JBSS
Journal of Biomedical & Space Sciences

LIASTRA INSTITUTE

Review

Neurocognitive and Mental Health Effects of Spaceflight, Spaceflight Analogs, and Extreme Environments

Marina Corrêa Freitas[1,*], Ana Beatriz Freitas Zagari Costa[1,2], Fabrício Corrêa Veloso[1,3], Letícia da Fonseca Paulo Andrade[1,4]
[1]International Center for Biomedical & Space Sciences (ICBS), LIASTRA Institute, Rio de Janeiro, Brazil
[2]Serra dos Órgãos University Center (UNIFESO), Rio de Janeiro, Brazil
[3]Henrique Lage State Technical School (ETEHL/FAETEC), Rio de Janeiro, Brazil
[4]Veiga de Almeida University (UVA), Rio de Janeiro, Brazil
*Correspondence: marinafreitas@liastra.com, marinacorreafreitas27@gmail.com | ORCID 0000-0003-1723-4113

DOI: 10.66234/bpt7jg08

SUMMARY

Long-duration spaceflight and terrestrial spaceflight analogs expose crews to microgravity, fluid redistribution, altered vestibular and sensorimotor inputs, isolation, confinement, circadian disruption, operational stress, and environmental monotony, potentially affecting neurocognitive performance and mental health. This PRISMA 2020-informed systematic review synthesized empirical human evidence on cognitive, psychological, sleep-related, stress-related, and behavioral outcomes in real and simulated spaceflight environments. Searches were conducted in PubMed/MEDLINE, PubMed Central, ScienceDirect, Frontiers, PLOS, NASA/ESA resources, Google Scholar/Crossref, and reference lists. Eligible studies reported neurocognitive or mental health outcomes during spaceflight, spaceflight analogs, or isolated, confined, and extreme environments. Reviews, editorials, non-human studies, and studies without relevant outcomes were excluded. Eighty-six records were identified; 21 duplicates were removed; 65 records were screened; 27 full texts were assessed; and 20 studies were included in qualitative synthesis. Meta-analysis was not performed because of heterogeneity in settings, designs, samples, instruments, and outcomes. The most consistent findings involved sleep disruption, altered alertness, mood fluctuations, stress responses, behavioral adaptation, and variable changes in vigilance, processing speed, attention, and cognitive throughput. Potential mechanisms include adaptive neuroplasticity, intracranial fluid shifts, neuroinflammatory signaling, and microglial activation. Exercise, structured routines, sleep protection, and individualized monitoring emerged as promising countermeasures. Standardized longitudinal protocols are needed for future missions.

KEYWORDS

Space Medicine; Microgravity; Neurocognition; Mental Health; Neuroplasticity; Neuroinflammation; Spaceflight Analogs; Extreme Environments.

INTRODUCTION

Human space exploration is entering a new phase characterized by longer missions, increased commercial spaceflight, renewed lunar exploration, and preparation for future Mars missions. These missions expose crews to a combined neurobiological and psychosocial stressor profile that includes microgravity, cephalad fluid redistribution, altered vestibular and proprioceptive input, sensorimotor unloading, radiation exposure, isolation, confinement, operational stress, altered circadian cues, sensory monotony, limited privacy, and delayed communication. Microgravity deserves particular attention because it directly changes the physical conditions under which the central nervous system operates, affecting intracranial fluid dynamics, sensorimotor integration, vestibular adaptation, and brain-body interaction. Therefore, long-duration missions require not only physiological resilience but also sustained neurocognitive performance, emotional stability, sleep regulation, and team functioning under conditions that challenge both neural adaptation and psychological well-being.

