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ORIGINAL ARTICLE

Microgravity Simulated by the 6° Head-Down Tilt Bed Rest Test Increases Intestinal Motility but Fails to Induce Gastrointestinal Symptoms of Space Motion Sickness

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Abstract

Background Space motion sickness (SMS) is the most relevant medical problem during the first days in microgravity. Studies addressing pathophysiology in space face severe technical challenges and microgravity is frequently simulated using the 6° head-down tilt bed rest test (HDT).

Aim We were aiming to test whether SMS could be simulated by HDT, identify related changes in gastrointestinal physiology and test for beneficial effects of exercise interventions.

Methods HDT was performed in ten healthy individuals. Each individual was tested in three study campaigns varying by a 30-min daily exercise intervention of either standing, an upright exercise regimen, or no intervention. Gastrointestinal symptoms, stool characteristics, gastric emptying time, and small intestinal transit were assessed using standardized questionnaires, ^{13}C octanoate breath test, and H_2 lactulose breath test, respectively, before and at day 2 and 5 of HDT.

Results Individuals described no or minimal gastrointestinal symptoms during HDT. Gastric emptying remained unchanged relative to baseline data collection (BDC). At day 2 of HDT the H_2 peak of the lactulose test appeared earlier (mean ± standard error for BDC-1, HDT2, HDT5: 198 ± 7, 139 ± 18, 183 ± 10 min; *p*: 0.040), indicating accelerated small intestinal transit. Furthermore, during HDT, stool was softer and stool mass increased (BDC: 47 ± 6, HDT: 91 ± 12, recovery: 53 ± 8 g/day; *p*: 0.014), indicating accelerated colonic transit. Exercise interventions had no effect.

Conclusion HDT did not induce symptoms of SMS. During HDT, gastric emptying remained unchanged, but small and large intestinal transit was accelerated.

Keywords Microgravity simulation · Space motion sickness · Head-down tilt · Breath test · Gastric emptying

Introduction

Humans fly into space for scientific, commercial, and even recreational purposes, and interplanetary missions might become reality within the next decades. However, adaptation of the human body to loss of gravity poses significant challenges to which the human body needs to adapt [36]. Space motion sickness (SMS) is the most frequent medical problem during the first 2–3 days in microgravity and only rarely persists for longer periods of time [17]. Up to 70 % of astronauts and cosmonauts are affected by SMS [6, 10]. Symptoms of SMS include vomiting (86 %), anorexia (78 %), headache (64 %), stomach awareness (61 %), and malaise (58 %) [10]. Therefore, missions include contingency planning that one or more crew members may be incapacitated by SMS, leading to delay of critical activities

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until after day 5 in space. Promethazine has been the drug of choice for the management of SMS during the last decades [10, 13], but a better understanding of gastrointestinal and/or brain physiology leading to SMS might improve management options. After day 2–3, SMS symptoms decrease in intensity, but most cosmonauts and astronauts continue to consume less calories than recommended and without proper precaution return to Earth with a reduced body weight [30].

Experiments in space are limited by restrictions in the availability of equipment and crew time. Therefore, attempts have been made to simulate microgravity on the ground. Microgravity can be induced by parabolic flights, but loss of gravity can only be sustained for less than half a minute. In contrast, for the 6° head-down tilt bed rest test (HDT), a simulation of microgravity can be maintained with reasonable effort for weeks or months. In this model, the bed is tilted with an angle of 6°. HDT is the standard ground methodology for simulation of microgravity and screening for countermeasures to alleviate the adverse effects of loss of gravity [1, 4, 18, 25, 34]. However, gastrointestinal pathophysiology during HDT has been insufficiently characterized. We therefore decided to rigorously test gastrointestinal symptoms and motility during HDT. The aims of these investigations were (1) to decide whether HDT was a reliable model to study gastrointestinal aspects of SMS, (2) to identify abnormal gastrointestinal physiology that could contribute to SMS during the first few days in space, and (3) to assess whether an exercise intervention could reverse the effects of HDT on gastrointestinal function and symptoms.

Materials and Methods

The gastrointestinal experiments described below were performed as a substudy of the short-term bed rest study 2009 for the evaluation of the use of artificial gravity of the European Space Agency (STBR-AG2, ESA contract number: 22126/08/NL/VJ). This study has been described in detail elsewhere [21].

