicine, USA
[7] Division of Sleep and Circadian Disorders, Brigham and Women's Hospital, USA
[8] Institute of Experimental Epileptology and Cognition Research, University of Bonn, Germany

Introduction: Normobaric hypoxia induces numerous adaptive changes, e.g., in cerebral blood flow, metabolism and electrical activity. Adenosine, as an inhibitory neuromodulator, is produced in and/or released to the interstitial space during hypoxia and assumed to mediate several of these effects. A1 adenosine receptor (A1AR) antagonism or knock-out attenuates this neuronal inhibition in mice. Here we tested the hypothesis that exposure to an interval of hypoxia compared to an interval of normoxia (control) reduces the availability of A1AR in the human brain, due to hypoxia-triggered rise of endogenous adenosine.
As exploratory objectives, we tested the hypotheses that psychomotor vigilance is affected during hypoxia and that cerebral blood flow is altered.

Methods: Ten healthy volunteers (32 ± 13 years, 3f) completed an 110-min bolus plus constant infusion [F-18]CPFPX PET-MRI hybrid experiment: Subjects spent the first 60 minutes of the scan in normoxia followed by 30 minutes of individually adapted normobaric hypoxia to achieve a peripheral oxygen saturation of 70 - 75 %, followed by 20 minutes of normoxia. Blood samples were used to calculate metabolite-corrected steady-state distribution volumes (VT) of A1AR (i. e., 40 - 100 min after start of [F-18]CPFPX administration). Brain perfusion was measured via arterial spin labelling. A 3-minute psychomotor vigilance test (PVT) was conducted every 10 minutes. Heart rate and peripheral blood oxygen saturation were measured continuously.

Results: Hypoxia reduced A1AR availability in the cerebral cortex by 11 % ($p = 0.033$). Compared to normoxia, brain perfusion increased during hypoxia by 36 % in cortical gray matter. Heart rate increased by 20 % ($p < 0.001$). PVT mean reaction time was longer by 12ms ($p = 0.027$).

Conclusions: Short term reduction of the oxygen saturation to 70 % (corresponding to an oxygen saturation at an altitude of approximately 6000 m) increases cerebral blood flow and impairs cognitive performance while A1AR availability is reduced. This indicates that acute hypoxia exposure increases cerebral adenosine concentration and receptor occupancy.

14

Ground-based validation of transcutaneous PCO_2 measurements by blood gas analysis

Fabian N. Möller[1,2], A. Betts[1], K. J. Carter[3], V. E. Ryder[4], A. T. Lovering[1], B. R. Macias[4], S. S. Laurie[3]

[1] University of Oregon, Department of Human Physiology, Eugene, USA
[2] Massachusetts Institute of Technology, Aerospace Physiology Lab, Cambridge, USA
[3] KBR, Houston, USA
[4] NASA Johnson Space Center, Houston, USA

Introduction: Mildly elevated ambient PCO_2 on the International Space Stations (ISS) has the potential to alter various physiological systems. Still, there have been no systematic assessments of arterial PCO_2 levels or the possible deleterious outcomes that may ensue. Based on the dependence of CO_2 absorption on the ISS, ambient CO_2 levels must be monitored continuously and accurately to detect even slight elevations, ensuring flight mission success and crew health. While the mean ambient PCO_2 level on ISS has been lowered over the past decade, elevated inspiratory PCO_2 levels may occur within areas of poor airflow, such as exercise facilities, confined spaces, and during sleep in personal cabins. These inspired levels may deviate from the average concentration measured throughout ISS. Transcutaneous measurements of carbon dioxide pressure ($P_{tc}CO_2$) may provide a continuous, non-invasive method to track CO_2 levels in individual crewmembers by application of a single heated sensor to the skin, allowing diffusion of gases to the sensor. However, the challenge to detect slight and acute changes in P_aCO_2 by $P_{tc}CO_2$ has not yet been validated against end-tidal PCO_2 ($P_{ET}CO_2$) by breathing gas analysis and the gold-standard arterial blood analysis (BGA) of P_aCO_2. We hypothesized (I) that transcutaneous CO_2 monitoring would underestimate P_aCO_2 and (II) that $P_{tc}CO_2$ would be superior to $P_{ET}CO_2$.

Methods: This ground-based study aims to validate a commercially available $P_{tc}CO_2$ monitor (Radiometer TCM5) against arterial P_aCO_2 by BGA and $P_{ET}CO_2$ during the conditions of supine and upright rest, voluntary hyperventilation to 30- and 20-mm Hg, hypercapnia of 3-, 6-, and 9-mmnHg above baseline, low and high-intensity exercise. The emphasis was on quantifying slight but potentially physiologically relevant changes during changes in posture and ventilatory responses. With additional data collection pending, this abstract shows preliminary results from five subjects (3 females).

