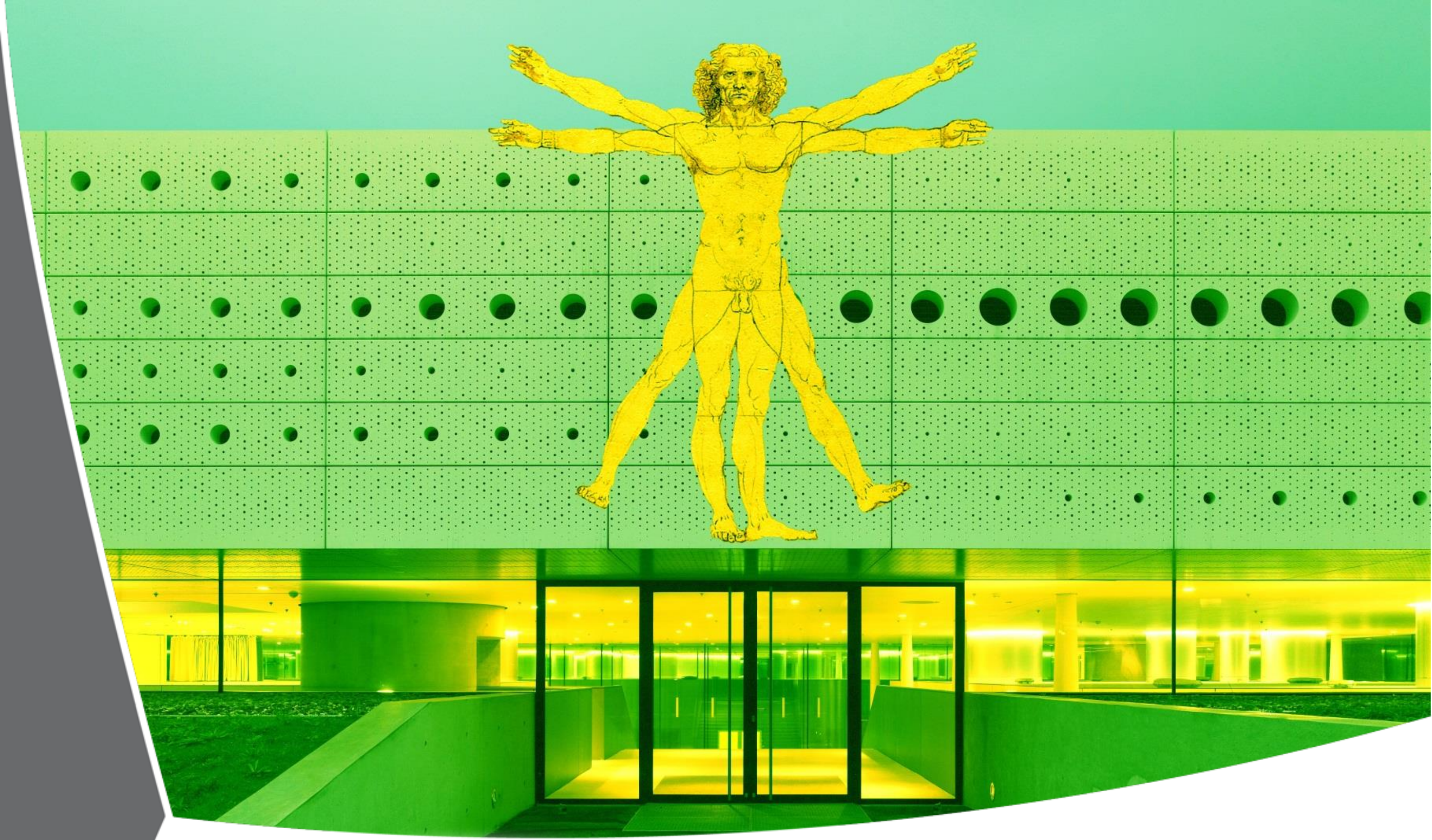

Human Physiology Workshop

8th of December 2018

Venue: DLR
:envihab
Forum
51147 Cologne
Germany
Planitzweg

Human Physiology Workshop

We are pleased to welcome you to the 3rd German Human Physiology Workshop 2018. 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, Tine Becker, Friederike Wütscher (German Aerospace Center (DLR), Institute of Aerospace Medicine, Cologne)
Katrin Stang, Michaela Girgenrath, Christian Rogon (German Aerospace Center (DLR), Space Administration, Microgravity Research and Life Sciences, Bonn)

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Stefan Schneider	German Sport University, Institute of Movement and Neurosciences, Cologne, Germany
Frank Weber	German Air Force Institute of Aviation Medicine, Fürstenfeldbruck, Germany

Print

Deutsches Zentrum für Luft- und Raumfahrt e.V. (DLR)

Program

Saturday, December 8, 2018

08:00 **Registration**

08:30 **Welcome (DLR)**

Session 1:

Chair: Joachim Fandrey & Kirsten Albracht

08:45 **Klein, T.:** Shades of Gravity - The influence of microgravity on cerebral blood flow and electrocortical activity

09:00 **Yilmaz, K.:** Assessment of vertical treadmill running under different levels of simulated gravity, using a vertical treadmill facility with a subject loading system (Avatar)

09:15 **Wilhelm, J.:** Change of lymphatic vessel density by induced muscle atrophy

09:30 **Bury N.-A.:** The Effect of Simulated Weightlessness on the Perception of Self-Motion

09:45 **Brix, B.:** Coagulation Changes during Lower Body Negative Pressure in Men and Women

10:00–10:30 Coffee break

Session 2:

Chair: Wilhelm Bloch & Ramona Ritzmann

10:30 **Schlager, B.:** Intrapleural pressure and its potential impact on spinal pathologies

10:45 **Dreiner, M.:** Reactive jumping under artificial gravity - A possible countermeasure against articular cartilage degeneration in space?

11:00 **Weber, J.:** The more exercise, the higher the benefit during space missions? A comparison of two different exercise schedules within a space-analog environment

11:15 **Thoolen, S.:** Operational performance for spaceflight: Robotic On-Board Trainer (ROBoT) skill acquisition and associated (neuro)physiological response

11:30 **Olsen, L.:** Cardiovascular Health: Can Exercise Replace the Loss of Estrogen in Postmenopausal Women? An *In* Vitro Model

11:45 **Deb, B.:** Sensory re-weighting: the use of vision for spatial orientation and balance control when vision is impaired

12:00–13:00 Lunch break

Session 3:

Chair: Nandu Goswami & Gabriele Pfitzer

13:00 **Hawliczek, A.:** Sinusoidal vibration as a proposed countermeasure to orthostatic intolerance through improvements in cardiopostural control. Implications for geriatrics and astronaut rehabilitation

13:15 **Staeudle, B.:** Functional implication on the gastrocnemius medialis muscle-tendon-unit after reconstruction of Achilles tendon rupture

13:30 **Fathi, A.:** Effect of orthostatic challenge upon nasal mucosal blood volume: a candidate indices of cephalad hemodynamic regulation

13:45 **Lawley, J.:** Contribution of sympathetic restraint on blood flow dynamics to the resting and active skeletal muscle

14:00 **Ritzmann, R.:** The effect of high intensity plyometric jump exercise on posture control, gait and functional mobility during 60 days of bed-rest: a randomized controlled trial including 90 days of follow-up

14:15–14:45 Coffee break

Session 4:

Chair: Justin Lawley & Anja Niehoff

14:45 **Austermann, K.:** Effects of an antioxidant cocktail on bone turnover markers during 60 days of 6°head-down tilt bed rest

15:00 **Koschate, J.:** Cardiorespiratory regulation in response to exercise - Effects of confinement in combination with restricted sleep

15:15 **Rabineau, J.:** Illustration of inotropic changes assessed by seismo- and ballistocardiography during long duration space flights

15:30 **Richter, C.:** In vivo fascicle and tendon length of the gastrocnemius medialis during running in simulated hypogravity using the vertical treadmill facility

15:45 **Haeger, M.:** Baroreceptor loading and unloading impairs cognition: A pilot study and future directions

16:00–17:00 Matthias Maurer: Horizons Mission Awards

17:00 Adjourn

Human Physiology Workshop

Abstracts

1

Shades of Gravity - The influence of microgravity on cerebral blood flow and electrocortical activity

Timo Klein[1,2], *Petra Wollseiffen*[1], *Marit Sanders*[3], *Jurgen Claassen*[3], *Heather Carnahan*[4], *Vera Abeln*[1], *Tobias Vogt*[5], *Heiko K. Strüder*[1], *Stefan Schneider*[1,2]

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Introduction: Changes in gravity conditions have previously been reported to be associated with changes in cerebral haemodynamic responses as well as neuronal activity. To better understand the effect of gravity on brain function and the underlying potential link between cerebral blood flow and brain cortical activity we aimed to test the combined responses during parabolic flights.