Participants

Ten healthy male volunteers, 20–45 years of age with a normal body mass index (20–26 kg m^{-2}) and a body height of 158–190 cm, were recruited. Each participant underwent a thorough screening process by the Institute of Aerospace Medicine, German Aerospace Center (Institut für Luft—und Raumfahrtmedizin, Deutsches Zentrum für Luft—und Raumfahrt e.V., DLR), Cologne, Germany. Exclusion criteria for participants included possible liver disease (ALAT, ASAT, AP, or γ-GT higher than two times the respective upper limit of normal), renal insufficiency (creatinine > 1.5 mg dl^{-1}), hypersensitivity to lactulose, galactosemia, bacterial overgrowth (negative lactulose H_2 breath test), current symptoms requiring medication that might alter gut function including anticholinergics, calcium channel blockers, beta blockers, laxatives, prokinetics, proton-pump inhibitors, non-steroidal anti-inflammatory drugs, and prior abdominal surgery other than uncomplicated appendectomy or hernia repair. The study was approved by the local ethics committee (Aerztekammer Nordrhein, Düsseldorf, Germany, number: 2008294).

Study Design

The study followed a randomized, non-blinded three-arm cross-over design. Participants were divided into three groups. During 30 min per day, one group followed a defined training program (locomotion replacement training, LRT). Another group was allowed to stand upright for 30 min (standing intervention, STA). The third group remained recumbent during the whole intervention time (control group, CON). Over the course of the three campaigns of the study, each participant alternated over all three training programs; however, the order of the programs was randomized for each participant.

Each campaign was divided into an adaptation phase (5 days), intervention phase (5 days), and a recovery phase (6 days, Fig. 1a). In both, the adaptation and the recovery phase, participants were allowed to maintain normal physical activity in the laboratory. In the intervention phase, the ten participants were set in 6° head-down tilt bed position. The gastrointestinal investigation (GI) module was performed on day 5 of the adaptation phase (baseline data collection day 5, BDC-1) and day 2 and 5 of HDT (HDT2 and HDT5).

During each of the three campaigns of the study, the volunteers received a strictly controlled individually tailored diet as foreseen in the ESA standardization plan. 29.7 ± 0.2 % of the daily energy intake was consumed as fat, 55.2 ± 0.2 % as carbohydrates, and protein was taken in the amount of 1.19 ± 0.05 g kg^{-1} d^{-1}. The fiber content of the meals was constant at 32 ± 2 g/day. All meals for the ambulatory and bed rest phases of this study were prepared in a metabolic kitchen where all foods were weighed to ±0.1 g using laboratory scales.

Digestive Symptoms

On each day of the GI module, gastrointestinal symptoms were assessed using the gastroparesis cardinal symptom index (GCSI) [26] and the Leeds dyspepsia questionnaire (LDQ) [20]. Before and during 240 min after the test, meal gastrointestinal symptoms were assessed every 15 min