Behavioral health risks are among the most complex challenges in long-duration exploration missions. Unlike many physiological risks, neurobehavioral risks may emerge gradually, fluctuate by mission phase, and be shaped by group dynamics, workload, monotony, individual traits, and coping strategies. Space agencies therefore rely heavily on terrestrial analogs, including Mars-500, NASA's Human Exploration Research Analog, HI-SEAS, Antarctic overwintering stations, head-down bed rest, and controlled ecological life-support confinement studies. These environments do not reproduce all features of spaceflight, but they offer controlled or naturalistic models of isolation, confinement, restricted autonomy, environmental monotony, and mission-like stress.

The neurocognitive outcomes of interest include attention, vigilance, working memory, processing speed, executive function, emotion recognition, risk-taking, and sensorimotor-cognitive integration. Mental health outcomes include mood disturbance, depressive symptoms, anxiety, stress, emotion regulation, sleep disturbance, interpersonal tension, adaptation, and subjective well-being. Previous studies suggest that these outcomes are heterogeneous: some individuals show sleep disruption, fatigue, reduced alertness, or mood changes, while others remain stable or adapt positively over time. This heterogeneity is central to astronaut selection, countermeasure development, clinical monitoring, and mission planning.

At the biological level, these outcomes may reflect the interaction between adaptive and potentially maladaptive neural responses. Microgravity and gravitational transitions can alter vestibular input, proprioceptive feedback, sensorimotor recalibration, intracranial fluid distribution, and brain structure, requiring continuous neuroplastic adaptation. In parallel, sleep disruption, chronic stress, circadian misalignment, radiation exposure, and environmental monotony may influence neuroendocrine and neuroimmune pathways. Microglia, the resident immune cells of the central nervous system, are increasingly recognized as regulators of neuroinflammation, synaptic remodeling, and plasticity. In the context of spaceflight, microglial activation has been proposed as a plausible pathway linking environmental stressors to cognitive dysfunction, altered emotional regulation, and neural health risks. However, direct human evidence remains limited, and these mechanisms should be interpreted as an explanatory framework rather than as definitive causal conclusions.

Systematic synthesis is necessary because the literature is distributed across space medicine, psychology, neuroscience, aerospace physiology, sleep research, Antarctic medicine, and human factors. This review therefore aimed to synthesize empirical human evidence on neurocognitive and mental health effects of real spaceflight, simulated spaceflight, and isolated, confined, and extreme environments relevant to space medicine.

1.1 Objective

To systematically identify and synthesize empirical human studies evaluating neurocognitive, psychological, sleep-related, stress-related, and behavioral outcomes during spaceflight, spaceflight analog missions, or isolated, confined, and extreme environments relevant to long-duration space exploration.

1.2 Review question

In adults exposed to spaceflight, spaceflight analogs, or isolated, confined, and extreme environments, what neurocognitive and mental health outcomes have been reported, and what factors appear to influence adaptation or impairment?

METHODS

2.1 Design and reporting framework

This review was designed as a PRISMA 2020-informed systematic review. PRISMA 2020 provides updated reporting guidance, including a 27-item checklist and revised flow diagrams for systematic reviews and meta-analyses.

Because the topic includes heterogeneous human analog studies rather than randomized clinical trials, the synthesis was qualitative. No meta-analysis was planned because of substantial heterogeneity in exposure types, study designs, sample sizes, outcome measures, and follow-up schedules.

2.2 Protocol and registration

No protocol was registered before conducting this preliminary review. This should be reported as a limitation. For a journal submission, registration in OSF or PROSPERO is recommended before repeating the final search and data extraction.

2.3 Information sources

The following sources were searched:

PubMed/MEDLINE; PubMed Central; ScienceDirect/Elsevier; Frontiers; PLOS; NASA/ESA resources; Google Scholar/Crossref through web-based searching; and reference lists of eligible articles.

Institutional database export from Scopus, Web of Science, Embase, and PsycINFO was not available during this preliminary version. Therefore, this review should be considered a robust open-source systematic search, but not a final institutional-database systematic review.