Methods: Seventeen participants (female: n=8, with a mean age of 37 ± 11 years) were tested under normal gravity (1G) conditions and microgravity (0G) conditions, during 15 bouts of 22 second intervals of weightlessness during a parabolic flight. Middle cerebral artery flow velocity (MCAv) was assessed with transcranial Doppler ultrasound. Two key drivers of MCAv, mean arterial pressure (MAP) and cardiac output (CO) were recorded via finger photoplethysmography. Cortical current density an indicator for brain cortical activity was measured using electroencephalography (EEG). Effects of gravity (1G vs. 0G) on MCAv, MAP and CO were compared using a t-tests. Changes in cortical current density was determined using repeated measures ANOVA with the within-group factors of "localization" (frontal, parietal, occipital, limbic, hippocampus, MCA, ACA, PCA) and "gravity" (1G, 0G).

Results: Key drivers of MCAv changed during 0G compared to 1G, where MAP (p<0.001) decreased and CO (p<0.001) increased during 0G. However, the averaged MCAv (p=0.28) remained unchanged during the microgravity phase in comparison to the normal gravity condition. Cortical current density decreased globally (p<0.001) during 0G compared to 1G.

Conclusion: Our data replicates earlier experiments reporting a decrease in brain cortical activity in microgravity. This decrease of activity, however, is unlikely to be dependent on haemodynamic changes and may be due to changes in fluid dynamics and membrane viscosity on a cellular level.

2

Assessment of vertical treadmill running under different levels of simulated gravity, using a vertical treadmill facility with a subject loading system (Avatar)

Kenan Yilmaz[1], *Jörn Rittweger*[1]

[1] DLR, Institute of Aerospace Medicine, Germany

Introduction: Prolonged exposure to microgravity during spaceflights leads to severe deconditioning in the physical performance of astronauts that affects dangerously crew health and safety during mission critical maneuvers. To understand the effectiveness of the existing inflight daily countermeasures, treadmill running in simulated microgravity under different levels of adjusted g-load is compared to usual treadmill running on earth.

Methods: For purposes of exercise planning onboard the ISS, the objective of this study was to assess the oxygen uptake under using spiroergometric assessment of men and women (n=26, 8 female and 6 male 20-30 years; 6 male and 6 female 50-60 years) during running on an horizontal treadmill and on a vertical treadmill under different levels of simulated gravity with the Vertical Treadmill Facility (VTF) and Subject loading system (SLS) from the European Space Agency (ESA) and took place in the Physiology Laboratory of the institute of Aerospace Medicine at the Department of Space physiology at the German Space Center (DLR) in Cologne, Germany.
After assessing the maximum oxygen uptake using the Bruce-protocol on the horizontal treadmill, an incremental running protocol on both the vertical and horizontal treadmill was performed in randomized order, starting at a speed of 4 kph and increasing every 4 min by 2.5 kph to a maximum of 19 kph. The runs on the vertical treadmill are performed under 0.3g, 0.6g and 1 g of body weight.

Results: 26 Subjects were included with a total of 93 runs (9 of 102 runs excluded).

Treadmill	horizontal	vert_1g	vert_0.6g	vert_0.3g
Maximum Speed [km/hr]	12.0 (2.1)	10.0 (4.2)	14.1 *** (5.4)	18.1 *** (1.2)
VO2 peak [ml/(min*kg)]	40.2 (7.2)	30.4 *** (6.3)	32.1 *** (7.1)	30.7 *** (5.2)
Heart Rate [beats/min]	163.1 (23.6)	147.7 * (29.2)	147 ** (22.7)	147.8 * (23.1)

The maximum speed was greater for 0.3g and for 0.6g on the vertical treadmill ($P < 0.001$, see Table above) than on the horizontal treadmill. By contrast, peak oxygen uptake was greater for the horizontal treadmill than for all conditions on the vertical treadmill ($P < 0.001$), and so was maximal heart rate ($P < 0.05$).

Conclusion: The reduction in peak oxygen uptake on the vertical treadmill was strikingly similar across the three simulated gravity conditions and cannot be explained by inability to run faster. Rather, gravity-related impediment of gas exchange, or impediment of perfusion in horizontal position can be suspected. If this should be the case, then this would constitute a substantial limitation to exercise in space.

3

Change of lymphatic vessel density by induced muscle atrophy

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[1] Dpt. Muscle and Bone Metabolism, Institute of Aerospace Medicine, German Aerospace Center (DLR), Cologne, Germany

Introduction: The functions of lymphatic system include homeostasis, drain of skeletal muscles and return of proteins and other macromolecules from interstitial tissue to the blood vessel system. A disability of the lymphatic efflux can induce grave consequences e.g. an increased loss of proteins. The trial "Exercise-Induced Decline in the Density of LYVE-1-Positive Lymphatic Vessels in Human Skeletal Muscle" from the Institute of Cardiology and Sports medicine, German Sport University Cologne "(…) investigated, if alterations in lymphatic density can be observed in human skeletal muscle as a response to endurance exercise (…) " It becomes apparent that the density of lymphatic capillaries within the extracted biopsy of M. vastus lat. decreased significantly after a cycling training intervention. (Gehlert et al. 2009). After it is asserted that raised endurance training leads to decreased density of lymphatic capillaries in human skeletal muscle, a change is also expected in an atrophied skeletal muscle. We hypothesize an increased density of lymphatic capillaries in human skeletal muscle and use biopsies of M. soleus to investigate the effects.

Methods: The extracted biopsies are results of the "NutriHep"-Trial which shows an induced muscular atrophy after load reduction within wearing "Hepahoios Orthese" for sixty days. (Schopen et al. 2016) It is expected that the atrophied muscle contains an increased density of lymphatic capillaries. 7 subjects were treated by Lupin-substitution and daily electrostimulations. The control group used Hepaistos Orthesis without any treatments. Biopsies were extracted pre and post induced atrophy. Lymphatic capillaries were stained by immunohistochemistry using Anti-LYVE-1 and Podoplanin antibodies for lymph specific staining and Anti-Caveolin-1 for detecting endothelial cells of lymphatic and blood vessels.

Results: For quantitative analysis of the fraction of lymphatic vessels in the total area of the muscle biopsies and the ratio of lymphatic to blood vessels we used ImageJ. Our preliminary results of NutriHep show the following percentages: lymphatic vessels in non-atrophic muscle 0,24+/-0,038%, in atrophic muscle 0,35+/-0,114%. For the ratio of lymphatic to blood vessels we found 3,6+/-1,612% in non- atrophic muscle, while in atrophy it was 5,59+/-1,84%

Conclusions: We could demonstrate that muscle atrophy increases the total fraction as well as the ratio in respect to blood vessels of lymphatic vessels in muscle biopsies. However not all data were taken into account and further analyzes are required. Especially the Lupin- and electrostimulating treatments may have significant influence on these preliminary results.

4

The Effect of Simulated Weightlessness on the Perception of Self-Motion

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[2] York University, Department of Electrical Engineering & Computer Science, Toronto, Canada

[3] University of Applied Sciences, Institute for Visual Computing, St. Augustin, Germany

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Key words: self-motion; visual-vestibular interactions; perception; underwater; leaky spatial integrator model

Introduction: In manned space missions, astronauts have to adjust to altered environmental conditions, independent of how long they will be weightlessness. Anecdotal reports from astronauts suggest an increased sensitivity to visually evoked sensations of linear motion under microgravity. This might challenge astronauts' spatial orientation and thus lead to performance errors, to the detriment of the mission's success. The objective of the present experiment was to assess the effectiveness of visual cues to linear motion in simulated weightlessness using water immersion and to compare these results with an ongoing overarching project that implements the present tasks in weightlessness (aboard the ISS and during microgravity flights).

Methods: Twenty-three participants (10 female; 25.5 ± 6.1 years) were tested in two *body postures* (lying supine / sitting upright) in each environmental *condition* – laboratory / underwater while looking at a visual display indicating upright continuously aligned with the long axis of the body. Water immersion reduced somatosensory cues to upright, and the supine posture put vestibular cues in conflict with the visual cues as to the participants' orientation. A hood occluded the visual surroundings beyond the screen. The experiment investigated the amplitude of self-motion evoked by optic flow by measuring the perception of "travel distance" in a simulated upright, visual environment. Participants performed two tasks: task 1: 'move-to-target' in which they moved to the position of a previously presented target (8m, 12m, 16m), and task 2: 'adjust-target' in which they adjusted the position of a target to match a previously experienced self-movement (8m, 12m, 16m). Data were fitted to the leaky spatial integrator model of Lappe et al. (2007, Exp Brain Res, Vol. 180:35-48) which determined gain and decay factors for each condition.

Results: The results for task 1 showed a slight overestimation for each distance. For task 2 participants underestimated travelled distance for short ranges (8m & 12m) and overestimated it for the larger ranges (16m). Further analysis will use the leaky spatial integrator model to reveal possible differences between the conditions and postures.

Outlook: The present experiment will reveal the influence of somatosensory cues in the perception of self-motion on earth. Any differences between the two conditions would confirm that these cues affect the perception of self- motion. Any differences between these results and the results of comparable experiments currently being carried out in space would quantify the relative importance of vestibular and somatosensory orientation cues to the perception of self-motion.

Acknowledgements: This research was supported by a VISTA Visiting Scholar Award funded by the Canadian First Research Excellence Fund, the York University (Toronto) and the University of Applied Science (Bonn-Rhein-Sieg). We thank Thomas Förster and Thomas Kesnerus for technical support, Jürgen Geiermann for hardware development and Dylan Stobbe for assistance with data collection and analysis.