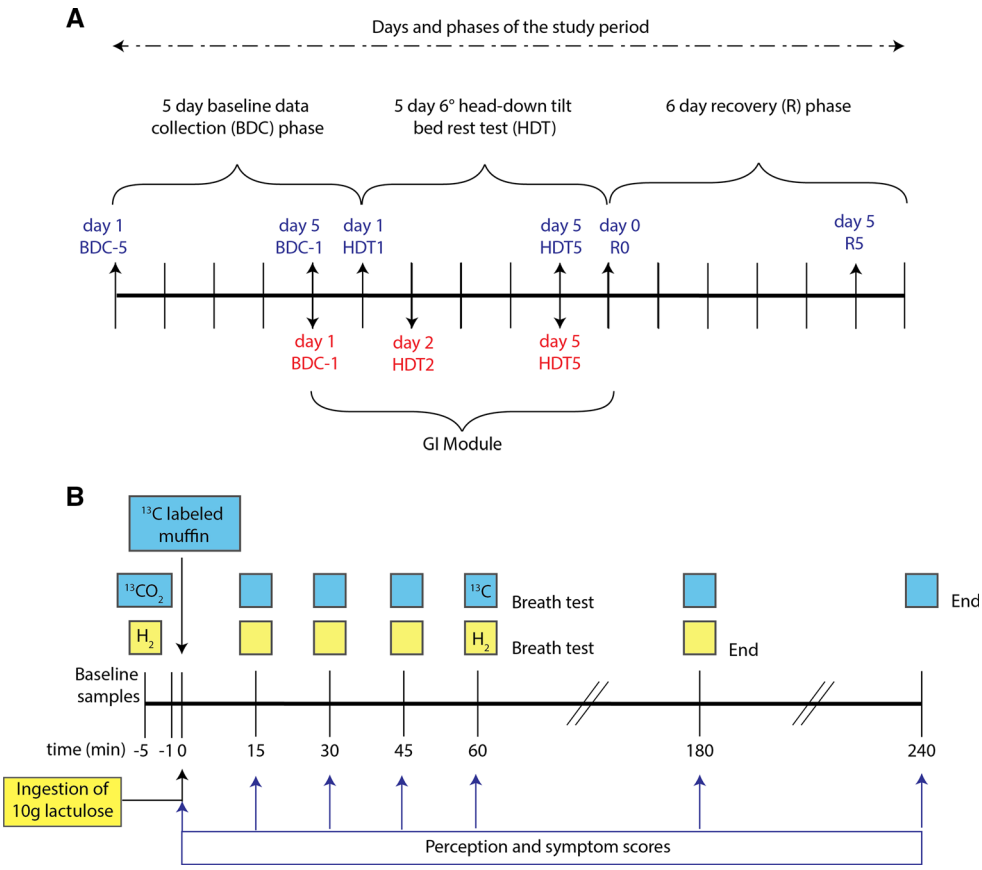

Fig. 1 Timing of the gastrointestinal investigation module and experimental procedures within the short-term bed rest study. **a** The three phases of the study used in all campaigns—baseline data collection, head-down tilt, and recovery phases are indicated. *GI* gastrointestinal investigation, *BDC* baseline data collection, *HDT* 6° head-down tilt bed rest test. **b** Experimental procedures during each GI module: After ingestion of the test meal, expiratory air was collected every 15 min, followed by analysis of ^{13}C and H_2 content of expiratory air

using a visual analog scale (VAS) and expressed as a value between 0 (no symptoms) and 100 (most severe symptoms). At every time point, hunger, quantity to eat, desire to eat, nausea, fullness, abdominal pain, and bloating were assessed.

Gastrointestinal Function

The GI module during BDC and HDT started 5 min before breakfast; base line breath test samples for H_2, CH_4, and $^{13}CO_2$ breath tests were collected for about 1–2 min. Subsequently, 10 g of lactulose syrup was administered to the participants together with 50 ml water or another liquid. Shortly thereafter, 125 mg of ^{13}C-sodium octanoate (chemical purity of 99.7 % and isotopic purity of 99.1 %) was administered in a 430 kcal solid muffin meal (35 % fat, 10 % protein, 54 % carbohydrates). After the meal, breath samples were collected every 15 min (Fig. 1b).

Breath samples were collected by exhalation separated for H_2, CH_4, and ^{13}C measurements into an evacuated 10-ml glass tubes (BD vacutainer®, Becton–Dickinson AG, 4002 Basel, Switzerland) and a bag, respectively. The ratio of $^{13}CO_2$ and $^{12}CO_2$ in the breath samples in the bags was determined by non-dispersive isotope-selective infrared spectroscopy (NDIRS, IRIS® Lab, Wagner Analysen Technik GmbH, Bremen, Germany) at the Gastrointestinal Physiology and Manometry Laboratory at the Division of Gastroenterology and Hepatology, University Hospital Zurich. The half emptying time (t_{50}) was calculated using several established methods [3, 8, 29].

Gastric emptying was analyzed using the Bluck-Coward algorithm [3]. Alternative algorithms including the Ghoos/Maes method [8] as well as the Wagner Nelson algorithm were used [29]. The Bluck-Coward algorithms and all additional calculation strategies used did not show any differences in gastric emptying under all conditions tested (not shown), and only the former results are shown.

Small bowel transit was assessed using a H_2/CH_4 lactulose breath test. These breath test samples were assessed without delay from the tubes after transfer to the laboratory of the DLR, Institute of Aerospace Medicine, using a Quintrom gas collection system (Quintrom Instrument Co., Milwaukee, WI).

Large bowel transit was not measured directly. Stool weight and stool consistency according to the Bristol Stool Scale (BSS) were used as surrogate measurements for colonic transit [19] during BDC, HDT, and the recovery phase.

Statistical Analysis

Each of the 10 subjects participated in all three campaigns varying in the exercise protocols—standing, exercise, and no exercise. Since the three campaigns were performed several months apart from each other, the overall study was regarded as a repeated measures study, where the same individual participated in three campaign protocols, unaffected by the earlier campaigns. Under each of these campaigns, the scores for describing several clinical symptoms were recorded on pre-specified days (for example, BDC-1, HDT2, HDT5) of the study. For continuous symptom observations during the 4-h test periods, such as the VAS score representing hunger, the individual values were averaged.