2.4 Search strategy

The search was conducted up to **9 April 2026** using combinations of the following terms:

“(spaceflight OR astronaut OR "space analog" OR "space analogue" OR Mars500 OR "Mars-500" OR HERA OR "HI-SEAS" OR NEEMO OR SIRIUS OR CELSS OR Antarctic OR Concordia OR "isolated confined extreme" OR ICE) AND (isolation OR confinement OR "isolated confined" OR overwintering OR “winter-over") AND (cognition OR cognitive OR neurocognitive OR psychological OR mood OR stress OR "mental health" OR sleep OR behavioral OR behavioural OR vigilance OR "processing speed" OR "working memory")”*

Searches were adapted to each platform according to indexing and search interface limitations.

A complementary mechanistic search was also conducted to support the biological interpretation of the findings, using the terms: (microgravity OR spaceflight OR astronaut*) AND (neuroplasticity OR brain plasticity OR neuroinflammation OR microglia OR microglial activation OR intracranial fluid shift OR vestibular adaptation OR sensorimotor adaptation). These references were used only to contextualize potential biological pathways and were not counted as included empirical studies in the PRISMA flow.

2.5 Eligibility criteria

Inclusion criteria: Studies were included if they met all of the following criteria: Human adult participants; Exposure to real spaceflight, simulated spaceflight, spaceflight analogs, Antarctic overwintering, isolated confined environments, or head-down bed rest relevant to space medicine; Reported at least one neurocognitive, psychological, sleep-related, stress-related, behavioral, or mood-related outcome; Empirical original research; Published in peer-reviewed journals or traceable academic sources.

Exclusion criteria: Studies were excluded if they were: Narrative reviews, scoping reviews, opinion papers, editorials, commentaries, or protocols without outcome data; Animal, cellular, or purely mechanistic studies without human neurobehavioral outcomes; Studies focused only on physiology without cognitive, psychological, sleep, stress, or behavioral measures; COVID-19 isolation studies without direct relevance to spaceflight analogs or ICE environments; Non-English full texts when essential extraction data could not be verified.

2.6 Selection process

Records were screened by title and abstract, followed by full-text assessment. Because this is a preliminary rapid systematic review, screening was performed by one reviewer. Before journal submission, two independent reviewers should repeat screening, resolve disagreements by consensus, and calculate agreement or at least document adjudication.

2.7 Data extraction

The following data were extracted: Author and year; setting or analog environment; sample size; exposure duration; study design; neurocognitive or mental health outcomes; instruments or assessment domains; main findings; and relevance to space medicine.

2.8 Risk-of-bias and quality appraisal

Given the heterogeneous study designs, formal quality appraisal was approached descriptively. The NIH/NHLBI study quality tools and JBI critical appraisal tools are appropriate for assessing internal validity, trustworthiness, relevance, and results in observational and quasi-experimental studies.

For this preliminary synthesis, studies were categorized as having **low**, **moderate**, or **high methodological concern** based on sample size, exposure definition, longitudinal design, objective outcomes, control/comparison conditions, completeness of reporting, and reproducibility of methods.

RESULTS

This section presents the results of the study selection process and the descriptive characteristics of the studies included in the qualitative synthesis. The findings are organized in accordance with the PRISMA 2020 reporting structure, beginning with the identification, screening, eligibility, and inclusion of records. The PRISMA flow diagram summarizes how the final sample of studies was obtained, while the study characteristics table provides an overview of the included evidence according to setting, exposure, design, outcome domain, and main contribution to the review question.

3.1. PRISMA Flow and Study Selection

The study selection process is summarized in the PRISMA 2020 flow diagram (Figure 1). A total of 86 records were identified through open-index database searches, institutional and agency resources, and reference list screening. After the removal of 21 duplicate records, 65 records were screened by title and abstract. Of these, 38 records were excluded because they did not meet the eligibility criteria or were not directly related to neurocognitive, psychological, sleep-related, stress-related, or behavioral outcomes in spaceflight-relevant environments.