5

Coagulation Changes during Lower Body Negative Pressure in Men and Women

Gerhard Cvirn[1], James E. Waha[2], Bianca Brix[2], Andreas Rössler[2], Andreas Jantscher[2], Axel Schlagenhauf [3], Martin Koestenberger[3], Willibald Wonisch[1], Thomas Wagner[4], Nandu Goswami[, 2]*

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Introduction: Application of lower body negative pressure (LBNP) is a surrogate to study physiological responses to blood loss, i.a., activation of the coagulation cascade. We investigated whether lower body negative pressure (LBNP) application leads to coagulation activation in whole blood (WB) samples in healthy men and women, and whether LBNP could be a suitable tool to identify healthy individuals with an elevated risk for future thrombotic events.

Methods: Twenty-four women and twenty-one men healthy young participants, with no histories of thrombotic disorders and not on medications, were included. LBNP was commenced at -10 mmHg and increased by -10 mmHg every-five minutes until a maximum of -40 mmHg, followed by a recovery phase of 10 minutes. Blood samples were collected at baseline, at end of LBNP and end of recovery. Haemostatic profiling included comparing the effects of LBNP on coagulation values in both men and women: standard coagulation tests, calibrated automated thrombogram, thrombelastometry, impedance aggregometry and markers of thrombin formation.

Results: Twenty-four women and twenty-one men were investigated. LBNP suction led to significant coagulation activation determined in both plasma and WB samples. At baseline, women are hypercoagulable compared with men, evidenced by, e.g., shorter 'Lag times' and higher thrombin peaks (CAT) and by shorter "Coagulation times" and 'Clot formation times' (TEM). Moreover, men were more susceptible to the LBNP suction, as evidenced by elevated FVIII levels and decreased 'Lag times' (TEM) following LBNP. Furthermore, LBNP led to coagulation activation without accompanying endothelial activation.

Conclusions: Women are a priori relative hypercoagulable compared with men, but men are more susceptible to coagulation changes during LBNP suction. LBNP could be a suitable tool for identifying individuals with a high risk for future (re-)thrombosis, even in those with previous histories of thrombosis.

6

Intrapleural pressure and its potential impact on spinal pathologies

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Introduction: The mechanical interaction between the physiology of the pleura, the abdominal organs and the spine is fairly unknown. Literature suggests a potential relevance of the thorax physiology on the development of idiopathic scoliosis. The intrapleural pressure (IPP), which is distributed across the inner chest wall, has as yet been widely neglected in etiology debates.

In this study, we investigated the potential mechanical interaction between the IPP and the spinal curvature, and propose a schematic diagram of the mechanical interactions within the thorax (see figure).

Methods: A parametric finite element (FE) model was created based on CT-data of an exemplary healthy (non-scoliotic) patient. This model included the vertebral levels T1 to S1, as well as the rib cage. The material properties of the passive structures of the vertebral segments and the costo-vertebral joints were calibrated using in vitro data. The spine was fixed at S1. To additionally investigate the influence of the IPP in an upright posture, the lateral displacement was fixed at T1.

Possible IPP values were deduced from published values and applied on the inner chest wall in the region of the lung. IPP distributions with a constant IPP gradient of -6 (Pa/mm) and an IPP of -300 Pa at the base of the lung was assumed. Furthermore, the influence of an asymmetry in the IPP distribution between the left and right hemithorax was investigated by reducing the gradient on one side and removing the pressure unilaterally within coronal sections. The numerical results were then compared to clinical data.

Results: The application of the IPP resulted in a reaction force of 22.3 N in the axial direction of the spine, which corresponds to 2.3 kg of weight, and a reaction moment of -2.8 Nm around the lateral axis at S1. An asymmetrical pressure between the left and right hemithorax resulted in lateral deviation of the spine towards the side of the reduced negative pressure. In particular, the pressure within the dorsal section of the rib cage had a strong influence on the vertebral rotation, while the pressure in medial and ventral region affected the lateral displacement.

Conclusions: An asymmetrical pressure caused spinal deformation patterns which were comparable to deformation patterns seen in scoliotic spines. The calculated reaction forces suggest that the IPP contributes in counterbalancing the weight of the intrathoracic organs. The intrapleural fluid, therefore, would be an important medium for counterbalancing the forces within the thorax and transmitting these to the chest and spine.

This study revealed that the IPP might have a strong influence on spinal curvature and be of relevance for understanding pathologies, Intraabdominal pressure such as adolescent idiopathic scoliosis.

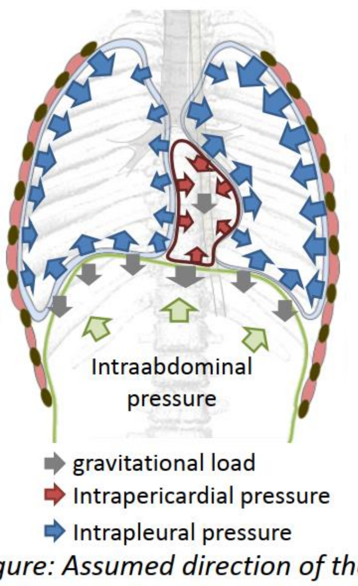

Figure: Assumed direction of the load vectors within the cross-section of the thorax in an upright posture.

7

Reactive jumping under artificial gravity – A possible countermeasure against articular cartilage degeneration in space?

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Introduction: A major challenge of long-duration spaceflight is the degeneration of skeletal muscle and bone tissue due to the exposure to microgravity (LeBlanc et al., 2007). The effects of microgravity on articular cartilage are less known but it is well established that articular cartilage health depends on an appropriate mechanical stimulus. Unloading and immobilization in animal and human studies have been shown to cause cartilage thinning and softening (Haapala et al., 2000; Hudelmaier et al., 2006). Recent studies have revealed that bed rest (Liphardt et al., 2017) and microgravity (Niehoff et al., 2016) initiate catabolic processes. Currently implemented exercise countermeasures for crew members of the International Space Station (ISS) have not been subject to cartilage related research. The purpose of the present study was to investigate the effects of reactive jumping under artificial gravity on serum biomarkers of articular cartilage metabolism to identify potential training methods to be implemented as a countermeasure for articular cartilage degeneration in space.

Methods: Each of 15 healthy male adults (26±4 years, 181±4 cm, 77.2±5.8 kg) participated on four different 30 min intervention protocols (P) on four different days: Centrifuge (P1), sledge jump system (P2), vertical jumps (P3) and running (P4). During the interventions P1, P2 and P3, 15 series of 15 reactive jumps were performed. In the P4 intervention, the subjects ran on a treadmill (2.2 m/s). Blood samples were taken before (T0) and after 30 min rest (T1), and on three time points after the interventions (immediately (T2), 0.5 h (T3) and 1.0 h (T4) after the interventions). Serum concentrations of cartilage oligomeric matrix protein (COMP, AnaMar), hyaluronic acid (HA, TECOmedical) and chitinase-3-like protein 1 (CHI3L1/YKL-40, TECOmedical) were determined using commercially available sandwich enzyme-linked immunosorbent assays (ELISA). Peak forces and ground contacts were determined by force plates (AMTI® and Novotec Medical GmbH). A two-way (time*group) repeated-measures analysis of variance (ANOVA) was used to detect significant differences ($p<0.05$) between groups (Duncan's post-hoc test).

Results: Peak forces during the jumping interventions were significantly different ($p<0.001$) between P1, P2 and P3, with increasing peak forces from P1 to P3. No significant differences were found between the peak forces for the interventions P2 and P4. After multiplication of the peak forces with the ground contacts, all interventions were significantly different to each other ($p<0.001$), with the highest values for P4. Biomarker analyses revealed that serum COMP and YKL-40 levels increased significantly ($p<0.05$) during all interventions and decreased 0.5 h after the interventions. The intervention P4 had significant higher ($p<0.05$) serum COMP levels after the intervention compared to the other protocols, with the highest increase measured directly after the intervention (+30%). The relative increase in YKL-40 concentration from before to after the intervention was highest for P3 (+32%). HA analysis did not reach the necessary detection threshold for most of the participants.

Conclusions: Our study confirmed the mechanosensitivity of COMP and YKL-40 and all applied interventions could trigger this response. The biomarker response was greatest for the vertical jump or running interventions. Artificial gravity protocols resulting in greater gravitational forces on the countermeasure device might achieve a more pronounced response in cartilage metabolism.

