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Microgravity-induced cerebral neuroplasticity: a systematic review of structural and functional brain adaptations

Neuroplasticidade cerebral induzida pela microgravidade: uma revisão sistemática das adaptações estruturais e funcionais do cérebro

Neuroplasticidad cerebral inducida por la microgravedad: una revisión sistemática de las adaptaciones estructurales y funcionales del cerebro

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ABSTRACT

Prolonged exposure to microgravity constitutes a unique physiological challenge to the human body and represents a critical issue for long-duration space missions, particularly due to its potential effects on the central nervous system. Over recent decades, scientific evidence has demonstrated that microgravity induces significant alterations in brain structure and function; however, these findings remain fragmented across heterogeneous experimental models and methodological approaches, limiting an integrated understanding of cerebral adaptation. The objective of this study was to systematically synthesize and critically analyze PubMed-indexed evidence on cerebral neuroplasticity induced by microgravity.

A systematic review of the literature was conducted in accordance with PRISMA guidelines. The search was performed exclusively in the PubMed database and included studies published between 2015 and 2025. Eligible studies comprised investigations involving human spaceflight, validated ground-based microgravity analogs, and experimental animal models, provided that they assessed structural or functional cerebral outcomes using neuroimaging or neurophysiological techniques.

The results revealed consistent cerebral adaptations across different models, including cephalad cerebrospinal fluid redistribution, ventricular expansion, regionally specific gray matter reorganization, white matter microstructural alterations (particularly in cerebellar and sensorimotor pathways) and functional connectivity changes involving vestibular, visual, and motor networks. These findings indicate that cerebral adaptations result from the interaction between mechanical fluid shifts and experience-dependent sensory reweighting.

In conclusion, microgravity induces robust and multidimensional cerebral neuroplastic responses, encompassing both adaptive and potentially maladaptive processes. Understanding these mechanisms is essential for astronaut neurological health, the development of effective countermeasures, and the advancement of knowledge on human brain plasticity under extreme environmental conditions.

Keywords: microgravity, brain adaptation, cerebral neuroplasticity, neuroscience, spaceflight

RESUMO

A exposição prolongada à microgravidade constitui um desafio fisiológico singular para o organismo humano e representa uma questão crítica para missões espaciais de longa duração, especialmente em razão de seus potenciais efeitos sobre o sistema nervoso central. Nas últimas décadas, evidências científicas têm demonstrado que a microgravidade induz alterações significativas na estrutura e na função cerebral; entretanto, esses achados permanecem fragmentados em modelos experimentais e abordagens metodológicas heterogêneas, o que limita uma compreensão integrada da adaptação cerebral. O objetivo deste estudo foi sintetizar e analisar criticamente as evidências indexadas na base PubMed sobre a neuroplasticidade cerebral induzida pela microgravidade.

Foi conduzida uma revisão sistemática da literatura de acordo com as diretrizes PRISMA. A busca foi realizada exclusivamente na base de dados PubMed e incluiu estudos publicados entre 2015 e 2025. Foram considerados elegíveis estudos envolvendo voo espacial humano, análogos terrestres validados de microgravidade e modelos animais experimentais, desde que avaliassem desfechos estruturais ou funcionais cerebrais por meio de técnicas de neuroimagem ou métodos neurofisiológicos.

Os resultados revelaram adaptações cerebrais consistentes entre os diferentes modelos, incluindo redistribuição cefálica do líquido cefalorraquidiano, expansão ventricular, reorganização regional da substância cinzenta, alterações microestruturais da substância branca (especialmente em vias cerebelares e sensório-motoras) e mudanças na conectividade funcional envolvendo redes vestibulares, visuais e motoras. Esses achados indicam que as adaptações cerebrais resultam da interação entre deslocamentos mecânicos de fluidos e processos de reponderação sensorial dependentes da experiência.

Conclui-se que a microgravidade induz respostas neuroplásticas cerebrais robustas e multidimensionais, englobando processos tanto adaptativos quanto potencialmente maladaptativos. A compreensão desses mecanismos é essencial para a saúde neurológica de astronautas, o desenvolvimento de contramedidas eficazes e o avanço do conhecimento sobre a plasticidade cerebral humana em ambientes extremos.

Palavras-chave: microgravidade, adaptação cerebral, neuroplasticidade cerebral, neurociência, voo espacial.