Twenty-seven full-text records were assessed for eligibility. Seven full-text articles were excluded for the following reasons: review, commentary, or conceptual design without original outcome data; absence of direct neurocognitive or mental health outcomes; protocol or incomplete outcome reporting; or population/environment outside the scope of the review. Therefore, 20 empirical studies were included in the final qualitative synthesis. No meta-analysis was performed because the included studies presented substantial heterogeneity in exposure settings, sample size, mission duration, assessment instruments, and reported outcomes.

3.2. Characteristics of Included Studies

The characteristics of the 20 studies included in the qualitative synthesis are summarized in Table 1. The included studies were published between 2000 and 2024 and covered a wide range of spaceflight-related and terrestrial analog environments, including real spaceflight missions, the International Space Station, Mars-500, NASA's Human Exploration Research Analog, HI-SEAS, the Controlled Ecological Life Support System experiment, Antarctic overwintering stations, short-term isolation protocols, and head-down bed rest models.

The studies varied substantially in design, sample size, duration of exposure, and outcome assessment. Most investigations used observational, longitudinal, before–after, or analog mission designs. The main outcome domains included sleep and circadian rhythms, vigilance, cognitive per-

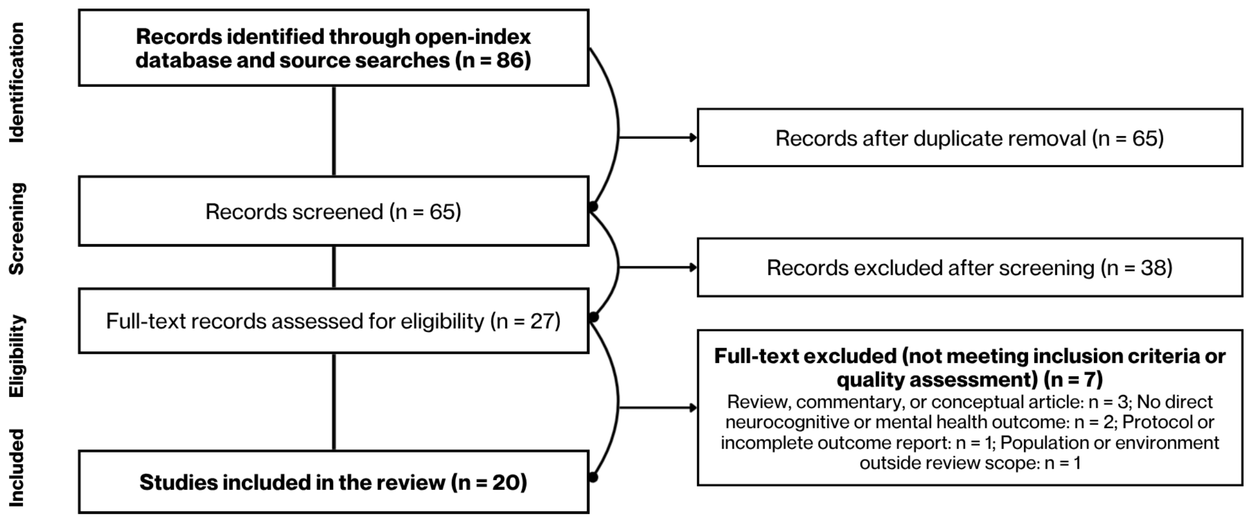

Figure 1. PRISMA 2020 flow diagram of study identification, screening, eligibility assessment, and inclusion.
PRISMA 2020 flow diagram showing the identification, screening, eligibility assessment, and inclusion of studies in the qualitative synthesis. A total of 86 records were identified, 21 duplicates were removed, 65 records were screened, 27 full-text articles were assessed for eligibility, and 20 empirical studies were included in the final qualitative synthesis. No meta-analysis was performed because of methodological and clinical heterogeneity across studies.

formance, mood, stress biomarkers, behavioral adaptation, psychosocial functioning, and the potential role of countermeasures such as exercise and structured routines. Although the studies differed methodologically, they collectively provided relevant evidence for understanding how isolation, confinement, operational stress, and extreme environments may influence neurocognitive and mental health outcomes.