Results: Preliminary data depicts mean values with standard deviation for resting measures in the supine (P_aCO_2 = 33 ± 4; $P_{ET}CO_2$= 38 ± 1; $P_{tc}CO_2$ = 41 ± 1 mm Hg) and upright position (P_aCO_2 = 36 ± 2; $P_{ET}CO_2$= 40 ± 1; $P_{tc}CO_2$ = 43 ± 3 mm Hg), and hypocapnia from voluntary hyperventilation to 30 mm Hg (n=3; P_aCO_2 = 29; $P_{ET}CO_2$= 30 ± 1; $P_{tc}CO_2$ = 33 ± 6 mm Hg) and subsequently to 20 mm Hg for 1 minute (n=5; P_aCO_2 = 19 ± 3; $P_{ET}CO_2$= 20 ± 1; $P_{tc}CO_2$ = 31 ± 6 mm Hg). Next, hypercapnia was induced by stepwise increases in inspiratory CO_2 above baseline by +3 mm Hg (P_aCO_2 = 38 ± 1; $P_{ET}CO_2$= 42 ± 1; $P_{tc}CO_2$ = 44 ± 2 mm Hg), +6 mm Hg (P_aCO_2 = 40 ± 1; $P_{ET}CO_2$= 46 ± 1; $P_{tc}CO_2$ = 47 ± 2 mm Hg), and +9 mm Hg (P_aCO_2 = 41 ± 1; $P_{ET}CO_2$= 48 ± 1; $P_{tc}CO_2$ = 50 ± 2 mm Hg). Following a recovery period, measurements were conducted pre-exercise (P_aCO_2 = 35 ± 2.0; $P_{ET}CO_2$= 35 ± 1; $P_{tc}CO_2$ = 39 ± 1 mm Hg) and at intensities below (P_aCO_2 = 35 ± 2; $P_{ET}CO_2$= 40 ± 2; $P_{tc}CO_2$ = 41 ± 1 mm Hg) and above the ventilatory threshold (P_aCO_2 = 29 ± 2; $P_{ET}CO_2$= 33 ± 2; $P_{tc}CO_2$ = 39 ± 3 mm Hg).

Conclusions: Repeated measures ANOVAs with Tukey post-hoc tests will be conducted for the full data sets, with the devices' agreement assessed using Bland-Altman plots. Based on preliminary data, transcutaneous measurements seem to over-estimate P_aCO_2 during supine and upright rest, contradicting our initial hypothesis. Furthermore, large changes in P_aCO_2 during hyperventilation led to severe over-estimation in the 20 mm Hg hyperventilation condition, not detecting the evident reductions in P_aCO_2. While the underlying reasons are speculative, a delay by changes in local skin perfusion or the sensor's response time will be investigated. More data are necessary to evaluate the potential for transcutaneous PCO_2 measurements to accurately detect the expected slight PCO_2 changes within spaceflight habitats.

15

Influence of muscle architecture on muscle perfusion in bed rest

Edoardo Calà[1,2], Rob C.I. Wüst[2], Jule Heieis[3,4,5], Wolfram Sies[1], Jochen Zange[1], Noah Tjiang[1], Thomas Voigtmann[3], Jörn Rittweger[1]

[1] Institute of Aerospace Medicine, German Aerospace Center, Cologne, Germany
[2] Laboratory for Myology, Faculty of Behavioral and Movement Sciences, Amsterdam Movement Sciences, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands
[3] Institute of Materials Physics in Space, German Aerospace Center, Cologne, Germany
[4] Children's Hospital, University of Cologne, Cologne, Germany
[5] Faculty of Medical Engineering and Technomatematics, FH Aachen University of Applied Science, Aachen, Germany

Introduction: Muscle fascicles are typically set at an angle with respect to the line of muscle pull. During muscle contractions, fascicles shorten which increases their pennation angle, both of which have implications for the physiological cross-sectional area and force output. Pressure accumulating in the muscle affects surrounding tissues, potentially altering blood flow and thereby local energy metabolism. Fluid dysregulation and muscle loss in the lower limbs may contribute to the orthostatic intolerance often observed after bed rest and spaceflight, but it is unknown if this intramuscular pressure is altered upon bed rest.