RESUMEN

La exposición prolongada a la microgravedad constituye un desafío fisiológico singular para el cuerpo humano y representa un problema crítico para las misiones espaciales de larga duración, especialmente debido a sus posibles efectos sobre el sistema nervioso central. En las últimas décadas, la evidencia científica ha demostrado que la microgravedad induce alteraciones significativas en la estructura y la función cerebral; sin embargo, estos hallazgos permanecen fragmentados entre modelos experimentales y enfoques metodológicos heterogéneos, lo que limita una comprensión integrada de la adaptación cerebral. El objetivo de este estudio fue sintetizar y analizar críticamente la evidencia indexada en la base de datos PubMed sobre la neuroplasticidad cerebral inducida por la microgravedad.

Se realizó una revisión sistemática de la literatura de acuerdo con las directrices PRISMA. La búsqueda se llevó a cabo exclusivamente en la base de datos PubMed e incluyó estudios publicados entre 2015 y 2025. Se consideraron elegibles investigaciones que involucraron vuelos espaciales humanos, análogos terrestres validados de microgravedad y modelos animales experimentales, siempre que evaluaran resultados estructurales o funcionales cerebrales mediante técnicas de neuroimagen o métodos neurofisiológicos.

Los resultados evidenciaron adaptaciones cerebrales consistentes entre los diferentes modelos, incluyendo redistribución cefálica del líquido cefalorraquídeo, expansión ventricular, reorganización regional de la sustancia gris, alteraciones microestructurales de la sustancia blanca (especialmente en vías cerebelosas y sensoriomotoras) y cambios en la conectividad funcional que involucran redes vestibulares, visuales y motoras. Estos hallazgos indican que las adaptaciones cerebrales resultan de la interacción entre desplazamientos mecánicos de fluidos y procesos de reponderación sensorial dependientes de la experiencia.

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En conclusión, la microgravedad induce respuestas neuroplásticas cerebrales robustas y multidimensionales, que abarcan procesos tanto adaptativos como potencialmente maladaptativos. La comprensión de estos mecanismos es esencial para la salud neurológica de los astronautas, el desarrollo de contramedidas eficaces y el avance del conocimiento sobre la plasticidad cerebral humana en condiciones ambientales extremas.

Palabras clave: microgravedad, adaptación cerebral, neuroplasticidad cerebral, neurociencia, vuelo espacial.

1. INTRODUCTION

Human spaceflight exposes the nervous system to a constellation of extreme and unprecedented environmental stressors, among which microgravity represents a central and defining factor. The absence of a constant gravitational vector profoundly alters vestibular signaling, proprioceptive loading, cerebrospinal fluid (CSF) dynamics, cardiovascular regulation, and multisensory integration. Astronauts frequently exhibit post-flight impairments in balance, locomotion, spatial orientation, and sensorimotor coordination, indicating substantial central nervous system adaptation during exposure to microgravity.

Historically, investigations into spaceflight-induced neural changes relied primarily on behavioral assessments and neurovestibular testing. However, the rapid development of advanced neuroimaging techniques, including high-resolution structural magnetic resonance imaging (MRI), diffusion-weighted imaging, and functional MRI, has enabled direct, in vivo characterization of cerebral adaptations associated with spaceflight. Longitudinal studies in astronauts and cosmonauts have demonstrated measurable alterations in brain morphology, CSF distribution, ventricular volume, and large-scale functional network organization, challenging earlier assumptions that neural adaptations to spaceflight are exclusively functional and transient (Roberts et al., 2017; Kramer et al., 2017).

One of the most robust and reproducible observations is the upward displacement of the brain within the cranial vault, accompanied by narrowing of CSF spaces near the vertex following long-duration spaceflight. These changes have been attributed to cephalad fluid shifts and altered intracranial compliance resulting from the absence of gravitational hydrostatic gradients (Roberts et al., 2015; Van Ombergen et al., 2018). In parallel, ventricular enlargement and redistribution of gray matter density have been consistently documented, raising critical questions regarding whether such findings reflect true tissue remodeling, morphological displacement, or an interaction between both mechanisms.