Table 1 provides a structured overview of each included study, including author and year, study setting, exposure context, outcome domain, and main contribution to the synthesis. This table was used to support the qualitative comparison of findings across different analog platforms and real spaceflight conditions.

The qualitative synthesis included 20 empirical studies. Additional references were used only to support methodological reporting and mechanistic interpretation and were not counted as included studies in the PRISMA flow.

3.3 Methodological Quality of Included Studies

Overall, the included studies presented moderate methodological concern, mainly because of small sample sizes, heterogeneous exposure conditions, limited control groups, and variability in cognitive, psychological, sleep-related, and biomarker assessment tools. Longitudinal analog studies and real spaceflight investigations provided valuable ecological relevance, but most findings should be interpreted cautiously because participants were highly selected and mission conditions differed substantially across studies. No study was excluded solely on the basis of methodological quality, but these limitations were considered in the qualitative interpretation of the evidence.

3.4 Synthesis by outcome domain

3.4.1 Sleep, circadian rhythm, and alertness

Sleep disruption was one of the most consistent domains across spaceflight and analog studies. In the Mars-500 simulation, Basner et al. reported protracted crew hypokinesis and altered sleep duration and timing during a 520-day simulated mission.

In actual astronauts, Barger et al. found that sleep deficiency was prevalent before, during, and after shuttle and ISS missions, indicating that sleep risk begins before launch and persists during mission operations.

In HERA, Nasrini et al. found that short-duration confinement alone did not produce a strong cognitive decline across all domains, but total sleep deprivation significantly impaired psychomotor vigilance and cognitive throughput.

Overall, sleep appears to be a key pathway linking isolation, workload, circadian disruption, and cognitive efficiency. Sleep disruption is clinically important because it may compromise attention, decision-making, psychomotor vigilance, mood regulation, and emergency performance.

3.4.2 Cognitive performance

Table 1. Characteristics of the studies included in the qualitative synthesis.

Study	Setting	Sample/Exposure	Main outcome domain	Main contribution
Basner et al., 2013	Mars-500	520-day simulated Mars mission	Sleep, activity, alertness	Demonstrated hypokinesis and altered sleep timing/duration during long confinement.
Basner et al., 2014	Mars-500	6 male crew members, 520 days	Psychological and behavioral adaptation	Showed behavioral health risks and strong individual variability during prolonged confinement.
Wang et al., 2014	Mars-500	520-day confinement	Mood, affective stimuli, hormones	Found stage-related mood and endocrine changes during confinement.
Schneider et al., 2010	Long-term confinement	Simulated confinement	Mood, electrocortical activity, exercise	Suggested exercise as countermeasure to psychophysiological deconditioning.
Schneider et al., 2013	Mars-500	Simulated Mars mission	Prefrontal cortex and cognition	Evaluated exercise effects on prefrontal activity and cognitive performance.
Tafforin, 2013	Mars-500	Crew ethology	Behavior and adaptation	Found time, cultural, and individual effects on crew behavior.
Tafforin, 2015	Mars analog environments	Confinement vs isolation	Ethology and social behavior	Compared behavioral manifestations of confinement and isolation.
Abeln et al., 2015	Antarctic Concordia	8-month isolation	EEG, mood, cognition, exercise	Supported voluntary exercise as a mental well-being countermeasure.
Connaboy et al., 2020	Antarctic ICE	Prolonged ICE exposure	Cognitive performance	Examined cognition across prolonged isolated, confined, and extreme exposure.
Alfano et al., 2021	Antarctica	Coastal and inland stations	Mental health, symptoms, stress biomarkers	Tracked mental health and stress during Antarctic exposure.
Klein et al., 2023	Short-term isolation	30–45 days	Brain, sleep, affect, cognition	Examined exercise dose during isolation.
Palinkas et al., 2000	Antarctica	Winter-over crews	Mood and behavior	Reported seasonal changes in mood and behavior during Antarctic winter.
Palinkas et al., 2001	Antarctica	McMurdo winter-over	Thyroid function and mood	Linked seasonal endocrine changes with mood.
Zimmer et al., 2013	Antarctica	Antarctic stay	Psychological changes	Reported psychological changes associated with Antarctic residence.
Nasrini et al., 2020	NASA HERA	2-week analog missions plus sleep restriction	Cognitive performance	Found sleep deprivation impaired vigilance/ cognitive throughput more clearly than short confinement alone.
Dunn Rosenberg et al., 2022	HI-SEAS	Three 8–12 month missions	Stress and psychosocial adaptation	Proposed phased stress model for Mars-like isolation and confinement.
Yuan et al., 2019	CELSS	180-day closed ecological system	Physiological and psychological adaptation	Studied multisystem adaptation during long confinement.
Dev et al., 2024	ISS	6-month low Earth orbit missions	Cognition across 10 domains	Found no systematic global cognitive decline in professional astronauts.
Tays et al., 2022	Head-down bed rest and artificial gravity	60-day analog	Cognitive and sensorimotor performance	Artificial gravity did not broadly mitigate cognitive/ sensorimotor changes but affected some task performance.
Barger et al., 2014	Space shuttle and ISS	Astronaut sleep observations	Sleep deficiency and hypnotic use	Found sleep deficiency common before, during, and after spaceflight.