Methods: We estimated intramuscular compressive stress from muscle torques, together with blood flow in twelve participants (35±7 years), before and after 30 days of 6° head-down tilt bed rest. Participants were split into an intervention group (horizontal cycling and thigh pressure cuffs) and a control group (n=6 each). Doppler-Ultrasound at the superficial femoral artery and B-mode pictures of the gastrocnemius medialis were taken during isometric plantar flexion torque at 25, 50, and 75% of maximum voluntary contraction.

Results: Preliminary results from this experiment showed a significant reduction of flow due to intramuscular compressive stress ($p<0.05$) in both groups at baseline, but this relationship was absent in the intervention group after bed rest. In both groups, produced muscle torque was not different after bed rest, as well as morphological features of the gastrocnemius were unchanged.

Conclusions: The present study indicates a significant contribution of intramuscular compressive stress to muscle blood flow. Whether bed rest had an impact on this relationship or not is on the border of statistical significance on basis of the data analyzed so far. We are currently analyzing data from another 12 subjects and trust to thereby amass the statistical power required to fully address our research question.

16

The effect of reduced rostrocaudal gravitational load on cardiac function

Victorien Faivre-Rampant[1,2,4], *Igor B. Mekjavic*[2], *Hervé Normand*[1], *Amir Hodzic*[1,3]

[1] Normandie Univ, UNICAEN, Inserm Comete, GIP Cyceron, 14000 Caen, France
[2] Department of Automatics, Biocybernetics, and Robotics, Jozef Stefan Institute, Ljubljana, Slovenia
[3] Normandie Univ, UNICAEN, CHU Caen Normandie, Department of Cardiology, Caen, France
[4] Jozef Stefan International Postgraduate School, Ljubljana, Slovenia

Introduction: Left ventricular end-diastolic pressure (LVEDP) reflects the degree of cardiac myocyte stretching prior to ventricular contraction, and together with ventricular contractility and afterload, determines the stroke volume. One of the factors affecting LVEDP is thoracic blood volume. *In vitro* experiments have demonstrated that LVEDP is also affected by intracardiac hydrostatic pressure gradients, which can be modified by the orientation of the heart in the thoracic cavity or the rostrocaudal gravitational load (gload). As a consequence, cardiac function will be altered during exposures to reduced gravity such as would be experienced on Mars (3.71 $m.s^{-2}$) compared to that on Earth (9.8$m\text{-}s^{-2}$). The aim of the present study was to test this hypothesis *in vivo* in human subjects. In order to isolate the effect of heart orientation, we investigated cardiac function during reduction in the pressure surrounding the lower body (lower body negative pressure, LBNP) in a supine position (inducing fluid shift only), and separately with several head-up tilt (HUT) angles without LBNP (simulating fluid shifts and altered intracardiac hydrostatic pressure gradients ranging from that anticipated on Mars to that on Earth).

Methods: Following a 10-min supine rest period on a tilt table with a lower body pressure box, 4 subjects (more data will be presented during the workshop) were exposed to 4 levels of LBNP in supine position and 4 HUT angles simulating different levels of rostrocaudal g-load on the cardiovascular system. The order between HUT and LBNP conditions was randomized, while the intensities (angles and pressures) were progressive, but interspersed with 3min breaks in the supine position to restore a cardiovascular baseline. For each tilt angle or LBNP level, the condition was applied for 3min to ensure steady state for the last minute of the stage. The HUT angles were: 80° (simulating 1g on Earth), 58° (0.85g), 42° (0.66g) and 22° (simulating 0.37g on Mars). While the LBNP levels were: 10, 20, 35 and 50 Torr. During the experimental session, arterial blood pressure was monitored with a continuous non-invasive method (Finapress Nova NC, Enschede, Netherlands). Fluid shifts in the different body segments were measured with bioelectrical impedance and then derived with Geddes's formula (Geddes & Sadler, 1973).

Results: The effect of LBNP and tilt angle on fluid shifts in the thoracic region were equivalent, resulting in equivalent modifications in preload. Fluid shifts in other regions (abdomen, pelvis and legs) exhibited differences most likely reflecting regional differences in blood flow distribution. There were no significant differences in heart rate (HR), stroke volume (SV) and cardiac output (CO) between the two conditions (LBNP and tilt angle). Whereas systolic blood pressure was progressively reduced with increasing LBNP (From 125.2 ± 16.0mmHg at 10 Torr to 114.17 ± 18.8mmHg at 50 Torr), it remained stable during the different HUT angles (125.5 ± 14.2mmHg at 22° and 124.8 ± 16.8mmHg at 80°). In contrast, diastolic blood pressure increased significantly ($p = 0.027$) with HUT (from 77.7 ± 9.1mmHg at 22° to 83.1mmHg at 80°).