The observations from 3 protocols × 3 days of observation × 10 subjects were analyzed using repeated measures ANOVA with SPSS software. Using repeated measures ANOVA, three analyses were performed for each measurement to show its variation: with day alone, with exercise protocol alone, or simultaneously depending on day and protocol. Figures 2, 3, 4, 5, and 6 show the mean values of the observations, along with their corresponding standard errors. The p values shown in the data were calculated using one-way repeated measures ANOVA and represent the significance levels for the "day" or "exercise protocol" being a factor that influences the observations.

Results

Digestive Symptoms

The overall burden of gastrointestinal symptoms during BDC and HDT was mild. There were no differences in symptom scores on either questionnaire between baseline and HDT2, the time period during which space motion sickness is expected to be prevalent in microgravity (Fig. 2). Similarly, no significant difference between BDC-1 and HDT2 could be detected when subscales of GCSI for hunger, nausea, and bloating were considered (not shown). Overall symptoms tended to increase at HDT5 (no statistical significance).

At day 5 of HDT, symptoms remained mild with a trend to less hunger/desire to eat and slightly more abdominal pain and nausea in simulated microgravity conditions (Fig. 3). None of these differences reached statistical significance, and this increment in symptom change is not likely to be clinically relevant in healthy individuals. Using a linear regression analysis, no significant correlation between different symptoms was detected. As might be expected, repeated assessment of the same symptom ("hunger," "desire to eat," and the "quantity subjects estimated they could eat") yielded significant correlations (R^2: 0.66 − 0.8, $p < 0.001$). Taken together, the 6° head-down tilt position before and after food challenge did not reproduce the pronounced and prevalent space motion sickness symptoms reported by astronauts during day 1 and 2 of space travel.

Gastrointestinal Function

There was no difference in calculated gastric emptying time between BDC-1 and HDT2 or HDT5 as assessed by the ^{13}C-octanoate breath test (Fig. 4). In line with these observations, alternative algorithms for the assessment of gastric emptying [8, 29] and simple calculations (including area under the curve, lag time, time to reach maximum ^{13}C excretion) were concordant for all 3 days of GI measurements during all three study campaigns. No correlations between symptoms during the meal and parameters of gastric emptying were observed (data not shown). We conclude that differences in gastric emptying induced by 2 or 5 days of 6° head-down tilt bed rest test are either non-

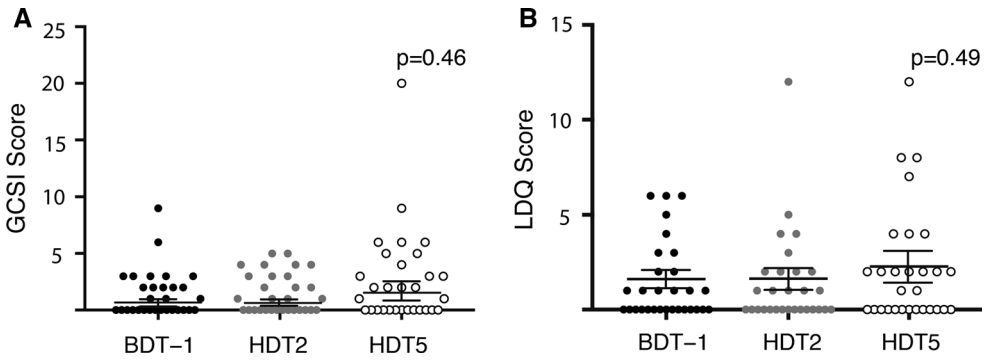

Fig. 2 Global scales for gastrointestinal symptoms. **a** gastroparesis cardinal symptom index (ranging from 0 to no symptoms to 45 most severe symptoms); mean values are indicated; *error bars* represent standard error of all measurements. Statistical analysis was performed using repeated measures ANOVA considering that 10 individuals repeated the same test three times. **b** Leeds Dyspepsia Questionnaire (ranging from 0 to no symptoms to 40 most severe symptoms); plot and analyses were performed as described in **a**