References: Happala et al. (2000). Int J Sports Med 21(1):76-81; Hudelmaier et al. (2006). J Musculoskelet Neuronal Interact 6(3):284-290; LeBlanc et al. (2007). J Musculoskelet Neuronal Interact 7(1):33-47; Liphardt et al. (2017). J Orthop Res 36(5):1465-1471; Niehoff et al. (2016). Osteoarthritis Cartilage 24(1):144-145

8

The more exercise, the higher the benefit during space missions? A comparison of two different exercise schedules within a space-analog environment

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Introduction: The increasing demand of space flights requires efficient countermeasures to prevent (neuro)psychophysiological impairments. Meanwhile it is well know that physical activity can counteract loss of bone and muscle mass, less is known about the effects on the brain and the (neuro-)hormonal system during space missions.
Furthermore, it is still highly under debate how much physical activity is adequate in order to prevent (neuro)psychophysiological deteriorations and how much is really necessary in order to not restrict the valued time during space missions. Therefore, we compared the outcomes of stress markers, neurotrophic factors, cortical activity and subjective wellbeing of two different campaigns of the *Human Exploration Research Analog* which differed in length and the amount of physical activity performed. It was hypothesized that less physical activity would lead to enhanced stress secretion, higher cortical arousal and mood impairments.

Methods: Both campaigns (C3 & C4) consisted of 16 participants (*C3 aged: 36.3 years; C4 aged: 39.4 years*). In campaign C3 participants were isolated for 30 days and performed physical activity on a daily basis. In campaign C4 participants were isolated for 45 days and performed physical activity only every second day. On several mission days participants completed the Positive Affect and Negative Affect Scale (PANAS-X) and a five-minutes resting electroencephalography. Also, intravenous morning cortisol, melatonin, and IGF-1 were assessed. Effects of both interventions were determined using a repeated measures ANOVA design.

Results: Cortisol levels were significantly increased in both groups during the isolation period. There was further a significant group effect and time by group interaction with higher cortisol secretion during the isolation period in participants from C3 compared to C4. Melatonin showed a significant time effect in terms of increased melatonin levels during isolation and a significant group difference with overall higher values for participants of C4. IGF-1 revealed significant changes for both groups, but did not differ between groups over time. Cortical activity, defined by frequency spectrums did not change over time or differed between both groups. In regards to mental changes, the general positive affect (GPA) of the PANAS-X was reduced over time for both groups, but did not show a significant contrast between the groups. The general negative affect did not change over time, but revealed a significant group effect which might be explained due to high baseline differences.

Conclusions: These results provide highly interesting information considering the effects of physical activity and the intensely debated question about how much physical activity is necessary to prevent impairments of the physiological homeostasis. Our results might give a first hint that physical activity does not necessary be performed on a daily basis, but rather that physical exercise every second day might already be sufficient to counteract (neuro)psychophysiological impairments. This could be demonstrated by the significantly higher cortisol secretion in the C3 campaign, although exercise was performed twice as much as in C4.

9

Operational performance for spaceflight: Robotic On-Board Trainer (ROBoT) skill acquisition and associated (neuro)physiological response

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[3] Center for Space Medicine, Baylor College of Medicine, Houston TX, USA

Introduction: Robotic On-Board Trainer (ROBoT-r) is under investigation by NASA for quantitative operational performance assessment in astronauts. A better understanding of the learning effects in the ROBoT-r task, and potential risks to performance of this complex task, is needed.

Methods: ROBoT-r skill acquisition in a new two-week protocol (MP) was determined in five healthy participants and compared to previously used protocols (HERA; Neumayer). Simultaneous multimodal (neuro)physiological monitoring was performed with a self-contained recording system (NINscan) to investigate the relationship between physiological parameters and performance.

Results: Between HERA and MP, angular error at capture was different over training sessions (F=1.8, p=0.039). Between Neumayer and MP, overall success rate (F=5.8, p=0.000), weighted performance score (F=5.3, p=0.000) and trial duration (F=4.2, p=0.000) were all different when compared across sessions. Using near-infrared spectroscopy, the oxygenated haemoglobin response changed over sessions at the right medial prefrontal cortex (F=1,9, p=0.024), and was correlated to weighted performance score (rrm=-0.32, p=0.002) and angular error (rrm=0.24, p=0.021). EEG theta (F=2.4, p=0.004) and alpha (F=2.1, p=0.015) activity response changed over sessions, and was correlated to weighted performance score (theta: rrm=-0.30, p = 0.003; alpha: rrm=-0.32, p=0.002) and angular error (alpha: rrm=0.21, p=0.050). Heart rate response was correlated to weighted performance score (rrm=- 0.21, p=0.047). Heart rate variability and electrodermal activity showed no significant changes.

Conclusions: This study provides preliminary data on skill-acquisition and associated (neuro)physiological correlates on a spaceflight- and operationally-relevant task (ROBoT-r). Compressed training protocols appear adequate for pre- and inflight training, and NINscan may help to provide indicators of physiological indicators associated with risk of performance decrements. However, higher statistical power and further comparison within and between different training protocols is needed.

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Cardiovascular Health: Can Exercise Replace the Loss of Estrogen in Postmenopausal Women? An *In Vitro* Model

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Background: The menopausal transition is associated with a loss of estrogen and a consequent increased risk of cardiovascular disease. Muscle contraction can stimulate some of the same molecular pathways as estrogen in rat myotubes through activation of estrogen-response elements (EREs) and regular exercise is therefore likely useful strategy to counteract the decline in cardiovascular health.

Objective: The current investigation is a sub-study of a larger intervention study with the aim to assess the efficacy of aerobic exercise training on vascular function in late postmenopausal women. The objective of the present sub-study is to investigate the activation of EREs by either estrogen or electrical stimulation in cultured human myotubes and endothelial cells isolated from muscle biopsies.

Hypothesis: We hypothesize that electrical stimulation of myotubes will lead to activation of EREs through ERRα, similarly to activation of EREs through ERα and ERβ. ERE activation will lead to upregulation of downstream proteins.

Study Design: Skeletal muscle myocytes and endothelial cells have been isolated from muscle biopsies obtained from m.v.lateralis and pilot studies are currently being conducted to optimize the protocol. Cultured myotubes will be stimulated either electrically or with estrogen and the extracellular media from these myotubes will be added to microvascular endothelial cells. In addition, the endothelial cells will also be treated with acute or chronic estrogen stimulation. The samples will be analyzed for mRNA and protein content of a number of factors relating to vascular function (e.g.NADPH oxidase, SOD2, NO, eNOS and ET-1), and angiogenesis (e.g. VEGF, VEGFR2, TSP1, Tie2and Ang2).In addition, the content of ERRα and estrogen receptors (ERα, ERβ and GPER)and the related target genes (e.g.PGC-1α, AMPK and PI3K) will be assessed. I expect to be able to present the first results from the cell experiments at the work-shop.

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Sensory re-weighting: the use of vision for spatial orientation and balance control when vision is impaired.

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Introduction: Falls are the foremost cause of injury in the elderly, with a third of people aged over-65 falling at least once per year. Falls risk has been linked to increased visual field dependence for spatial orientation and balance control, even though vision typically deteriorates with age similar to vestibular and proprioceptive sensitivity. Likewise, though many ISS astronauts experience reduced visual acuity from long duration spaceflight, visual dependence for spatial orientation is typically upregulated as both vestibular and proprioception are disrupted in microgravity. Cambridge Simulation Glasses (CSGs) provide a way to controllably degrade the visual field in healthy subjects that was not possible till now without total removal of functional vision. Thus, this study seeks to assess the effect of graded visual impairment upon visual field dependence.

Methods: Two groups of healthy subjects (Stable: n = 11, mean age ± SD = 21.1 ± 1.45; Foam: n = 11, age = 29.6 ± 7.75) with no sensory deficits or established falls risk were randomly assigned six levels (L0 to L5) of visual impairment using CSGs, and performed Rod & Disk Tests whilst standing upon either stable, or foam surfaces. At each CSG level, subjects were asked to correct an onscreen rod to vertical after it was randomly set to 20° CW/CCW, for 4 trials with motionless dots (static), and 4 with dots rotating (roll velocity 30° s^{-1}). Spatial orientation was measured through deviation in subjective visual vertical (SVV) averaged per visual condition (SVV_{static}, $SVV_{rotating}$), with $\Delta(SVV_{rotating} - SVV_{static})$ expressed as $SVV_{dynamic}$. Balance control was assessed using computerised centre-of-pressure sway area (SA_{static}, $SA_{rotating}$). Within- and between-subject effects of CSG level and support surface respectively upon SVV and SA were evaluated by mixed model analyses of variance. Subjective ratings of difficulty seeing, difficulty correcting the rod, vection score, vection/vision ratio, and balance confidence were recorded after each CSG level and evaluated by Spearman's rank correlations.

Results: Visual impairment and support surface stability did not interact but were significantly associated individually with increased $SVV_{rotating}$ (CSG level: $F_{5,100} = 3.850$, $p = 0.003$; support surface: $F_{1,20} = 10.24$, $p = 0.004$) and $SVV_{dynamic}$ (CSG level: $F_{5,100} = 5.055$; support surface: $F_{1,20} = 10.525$, $p = 0.004$). $SA_{rotating}$ was greater in the foam condition vs. stable surface (support surface: $F_{1,20} = 4.481$, $p = 0.047$), though there was no statistically significant effect of visual impairment on SA. A U-shape pattern was present in both SVV and SA data, exaggerated further by the foam condition; maximal visual dependence was reached at L3 impairment before returning towards baseline, though this was not statistically significant. All subjective ratings positively correlated with CSG level ($p < 0.01$).