Conclusions: Elevated reductions in the surrounding pressure of the lower body (LBNP) induces an equivalent stress on the cardiovascular system as HUT. Hence, an LBNP of 10 Torr induces the same modifications in HR, SV and CO as a rostrocaudal gravitational load of about 0.37g (Mars' gravity), while 50 Torr is equivalent to a gravitational load of 1g. The elevated diastolic and maintained systolic blood pressure with higher HUT may reflect either an improvement in diastolic loading due to intracardiac hydrostatic gradients, a modification in vascular peripheral resistances induced by the fluid shift or a vestibular reflex leading to modified cardiovascular regulation. Further explorations with transthoracic echocardiography are planned and should help us to have a better understanding on the underlying phenomenon.

Acknowledgements: Victorien Faivre-Rampant is recipient of the Slovene Research Agency Young Researcher scholarship.

17

Exploring the role of the Hippo pathway member Yap in a model of Duchenne Muscular Dystrophy

Marius Meinhold, Martin Schönfelder, Henning Wackerhage

Technical University Munich, TUM School of Medicine and Health, Associate Professorship of Exercise Biology, Germany

Introduction: The Duchenne muscular dystrophy (DMD) is a progressive, X-linked muscle disorder leading to impaired regeneration and differentiation, severe fibrosis and subsequent loss of function. Several findings in the literature point to a role of the mechano-sensitive Hippo pathway member Yap in models of DMD. Among many other therapeutic approaches, Simvastatin was shown to improve muscle function and drastically improve fibrosis in mdx mice. Interestingly, Simvastatin was also found to be a potent inhibitor of Yap. Therefore, we aimed to find out 1) whether Yap is constitutively active in dystrophic, human myotubes and 2) whether Simvastatin inhibits Yap in dystrophic, human myotubes.

Methods: We cultured immortalized, human myoblasts from one healthy donor and from two DMD donors provided by Dr. Vincent Mouly from the Center for research in Myology (Paris, France). To study Yap localization in myotubes, myoblasts were grown to confluence, switched to differentiation medium and fixed on days 2, 4, 6 and 8 of differentiation and immunolabelled for Yap. For Yap phosphorylation status, we detected total and phospho-Yap (S127) using Western Blots. Furthermore, we performed RT-qPCR and quantified the expression of Yap target genes (*Ctgf*, *Ankrd1*, *Cyr61)*. To study the effects of Simvastatin on Yap, we treated immortalized, human myotubes on day 7 for 24 hours (10µM) and used the above-mentioned methods to investigate Yap subcellular localization, phosphorylation and target gene expression.

Results: Using immunofluorescence, we found that Yap can be both nuclear and cytosolic in immortalized, human myotubes with no apparent difference between healthy donor cells and those of DMD patients. There was also no meaningful difference between different time points during differentiation. To validate these findings, we performed Western Blots using antibodies against total and phosphorylated Yap (S127) and as expected, differences appear to be minimal. In contrast to the literature, we did not find that Yap target gene expression is increased in dystrophic compared to healthy myoblasts or myotubes. To find out, whether the dystrophy-alleviating effects of Simvastatin are potentially explained by inhibition of Yap, we treated healthy and dystrophic myotubes and found that Yap nuclear localization is decreased, Yap phosphorylation increases and that Yap target genes expression decreases. These results were similar between healthy and dystrophic myotubes and also similar between the two DMD donor cells.

Conclusions: In this in-vitro study, we found little support for previous findings that Yap is constitutively active in models of DMD. However, we show that Simvastatin is a potent inhibitor and Yap in muscle cells of healthy and dystrophic patients. Moreover, Simvastatin reduced the expression of fibrosis-driving gene *Ctgf*. This is not only interesting for the treatment of DMD but potentially also for the treatment of disuse-induced fibrosis. Lastly, our results raise the question whether 2D cell culture is an appropriate model to study the role of mechano-sensitive pathways in DMD.