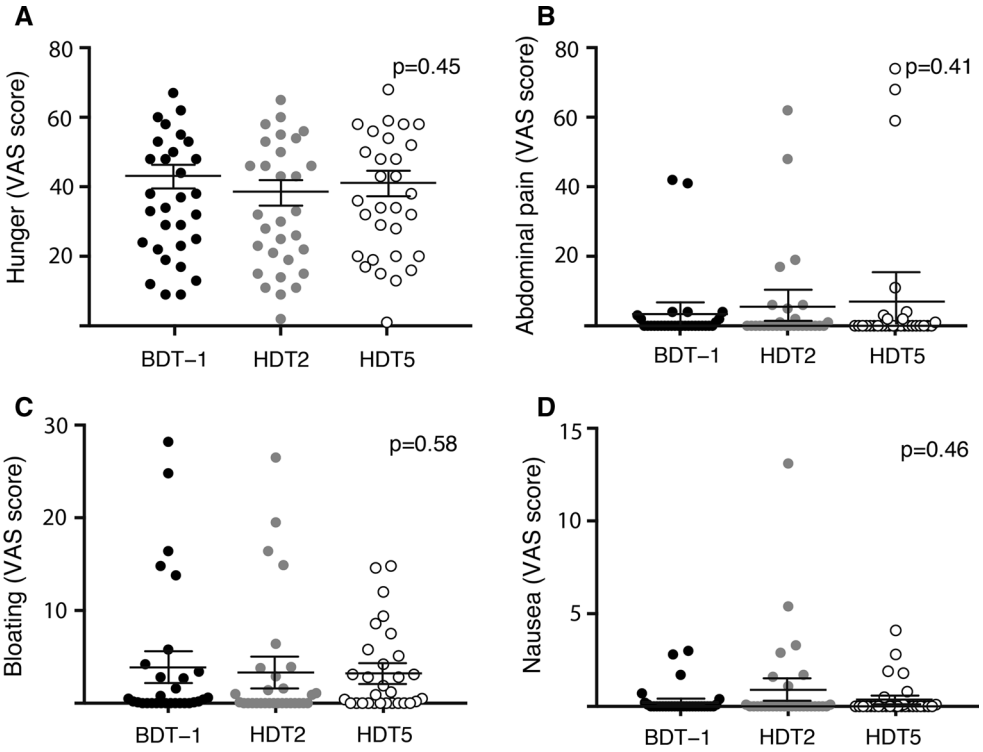

Fig. 3 Clinical symptoms during the test meal/lactulose challenge. Scatter of self-reported symptoms on a visual analog scale (VAS) ranging from 0 to 100 during the 4-h test period are plotted for: **a** Hunger, **b** abdominal pain, **c** bloating, **d** nausea. For each 4-h test period, the mean VAS value was calculated; plot and analyses were performed as described for Fig. 2. Mean and standard error of the mean are indicated as well

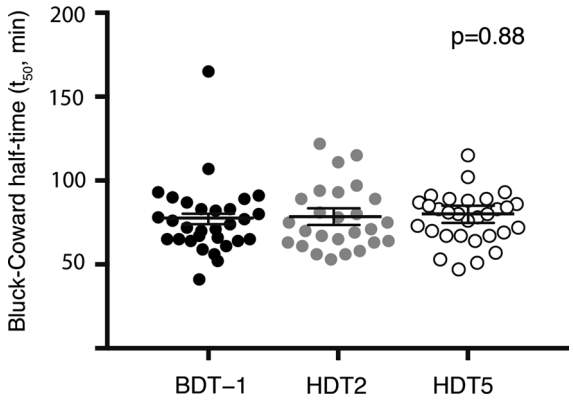

Fig. 4 Gastric emptying time during study period: ^{13}C-octanoate data were analyzed using the Bluck-Coward algorithm [3] to calculate half-time (t_{50}) of gastric emptying. Plot and analysis were performed as in Fig. 2, but no significant variation of t_{50} could be detected

existent or minor and beyond the detection threshold of the ^{13}C octanoate breath test.

Intestinal transit was assessed by the lactulose H_2 breath test (Fig. 5). After lactulose intake, the time to reach maximum in the H_2 signal (Fig. 5b) was shorter at HDT2 compared to baseline (time for maximum H_2 signal on BDC-1, HDT2, HDT5: 198 ± 7, 139 ± 18, 183 ± 10 min; $p = 0.040$). In line with these observations, time until a signal of >10 ppm above baseline was reached (Fig. 5d) tended to be shorter at HDT2 compared to baseline (time for $H_2 > 10$ ppm on BDC-1, HDT2, HDT5: 91 ± 12, 46 ± 25, 114 ± 17 min; $p = 0.330$). The picture did not change, whether the H_2 signal alone or the sum of H_2 and CH_4 was considered (data not shown). At HDT5, the results were closer to baseline than to HDT2, suggesting that any changes induced by the 6° head-down tilt position were mainly reversed at day 5. As described for gastric emptying, no correlation between symptoms and the H_2 or CH_4 signal was detected.