Conclusions: Graded visual impairment increased spatial disorientation and postural sway, particularly when ankle proprioception was simultaneously disrupted. As vision worsened, visual dependence appeared to reach a maximum at the region of VA possessed by many over-65s before returning towards baseline. Reduced visual stabilisation may combine with unopposed visual motion detection at mild-moderate visual impairment and lead to enhanced vection and disorientation. The resulting within-subject group variability may explain the lack of a significant effect of CSG level upon SA. At higher CSG levels, visual impairment may be severe enough to trigger sensory reweighting away from vision. The transition from using exocentric visual cues to egocentric references appears dissociated with subjective ratings. Thus, a 'vulnerable zone' of visual impairment may cause sensory conflict in people with degradations in other senses, increasing falls risk.

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Sinusoidal vibration as a proposed countermeasure to orthostatic intolerance through improvements in cardiopostural control. Implications for geriatrics and astronaut rehabilitation

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Introduction: Orthostatic intolerance is a multifaceted condition with serious consequences due to the possible risk of injuries. Sinusoidal vibration is a countermeasure that proved its efficiency against the plethora of major health concerns for both the elderly, and the astronauts, including (but not limited to): muscle atrophy, bone mineral density loss, and insulin insensitivity. It is possible to combine vibration with other forms of rehabilitation, such as exercise or electromyostimulation to improve its efficiency.

Methods: The pilot study under the ethical approval of Medical University of Graz conducted two consecutive stand tests, before and after 15 minutes of 13 Hz sinusoidal vibration on the Galileo vibration platform attached to the foot of a bed tilted up by 15°; the intervention was preceded and proceeded by baseline and recovery recordings.

Results: Selected cardiac parameters were analyzed for 5 young healthy individuals (1 female, 4 males; mean age 25.6 years ± 2.245) and analyzed statistically with repeated measures one-way ANOVA. It revealed that HR values post-vibration (68.27 ± 13.64) were decreased in comparison to baseline (56.69 ± 10.32), systolic blood pressure was elevated (119.47 ± 7.46 became 103.27 ± 11.17), and diastolic BP similarly decreased from 75.09 ± 5.95 to 65.91 ± 9.29. Minute by minute, only heart rate showed significant differences at all time points. Blood pressure was significantly different exclusively for diastolic, and only at 2 separate time points during control and post-vibration.

Conclusions: It is concluded that both heart rate and diastolic blood pressure showed significantly different values following the vibration intervention ($p=0.0022$ and $p=0.0288$ respectively), even though it was passively performed at low frequency and on the tilted bed. Vibration is a promising method to improve cardiopostural response to orthostatic stress, with benefits available to patients confined to bedrest, as well as returning astronauts. Further research is needed to ensure that the countermeasure's full capacity for the future benefit of individuals affected by orthostatic intolerance, irrelevant of its cause and origin.

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Functional implication on the gastrocnemius medialis muscle-tendon-unit after reconstruction of Achilles tendon rupture

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Introduction: After complete Achilles tendon rupture (ATR), long-term deficits in force generation of the triceps surae muscle-tendon-unit (MTU) and functional limitations have been described. Surgical reconstruction and early functional treatment of Achilles tendon rupture can lead to a lengthened Achilles tendon causing a lack of tension in the triceps surae MTU. As a consequence, an excessive sarcomere overlap forces the muscle fascicles to operate in a disadvantage length for force generation. In order to restore function, we hypothesize that a re-organization of in-series sarcomeres may compensate for changes in work constraints imposed by the longer tendon. Tendon stiffness has already been described to increase after ATR, which might also be an actuator to compensate for tendon lengthening. To clarify the mentioned deficits, this study investigates the mechanical and morphological properties of the triceps surae MTU post rupture and their effect on force generation.

Methods: Eleven male subjects (44 ± 11 yrs) who underwent acute surgical repair of a complete AT rupture were analyzed 4.6 ± 2 years after rupture. Tendon stiffness and morphology as well as muscle architecture were determined using ultrasonography. Further, force-length relation was assessed in maximal plantarflexion effort in five different ankle angles (20° dorsiflexion to 20° plantar flexion) capturing gastrocnemius medialis muscle architecture via ultrasonography simultaneously. The unaffected leg served as control. Additionally, MTU simulations (OpenSim) were used to obtain a better understanding of the influence of affected MTU properties in force generation.

Results: The affected tendons of the gastrocnemius medialis muscle (GM) are significantly longer (13±10%, p=0.009), have a greater CSA (105±28%, p<0.001) and tendon stiffness (54±24%, p<0.001) while no significant differences were found for tendon material properties. The maximal moment produced at optimal ankle joint angle differed significantly (15±15%, p=0.007) and occurred in a significantly more dorsiflexed position (9±2°, p<0.001). A mean deficit in plantarflexion moment of 35±15% (p<0.001) occurred. Shorter muscle fascicles (32±12%, p<0.001) and greater pennation angles (21±13%, p<0.001) as well as decreased muscle thickness (14±10%, p=0.008) were observed in the GM muscle at rest.

Conclusion: Our findings confirm previous reports indicating elongated and stiffer tendons in Achilles tendon rupture patients with a remaining deficit in force generation. In addition, ultrasound measurements showed for the first time a decrease in fascicle length and an increase in pennation angle of the GM muscle, indicating an architectural re-organization of the triceps surae due to a longer Achilles tendon long-term post-surgery. These changes were accompanied by a shift in the optimal ankle joint angle of force production towards more dorsiflexed positions. Taken together, these data suggest that the lengthening of the Achilles tendon seen in ATR patients may partly be compensated for by an increase in stiffness and a reduction of in series sarcomeres. However, years after surgery, the longer tendon may still not be fully accounted for. Therefore, when aiming for full return of function and strength, an important goal for surgery and early functional treatment appears to be to minimize tendon lengthening.

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Effect of orthostatic challenge upon nasal mucosal blood volume: a candidate indices of cephalad hemodynamic regulation

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Introduction: Microgravity-induced cephalad fluid redistribution are suggested to increase intra-ocular (IOP) and intra-cranial (ICP) pressures in some astronauts and may lead to visual impairment. As such physiological changes represent a significant issue for future space exploration missions. Interestingly, nasal congestion is also commonly associated with spaceflight, and orthostatic intolerance is a significant issue Post-flight. Therefore, this study sought to determine if a novel non-invasive measurement of nasal mucosal blood volume (NMBV) is sensitive to orthostatic challenge.

Methods: Nine healthy participants (mean age: 26.2 ± 5.6, 44% male, body mass index 21.2 ± 2.1 kg m^{-2}) gave written informed consent to be tilted on a tilt-table whilst nasal tissue optical density (OD) was recorded (2Hz) using Near Infra-Red Spectroscopy (Rhinolux, Rhios GmbH, DE). Each participant completed a pre-defined six-phase (each 10 minutes) protocol consisting of three test, and three baseline conditions: i) supine (baseline), ii) 60 degrees head down tilt (HDT), iii) supine (baseline 2), iv) 60 degrees head down tilt + 40 mmHg lower body negative pressure (HDT LBNP), v) supine (baseline 3), and vi) head up tilt (HUT). The study was concluded with a 3-minute supine recovery phase. Total change in nasal mucosal blood volume defined as the area under the curve (AUC), and maximal responses amplitude (MRA) were determined for each phase. The effect of orthostatic challenge was determined by one- way ANOVA with post-hoc Tukey's analysis.

Results: Orthostatic challenge significantly modulated nasal mucosal blood volume [$F(3,33) = 4.14$; $p = 0.01$]. Post-hoc analysis revealed a significant increase in NMBV in the HDT position as compared with HDT LBNP ($p = 0.02$), and HUT ($p = 0.02$). Conversely, there was no significant change in NMBV between HDT LBNP and HUT, and between supine and test conditions. We also report significant differences in MRA in response to the direction of tilt [$F(2,24) = 13.87$; $p < 0.001$] with a significant increase during HDT compared with HDT LBNP ($p = 0.002$) and HUT ($p < 0.001$). However, no difference between HDT LBNP and HUT was observed.

Conclusions: Our results show that novel non-invasive measurement of nasal mucosal blood volume is sensitive to orthostatic challenge-induced fluid shifts. Studies are currently ongoing to determine the relationship between NMBV and other indices of orthostatic intolerance.

Doctoral degree: MD since June 2018

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Contribution of sympathetic restraint on blood flow dynamics to the resting and active skeletal muscle.

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Introduction: During cycling exercise, there is an increase in muscle sympathetic nerve activity (1,2) retrograde blood flow (3,4) and a reduction in brachial artery vascular conductance to non-active skeletal muscle (3). Yet the contribution of α-adrenergic control of these processes is unclear. The aim of this study was to establish the contribution of α-adrenergic control of brachial artery retrograde conductance at 1) rest, 2) during sympathoexcitation via moderate intensity cycling exercise in non- active skeletal muscle and 3) during sympathoexcitation in active skeletal muscle. We hypothesized that local α-adrenergic blockade will abolish brachial artery retrograde vascular conductance at rest and attenuate the increase in retrograde conductance in non-active and active skeletal muscle.