18

Physical inactivity does not explain exercise intolerance and skeletal muscle adaptations in long COVID

Braeden T. Charlton[1,2], Brent Appelman[3], Paul Hendrickse[4], Richie P. Goulding[1,2], Moritz Eggelbusch[1,2], Ellen Breedveld[1,2], Tom Kerkhoff[1,2], Jörn Rittweger[5,6], Edwin Mulder[5], Frank Bloemers[2,7], Jelle Posthuma[2,7], Michele van Vugt[8], Rob C.I. Wüst[1,2]

[1] Department of Human Movement Sciences, Faculty of Behavioral and Movement Sciences, Vrije Universiteit Amsterdam, the Netherlands
[2] Amsterdam Movement Sciences, Amsterdam, the Netherlands
[3] Amsterdam Medical Centre, Center for Experimental and Molecular Medicine, the Netherlands
[4] Lancaster Medical School, Lancaster University, Lancaster, UK
[5] Institute of Aerospace Medicine, German Aerospace Center (DLR), Cologne, Germany
[6] Department of Pediatrics and Adolescent Medicine, University of Cologne, Cologne, Germany
[7] Department of Trauma Surgery, Amsterdam UMC location University of Amsterdam, the Netherlands
[8] Division of Infectious Diseases, Tropical Medicine, Department of Medicine, Amsterdam UMC location University of Amsterdam, the Netherlands

Introduction: Patients with long COVID (or post-acute sequalae of COVID) present a unique set of symptoms, marked by a reduced exercise capacity and post-exertional malaise, which is the worsening of symptoms following mental or physical exertion. The combination of these symptoms renders many patients unable to perform daily physical tasks, which limits their movement and ultimately leads to a severely inactive lifestyle. Physical inactivity *per se* causes physiological alterations in skeletal muscle that can underly the reduced exercise capacity and increased feeling of fatigue. It is unknown to what extent the changes in exercise capacity are a consequence of long COVID, or due to physical inactivity. The current study aims to compare the exercise capacity and skeletal muscle alterations in patients with long COVID with those occurring after long term bed rest, which is used as a model for extreme physical inactivity.

Methods: Exercise capacity (by means of a cardiopulmonary exercise test) was assessed in 25 patients with long COVID, in 21 healthy participants, and in 24 participants before and after 60 days of bed rest. For each condition, vastus lateralis muscle biopsies were stained for fibre cross-sectional area, muscle fibre type distribution, oxidative enzyme activity, and capillarization.

Results: Peak power output was 23% lower in patients with long COVID and 26% lower after bed rest. Long COVID patients had a 20% lower $\dot{V}O_{2peak}$ which was similar after bed rest (-23%). However, the skeletal muscle adaptations underlying the reduction in exercise tolerance were different: whereas long COVID patients showed no signs of a lower fiber cross-sectional area relative to age-matched controls, fiber cross-sectional area decreased markedly across all muscle fiber types after 60 days of bed rest. Muscle fiber type did not change after bed rest, but long COVID patients had a lower percentage of type I and a higher percentage of type IIx muscle fibers, compared to healthy controls. Succinate dehydrogenase (SDH) activity was lower after bed rest, but not different between long COVID patients and healthy controls. Similarly, capillary-to-fiber ratio did not differ between long COVID patients and controls, while 60 days of bed rest resulted in a decreased capillary-to-fiber ratio.

Conclusions: While both extended bed rest and long COVID result in decreased exercise tolerance, the accompanying skeletal muscle adaptations in both conditions diverge. As such, we conclude that the decreased exercise capacity observed in long COVID patients is not simply a matter of physical inactivity, and that further research is needed to resolve the underlying adaptations in patients with long COVID.

19

The effects of a one-year antarctic sojourn at the Concordia Research Station on olfactory and gustatory functions

Bea Klos, Andrea Meyer, Daniela Reinhardt, Paul Enck, Isabelle Mack

Department of Psychosomatic Medicine and Psychotherapy, University Hospital Tübingen, Tübingen, Germany

Introduction: In extreme environments, it's crucial to maintain a healthy body weight. Sensory functions, specifically the senses of smell and taste, are of significant importance in the context of dietary intake, representing key factors in maintaining appropriate energy intake and body weight. In a hypoxic extreme environment, such as the Concordia Station in the mainland of Antarctica, it is believed that there may be potential changes in these sensory functions. However, existing data are scarce.

Methods: We investigated olfactory function (threshold, identification, discrimination) using ODOFIN Sniffin' Sticks and gustatory function using ODOFIN Taste Strips (taste identification test for the taste qualities sour, salty, sweet and bitter) as part of the 'Immune and Microbiome Changes in Environments with Limited ANtigen Diversity' project (ICELAND). The 19 participants of the winter-over periods 2019/2020 and 2021/2022 (39.2±10.9 years, 3/19 female) were examined upon baseline (T0) and three times during the Antarctic sojourn (T1-T3) by trained staff. Taste was also tested six months post Antarctica (T4).