Colonic transit was assessed by surrogate measurements of stool volume and stool consistency. Stool weight increased from on average 47 ± 6 g/day at the baseline period to 91 ± 12 g (stool weight on BDC-1, HDT2, HDT5: 47 ± 6, 91 ± 12, 53 ± 8 g/day; $p = 0.014$) during the time spent in 6° head-down tilt position (Fig. 6a). Similarly, stool was significantly softer and less formed on the Bristol Stool Scale during the time in simulated microgravity (Bristol Stool Scale index during BDC, HDT, recovery phases: 1.15 ± 0.13, 1.70 ± 0.23, 1.03 ± 0.11; $p = 0.004$, Fig. 6b).

These findings indicate that both small bowel transit time and colonic transit time are faster during simulated microgravity conditions.

Exercise Interventions

Finally, we repeated all analyses considering the three different exercise protocols all subjects underwent during the study. No difference was detected in any of the

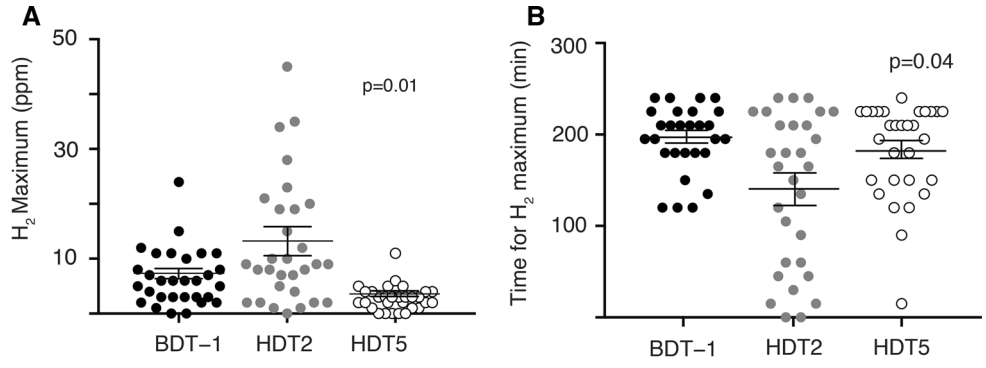

Fig. 5 Lactulose breath test: H_2 signal over baseline from lactulose breath test was analyzed. **a** Maximum value of H_2 during the 240-min test period, **b** time at which this maximum occurs, **c** probability that H_2 at 45 min is greater than 10 ppm and **d** time when H_2 signal exceeds 10 ppm. Plot and repeated measures ANOVA was performed as described in Fig. 2

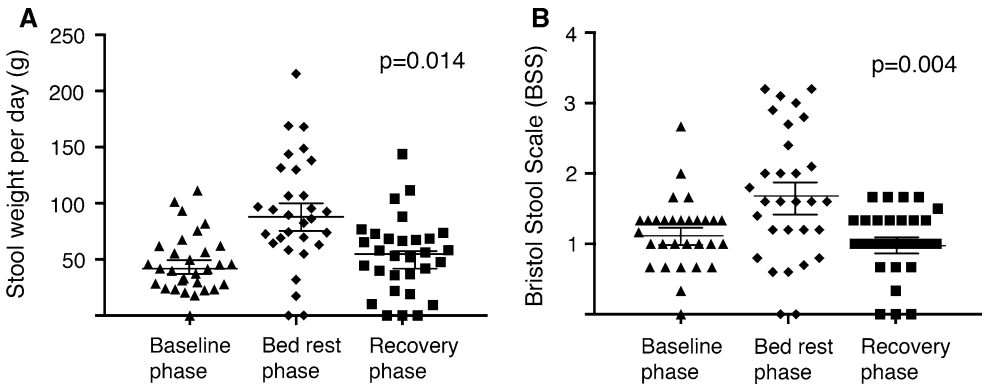

Fig. 6 Stool weight and consistency during the different phases of the short-term bed rest study. **a** Averaged stool weight per day and **b** Bristol Stool Scale (BSS) for describing stool consistency ranging from 1 (very hard stool) to 7 (liquid/watery stool). Values for all days of the respective study phases were averaged. Plot and repeated measures ANOVA were performed as in Fig. 2. Please note that in contrast to Figs. 2, 3, 4, and 5, this figure compares different phases of the study rather BDC-1 and HDT2 and HDT5 as in the other figures

parameters described in Figs. 2, 3, 4, 5, and 6 and in all additional comparisons performed (data not shown).