Beyond macrostructural effects, functional neuroimaging studies have revealed systematic reorganization within vestibular, sensorimotor, cerebellar, and multisensory integration networks. Resting-state functional connectivity analyses indicate altered coupling between cortical and subcortical regions involved in balance control, spatial orientation, and motor planning. These network-level changes are commonly interpreted within the framework of sensory reweighting, whereby the central nervous system dynamically adjusts the relative contribution of visual, vestibular, and proprioceptive inputs to maintain functional performance in a gravity-deprived environment (Cassady et al., 2016; Pechenkova et al., 2019).

Objective: This study aimed to systematically review and synthesize PubMed-indexed evidence on microgravity-induced cerebral neuroplasticity, integrating structural and functional findings across human spaceflight, validated ground-based analogs, and experimental models, while identifying convergent mechanisms, methodological limitations, and priorities for future research.

2. THEORETICAL FRAMEWORK

Cerebral neuroplasticity refers to the brain's capacity to reorganize its structure and function in response to environmental demands. In microgravity, altered vestibular input, proprioceptive feedback, and intracranial fluid dynamics jointly create a unique neurobiological context. Current models emphasize the interaction between **sensory reweighting mechanisms** and **mechanical effects related to CSF redistribution** in shaping cerebral adaptations.

3. METHODOLOGY

The his systematic review was designed and conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020), with methodological adaptations appropriate for neuroscience and space medicine research.

3.1 Study design

A qualitative systematic review design was adopted to comprehensively synthesize evidence on cerebral neuroplasticity induced by microgravity. Given the substantial heterogeneity in exposure paradigms, neuroimaging modalities, and outcome measures, quantitative meta-analysis was deemed inappropriate. Instead, a structured narrative synthesis was employed to preserve methodological nuance while enabling integrative interpretation.

3.2 Data source and search strategy

The literature search was conducted exclusively in PubMed (National Library of Medicine) to ensure methodological consistency and reproducibility. Searches covered publications from January 1, 2015, to December 31, 2025. The following search string was applied:

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("microgravity" OR "spaceflight" OR "weightlessness" OR "head-down tilt") AND ("neuroplasticity" OR "brain plasticity" OR "functional connectivity" OR "diffusion" OR "gray matter" OR "white matter") AND ("brain" OR “cerebral”).

The full search strategy and query components are summarized in Table 1.

Table 1. Search strategy and query components used in the systematic review

Conceptual block	Keywords / descriptors	Boolean operators
Exposure	microgravity; spaceflight; weightlessness; head-down tilt	OR
Outcomes	neuroplasticity; brain plasticity; functional connectivity; gray matter; white matter; diffusion MRI	OR
Anatomy	brain; cerebral; central nervous system	OR
Combined strategy	(Exposure) AND (Outcomes) AND (Anatomy)	AND

Source: Prepared by the authors.

3.3 Eligibility criteria

Eligibility criteria were defined according to the Population, Exposure, Outcome, and Study design (PEOS) framework. Inclusion criteria comprised peer-reviewed PubMed-indexed original studies involving human spaceflight, parabolic flight, ground-based microgravity analogs, or validated animal models, provided that objective cerebral structural or functional outcomes were assessed. Exclusion criteria included non-neural outcomes, reviews, editorials, conference abstracts, and studies lacking sufficient methodological detail.

3.4 Study selection and data extraction

Study selection followed the PRISMA stages of identification, screening, eligibility, and inclusion. Two-stage screening was performed based on titles/abstracts and full-text assessment. Data extraction was conducted using a standardized form capturing study design, sample characteristics, exposure duration, neuroimaging modality, brain regions analyzed, and principal findings. The selection process is illustrated in the PRISMA flow diagram (Figure 1).

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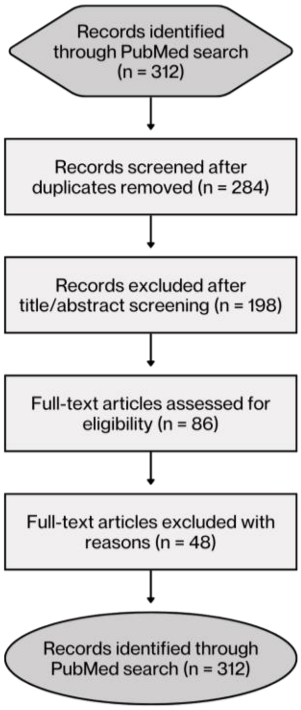
Figure 1. PRISMA 2020 flow diagram of study selection



Source: Prepared by the authors according to PRISMA 2020.

