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Counteracting inactivity deconditioning with graded hypergravity loading: From clinical neurorehabilitation to space medicine

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ABSTRACT

Background: Neuromuscular and neurodegenerative diseases such as Parkinson's disease result in progressive mobility restrictions, accelerating cardiovascular, muscular, and functional deconditioning. Such changes resemble the multisystem deconditioning that occurs during microgravity exposure, highlighting shared physiological consequences of reduced mechanical loading, even though the underlying mechanisms differ. Objective: This study evaluated short-arm human centrifugation (SAHC) training as a whole-body rehabilitation intervention for patients with multiple sclerosis and neurodegenerative diseases with restricted mobility.
Methods: Twenty patients received SAHC training at 1.7–2 g for 30 min, three sessions per week, over 30 weeks. Cardiovascular parameters—cardiac output (CO, L/min), mean arterial pressure (MAP, mmHg), systolic blood pressure (SBP, mmHg), diastolic blood pressure (DBP, mmHg), stroke volume (SV, mL/beat), heart rate (HR, bpm); oxygen saturation (SpO_2, %), blood-gas indices, hematology values, handgrip strength (kg), and stance balance (CoP) were longitudinally assessed. Nonparametric repeated-measures ANOVA and Friedman tests with Wilcoxon post-hoc comparisons (Holm correction) were applied. Functional mobility was also measured with a questionnaire at baseline and after the 30weeks.
Results: SAHC training produced significant longitudinal changes in CO (↑), SBP (↓), HR (↓), and MAP **(↑)** (all $p<.001$), while hematology remained stable; grip strength increased bilaterally, stance balance was preserved, and FMQ-Short scores significantly improved from baseline to the 30-week assessment Conclusions: Artificial gravity training via short-arm centrifugation significantly improves cardiovascular performance and upper limb strength while maintaining postural stability in patients with neuromuscular and neurodegenerative diseases. These findings highlight AG as a promising terrestrial rehabilitation countermeasure with reciprocal applications for clinical neurorehabilitation and the mitigation of spaceflight deconditioning.

1. Introduction

Multiple Sclerosis (MS) and neurodegenerative disorders of the central nervous system, like Parkinson's disease, are associated with gradual neurologic impairment affecting ambulation, often manifesting as profound physical inactivity. Individuals with neuromuscular and neurodegenerative diseases are physically far less active than healthy adults, and this physical inactivity worsens as disease severity progresses (Sandroff et al., 2012; Motl et al., 2005; Beckerman et al., 2010). Notably, some autonomic irregularities observed in conditions such as multiple sclerosis may be partially attributed to physical deconditioning rather than primary autonomic dysfunction, suggesting that such

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impairments could be at least partially responsive to structured physical interventions like AG (Feltham et al., 2013). This reduced mobility contributes to loss of independence, decreased quality of life, and increased healthcare burden (Bloem et al., 2021; Walton et al., 2020), while existing rehabilitation approaches such as physiotherapy and exercise training often provide only partial or short-term improvements (King and Horak, 2009; Motl and Pilutti, 2012). The implications are not limited to muscular deconditioning, but also pertain to cardiovascular deconditioning, central autonomic impairment, and a more general deterioration in whole-body physiology (Motl et al., 2011). These adaptations share features with multisystem deconditioning observed after prolonged microgravity exposure. Microgravity-induced unloading leads to rapid deterioration in cardiovascular function, bone density, muscular strength, and autonomic regulation, like aging or severe immobilization (Vernikos, 2018). Short-arm human centrifugation (SAHC) has been a widely studied countermeasure to prevent these types of spaceflight deconditioning (Clément and Pavy-Le Traon, 2004; Hoenemann et al., 2023). Daily AG exposure mitigates orthostatic intolerance and maintains cardiac output following bed rest (Hoenemann et al., 2023). Furthermore, intermittent SAHC training appears to be effective in retaining autonomic cardiovascular control and blood pressure regulation (Stenger et al., 2012; Goswami et al., 2015). A preliminary pilot study of our team, involving a 4-week short-arm centrifugation program in a small clinical cohort, demonstrated the feasibility and immediate physiological responses to graded hypergravity loading, and directly informed the design of the present 30-week protocol (Kourtidou-Papadeli et al., 2022). The same group recently reported additional operational insights from repeated short-arc centrifugation exposures in a separate cohort, further supporting the translational potential of this intervention (Kourtidou-Papadeli et al., 2025).

Although the idea of AG as an approach to counteract microgravity-induced deconditioning is not new, its use in clinical rehabilitation for terrestrial populations remains underexplored. Recent reviews have suggested that artificial gravity may have broader medical applications, including the rehabilitation of neurological and musculoskeletal diseases (Isasi et al., 2022; Kourtidou-Papadeli et al., 2022). Instead of considering these patients as terrestrial analogs of astronauts, their relevance lies in the shared pattern of multi-system deconditioning resulting from markedly reduced mechanical loading. In this study, we evaluated short-arm human centrifugation as an innovative method of whole-body rehabilitation for patients with neuromuscular and neurodegenerative diseases, who typically present with reduced mobility and diminished musculoskeletal loading. We hypothesized that graded hypergravity loading would counteract systemic deconditioning by improving cardiovascular function, muscular strength (assessed through bilateral handgrip force), and postural stability (assessed through stance balance measures). By demonstrating functional improvements, our results highlight the bidirectional translational relevance of this intervention, suggesting important clinical applications in neurorehabilitation while also informing countermeasure development for long-duration human spaceflight.

2. Materials and methods

2.1. Subjects

A total of 20 patients with neuromuscular and neurodegenerative disorders (including multiple sclerosis and Parkinson's disease) were enrolled in the study (Table S1). No participants were excluded before baseline assessment, and there were no dropouts during the 30-week SAHC program; all participants completed the full intervention. The cohort was entirely independent of the 12-patient group reported in our Acta Astronautica study (Kourtidou-Papadeli et al., 2025), which examined acute cardiovascular responses to graded hypergravity. None of the participants in the present study had any prior exposure to short-arm human centrifugation before enrollment. All outcome measures were collected over the complete 30-week period. Handgrip strength and stance balance were assessed every week for 20 weeks. Functional mobility (FMQ) was assessed at baseline and at the end of the 30-week protocol. Although FMQ is routinely performed every 3 months in our clinical practice, only the baseline and 30-week evaluations were used in the present study. No mid-program FMQ measurements were included in the analysis. Inclusion criteria were mobility restrictions preventing effective conventional exercise, a stable medication regimen for $\geq$3 months, and absence of contraindications to artificial gravity training (e.g., uncontrolled cardiovascular disease, vertigo, epilepsy, kidney stones).