In additional analyses, we compared results of the three study campaigns to exclude sequence effects. We found significant differences with higher scores in campaigns B and C for "hunger" (average VAS scores for campaigns A, B, C: 28.5 ± 4.2, 37.5 ± 5.0, 40.5 ± 5.5; $p = 0.037$; compare Fig. 3a), but no significant differences for all other types of evaluations referred to in this study (data not shown) and sequence effects are unlikely to affect our conclusions.

Discussion

Space motion sickness constitutes a major health problem for astronauts, especially during the first days of a space mission. The pathophysiology of SMS remains incompletely understood but has been explained by two non-mutually exclusive theories: (1) The "fluid shift" hypothesis suggests that the pronounced redistribution of fluids from the legs to upper parts of the body in microgravity is responsible for gastrointestinal symptoms. (2) The "sensory conflict" hypothesis proposes that a contradiction in

inputs from the brain from visual and proprioceptive signals with labyrinth signals during space flight results in gastrointestinal symptoms [10, 16, 24]. Clarifying the pathophysiology of SMS would greatly facilitate treatment of gastrointestinal symptoms during the early days of a space flight.

HDT is considered the standard ground model for studying microgravity and several aspects of a space travel, especially the above-mentioned fluid shift from the legs to the remaining body are reproduced by HDT. Specifically, HDT results in similar changes in body mass, plasma volume, urinary calcium, muscle mass, and insulin resistance as during a space flight [25].

Despite this well-documented fluid shift, in our experiments, HDT did not reproduce the whole range of gastrointestinal symptoms experienced during space flight. In space, nausea, sickness, and vertigo are present in 7, 23, and 35 % of astronauts with severe, moderate, and mild intensity, respectively [25]. Our systematic study exposed healthy volunteers 3 times to the 6° head-down bed rest test but failed to induce relevant gastrointestinal symptoms. Therefore, HDT at best reproduces a part of the physiological changes leading to space motion sickness. Previously, effects of HDT on gastrointestinal symptoms had only been insufficiently studied: In a narrative review, nausea was reported to be rare and vertigo seems to be present in approximately 10 % of individuals [25], but no controlled data are available.

Importantly, our negative results still contribute to our understanding of the pathophysiology of SMS: Since HDT can reproduce microgravity-related fluid shifts well, our data strongly argue for a major role of central effects, such as those proposed by the sensory conflict hypothesis, in the pathogenesis of SMS. In line with this interpretation, no correlation of changes in gastrointestinal motility and symptoms could be observed in our study.

In addition, our results clarify changes in gastrointestinal motility induced by the fluid shift upon prolonged 6° head-down tilt position. These data are of value since experiments in space are exceedingly challenging. Of note, no changes in gastric emptying could be detected using a ^{13}C breath test. Since ^{13}C breath test compares well with the gold-standard scintigraphy [3, 5, 7, 8, 23, 32], especially for healthy individuals ([11] and many other studies), our results exclude marked changes in gastric emptying upon HDT [31, 35].

In contrast, the results of the H_2 breath test suggest accelerated transit of the small intestine. Faster intestinal movements would shorten the time until the colon is reached, resulting in an early signal in the lactulose H_2 breath test as observed in our subjects on day 2 of HDT. The mechanism by which a fluid shift accelerates intestinal transit remains unknown. Interestingly, on day 5 of the bed rest, intestinal movements had returned to baseline, suggesting that adaptations of intestinal motility to HDT conditions may have occurred.

In addition to the increase in small intestinal transit, our results also suggest an acceleration of colon transit during HDT. Direct measurement of colonic transit by marker studies or scintigraphy was not performed; however, it has been demonstrated that stool consistency measured by the Bristol Stool Scale is inversely correlated with colonic transit at least at the extremes of the BSS [19, 28]. Stool weight has been less intensively studied, but the sudden increase in stool weight upon HDT is wholly consistent with accelerated colonic transit. These results indicate that simulated microgravity affects motility of the small and large intestine but not the stomach.