3.5 Quality assessment and risk of bias

Methodological quality was assessed qualitatively, considering study design robustness, longitudinal completeness, imaging protocol consistency, statistical rigor, and transparency of reporting. Quality assessment informed interpretation of findings but was not used as an exclusion criterion.

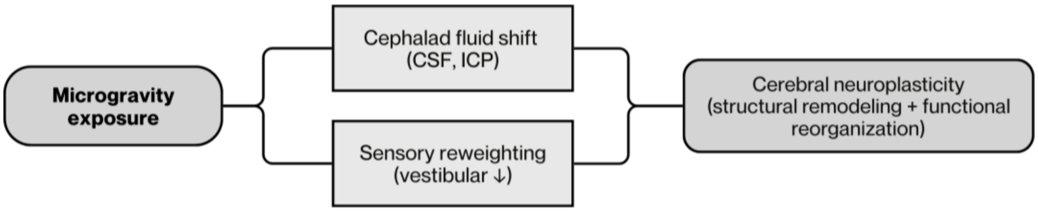
4. RESULTS AND DISCUSSIONS

4.1 General overview of findings

A A total of 38 PubMed-indexed studies were included in this systematic review, encompassing longitudinal investigations of astronauts and cosmonauts, controlled parabolic flight experiments, ground-based microgravity analogs, and validated animal models. Despite methodological heterogeneity, the evidence converges on the conclusion that microgravity exposure induces reproducible cerebral adaptations at macrostructural, microstructural, and functional network levels.

The neuroplastic effects of microgravity arise from parallel and interacting mechanical and neurofunctional mechanisms. Prolonged exposure to weightlessness promotes cephalad cerebrospinal fluid redistribution and intracranial pressure changes, leading to mechanical brain displacement and associated structural remodeling. In parallel, altered gravitational input drives experience-dependent sensory reweighting, resulting in functional reorganization and changes in large-scale brain connectivity. Together, these converging pathways promote multidimensional cerebral neuroplasticity. The mechanistic model underlying these processes is summarized in Figure 2.

Figure 2. Mechanistic model of microgravity-induced cerebral neuroplasticity. Prolonged exposure to microgravity triggers two interacting pathways: (i) a mechanical pathway involving cephalad cerebrospinal fluid redistribution and intracranial pressure changes, and (ii) a functional pathway driven by altered vestibular input and sensory reweighting. These mechanisms act in parallel and converge to promote cerebral neuroplasticity, encompassing both structural remodeling and functional



reorganization.
Source: Prepared by the authors.

To provide a comparative overview of the experimental models, exposure paradigms, and principal cerebral outcomes identified across the included studies, a structured synthesis is presented in **Table 2**.

Table 2. Comparative synthesis of cerebral neuroplasticity findings across experimental models

Model	Primary exposure	Neuroimaging modality	Key cerebral findings
Astronauts	Long-duration spaceflight	Structural MRI / fMRI / DTI	Upward brain shift; ventricular expansion; GM redistribution; vestibular network reorganization
HDBR	6° head-down tilt ± CO_2	Structural MRI / rs-fMRI	CSF redistribution; cortical displacement; altered sensorimotor connectivity
Parabolic flight	Acute gravity transitions	fMRI	Transient disruption of multisensory integration networks
Animal models	Simulated microgravity	Histology / MRI	Synaptic remodeling; altered cerebellar and vestibular pathways

Source: Prepared by the authors.

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4.2 Cerebrospinal fluid dynamics and ventricular remodeling

Structural neuroimaging studies consistently demonstrated cephalad redistribution of cerebrospinal fluid and associated ventricular expansion following exposure to microgravity. Long-duration spaceflight was associated with more pronounced ventricular enlargement and narrowing of cerebrospinal fluid spaces near the vertex, supporting a dose–response relationship. Comparable, albeit attenuated, effects were observed in head-down tilt bed rest analogs, reinforcing the mechanistic role of altered intracranial fluid dynamics.

These findings highlight the importance of interpreting volumetric changes in the context of fluid redistribution. Advanced tissue-fraction modeling indicates that some apparent gray matter volume changes may reflect morphological displacement rather than true neuronal loss or gain.

4.3 Gray matter reorganization and sensorimotor cortical plasticity

Several studies reported regionally specific gray matter changes consistent with experience-dependent neuroplasticity. Increases in gray matter volume were frequently observed in medial sensorimotor cortices, particularly regions associated with lower limb representation, whereas decreases were reported in frontal, temporal, and orbitofrontal areas. These patterns are consistent with altered motor strategies and sensory demands in a gravity-deprived environment.