Results: At T0, 3 out of 19 participants exhibited hypogeusia. This proportion increased to 6 out of 19 participants 2-month post-arrival at the Concordia Station (T1) and subsequently stabilized at 4 out of 19 participants (T2-T4). The sweet taste quality consistently yielded the highest identification rates over all times. Notably, a significant decrease in cumulative salty taste scores was observed over the course of the Antarctic stay, returning to baseline levels at T4. At both T0 and T1, 4 out of 19 individuals experienced hyposmia. This prevalence increased to 7 out of 19 participants during the Antarctic winter, remaining stable until the end of the Antarctic stay. Overall, olfaction sum scores exhibited a downward trend from baseline throughout the duration of their time in Antarctica.

Conclusions: Living one year in an extreme and hypoxic environment as Concordia Station in Antarctica affects olfactory and gustatory function individually to different extents. Some individuals may temporarily exhibit extreme reduced taste and/or olfactory function.

20

Resistance exercise and training alters desmin phosphorylation in human skeletal muscle and makes it less prone to degradation

Daniel Jacko[1], Kirill Schaaf[1], Lukas Masur[1], Käthe Bersiner[2], Wilhelm Bloch[1], Sebastian Gehlert[2]

[1] German Sport University Cologne, Institute for Cardiovascular Research and Sport Medicine, Department for Molecular and Cellular Sport Medicine, Cologne, Germany
[2] University of Hildesheim, Institute of Sport Science, Department for Biosciences of Sports, Hildesheim, Germany

Introduction: In skeletal muscle (SKM), the desmin intermediate filaments (IF) network plays a crucial role in lateral force transmission and maintaining the overall mechanical stability of myofibers. In our previous work, we demonstrated that resistance training rapidly upregulates desmin content and enhances mechanical stress resistance. Conversely, IF solubilization and degradation are prerequisites for myofibril disassembly, contributing to muscle wasting. Desmin stability is regulated by posttranslational modifications, including initial phosphorylation and subsequent ubiquitination, which primes desmin for calpain-dependent degradation. Therefore, investigating desmin phosphorylation (pDes) is highly relevant for understanding muscle atrophy in conditions such as disuse, aging, or catabolic states. While pDes has been studied in pathological states in cell culture, animal models, and cardiomyocytes, there is currently no data available on this mechanism in healthy human muscles. Furthermore, it remains unknown whether specific interventions can modulate desmin's posttranslational modification.

Methods: First, we assessed the baseline phosphorylation levels at four prominent sites (serine 31, 60; threonine 17, 76/77) in biopsies obtained from healthy human SKM in an unadapted state using western blotting. We then investigated whether acute resistance exercise led to modifications in these phosphorylation levels. Additionally, we conducted a degradation assay to determine whether changes in desmin's phosphorylation state were associated with reduced susceptibility to degradation. Subsequently, we examined whether resistance training, and the resulting muscle adaptation, affected acute post-exercise phospho-regulation and baseline desmin phosphorylation levels.

Results: In the unadapted state, desmin exhibited phosphorylation at all four investigated sites. Acute resistance exercise led to a downregulation of pS31 and pT17, while pS60 and pT76/77 remained unaffected. Notably, desmin in resting SKM was found to be more susceptible to degradation than after exercise. In the adapted state, only pS31 showed a significant decrease following acute exercise. However, baseline phosphorylation levels were altered for three of the four sites: pS31 increased, while pS60 and pT17 decreased. Furthermore, total desmin content increased.

Conclusions: These findings indicate that desmin phosphorylation is not exclusive to diseased muscles but is also present in healthy SKM. Importantly, it is possible to modulate this phosphorylation through acute resistance exercise and training. Additionally, exercise-induced dephosphorylation of desmin renders it less susceptible to degradation, suggesting a mechanism for acute stress protection to maintain myofibrillar integrity under conditions of high mechanical demand. The potential long-term impact of training-induced modifications in baseline/resting-state phosphorylation levels on desmin stability will be the focus of future investigations.