It is interesting to note that promethazine, the treatment of choice against SMS [10, 13], has anti-dopaminergic but also anticholinergic properties that could inhibit GI contractility and slow gastrointestinal transit. In that respect, it can be speculated that faster intestinal transit could render an individual more vulnerable to "sensory conflicts" between central and peripheral sensors and thus contribute to SMS [10, 13].

Our results are in agreement with a previous Russian study in a small group of subjects [2]. The authors used a different technique to simulate microgravity (dry immersion) and a ^{13}C-acetate test and an H_2 inulin test for the assessment of gastric emptying and intestinal transit, respectively. As in our study, no changes for gastric emptying but an accelerated intestinal motility were observed. Interestingly, in dry simulation, pronounced stool retardation has been described ([2] and references therein), but stool retardation might also be a result of the inconvenience of the defecation procedure which could be more pronounced in dry immersion compared to the bed red tests.

Whether gastrointestinal motility and transit under true microgravity conditions in space are increased or decreased remains unknown. Indirect tests in space have reported markedly decreased bowel sounds in subjects affected by SMS, [33] and gastric myoelectric activity was shown to be reduced, especially on day 1 in microgravity [9]. In a case study of one individual, upon acute exposure to microgravity fasting plasma levels of motilin, pancreatic polypeptide, vasoactive intestinal peptide, and secretin were increased, accompanied by a decrease in cholecystokinin concentration [27]. For all these observation, the impact on transit remains unclear and more studies applying direct tests are needed.

During our study, the effect of exercise was tested in a non-blinded randomized cross-over study design. During the three study campaigns, each participant completed either the exercise module of locomotion replacement

training, the standing intervention, or remained within the control group. Strikingly, no difference in gastrointestinal symptoms or in the results of the breath tests could be observed. For a relevant change in gastrointestinal symptoms, a daily 30-min intervention might have a too short duration. Since HDT did not reproduce gastrointestinal symptoms of SMS, it cannot be excluded that such an exercise program has an impact on gastrointestinal symptoms in space. Exercise programs before exposure to microgravity are likely inefficient since in the previous shuttle experience pre-flight aerobic fitness did not correlate with the development of SMS [14].

This study has several strengths and limitations. Strengths include the rigorous and well-controlled, randomized cross-over study design. However, we would like to point out the following limitations: (1) In our experiments, gastric emptying and small intestinal transit were measured simultaneously and we cannot exclude effects of the test meal on lactulose transit and effects of lactulose on gastric emptying. However, during all study days, tests were carried out identically, and even though confounders might affect absolute numbers, changes between baseline and HDT cannot be explained by combined testing. (2) We did not rigorously rule out development of small intestinal bacterial overgrowth (SIBO), which would also result in an early H_2 signal even if small intestinal transit remained constant. SIBO could be relevant in space medicine given reports of increased bacterial virulence in microgravity [15, 22] and dysbiosis after landing [12]. However, in clinical practice, SIBO typically develops predisposed individuals and is usually accompanied by symptoms such as bloating or diarrhea. Furthermore, SIBO is unlikely to develop within only 2 days and to resolve on day 5. (3) As discussed, using HDT, we were unable to reproduce the whole set of symptoms of SMS, and some of our results are negative. However, rigorous testing in space is clearly not feasible and more valid data are unlikely to be available in the foreseeable future.

In summary, the 6° head-down tilt bed rest test cannot reproduce gastrointestinal symptoms of SMS and therefore at best partially reproduces pathophysiological changes in microgravity leading to SMS. Our results therefore strongly argue for a role of "sensory conflict" for the pathogenesis of SMS. In addition, we demonstrate that a fluid shift away from the lower parts of the body as induced by HDT can accelerate intestinal but not gastric motility. Exercise interventions tested in our study had no impact on gastrointestinal transit and symptoms and did not modify motility changes induced by HDT.

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Conflict of interest The authors declare no conflicts of interest.

Glossary

BDC	Baseline data correction
BSS	Bristol Stool Scale
CON	Control group
DLR	German Aerospace Center ("Deutsches Institut für Luft- und Raumfahrt")
ESA	European Space Agency
GCSI	Gastroparesis cardinal symptom index
GI	Gastrointestinal investigation
HDT	6° head-down tilt bed rest test
LDQ	Leeds dyspepsia questionnaire
LRT	Locomotion replacement training
SIBO	Small intestinal bacterial overgrowth
SMS	Space motion sickness
STA	Standing intervention
VAS	Visual analog scale

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