Methods: Ten young healthy male subjects (age: 26.7±4.0yrs; weight 76.1±8.7kg; height 177.3±5.8cm) participated. Subjects performed three maximal voluntary contractions using a handgrip device.
Subjects then performed rhythmic handgrip exercise at 15% of their maximal voluntary contraction for three minutes. After a short rest, subjects cycled on a semi-recumbent ergometer at 60% peak wattage for five minutes, and then repeated 15% handgrip exercise whilst cycling. The protocol was repeated after local forearm □ and □-adrenergic blockade. Continuous recordings were obtained of brachial artery flow dynamics (anterograde, retrograde and mean blood flow) via ultrasonography and blood pressure through a brachial arterial catheter at each time point. Forearm vascular conductance = flow / pressure * 100. Data were compared by paired t-test.

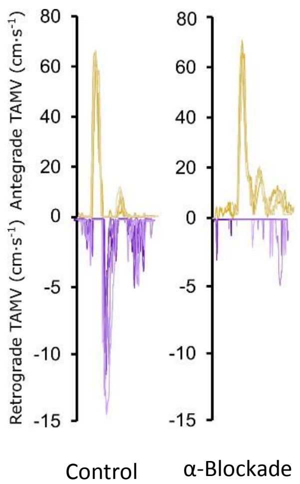

Fig. 1 Effect of α-blockade on brachial retrograde velocity at rest.

Results: Resting brachial retrograde conductance was almost abolished after □-adrenergic blockade (-10.0±5.0 to -0.5±0.4, $ml \cdot min^{-1} \cdot 100 \cdot mmHg^{-1}$, P<0.01, Fig. 1). Cycling exercise caused an increase in brachial retrograde conductance (Δ-59.3±33.1, $ml \cdot min^{-1} \cdot 100 \cdot mmHg^{-1}$), which was attenuated by 55% after α-adrenergic blockade (P<0.01). Cycling exercise also caused a substantial reduction in total brachial conductance (49.1±14.1 to 29.5±14.8, $ml \cdot min^{-1} \cdot 100 \cdot mmHg^{-1}$, P<0.01), but brachial blood flow was maintained (45.0±11.6 to 35.7±17.5, $ml \cdot min^{-1}$, P=0.16) due to the exercise pressure response. Finally, cycling caused an increase in brachial retrograde conductance during handgrip exercise (Δ-30.3±27.0, $ml \cdot min^{-1} \cdot 100 \cdot mmHg^{-1}$), which was also attenuated by ~70% (Δ-10.2±25.7, $ml \cdot min^{-1} \cdot 100 \cdot mmHg^{-1}$, P<0.01) after α-adrenergic blockade.

Conclusions: The primary findings of this study were that at rest and during cycling exercise, a substantial component of brachial retrograde conductance is due, in part, to α-adrenergic vasoconstrictor tone in non-active and active skeletal muscle. Thus, precise measurements of brachial artery flow dynamics may provide a window to assess sympathetic control of vascular function during physiological increases in sympathetic activity.

References: (1) Saito et al. 1993; (2) Moralez et al. 2018; (3) Simmons et al. 2010; (4) Thijssen et al. 2009

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The effect of high intensity plyometric jump exercise on posture control, gait and functional mobility during 60 days of bed-rest: a randomized controlled trial including 90 days of follow-up

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Introduction: During prolonged space missions, astronauts adapt to the microgravity environment. As a consequence, they suffer from structural and functional changes associated with a progressive deconditioning of the human body. Deficits in balance and gait control predisposing individuals to an increased fall and injury risk are the space agencies' major concerns regarding manned inter-planetary space flights scheduled in the future. In order to maintain health and fitness during space missions, astronauts have to perform physical exercise during spaceflight, which can allow them to preserve the capability to perform critical mission tasks and to counteract microgravity-induced impairments. This study aimed to assess the efficiency of a plyometric jump exercise as a countermeasure to prevent detrimental effects on gait, posture control and functional mobility in the microgravity analog bed rest.

Methods: 23 healthy male participants (aged 30±7 years) were selected after standardized screening procedure and confined to bed in the Envihab facilities of the DLR. The study was divided in three phases: a 15-day baseline measurement phase, a 60-day head-down-tilt bed-rest phase and a 90-day follow up phase. Participants were randomly allocated to the control group (CTRL, n = 11) or the training group (JUMP, n = 12). We assessed sway path and electromyographic activity in monopedal stance, spatiotemporal, kinematic and variability characteristics in gait, functional mobility with repeated chair-rises and Timed Up and Go tests.

Results: The JUMP group showed no significant changes after bed-rest, whereas the CTRL group exhibited substantial degradations: an increased sway path ($p<0.05$) was found concomitant with an increased co-contraction of antagonistic muscles encompassing the knee and ankle joint ($p<0.05$). A reduced locomotor speed ($p<0.05$) was accompanied by reduced angular excursions in the ankle and knee joints ($p<0.05$), adverse gait rhythmicity ($p<0.05$), and a marked increased gait variability ($p<0.05$). Chair-rising time was increased ($p<0.05$) and rises were executed with reduced peak power ($p<0.05$). Duration to accomplish the Timed Up and Go tests was increased ($p<0.05$). The deconditioning effects in CTRL persisted for almost one month after bed-rest. Increases in sway path were correlated to decreases in gait speed.

Conclusions: The plyometric jump exercise has been justified in being a successful countermeasure to prevent the detrimental effects of physical deconditioning during two months of bed-rest. It preserved neural activation patterns involving antagonistic muscle coordination when controlling postural equilibrium. Furthermore, it allowed to effectively maintain functional mobility and the ability to perform complex locomotor movements including bipedal gait at maximal speed as well as technics involving turns and rises. In view of manned inter-planetary space flights, we recommend plyometric jumps as an appropriate strategy combatting functional deconditioning of the human body during space missions.

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Effects of an antioxidant cocktail on bone turnover markers during 60 days of 6°head-down tilt bed rest

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Introduction: Inactivity during space flight and in ground based analogs, such as 6°head-down tilt bed rest (HDBR) is associated with bone loss. This bone loss is mainly induced by decreased mechanical loading. Additionally, oxidative stress resulting from excessive formation of reactive oxygen species (ROS) or dysfunction of the antioxidant defense systems leads to increased bone resorption processes. Antioxidants like polyphenols, omega-3-fatty acids, vitamins and micronutrients may mitigate the damaging effects of ROS on bone turnover and mediate the scavenging of free radicals.

We hypothesized that antioxidant supplementation during 60 days of HDBR reduces bone resorption and increases bone formation compared to non-supplemented controls.

Methods: A randomized, controlled, single-blind intervention study, in a parallel design was conducted at the Institute for Space Medicine and Physiology, Toulouse, France with 20 healthy male volunteers (age 34 ± 8 y, weight 74 ± 6 kg). The study was divided into two campaigns and each campaign consisted of a 14-d adaptation-, a 60-d HDBR- and a 14-d recovery phase. Ten volunteers participated in each campaign. In both campaigns, five volunteers were randomly allocated to the intervention group and five volunteers to the control group. In the intervention group volunteers received an antioxidant cocktail, consisting of 741 mg polyphenols, 2.1 g omega-3-fatty acids, 168 mg vitamin E and 80 µg Selenium. In the control group volunteers received no supplement. All volunteers received an individually tailored and strictly controlled diet. Serum calcium, parathyroid hormone (PTH), osteocalcin, and bone formation markers aminoterminal propeptide of type I collagen (P1NP) and bone alkaline phosphatase (bAP) were measured at different time points during adaptation-, HDBR- and recovery period, along with urinary calcium and bone resorption markers C-telopeptide of type I collagen (CTX) and N-telopeptide of type I collagen (NTX). Data were analysed by linear mixed models, with baseline values, bone mineral density and VO_2max as covariates.

Results: We found a significant time effect for all parameters, but no antioxidant supplement effect. Serum calcium was alleviated during bed rest and decreased in the recovery phase ($P<0.001$). Serum PTH decreased during HDBR and increased in recovery period ($P<0.001$). Serum osteocalcin and undercarboxylated osteocalcin and the bone formation markers bAP and P1NP increased in recovery phase ($P<0.001$). Calcium excretion increased during HDBR and decreased again during recovery period ($P<0.001$). The bone resorption markers urinary CTX and NTX, and serum ßCTX increased during bed rest ($P<0.001$). During the recovery period resorption markers decreased ($P<0.001$) and 30 days after the end of bed rest they were back to pre-bed rest levels.

Conclusions: The antioxidant supplement applied as a countermeasure in this study did not reduce the deleterious effects induced by 60 days of HDBR on bone turnover.

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Cardiorespiratory regulation in response to exercise – Effects of confinement in combination with restricted sleep

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Introduction: Cardiorespiratory kinetics are slowed in astronauts, returning from six month missions on-board the International Space Station (ISS; Hoffmann et al., Eur J Appl Physiol 116: 503-511, 2016). Despite microgravity, several other factors influence cardiorespiratory kinetics on-board the ISS. Inside the Human Exploration Research Analog (HERA) facility some of these factors were controlled: The effects of 45 d of confinement in combination with restrictions for sleep and a defined physical training on muscular oxygen uptake (V'O2musc) kinetics and cardiovascular regulation during exercise were investigated.