The centrifuge rotated in a single fixed direction for all participants and all sessions; the rotation direction was not alternated to avoid vestibular perturbations associated with changes in angular direction. During the centrifugation periods, participants were instructed to remain still, keep their head in a neutral position, and avoid any voluntary head or trunk movements. Hands were placed alongside the body, and communication with the operator was maintained throughout the session. These procedures were implemented to minimize stimulation of the semicircular canals and maintain vestibular input at negligible levels. All participants provided written informed consent, which was approved by the Bioethics Committee of the School of Medicine, Aristotle University of Thessaloniki (document number 179/19.03.2020). The protocol was registered with ClinicalTrials.gov (NCT04369976).

2.2. Experimental design

This single-cohort, within-subject pre/post-intervention study delivered 30 weeks of SAHC training. High-frequency cardiopulmonary/hematology measures were collected at weeks 1, 5, 10, 15, 20, 25, 30; handgrip and stance balance were assessed weekly for 20 consecutive weeks (weeks 1–20). Participants first underwent a familiarization centrifugation session at 1 g for 10 min. Those tolerating the procedure without dizziness, nausea, or pre-syncope were enrolled in the study. They were instructed to abstain from caffeine on training days, avoid alcohol for the preceding 12 h, refrain from eating for the preceding 2 h, and avoid heavy exercise for the preceding 24 h. Each was subjected to stepwise centrifugation at progressively increasing loads of gravitation (1.5, 1.7, 1.7, 2.0, and 2.0 g) for 6 min each load and 5 min pause (Fig. 1). All participants continued their regular lives throughout the study period, with the only systematic intervention being artificial gravity training via centrifugation. Medication regimens and other rehabilitation therapies were required to be stable for at least 30 weeks before and throughout the intervention; any change in pharmacotherapy or the addition of new therapies was an exclusion criterion. Three measurement conditions were defined: (1) Pre: measurements obtained before centrifugation, while the participant was in a sitting position immediately upon arrival. (2) Lying: measurements obtained after positioning the participant in a supine position on the centrifuge bed, immediately before centrifugation, following a brief stabilization period.

(3) Post: measurements obtained immediately after completing the centrifugation protocol, with the participant still in the supine position. In all cases, posture was kept consistent within each measurement condition to ensure physiological changes reflected the effects of SAHC rather than postural transitions.

Systolic blood pressure (SBP, mmHg), diastolic blood pressure (DBP, mmHg), mean arterial pressure (MAP, mmHg), cardiac output (CO, L/min), stroke volume (SV, mL/beat), and heart rate (HR, bpm) were monitored continuously and non-invasively with a finger-cuff hemodynamic system (Edwards Life Sciences) (Fig. 1). Non-invasive optical monitoring (Cnoga TensorTip MTX) estimated partial pressure of oxygen (pO_2, mmHg), partial pressure of carbon dioxide (pCO_2, mmHg), oxygen content (O_2), carbon dioxide content (CO_2), and oxygen

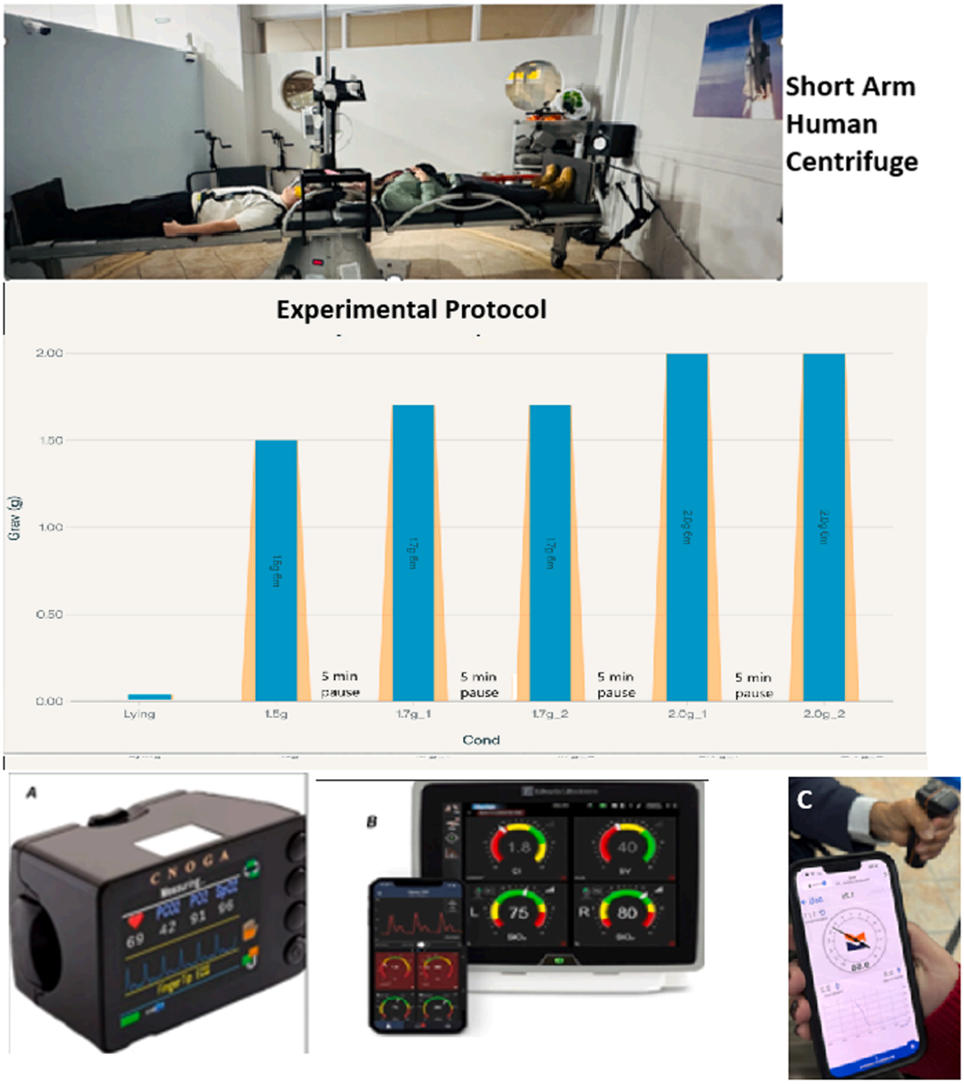

Fig. 1. SAHC protocol and devices: A. Clear Sight device (Edwards Life Sciences), B. Cnoga Medical Tensor Tip (MTX device), and C. Kinvent for grip and Stance. The g-levels refer to the longitudinal (Gz) load at the feet, with a decreasing gradient toward the head due to proximity to the axis of rotation.

saturation (SpO_2, %) as well as hemoglobin (Hb), hematocrit (Hct), and red blood cells (RBC) (Fig. 1).