Table 1. Characteristics of the studies included in the qualitative synthesis.
Characteristics of the 20 studies included in the qualitative synthesis. The table summarizes the author and year of publication, study setting, exposure context, main neurocognitive or mental health outcome domain, and principal contribution of each study to the review. Included studies covered real spaceflight, simulated Mars missions, spaceflight analogs, Antarctic overwintering, controlled ecological life-support confinement, and isolated, confined, and extreme environments.

Cognitive outcomes were heterogeneous. Short analog confinement did not consistently impair all domains, while sleep deprivation and mission phase were more clearly associated with deficits. Nasrini et al. showed that sleep deprivation reduced psychomotor vigilance and cognitive throughput in HERA participants, even when confinement effects were less pronounced.

In professional astronauts, Dev et al. assessed cognitive performance across 10 domains during 6-month ISS missions and reported no evidence of systematic global cognitive decline, although specific domains such as processing speed, working memory, sustained attention, and risk-taking showed phase-specific variation.

In Antarctic and ICE settings, cognitive performance also showed mixed results. Some studies reported stable or improved performance in selected domains, suggesting adaptation, practice effects, or strong preselection of resilient participants.

The available evidence therefore does not support a simple model of universal cognitive deterioration. Instead, the most plausible interpretation is that cognitive vulnerability depends on domain, sleep state, mission phase, workload, individual resilience, and environmental stress load.

3.4.3 Mood, affect, and psychological adaptation

Mood and psychological adaptation varied across individuals and mission phases. In Mars-500, Basner et al. reported behavioral and psychological reactions during 520 days of confinement in a multinational crew, emphasizing that behavioral health risks are serious challenges for long-duration exploration.

Wang et al. found that 520 days of Mars-500 confinement affected affective stimulus assessment, mood stage, and plasma hormone levels, suggesting interaction between affective processing and endocrine adaptation.

In Antarctica, Palinkas et al. reported seasonal changes in mood and behavior during winter-over periods, including changes in tension, depression, anger, confusion, fatigue, and vigor.

Alfano et al. examined mental health, physical symptoms, and stress biomarkers in Antarctic stations, supporting the use of Antarctica as an Earth-based analog for long-duration spaceflight stressors.

Together, these findings suggest that mood outcomes are not static. They fluctuate across exposure phase and may include both negative symptoms and adaptive responses. This supports the need for longitudinal monitoring rather than one-time screening.