Methods: To date, fourteen healthy individuals (5 females, 9 males, 37±7 y, 23±3 $kg \cdot m^{-2}$) were analyzed 8 d before the mission (MD-8), on mission day 22 (MD22), mission day 42 (MD42) and 4 d after (MD+4) a simulated mission to an asteroid. At all test days a cycle exercise test beginning with 300 s of rest (Rest), 300 s of 30 W (Low), 300 s of pseudo-random binary work rate changes (WR) of 30 W and 80 W (PRBS1 & PRBS2) and 300 s of 80 W (High) were completed. On MD-8 and MD+4 an incrementally increasing step protocol (25 W min^{-1}) to assess peak oxygen uptake (V'O2peak) was added. Heart rate (HR) and mean arterial blood pressure (MAP) were measured beat-to-beat and pulmonary oxygen uptake (V'O2pulm) breath-by-breath. V'O2musc was estimated from HR and V'O2pulm. Kinetics responses were calculated using time series analysis: Higher maxima of the cross correlation function (CCFmax) between WR and the respective parameter indicate faster kinetics (Hoffmann et al., Eur J Appl Physiol 113:1745- 1754, 2013). During the mission, exercise training sessions were scheduled every second day with a maximal HR restricted to below 85% of the age-related maximum. Sleep was restricted to 5 h per weekday and 8 h at the weekends. Statistical analyses of the kinetics parameters were performed by means of repeated measures ANOVA (MD-8, MD22, MD42, MD+4) for V'O2musc and the Friedman-test for V'O2pulm, MAP, and HR. V'O2peak at MD-8 and MD+4 was compared using a Wilcoxon-test. Further, differences in V'O2peak and kinetics from MD-8 to MD+4 were calculated and correlated with the values measured at MD-8 using the Pearson test. Level of significance was set to $\alpha = 5\%$.

Results: HR kinetics did not change significantly throughout the mission (MD-8 vs. MD22 vs. MD42 vs. MD+4; mean ± standard deviation [a.u.]: 0.31±0.12 vs. 0.32±0.07 vs. 0.36±0.12 vs. 0.33±0.09; p=0.216) just as V'O2pulm (0.34±0.12 vs. 0.32±0.07 vs. 0.32±0.06 vs. 0.30±0.05; P=0.543), MAP (0.25±0.07 vs. 0.28±0.09 vs. 0.26±0.05 vs. 0.23±0.04; P=0.216) and V'O2musc kinetics (0.32±0.07 vs. 0.33±0.05 vs. 0.33±0.05 vs. 0.30±0.05; P=0.182). V'O2peak differed not significantly (P=0.221) between MD-8 (37.8±5.8 ml min^{-1} kg^{-1}) and MD+4 (38.9±4.6 ml min^{-1} kg^{-1}). Changes in CCFmax(HR) correlated significantly with CCFmax(HR) at MD-8 ($r = -0.839$, $P < 0.001$), changes in CCFmax(V'O2musc) correlated significantly with CCFmax(V'O2musc) at MD-8 ($r = -0.641$; $P = 0.014$) and the difference in V'O2peak correlated with V'O2peak at MD-8 ($r = -0.614$; $P = 0.019$).

Conclusions: Forty-five days of confinement in combination with sleep restrictions and physical training, had no significant effect on HR, V'O2musc and V'O2pulm kinetics and V'O2peak. However, those individuals who started with slow kinetics or a low V'O2peak benefited from the exercise training during the mission. The volume and/or intensity of the exercise training intervention might have been higher during the HERA C4 missions compared to most of the crew members' everyday life activities.

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Illustration of inotropic changes assessed by seismo- and ballistocardiography during long duration space flights

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Introduction: Long-term exposure to microgravity is known to result in cardiovascular adaptations, however with non- negligible inter-subject variability. The aim of this analysis is to evaluate intra- and inter-subject changes in the inotropic state of the heart during and after a long-duration mission on the ISS, by measuring the vibrations on the surface of the body resulting from cardiac activity. In addition, we aim at improving the physiological understanding by using a numerical model of the cardiovascular system.

Methods: Data was recorded using CARDIOVECTOR-1 on 8 cosmonauts (7 males), asked to perform an alternation of controlled and non-controlled breathing protocols. 1-axis dorsoventral Seismocardiography (SCG, linear accelerations recorded on the apex) and 6 degrees of freedom Ballistocardiography (BCG, 3-axis linear accelerations and 3-axis angular velocities, recorded close to T8-T9 vertebrae) were performed. In addition, ECG and plethysmography were recorded simultaneously, which enabled to split the SCG and BCG records in each of their related heartbeats and to associate them to a respiratory phase. Ensemble averaged was performed on the different signals for all the beats of a given respiratory phase. Then, the resulting signals were processed to compute parameters such as the kinetic energy and power transferred to the body by cardiac contraction and blood flow in the arterial tree. In parallel, we designed a model of the cardiovascular system, where the 55 main arteries are considered to compute pressure and blood flow at any given time of the cardiac cycle, in order to generate an artificial BCG signal. To do so, each artery is split in smaller parts on which we solve simplified fluid mechanics equations. By adapting the input according to the modifications known to happen in space, we test the capacity of the model to reproduce the results observed in space.

Results: Measurements on Earth and in space are not directly comparable, since the position of the subject greatly influences the SCG and BCG signals, and consequently the computed parameters as well. No matter of the respiration phase, we notice that the amplitude of the BCG signals is far higher in space than on Earth, which is also seen on most of the BCG-derived metrics. As concerns SCG, the inflight values of most of the computed metrics stabilize between their supine and standing pre-flight values. As expected, inter-subject differences are high, but some common intra-subject trends are still observed. In particular, kinetic energy measured on the BCG sensor is decreasing all along the space flight. This is to be put in context with our recent results showing a significant positive correlation between changes in this parameter and changes in stroke volume. In addition, the model confirms that a decrease in stroke volume could indeed lead to a decrease in BCG kinetic energy, even though it also shows that many other parameters also influence this metric.

Conclusions: BCG parameters collected in microgravity cannot easily be compared to those collected on ground because of mechanical coupling with the bed or the ground, which is apparently less the case for SCG parameters. Consequences of cardiovascular changes after several months in microgravity are observed differently on SCG and BCG. Intra-subject evolution of some BCG-derived parameters indicates the possibility to easily assess consequences of a cardiovascular condition evolution and ultimately efficiency of countermeasures. The changes observed in space can be reproduced in a numerical model of the cardiovascular system, which gives indications concerning the potential causes of changes observed.

In vivo fascicle and tendon length of the gastrocnemius medialis during running in simulated hypogravity using the vertical treadmill facility

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Introduction: Astronauts exposed to microgravity experience physiological deconditioning, especially systems sensitive to force loading such as the musculoskeletal system. In order to attenuate these adverse effects, current ISS crew members perform a daily physical exercise countermeasure program, including treadmill running. However, the maximum vertical loading applied is usually not more than 70-80% of body weight (BW). As the triceps surae is one of the muscles most affected by immobilization but at the same time contributes significantly to vertical support and horizontal propulsion of the human body, it is important to examine the behaviour of its fascicles and tendon under unloading conditions to get a deeper understanding of what might cause the wasting and loss of function. Therefore, the aim of this study was to determine fascicle, tendon and muscle-tendon-unit (MTU) length of the gastrocnemius medialis muscle (GM) during running at 0.38g (Martian gravity), 0.7g (70% BW) and 1g.

Methods: Eight male subjects (31.9 ± 4.7 yrs) ran at 125% of their preferred walk-to-run transition speed at 0.38g and 0.7g on the vertical treadmill facility. In addition, running without unloading (1g) served as a control condition. GM fascicle length and pennation angle were scanned and measured via ultrasonography. Additionally, joint kinematics (goniometers) were analysed to determine GM tendon and MTU length. Further, plantar pressure (loadsol) was measured to determine gait-cycle events. A repeated measure one-way ANOVA for dependent samples and Holm-Sidak's multiple comparisons test was used to test whether changes in fascicle, tendon and MTU length during the stance phase are significantly influenced by different gravity levels.

Results: Compared to 1g, maximum ankle dorsiflexion (-38.2 ±21. 9%, $p= 0.003$) and maximum knee flexion (-21.4 ± 9.4%, $p = 0.001$) is significantly smaller during midstance at 0.38g, whereas for 0.7g no significant differences were found. MTU and tendon elongation is significantly smaller during running at 0.38g (-47.3 ± 17.3%, $p < 0.001$; -35.2 ± 11.5%, $p < 0.001$) and 0.7g (-25.50 ± 20.3%, $p = 0.008$; -18.70 ± 13.7%, $p = 0.005$) compared to 1g. Although, GM fascicles operate at a significantly longer length and corresponding smaller pennation angle at 0.38g (+12.4 ± 6.4%, $p < 0.001$; -9.5 ± 5.9%, $p = 0.007$) and 0.7g (+8.9 ± 5.8%, $p = 0.024$; -8 ±4.4%, $p= 0.008$), fascicle shortening shows no significant differences.