Speakers

Badalì, Constance: German Sport University Cologne, Institute of Movement and Neurosciences, Cologne, Germany

Böcker, Jonas: Department of Muscle and Bone Metabolism, Institute of Aerospace Medicine, German Aerospace Center, Cologne, Germany

Bothe, Tomas L.: Charité Universitätsmedizin Berlin, Institute of Physiology, Center for Space Medicine and Extreme Environments, Berlin, Germany

Burger, Nicole: Laboratory for Translational Research "Stress & Immunity", Dpt. of Anesthesiology, LMU University Hospital, LMU Munich, Germany

Calà, Edoardo: Institute of Aerospace Medicine, German Aerospace Center, Cologne, Germany; Laboratory for Myology, Faculty of Behavioral and Movement Sciences, Amsterdam Movement Sciences, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands

Charlton, Braeden T.: Department of Human Movement Sciences, Faculty of Behavioral and Movement Sciences, Vrije Universiteit Amsterdam, the Netherlands; Amsterdam Movement Sciences, Amsterdam, the Netherlands

Ebner, Ines: Dept. of Internal Medicine 3 – Rheumatology & Immunology, Universitätsklinikum Erlangen & Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg, Germany; Deutsches Zentrum Immuntherapie (DZI), Universitätsklinikum Erlangen & FAU Erlangen-Nürnberg, Germany

Faivre-Rampant, Victorien: Normandie Univ, UNICAEN, Inserm Comete, GIP Cyceron, 14000 Caen, France; Department of Automatics, Biocybernetics, and Robotics, Jozef Stefan Institute, Ljubljana, Slovenia; Jozef Stefan International Postgraduate School, Ljubljana, Slovenia

Fisher, Jason T.: Department of Automatics, Biocybernetics and Robotics, Jozef Stefan Institute, Slovenia

Henkel, Sara: University of Bonn, Institute of Nutritional and Food Sciences, Bonn, Germany

Jacko, Daniel: German Sport University Cologne, Institute for Cardiovascular Research and Sport Medicine, Department for Molecular and Cellular Sport Medicine, Cologne, Germany

Klos, Bea: Department of Psychosomatic Medicine and Psychotherapy, University Hospital Tübingen, Tübingen, Germany

Kowalski, Tomasz: Department of Physiology, Institute of Sport, National Research Institute, Warsaw, Poland

Luciano, Francesco: University of Milano, Dept. of Pathophysiology and Transplants, Italy

Meinhold, Marius: Technical University Munich, TUM School of Medicine and Health, Associate Professorship of Exercise Biology, Germany

Michno, Manuel: Forschungszentrum Jülich, Institute of Neuroscience and Medicine (INM-2), Germany

Möller, Fabian N.: University of Oregon, Department of Human Physiology, Eugene, USA

Possnig, Carmen: University of Innsbruck, Innsbruck, Austria

Son, Yuliya: Laboratory of Translational Research "Stress and Immunity", Department of Anesthesiology, LMU University Hospital, LMU Munich, Germany

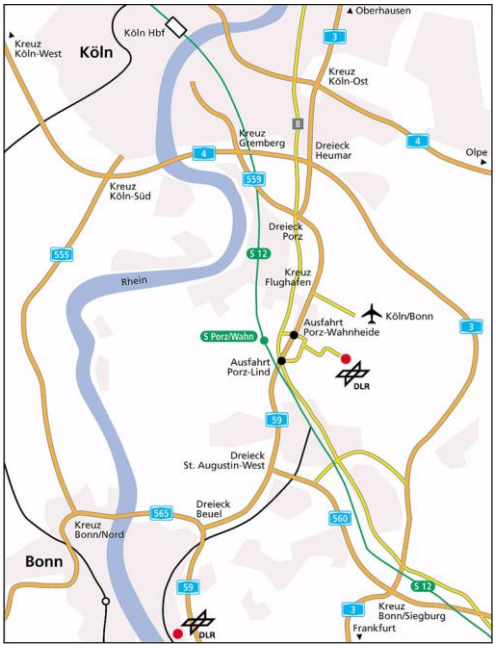
Tang, Ge: Institute for Neuroradiology, LMU Hospital Munich, Germany; Graduate School of Systemic Neurosciences, LMU Munich, Germany

Travel Instructions (see also: DLR - envihab - How to reach us)

DLR Cologne, Planitzweg, 51147 Cologne, Tel.: +49 2203 601-0

How to reach us:

Arrival by train
The local trains ("S-Bahn") S 12 or S 19 leave from Koeln Hauptbahnhof (Hbf), Siegburg and Troisdorf. The local train S 19 also leaves from Koeln Bonn Airport. Daytime departures take place every 20 min for both trains so that there is a train every 10 minutes. Get off at the railway station "Porz-Wahn" and continue from there by KVB bus number 162, direction "DLR". See instructions "By bus" below.