Handgrip strength (kg) was measured weekly for 20 consecutive weeks using a KINVENT K-Grip dynamometer (three 3–5 s maximal voluntary contractions (MVCs) per hand, best value analyzed), and stance/balance was assessed on KINVENT K-Force Plates via center-of-pressure (CoP) metrics (two 30-s quiet-standing trials; sway path/area/velocity and weight distribution) (Fig. 1). Data were captured with the KINVENT Physio application and exported for analysis. Raw force/CoP data were exported from KINVENT Physio and processed using pre-specified scripts. Trials with obvious artifacts (loss of contact, coughing, stepping) were flagged a priori and re-acquired. Functional mobility was assessed using a validated Functional Mobility Questionnaire administered at baseline and after 30 weeks. Total and subscale scores were recorded according to the instrument's scoring guidelines. All figures and tables were organized to follow the chronological order of the experimental protocol and outcome evaluation. Cardiovascular plots were condensed to the main integrative variables CO and MAP, while all other cardiovascular measures were summarized in a single table (Table S5). Stance and grip figures were consolidated to minimize redundancy and enhance interpretability. Handgrip and stance balance were assessed for the first 20 weeks because these variables show earlier adaptation, and weekly testing beyond 20 weeks would not provide additional information while increasing participant burden.

2.3. Intervention protocol

The intervention consisted of three sessions per week centrifugation sessions for 30 weeks, each including a duration of 30 min of total centrifugation with a standard protocol of g loads of 1.5, 1.7, 1.7, 2.0, and 2.0 g, typically structured in 6-minute intervals with 5-minute rest periods in between (Fig. 1). The structure of the 30-week SAHC program (session duration, incremental g-step progression, and safety thresholds) was informed by an earlier 4-week pilot investigation conducted by our group, which established patient tolerance and guided refinement of the clinical protocol (Kourtidou-Papadeli et al., 2022). Additional insights from a subsequent cohort study reported in Acta Astronautica (Kourtidou-Papadeli et al., 2025) also contributed to the finalization of operational procedures. All g-levels described in this study refer to the longitudinal body axis component (Gz) measured at the feet, where centrifugal acceleration is maximal. Because participants were positioned supine with the head near the axis of rotation, the actual g-load decreased along the cephalad direction, resulting in a partial g-gradient. The term '1 *g*' used during the familiarization session, therefore, denotes 1 g at the feet, not resultant g. This convention was applied to all centrifugation amplitudes.

Target g-levels were defined at the feet, and rotation rate (rpm) was individualized for each participant based on their foot-to-axis distance. The required rpm was calculated using the standard centripetal acceleration formula ($g = r{\cdot}\omega^2/g_0$), ensuring that all participants experienced the same longitudinal Gz-load at the feet regardless of stature. The head was positioned close to the axis of rotation. Because the head was positioned approximately 10 cm from the axis of rotation, the centrifugal g-load at the head was extremely small (≈0.03 g), with the full prescribed longitudinal Gz-load applied only at the feet, where centrifugal acceleration was maximal. Angular acceleration and deceleration were standardized: the centrifuge ramped from 0 rpm to the subject-specific rotation rate over 20–25 s and returned to rest over the same duration to minimize vestibular stimulation and ensure participant comfort.

The position of the subject was supine, head near the axis to minimize Coriolis forces, and continuous cardiovascular monitoring (CO, MAP, HR, SpO_2) with session termination criteria included pre-syncope symptoms or critical hemodynamic changes (e.g., SBP drop >20 mmHg, HR drop >15 bpm).

2.4. Short-Arm human centrifuge (SAHC) device

Training was performed on a custom-built SAHC (patent #1009,812/13/09/2019) located at the "Joan Vernikos" Laboratory of Aerospace and Rehabilitation Applications, Thessaloniki, Greece (Fig. 1). The centrifuge has a 4 m diameter; maximum +Gz at the feet was 3.5 g. The device consists of a central rotating shaft with supine beds, safety harnesses, and integrated exercise modules (bicycle ergometer and resistance bands, though no additional exercise was included in this protocol). The g-load gradient ensured near-zero g at the head and maximal g at the feet.

2.5. Statistical analysis

Data analysis was performed using the R programming language at a minimum significance level of 5 %. Given significant deviations from normality in most variables, longitudinal cardiovascular, blood-gas, and hematological parameters were analyzed using rank-based nonparametric analysis of longitudinal data (nparLD in R), following the method of Brunner, Domhof & Langer (2002) (Brunner et al., 2002). This approach evaluates the main effects of time (weeks 1–30), condition (pre, lying, post), and their interaction, using Wald-type ANOVA-type statistics (ATS), which are F-approximated test statistics appropriate for nonparametric repeated-measures designs. Post-hoc contrasts were adjusted using the Holm correction.

For handgrip strength and stance stability, which were measured weekly over the first 20 weeks, we used Friedman tests to assess the overall effect of the intervention. When a significant effect was detected, planned comparisons (week 1 vs weeks 5, 10, 15, and 20) were performed using Wilcoxon signed-rank tests with Holm's correction, following Aickin & Gensler (1996) (Aickin and Gensler, 1996). Effect sizes were expressed as Kendall's W for Friedman analyses and as relative effect sizes for nparLD models.

Diagnostic subgroup effects (Multiple Sclerosis vs Other Neurodegenerative Disorders) for grip and stance outcomes were examined using factorial nparLD models, with Group as a between-subject factor and Time as a within-subject factor. Cardiovascular and blood-gas analyses included only within-subject factors (Time and Condition).

The three F-type statistics reported in Supplementary Table S2—FT, FC, and FI—correspond to the ANOVA-type statistics (ATS) generated by the nparLD models: FT (F for Time) tests the main effect of time (changes across weeks, averaged over conditions), FC (F for Condition) tests the main effect of condition (pre, lying, post, averaged over weeks), and FI (F for Interaction) tests the time × condition interaction (whether temporal changes differ across the three conditions). These indices clarify whether observed effects arise from time, condition, or their combination.

Hematological parameters (Hb, Hct, RBC) were also analyzed longitudinally using the nparLD framework to evaluate potential effects of SAHC training on erythrocyte-related and oxygen transport variables.

3. Results

3.1. Hemodynamics

All values were obtained in the standardized pre, lying, and post-measurement conditions. For the hemodynamic parameters, nonparametric repeated measures ANOVA were performed and indicated a significant main effect of time on SBP ($F = 7.4$, $p < .001$), MAP ($F = 2.7$, $p < .001$), HR ($F = 3.4$, $p < .001$), and CO ($F = 140.8$, $p < .001$) (Table S2). Accordingly, a significant interaction of condition with time emerged for the parameters SBP ($F = 3.1$, $p < .001$), DBP ($F = 4.8$, $p < .001$), HR ($F = 4.3$, $p < .001$), and CO ($F = 10.1$, $p < .001$) (Table S2). Post-hoc analysis showed a significant decrease in the mean value of HR between the 1st and 5th week ($p < .001$) and between the 1st and 20th week ($p = .041$). Also, analysis showed a significant decrease in the mean value of SBP between the 1st and 25th week ($p = .005$). Finally, post-hoc analysis showed a substantial increase in the mean value of CO between 1st and 5th week ($p < .001$), 1st and 10th week ($p < .001$), 1st and 15th week ($p < .001$), 1st and 20th week ($p < .001$), 1st and 25th week ($p < .001$) and 1st and 30th week ($p < .001$) (Table S2). The evolution of SBP across the three conditions (pre, lying, and post) over the 30 weeks is depicted in Figure S1. The data show a significant effect of both the testing condition and time on systolic pressure as confirmed by nonparametric repeated measures ANOVA (main effect of condition: FC = 16.2, $p < .001$; main effect of time: FT = 7.4, $p < .001$; interaction: FI = 3.1, $p < .001$). Notably, post-hoc analysis indicates a statistically significant decrease in systolic pressure between the first and 25th weeks ($p = .005$), demonstrating a measurable cardiovascular response to the intervention over time (Table S2).