3.4.4 Stress biomarkers and endocrine responses

Several studies linked psychological outcomes with physiological stress markers. Wang et al. reported mood and plasma hormone changes during Mars-500 confinement.

Palinkas et al. evaluated hypothalamic–pituitary–thyroid function and mood during extended Antarctic residence, suggesting that seasonal endocrine changes may interact with mood in polar environments.

Alfano et al. integrated mental health, physical symptoms, and biomarkers of stress during Antarctic exposure, strengthening the view that neurobehavioral adaptation should be assessed as a psychophysiological process rather than solely through questionnaires.

These findings are clinically relevant because biomarkers may help identify individuals at increased risk before subjective symptoms become severe or operationally relevant.

3.4.5 Behavioral adaptation and crew dynamics

Behavioral adaptation was most directly assessed in ethological studies. Tafforin found that Mars-500 crew behavior varied by time, culture, and individual differences, suggesting that adaptation during confinement is dynamic and socially patterned.

The comparison between confinement and isolation indicated that confinement may generate stress manifestations, whereas isolation may enhance certain social relationships, depending on context and group structure.

HI-SEAS data also suggested phased psychosocial stress responses across long Mars-like analog missions, including initial eustress, deprivation, disruption of team dynamics, and asynchronous coping.

These findings support the importance of team composition, leadership, communication, autonomy, privacy, structured routines, and psychosocial monitoring during exploration-class missions.

3.4.6 Exercise and countermeasures

Exercise appeared repeatedly as a promising countermeasure. Schneider et al. concluded that confinement is accompanied by psychophysiological changes and that exercise may counteract psychophysiological deconditioning.

During Mars-500, Schneider et al. examined the influence of exercise on prefrontal cortex activity and cognitive performance, indicating that exercise may influence neurocognitive functioning under confinement.

At Antarctic Concordia, Abeln et al. reported that voluntary regular exercise supported subjective mental well-being during long-term isolation. Klein et al. also examined isolation, sleep, affect, neurobehavioral function, and exercise dose, reinforcing the relevance of exercise as a behavioral and neurophysiological countermeasure.

Exercise may therefore operate through several mechanisms: maintaining routine, improving sleep, reducing stress, supporting mood regulation, preserving cortical function, and improving perceived autonomy.

Although the included empirical studies primarily assessed behavioral, psychological, cognitive, sleep-related, and stress-related outcomes, the observed patterns also support the need for mechanistic interpretation. In particular, future work should examine whether microgravity-related brain adaptation, neuroplastic remodeling, neuroinflammatory signaling, and microglial activation help explain individual differences in cognitive efficiency, mood regulation, and resilience during long-duration missions.

DISCUSSION

4.1 Principal findings

This systematic review found that spaceflight, spaceflight analogs, and ICE environments are associated with variable neurocognitive and mental health outcomes. The strongest and most consistent evidence concerns sleep disruption, altered alertness, mood fluctuation, stress responses, behavioral adaptation, and domain-specific cognitive changes.

However, the evidence does not support a universal or linear decline in cognition or mental health. Some participants remain stable, some improve in selected tasks, and others show vulnerability in specific domains. This heterogeneity is especially important for astronaut selection, clinical monitoring, and mission design.

4.2 Interpretation of cognitive findings

The cognitive evidence suggests that astronauts and analog participants can maintain overall function under prolonged exposure, especially when they are highly selected, trained, and supported. However, specific domains such as processing speed, vigilance, sustained attention, working memory, and cognitive throughput appear more vulnerable to sleep loss, stress, monotony, or mission phase.

This is clinically meaningful because small declines in speed, vigilance, or decision-making may have disproportionate consequences in high-risk operational environments. A mission does not require global cognitive collapse to become unsafe; subtle performance slowing may matter during emergency procedures, medical decision-making, docking operations, extravehicular activities, or conflict management.