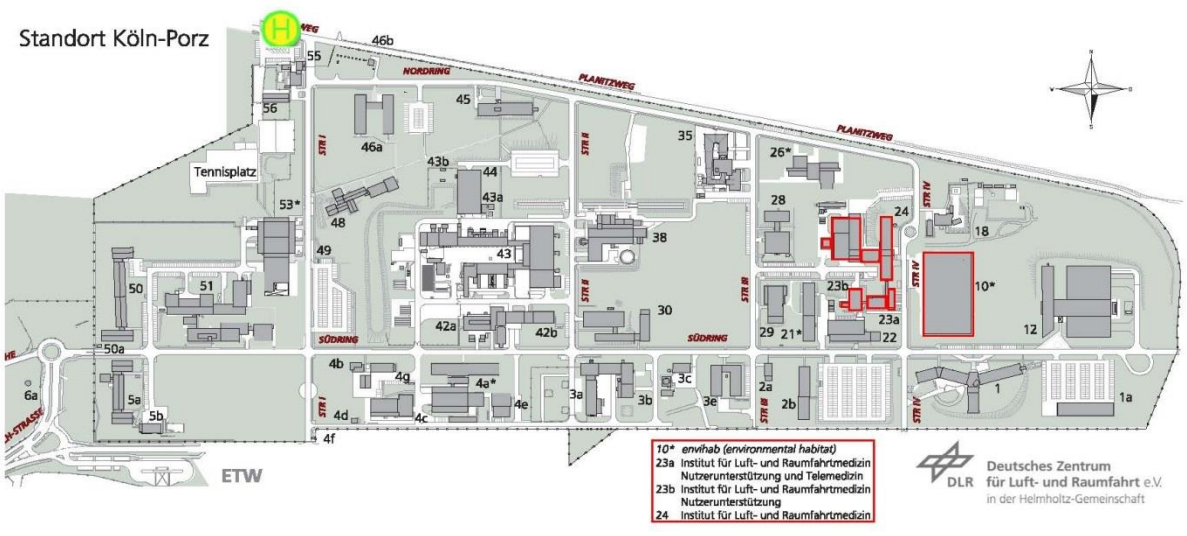
Arrival by bus
To get to DLR Koeln by bus, take the KVB bus number 162 from Porz-Wahn. The bus sign will show "DLR". Please be sure that you take the one saying "DLR" as there are different routes for bus number 162. Exit at the last stop and you have arrived at the main gate of the German Aerospace Center DLR Koeln.

Arrival by taxi
Upon arrival at Koeln Hauptbahnhof (central station) take a taxi to "Porz-Wahnheide, DLR". Taxi stands are located on both, the north and south exit of the station. Taxis are available almost everywhere in Cologne. However, if you can't find one, you can call Tel. 19410 and ask to be picked up. Tell the driver to take you to "Porz-Wahnheide, DLR". The price will very much depend on daytime and traffic but from Cologne central station to DLR without any traffic jam it should not exceed 35 Euros.

Arrival by car
Have a look at the map (How to reach us): Arriving from Frankfurt (A3) or from Bonn (A59): follow the indications to Koeln Bonn Airport (A59) until the exit Porz-Wahn/Wahnheide. At the exit take the right (Porz-Wahnheide) and follow the DLR sign.
Arriving from Cologne (A59) or Oberhausen/Duesseldorf (A3): follow the indications to Koeln/Bonn Airport (A59), then do not exit at the interchange "Flughafen Köln/Bonn" but take the next exit Porz-Wahn/Wahnheide. At the exit drive left (Porz-Wahnheide) and follow the DLR sign.

Note: If you use a navigation system, enter your destination as "Planitzweg" instead of Linder Höhe.

Arrival by air
Upon arrival at Koeln Bonn Airport there's two possibilities: Take a taxi in front of the terminal and ask the driver to take you to "DLR in Porz-Wahnheide". Or take the local train S 19 direction "Troisdorf" from the railway station "Köln/Bonn Flughafen", which is located in the basement of the airport, to the station "Porz-Wahn" which is your first stop after boarding the train. Continue from there by KVB bus number 162, direction "DLR". See also above instructions "By train" and "By bus".



Human Physiology Workshop 2023

If you have any questions please contact:

Organizers

Jörn Rittweger, Claudia Kaiser-Stolz, Alexandra Noll, Willi Pustowalow, Friederike Wütscher (German Aerospace Center (DLR), Institute of Aerospace Medicine, Cologne)
Katrin Stang, Michaela Girgenrath, Christian Rogon (German Space Agency at DLR, Bonn)

→ humanphysiologie-ws@dlr.de