The pattern of DBP across the three conditions (pre, lying, and post) during the 30-week intervention period is depicted in Figure S2. The statistical analysis indicated a significant interaction effect of both condition and time on diastolic pressure (main effect of condition: FC = 1.1, $p = .325$; main effect of time: FT = 2.3, $p = .051$; condition × time interaction: FI = 4.8, $p < .001$). While diastolic blood pressure remained generally stable, there was a significant interaction suggesting subtle variations depending on testing condition and time point.

To improve clarity and reduce redundancy, cardiovascular results were consolidated. Graphical plots were retained only for cardiac output (CO) and mean arterial pressure (MAP), as these variables provide a comprehensive representation of systemic hemodynamic behavior during SAHC (Figs. 2 and 3). All additional cardiovascular parameters (heart rate, systolic and diastolic blood pressure) are summarized in Table S2 across pre-, lying-, and post-conditions throughout the 30-week intervention.

3.2. Hematology

The results for the hematology parameters are presented in Table S3. Nonparametric repeated measures ANOVA indicated that there was no effect of the intervention on any of the three hematology parameters (Hb, Hct, and RBC).

3.3. Blood gas

The results are presented in Table S4. Nonparametric repeated-measures ANOVA indicated a significant main effect of time for SpO_2, pH, pCO_2, pO_2, O_2 content, and CO_2 content (all $p<.001$), with significant time×condition interactions for the same variables (all $p\leq.002$). Post-hoc tests showed SpO_2 decreased from week 1 to weeks 20 and 30 (both $p<.001$). pH decreased from week 1 to weeks 15, 20, and 30 (all

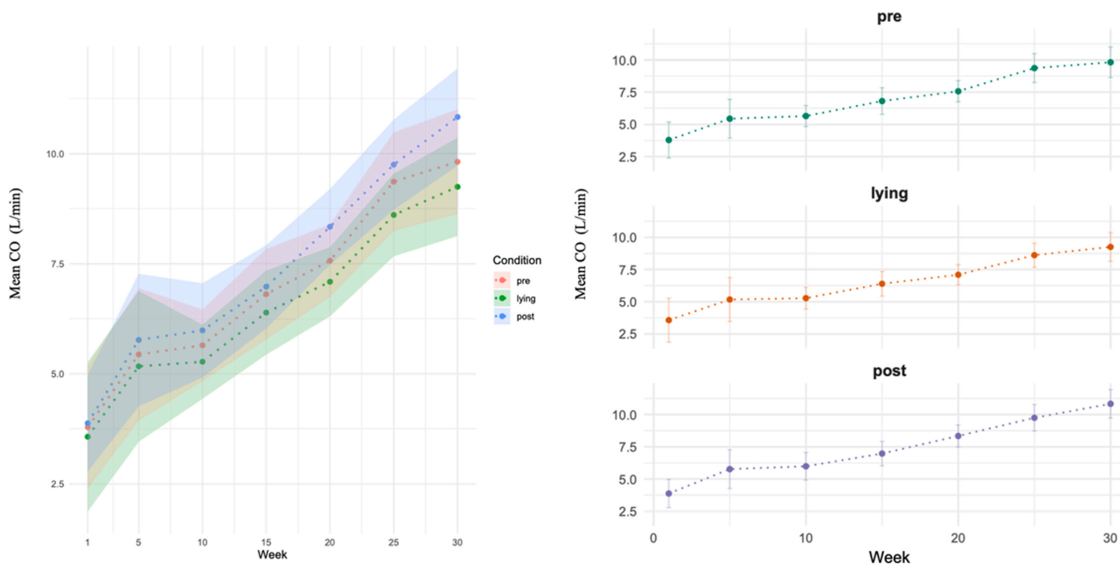

Fig. 2. Cardiac Output (CO, L/min) Pre, lying, post conditions from week 1 to week 30.

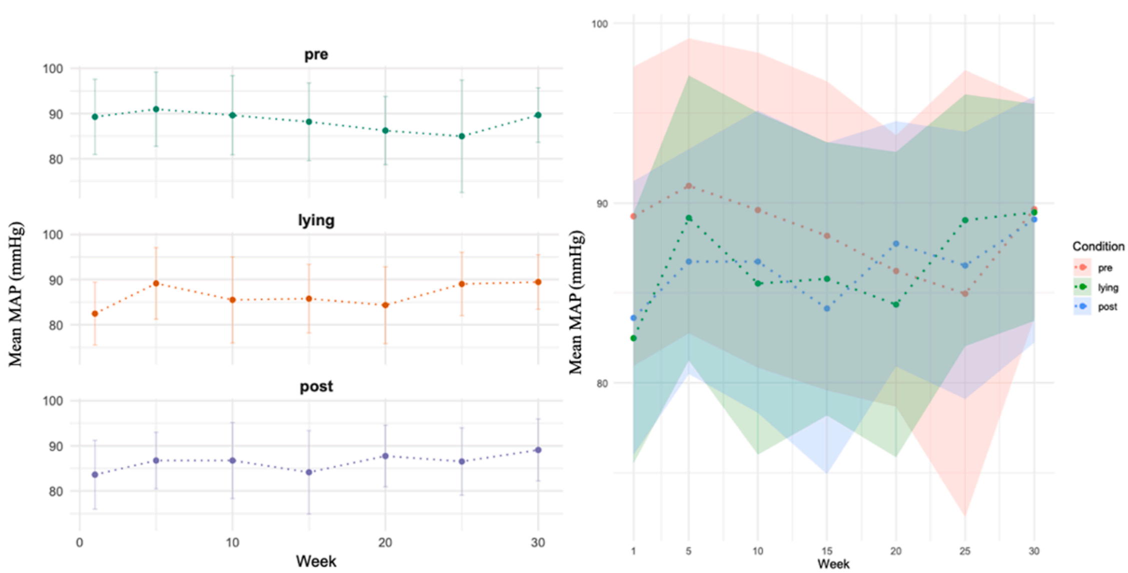

Fig. 3. Mean Arterial Pressure (MAP, mmHg) Pre, lying, post conditions from week 1 to week 30.