4.4 White matter microstructural alterations and cerebellar involvement

Diffusion MRI investigations revealed microstructural alterations within white matter tracts, notably within cerebellar and sensorimotor pathways. Such changes are particularly relevant given the cerebellum's central role in motor coordination, error correction, and vestibular integration. Evidence of persistence beyond the immediate post-flight period suggests that some white matter adaptations may be long-lasting.

4.5 Functional connectivity and large-scale network reorganization

Functional MRI studies consistently demonstrated altered intrinsic and task-related connectivity within vestibular, visual, and motor networks. Decreased connectivity within vestibular-related cortical regions was often accompanied by increased reliance on visual and somatosensory networks, supporting sensory reweighting models. Acute parabolic flight studies further showed that even short-term

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gravitational transitions can transiently disrupt connectivity in multisensory integration hubs such as the temporo-parietal junction.

4.6 Clinical and operational implications

The cerebral adaptations identified in this review have direct implications for astronaut health, mission performance, and post-flight recovery. Structural displacement effects have been implicated in spaceflight-associated neuro-ocular syndrome, whereas functional network reorganization may underlie sensorimotor impairments observed after landing. Understanding the balance between adaptive and potentially maladaptive neuroplastic responses is therefore critical for the development of effective countermeasures in long-duration exploration missions.

5. CONCLUSION

This systematic review provides a comprehensive synthesis of PubMed-indexed evidence demonstrating that exposure to microgravity induces profound and multidimensional cerebral neuroplastic adaptations. Across human spaceflight, validated ground-based analogs, and experimental models, convergent findings indicate that microgravity affects brain structure, cerebrospinal fluid dynamics, white matter microarchitecture, and large-scale functional networks.

The reviewed literature supports an integrated mechanistic framework in which cerebral adaptations arise from the interaction between cephalad fluid shifts and experience-dependent sensory reweighting. Structural phenomena such as upward brain displacement, ventricular expansion, and redistribution of cerebrospinal fluid appear largely driven by altered intracranial pressure gradients and mechanical constraints within the cranial vault. In parallel, regionally specific gray matter changes, white matter remodeling (particularly within cerebellar and sensorimotor pathways) and functional connectivity reorganization reflect adaptive neuroplastic processes supporting sensorimotor performance in a gravity-deprived environment.

Importantly, the evidence indicates that microgravity-induced neuroplasticity encompasses both adaptive and potentially maladaptive components. While functional network reorganization may facilitate short-term behavioral adaptation, persistent structural alterations raise concerns regarding long-term neurological consequences, including their potential contribution to spaceflight-associated neuro-ocular syndrome and prolonged post-flight sensorimotor impairment. Distinguishing beneficial neuroplastic remodeling from adverse mechanical effects therefore represents a critical challenge for space neuroscience.

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From an operational and translational perspective, these findings underscore the necessity of incorporating cerebral outcomes into astronaut health monitoring, risk assessment, and countermeasure development. Interventions such as artificial gravity, lower-body negative pressure, vestibular training, and optimized habitat design should be systematically evaluated for their capacity to mitigate or modulate neuroplastic changes at both structural and functional levels.

Several limitations of the current evidence base must be acknowledged. Most studies are constrained by small sample sizes, heterogeneous imaging protocols, variable post-flight assessment intervals, and incomplete control of confounding factors such as hydration status, ambient carbon dioxide levels, and pharmacological countermeasures. Additionally, methodological variability across neuroimaging pipelines limits direct quantitative comparison between studies, precluding formal meta-analytic synthesis.

Future research should prioritize harmonized longitudinal designs, standardized neuroimaging methodologies, integration of intracranial fluid dynamics with neural measures, and extended follow-up to characterize the reversibility or persistence of cerebral adaptations. International collaboration and open data practices will be essential to advance understanding of human brain plasticity under extreme environmental conditions.

In conclusion, microgravity-induced cerebral neuroplasticity represents a complex and clinically relevant phenomenon with direct implications for long-duration human space exploration. Elucidating its mechanisms not only supports astronaut neurological health and mission safety but also provides a unique natural experiment for advancing fundamental knowledge of human brain adaptability.

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