Conclusions: During unloaded walking, less mechanical work is required to propel the body forward leading to altered joint kinematics as well as GM fascicle and tendon behaviour. Reduced tendon elongation suggests that less force is acting on the Achilles tendon resulting in a reduced storage of elastic energy. Furthermore, we speculate that the longer fascicle length allows the GM to operate at an advantageous part of the force-length relationship leading to reduced muscle activation and a more economical force generation during locomotion. To determine if running with 70% of BW is sufficient to maintain muscle mass and function, additional measurements of torque and neuromuscular activation are required in order to estimate the strain imparted on the GM.

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Baroreceptor loading and unloading impairs cognition: A pilot study and future directions

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Introduction: A changing body position initiates baroreflex (BR) dependent adaptations in heart rate and blood pressure (Sheriff, Nadland, & Toska, 2007; Toska & Walløe, 2001). Especially an intrinsic BR stimulation seems to inhibit cortical activations (Elbert, Roberts, Lutzenberger, & Birbaumer, 1992). This might be based on afferent information from corresponding receptors which are forwarded via the medulla oblongata to different cortical areas (Rau & Elbert, 2001). A recent study reported an impact of baroreceptor activation on cognitive control processes during supine lying in a head-up and -down tilted position (Pramme, Schächinger, & Frings, 2015). Such an effect was previously described in a review in which BR-sensitivity (BRS) was reported to affect cognition and vice versa (Duschek, Werner, & Reyes Del Paso, 2013). However, there are also studies which find no effect from baroreceptor loading on psychomotor reactions or reaction times (Richter, Schulz, Port, Blumenthal, & Schächinger, 2009).
In our pilot study we will replicate the BR-cognition interaction in a tilt-seat with dynamic changes of body position. Since the main function of the BR is a short-term stabilization with fast adaptations, only a few studies used that. We assume that a passive change of body position activates the BR and simultaneously restricts cognition.

Methods: Ten healthy subjects (4 female, 29 ± 4.1y, 67 ± 8.6kg, 172 ± 8.6cm) were tested in a tilt-seat. The seat was adjusted to an upright starting position (i.e. 90°) and was tilted down three times to either 0° or -6° and back to 90° in randomized order. Each position was changed after 1 min. Heart rate (HR) and blood pressure (BP) were recorded beat-to-beat by Finapres NOVA (Finapres Medical Systems, Netherlands). Additionally, each subject performed a continuous reaction time task (developed with PsychoPy2, Version: PY3-1.90.3), and we recorded reaction times (RT) throughout the experiment. All variables were adjusted to the same course of time and we analyzed 16 s across tilting-down and –up sequences, since main adaptations in HR and BP take place in first 10 s. Thus, we conducted a 2 (angle: 0°, -6°) x 2 (tilt: down, up) x 8 (time: steps of 2s) analysis of variance (ANOVA) with repeated measurements for HR, BP, and RT. Subsequently, we used bivariate correlations to analyze relationships between HR, BP, and RT.

Results: Results indicated time-related changes in HR ($p < 0.01$), BP ($p < 0.01$), as well as RT ($p < 0.01$) with one single difference between angles of 0° and -6° for RT ($p < 0.05$). Merely HR ($p < 0.01$) and BP ($p < 0.01$) showed differences between tilting-sequences (i.e. up and down) which can be attributed to the BR (Table 1). Subsequent analyses for tilting-sequences up/down yielded a negative correlation between HR and RT ($r = -0.774$, $p < 0.01$) while tilting-up from -6° to 90°. Furthermore, we found the similar trend in HR and RT ($r = 0.586$, $p = 0.075$) while tilting-down from 90° to -6°.

Table 1: Mean values for both angles across the time course (M±SD)

	1	2	3	4	5	6	7	8
HR_{down}	62±9.3	63±9.9	64±10.3	67±11.1	64±9.6	56±9.9	54±6.3	53±6.2
HR_{up}	64±8.9	64±8.8	66±8.9	70±10.2	75±10.8	77±10.5	75±10.6	74±10.7
BP_{down}	98±9.2	96±9.9	93±10.6	95±9.3	99±9.8	99±10.4	96±10.2	94±9.5
BP_{up}	89±8.9	88±8.9	86±9.9	85±9.7	86±9.2	87±8.2	88±8.8	89±9.5

Conclusions: Our results showed the expected adaptations in HR and BP following tilting sequences. Furthermore, we found impaired RTs during tilts which reflect the above mentioned interactions in the central nervous system. In fact, reduced RTs indicate a prioritization of physiological mechanisms during the tilting process. However, we cannot finally confirm this, since we have no comparable values without a cognitive task. Another important aspect is the influence of a cognitive task on BRS. A previous study reported such a reversed approach where higher cognitive load impaired BRS (Yasumasu, Reyes Del Paso, Takahara, & Nakashima, 2006). Examining these interactions or prioritizations would be an interesting aspect for further studies. Additionally, other tilt-positions as well as cardiorespiratory variables should be investigated to analyze the influence of physical fitness on the BR.

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Travel Instructions (see also: http://www.dlr.de/envihab/en/desktopdefault.aspx/tabid-9657/)

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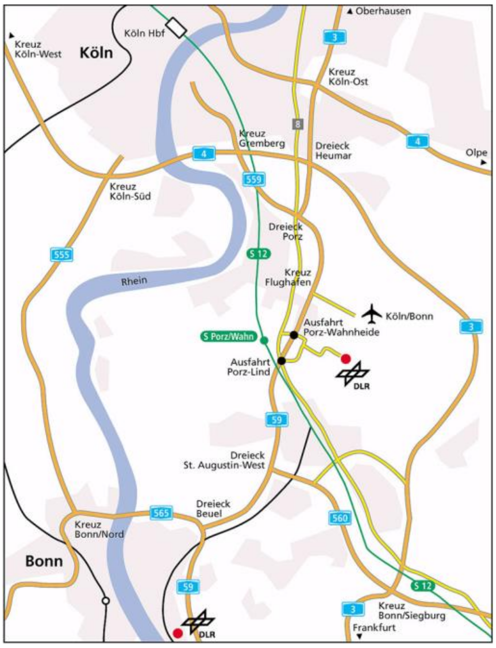
The DLR Cologne site is located south-east of Cologne, close to Cologne-Bonn airport.

How to reach us:



Arrival by train

The local trains ("S-Bahn") S 12 or S 13 leave from Koeln Hauptbahnhof (Hbf), Siegburg and Troisdorf. The local train S 13 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

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 at the main gate of the German Aerospace Center DLR Koeln.

Arrival by taxi

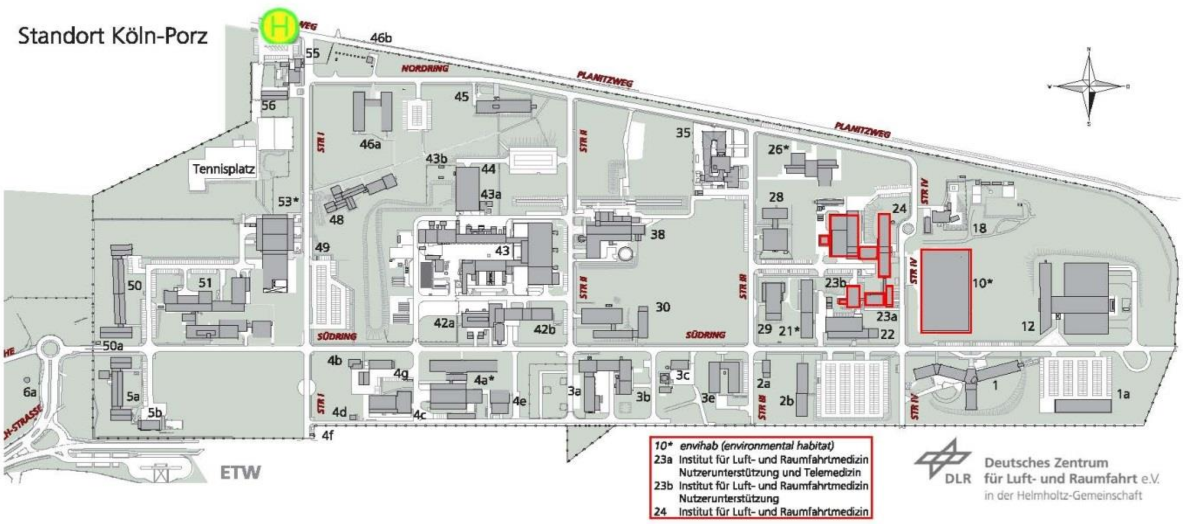
At Koeln Hauptbahnhof (central station) take a taxi to "Porz-Wahnheide, DLR". Taxi stands are located on both exits of the station. Taxi call for all locations in Cologne: Tel. +49/221/19410. Tell the driver to take you to "Porz-Wahnheide, DLR". The price will depend on daytime and traffic (normally it should not exceed 35 Euros).

Arrival by car

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 take the 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

From Koeln Bonn Airport : Either take a taxi in front of the terminal to "DLR in Porz-Wahnheide". Or take the local train S 13 direction "Troisdorf" from the railway station "Köln/Bonn Flughafen" (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".



Accommodation (example):

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