$p<.001$). pCO_2 decreased from week 1 to weeks 20, 25, and 30 (all $p<.001$). pO_2 increased from week 1 to weeks 10, 15, 25, and 30 (all $p<.001$). O_2 content increased from week 1 to weeks 5, 10, 15, 20, 25, and 30 (all $p<.001$). CO_2 content showed a mixed pattern consistent with the significant interaction (see Table S4 for cellwise values).

Post-hoc analysis revealed a significant decrease in SpO_2 from week 1 to weeks 20 and 30 (both $p < .001$). Given a significant time×condition interaction, SpO_2 patterns were condition-dependent (e.g., higher values in the post condition despite the overall time effect).

Similarly, a significant decrease in pH value was recorded between the 1st and 15th week ($p < .001$), 20th week ($p < .001$), and 30th week ($p < .001$) (Figure S2). Regarding pCO_2 measurements, post-hoc analysis showed that a significant decrease was recorded between the 1st and 20th week ($p < .001$), 25th week ($p < .001$), and 30th week ($p < .001$) (Figure S3). Furthermore, post-hoc analysis indicates a significant increase in the case of pO_2 between the 1st and 10th week ($p < .001$), 15th week ($p < .001$), 25th week ($p < .001$), and 30th week ($p < .001$) (Figure S4). Regarding O_2 content measurements, post-hoc analysis showed that there was a significant increase between the 1st and 5th week ($p < .001$), 10th week ($p < .001$), 15th week ($p < .001$), 20th week ($p < .001$), 25th week ($p < .001$), and 30th week ($p < .001$) (Figure S5). Also, CO_2 content analysis indicates a significant increase between the 1st and 5th week ($p < .001$), a substantial decrease between week 1 and 15th week ($p < .001$), a significant increase between the 1st and 25th week ($p < .001$), and a substantial decrease between the 1st and 30th week ($p < .001$) (Figure S6).

3.4. Stance balance (mm)

CoP metrics showed no significant change over 20 weeks; variability at week 5 reflected an individual outlier (Table S5; Figs. 4 and 5).

The results regarding the evolution of stance on the right and left side between MS and Other ND patients are given in Fig. 5. The data show that, on average, there is stationarity in stance on both sides (left and right) in both groups of patients. A large variation is recorded in stance values in the group of patients with other NDs at week 5. All stance

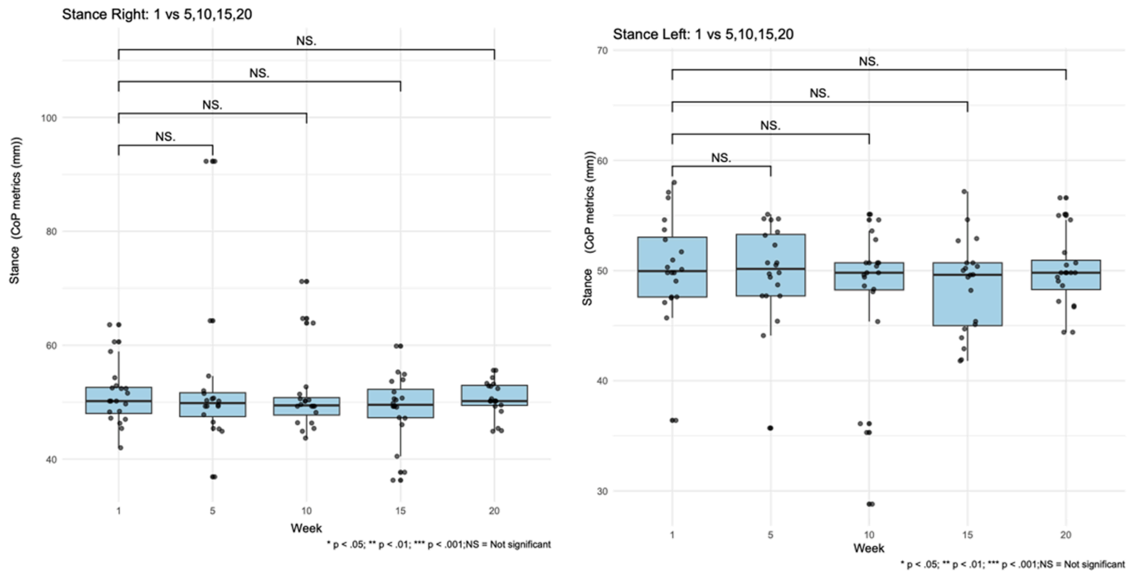

Fig. 4. Stance Stability – Post-hoc Comparisons (CoP, mm). Right and left stance post-hoc comparisons between weeks 1, 5, 10, 15, and 20.

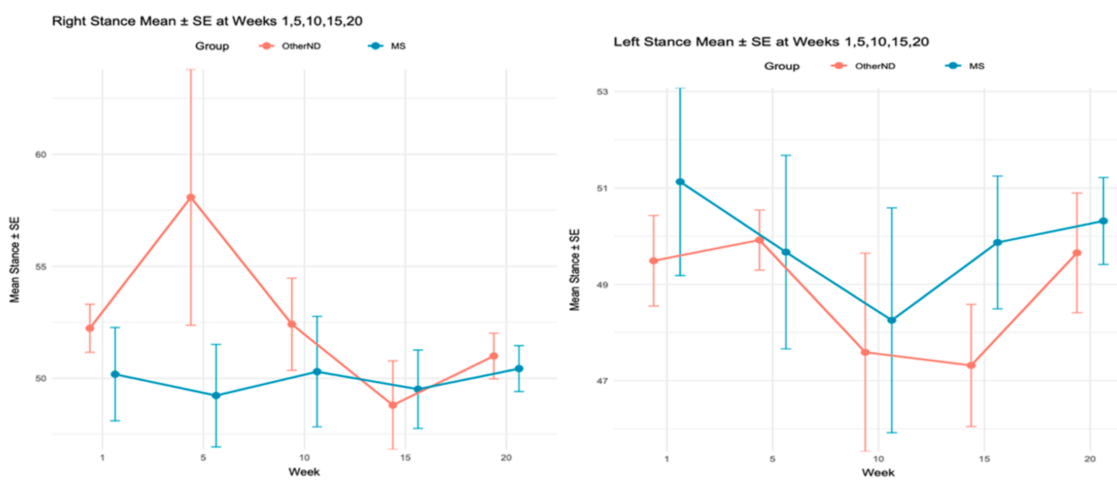

Fig. 5. Stance Stability (mm) by Patient Group. Mean ± 95 % CI for stance (right and left) per week for MS vs ND groups.

assessments were conducted with a rigorously calibrated device, using the same standardized measurement order for each participant. The device's calibration was verified before each session, ruling out technical error or procedural deviation as a source of variability. The unusually high mean value recorded for stance on the right in week 5 appears to result from an individual outlier who engaged in increased physical activity in the preceding days. Acute changes in physical condition—such as exercise-induced fatigue or neuromotor adaptation—are known to transiently affect postural balance scores, which may explain this observation despite strict adherence to protocol and technical quality assurance.

The results of the nonparametric repeated measures ANOVA showed that there is no significant effect of group on stance on the left and right sides. Furthermore, a non-significant interaction between group and time on the stance on the left and right side. From Figure S7, for patients with other ND, a sharp increase in the mean in stance on the right side was recorded at week 5, and then a decline and stagnation until the end of week 20. In the group of patients with MS, stationarity in mean stance on the right side is recorded from the first week.

3.5. *Hand grip (Kg)*

The results of the analysis of grip measurements (left and right) per week in the total of 20 patients are presented in Table S6, with hand grip strength measured in kilograms (kg). The mean and median values of grip on the left at week 1 were equal to 18.4 and 17.6, respectively. Furthermore, the mean and median values of grip on the left at week 20 increased to 26.5 and 27.8, respectively. Similarly, results show that the mean and median values of grip on the right in week 1 were equal to 20.8 and 23.9, respectively, and at week 20 increased to 29.3 and 28.2, respectively.

Fig. 6 shows an increasing trend in the average grip value on both the left and right sides, with the lowest value in both cases recorded in the first week and the highest value in both cases recorded in the twentieth week.

The results of the nonparametric Friedman test showed that there was a statistically significant difference in the mean grip on the right side ($\chi^2 = 179.69$, df = 19, $p < .001$) and the mean grip on the left side ($\chi^2 = 162.56$, df = 19, $p < .001$) over time. On the contrary, there was no significant difference in the mean stance on the right side ($\chi^2 = 16.41$, df = 19, $p = .623$) and the mean stance on the left side ($\chi^2 = 19.66$, df = 19,

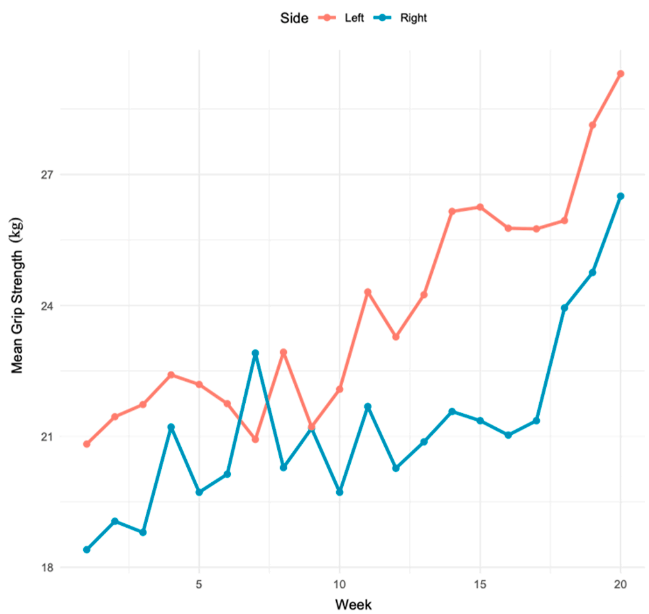

Fig. 6. Grip Strength (kg) – Longitudinal Trajectories. Mean grip strength (left and right) per week across all participants.

p = .416) over time.

The nonparametric Wilcoxon test (Holm's correction method) revealed that there was no statistically significant difference between the mean grip on the left side between weeks 1 and 5 (p = .294) and between weeks 1 and 10 (p = .294). On the contrary, there was a statistically significant increase in the mean grip on the left side between weeks 1 and 15 (p = .009) and between weeks 1 and 20 (p < .001) (Fig. 7).

The nonparametric Wilcoxon test (Holm's correction method) revealed that there was no statistically significant difference between the mean grip on the right side between weeks 1 and 5 (p = .280), between weeks 1 and 10 (p = .280), and between weeks 1 and 15 (p = .091). On the contrary, there was a statistically significant increase in the mean grip on the right side between weeks 1 and 20 (p < .001) (Fig. 7).

The results regarding the evolution of grip on the right and left side between MS and Other ND patients are given in Figure 15. The data shows that in both groups of patients, there is an increasing trend in the average grip on both sides (left and right).

The results of the nonparametric repeated measures ANOVA showed that there is a significant effect of group (p<.001) on grip on the right side. Furthermore, an analysis that a significant interaction between group and time (p < 0.001) on grip on the right side. From Fig. 8, for patients with other ND, there is an increasing trend in the average grip on the right side as early as the 5th week, while for patients with MS, the increase in the average occurs after the 15th week.

The results of the nonparametric repeated measures ANOVA showed that there is a significant effect of group (p<.05) on grip on the left side. Furthermore, the analysis showed a significant interaction between group and time (p < 0.001) on grip on the left side being recorded. From Figure S8, for patients with other ND, there is an increasing trend in the average grip on the left side as early as the 5th week, while for patients with MS, the increase in the average occurs after the 15th week.

4. Discussion

This study evaluated short-arm human centrifugation (SAHC) training as a novel whole-body rehabilitation intervention in patients with neurodegenerative diseases and restricted mobility. The findings demonstrate that three sessions per week of SAHC exposure at g loads (1.5, 1.7, 1.7, 2.0, and 2.0 g) for 30 weeks significantly improves cardiovascular parameters, enhances grip strength, maintains stance stability, and improves functional mobility.

4.1. Cardiovascular adaptations and autonomic benefits

The significant increases in cardiac output (CO) and mean arterial pressure (MAP) are consistent with prior studies in microgravity analogs. We observed modulated oxygenation parameters with increases in pO_2 and O_2 content and mixed SpO_2 patterns by time and condition. Hoenemann et al. showed that daily SAHC exposure during 60-day head-down tilt bed rest prevented orthostatic intolerance by preserving CO (Hoenemann et al., 2023). Similarly, Stenger et al. found that intermittent SAHC training prevented bed rest-induced cardiovascular deconditioning (Stenger et al., 2012). Our findings extend these results to a terrestrial clinical population, suggesting that graded hypergravity loading induces beneficial hemodynamic adaptations through enhanced

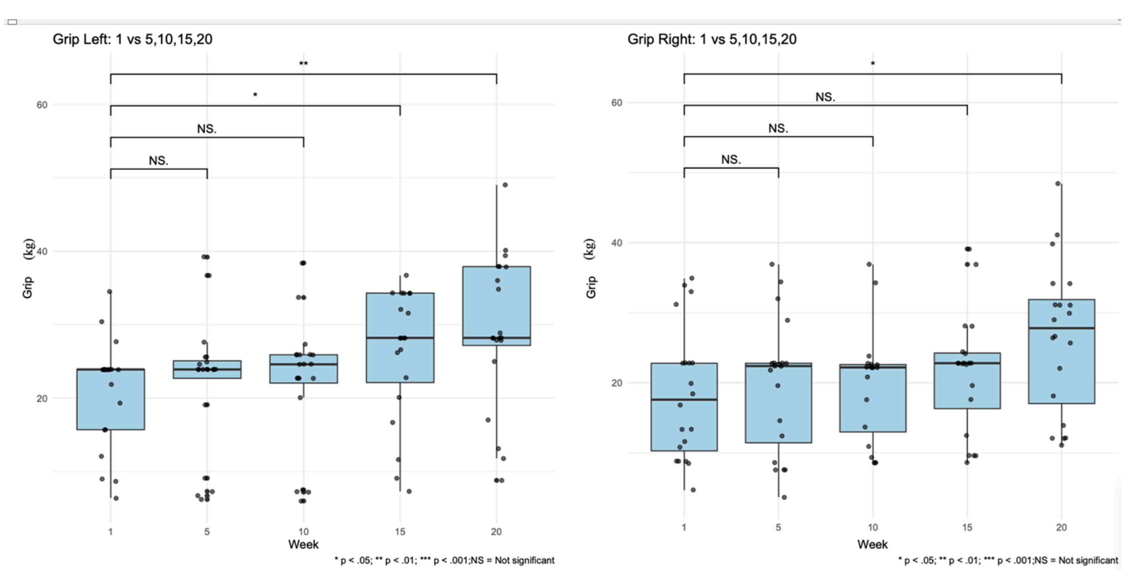

Fig. 7. Grip Strength (Kg) – Post-hoc Comparisons. A) Left-hand post-hoc comparisons (1, 5, 10, 15, 20 weeks), B) Right-hand post-hoc comparisons (1, 5, 10, 15, 20 weeks).

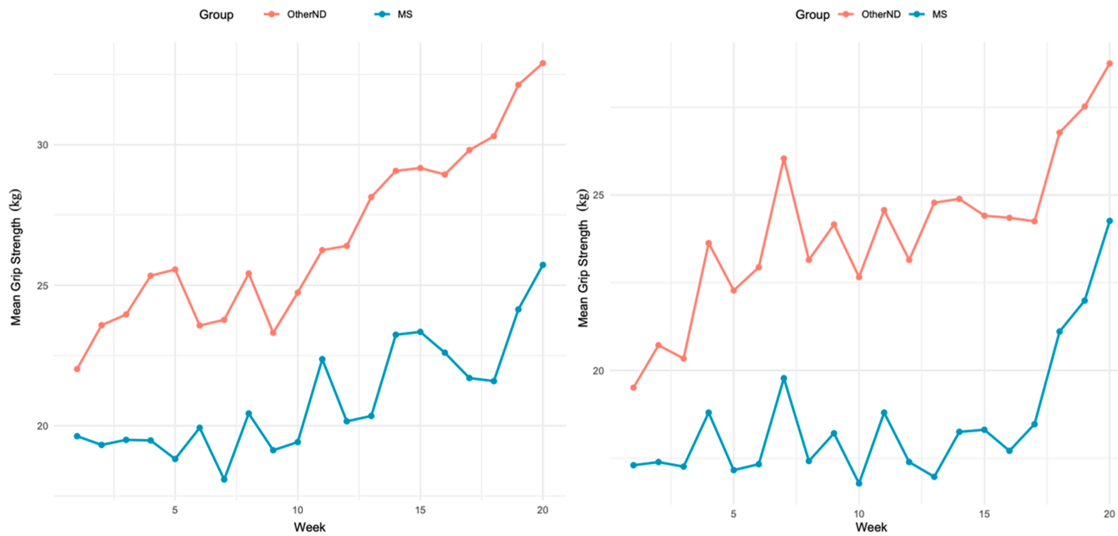

Fig. 8. Grip Strength (Kg) by Diagnostic Subgroup. Mean grip (left and right) per week for MS vs ND groups.

venous return, increased preload, and autonomic cardiovascular stimulation (Goswami et al., 2015).

The slight increase in mean arterial pressure (MAP) was observed primarily in the lying and post conditions following centrifugation, whereas the pre condition did not show notable changes. This improvement in MAP is indicative of a partial recovery of baroreflex-mediated blood pressure control, which is frequently compromised in neurodegenerative disorders due to autonomic imbalance (Low et al., 2015). The interaction F values (for condition and time) reflect changes between these different measurement positions (pre, lying, post) throughout the intervention period. The upward trend in MAP toward normative ranges in lying and post conditions may contribute to enhanced orthostatic tolerance and reduced syncope risk during daily activities.

Furthermore, the observed increases in pO_2 and O_2 content, with mixed SpO_2 patterns by time and condition, and reductions in pCO_2 levels suggest enhanced systemic gas exchange. These changes, detailed in Figures S3–S5 and Table S4, likely reflect improved pulmonary perfusion and more efficient oxygen delivery following SAHC-induced cardiovascular adaptation. The stabilization or mild improvement in blood pH also supports a balanced acid–base status, despite repeated exposure to moderate gravitational loads (Figure S9). These physiological effects may provide additional cardiopulmonary benefits for patients prone to ventilatory inefficiency and hypoxia. A growing body of research supports the observed improvements in arterial oxygen parameters and gas exchange following artificial gravity interventions. Previous studies have reported increases in oxygen uptake, improved cardiovascular adaptation, and a protective effect against spaceflight-induced hypoxia when SAHC was combined with exercise or implemented as a daily countermeasure during bed rest or microgravity simulations. These cardiopulmonary benefits align with our findings, further demonstrating that graded hypergravity loading may be an effective strategy for mitigating ventilatory inefficiency and oxygenation deficits in patients with neurodegenerative conditions, as well as in spaceflight populations (Clément et al., 2015).

Grip strength improvements and neuromuscular implications

Both right- and left-hand grip strength increased significantly over the 30-week intervention. Grip strength is a validated surrogate marker of global upper-limb function, overall strength, and frailty in neurological populations (Bohannon, 2001). The passive gravitational loading provided by SAHC likely activates mechanoreceptors, enhances peripheral circulation, and stimulates neuromuscular pathways, promoting strength gains even in the absence of active resistance training (Isasi et al., 2022). These improvements are clinically meaningful for activities of daily living in severely mobility-impaired individuals.

When examined by diagnostic subgroup, both MS and other neurodegenerative (ND) patients showed significant improvements, but with different temporal patterns. The ND group demonstrated earlier gains (beginning around week 5), whereas patients with MS exhibited a delayed but still robust improvement that became evident after week 15. This delayed response in MS is consistent with demyelination-related conduction deficits and reduced neuromuscular efficiency, which may slow adaptation. Although several MS participants spontaneously reported subjective improvements in daily manual tasks (e.g., opening containers, stabilizing objects), these observations were not formally quantified.

No consistent subgroup differences were observed in cardiovascular, stance, or FMQ outcomes. The overall pattern of improvement aligns with emerging evidence showing that gravitational loading can enhance vascular, muscular, and functional outcomes in clinical populations, including recent reports of successful artificial gravity therapy in patients with systemic sclerosis and endothelial dysfunction (Isasi et al., 2022).

4.2. Functional mobility gains

The Functional Mobility Questionnaire (FMQ–Short) results after the 30-week SAHC rehabilitation program demonstrated a statistically significant improvement, suggesting perceived and clinically assessed gains in overall mobility (Table S7). Because of the progressive nature of neurodegenerative diseases, these gains could manifest clinically as sufficient to stabilize and possibly reverse some aspect of inactivity-induced deconditioning (Sandroff et al., 2012; Motl et al., 2011).

Maintenance of stance balance and intervention safety

No deterioration in stance stability was found, suggesting that SAHC training does not negatively affect postural control. Previous studies emphasize that vestibular and proprioceptive stimulation during SAHC may support balance and spatial orientation adaptations (Clément and Pavy-Le Traon, 2004). Safety was established with no treatment-related cardiovascular or vestibular side effects observed, indicating SAHC's feasibility in such a patient group.

In addition, hematological parameters such as hemoglobin (Hb), hematocrit (Hct), and red blood cell count (RBC) remained stable throughout the intervention (Table S3). This suggests that SAHC training, while inducing cardiovascular and neuromuscular adaptations, does not impose hematologic stress or alter oxygen-carrying capacity in patients, reinforcing its safety profile.

4.3. Clinical implications and spaceflight countermeasure relevance

Graded hypergravity loading via SAHC provides systemic physiological and functional benefits analogous to medium intensity exercise (Qiu et al., 2023), an effective form of rehabilitation for individuals who are not ambulatory secondary to profound neurologic loss, and it represents an alternative medical approach for treating loss of tissue mass and neuromuscular function due to bed rest. In clinical neurorehabilitation, such interventions address the critical challenge of inactivity-induced cardiovascular, musculoskeletal, and autonomic deconditioning, which accelerates functional decline and worsens quality of life in neurodegenerative diseases.

Artificial gravity offers a unique rehabilitative stimulus by reintroducing gravitational loading through centrifugation-induced hydrostatic pressure gradients and vestibular stimulation. This integrated loading simulates the physiological stresses of upright posture and ambulation, promoting cardiovascular acclimatization, baroreflex stimulation, and neuromuscular recruitment even in completely bedridden patients. Such systemic stimulation is hard to achieve with conventional passive rehabilitation approaches, and graded hypergravity loading with SAHC may be considered as a complementary therapy to preserve or improve cardiovascular function, muscle strength, and, more generally, physiological reserve in immobile or severely deconditioned patients.

Although neurodegenerative patients experience profound physical inactivity, they should not be considered terrestrial analogs of astronauts, who are medically healthy during missions and protected by structured countermeasures. The similarity lies not in their overall physiology but in the shared pattern of multi-system deconditioning driven by reduced or absent mechanical loading. Prolonged inactivity in clinical populations leads to cardiovascular, musculoskeletal, and autonomic decline, paralleling some aspects of the deconditioning observed in astronauts following exposure to microgravity.

In this context, studying short-arm human centrifugation in patients offers a valuable opportunity to investigate gravitational loading as a countermeasure for inactivity-induced decline, while fully recognizing that the two populations differ fundamentally in baseline health status and underlying etiology. This approach preserves the clinical relevance of gravitational rehabilitation while informing spaceflight countermeasure development without implying physiological equivalence.

From a broader perspective, insights gained from applying graded gravitational loading in patients with restricted mobility can inform both domains: (1) rehabilitation medicine, by demonstrating that hypergravity exposure may mitigate cardiovascular decline, orthostatic intolerance, and musculoskeletal deterioration, and (2) space medicine, by providing practical information about human tolerance, optimal loading protocols, and systemic adaptations that support the design of artificial gravity countermeasures for long-duration missions. Understanding these responses in clinically vulnerable populations can refine safety guidelines, operational procedures, and device requirements for future exploration-class missions.

4.4. Limitations

This study had several limitations. An additional control group of healthy volunteers was not included since, by definition, healthy controls without rehabilitation would not manifest a detectable change in functional or physiological measures. The focus was to assess SAHC effects specifically in patients representing a clinical analog of inactivity-induced deconditioning. The absence of a randomized control group limits the ability to draw causal inferences about graded hypergravity loading with SAHC-specific effects.

The sample size was modest ($n = 20$), and subgroup analyses (MS vs Other ND) were exploratory and underpowered. We fully recognize that a modest sample size ($n = 20$) limits the breadth of subgroup analyses and increases the potential for a type II error, especially regarding secondary endpoints such as stance stability. However, several factors justify this sample size for the present study. Despite modest size, the study achieved complete longitudinal follow-up, yielding robust, repeated-measures data across six months. Each patient served as their own control, enhancing analytical power for detecting within-subject effects.

Functional mobility outcomes were assessed with a short questionnaire; inclusion of additional objective gait or transfer assessments would strengthen the conclusions and provide more robust evidence for the observed improvements. The sustainability of the intervention effects in the long term is not known.

Future research should include controlled trials with larger sample sizes, disease-specific analyses, and long-term follow-up to evaluate the sustainability of SAHC-induced adaptations.

4.5. Neurophysiological integration and mechanistic implications

Gravitational neuromodulation has been proposed as a broader conceptual mechanism; however, in the present protocol, vestibular stimulation was intentionally minimized by placing the head near the axis of rotation and restricting head movements. Thus, vestibulo-autonomic contributions should be considered theoretical rather than primary drivers of the observed outcomes. Prior studies have shown otolith-driven vestibulo-sympathetic influences on cardiovascular regulation (Hallgren et al., 2015; Yates et al., 2014), and central neural efficiency changes with repeated gravitational loading (Tays et al., 2023), but these mechanisms were unlikely to be substantially activated under our minimized-vestibular-load. conditions.

5. Conclusion

Short-arm centrifugation, which delivers artificial gravity at graded g-loads, is associated with improvements in cardiovascular parameters, grip strength, and functional mobility, while maintaining stance stability, in patients with neurodegenerative diseases and restricted mobility. Artificial gravity represents a novel, feasible, and effective rehabilitation countermeasure bridging terrestrial clinical rehabilitation needs with space physiology countermeasure development for astronaut health maintenance during long-duration missions.

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CRediT authorship contribution statement

Chrysoula Kourtidou-Papadeli: Writing – original draft, Visualization, Resources, Methodology, Investigation, Conceptualization. **Gerasimos Terzopoulos:** Methodology. **Sofia Kourtidou:** Methodology, Data curation. **Eleni Dafli:** Investigation. **Dimitrios Karnaras:** Investigation. **Kalliopi Galanopoulou:** Investigation. **Evangelia Theodorou:** Methodology. **Anna Kontogianni:** Methodology. **Nicholas Georgiou:** Resources, Methodology. **Panagiotis D. Bamidis:** Writing – review & editing, Supervision. **Joan Vernikos:** Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.lssr.2025.12.001.

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