4.3 Biological mechanisms: microgravity, neuroinflammation, microglia, and neuroplasticity

The neurocognitive and emotional findings identified in this review should be interpreted not only as behavioral responses to isolation and confinement, but also as possible manifestations of underlying biological adaptation to the spaceflight environment. Microgravity is a central factor in this process. By reducing gravitational loading, altering vestibular and proprioceptive input, and promoting cephalad fluid redistribution, microgravity may affect intracranial fluid dynamics, sensorimotor recalibration, and structural or functional brain organization. These changes may contribute to alterations in vigilance, processing speed, sensorimotor performance, and executive control, particularly during mission phases requiring rapid adaptation to altered gravitational contexts.

Neuroplasticity provides one of the most important frameworks for interpreting these findings. Some changes observed during spaceflight and analog exposure may represent adaptive plasticity, allowing the nervous system to recalibrate motor control, spatial orientation, attention, and behavioral responses to novel environmental demands. However, adaptive plasticity may coexist with transient dysfunction, especially when microgravity is combined with sleep disruption, stress, circadian misalignment, high workload, and social confinement. This dual pattern may help explain why some participants maintain or improve performance in selected domains, whereas others show fatigue, mood instability, reduced alertness, or slower cognitive throughput.

Neuroinflammatory mechanisms may also be relevant. Chronic stress, disrupted sleep, radiation exposure, and altered immune regulation may influence neuroimmune signaling. Microglia, as resident immune cells of the central nervous system, regulate synaptic remodeling, cytokine signaling, and responses to neural injury or stress. In spaceflight and microgravity research, microglial activation has been proposed as a potential mechanism contributing to neuroinflammation, synaptic plasticity disruption, and cognitive vulnerability. Although most direct evidence remains preclinical or mechanistic, this pathway is important because it links environmental stressors to neural circuit efficiency, emotional regulation, and long-term brain health.

Therefore, future neurobehavioral space medicine studies should integrate cognitive testing with biological markers, including neuroimaging, inflammatory biomarkers, endocrine measures, sleep metrics, and, where feasible, neuroimmune indicators. Such integration would help distinguish adaptive neuroplastic remodeling from maladaptive neuroinflammatory responses and would strengthen causal interpretation of neurocognitive and mental health outcomes during long-duration missions.

4.4 Sleep as a central mechanism

Sleep may be the most actionable clinical target identified in this review. Evidence from astronauts, Mars-500, and HERA suggests that sleep timing, sleep duration, and sleep deprivation affect alertness and cognitive throughput. Sleep monitoring should therefore be integrated with cognitive testing, mood assessment, light exposure control, workload planning, and countermeasure scheduling.

Future missions should treat sleep as a mission-critical health variable rather than only a wellness issue.

4.5 Mental health and behavioral adaptation

Mood and stress responses appear to fluctuate across phases. Early mission periods may involve novelty and eustress, mid-mission periods may involve monotony and deprivation, and later periods may involve fatigue, interpersonal strain, or asynchronous coping. This pattern suggests that psychosocial countermeasures should be phase-specific rather than uniform across a mission.

Psychological monitoring should include self-report, observer-based ratings, behavioral indicators, sleep data, and biomarkers when feasible.

4.6 Exercise as a countermeasure

Exercise appears to be one of the most promising countermeasures because it targets physical, psychological, and neurophysiological domains simultaneously. Evidence from confinement and Antarctic studies suggests beneficial effects on mood, electrocortical activity, subjective well-being, and possibly cognitive performance.

However, the optimal exercise type, intensity, timing, and frequency for neurobehavioral protection remain unclear. Future studies should compare endurance, resistance, combined, and short-bout exercise protocols using standardized cognitive and mood outcomes.

4.7 Clinical and translational relevance

The findings have relevance beyond astronaut health. Spaceflight analog research can inform terrestrial medicine in populations exposed to isolation, confinement, sensory monotony, circadian disruption, or extreme stress, including submarine crews, polar workers, military teams, offshore workers, intensive care patients, long-term care residents, and people experiencing prolonged social isolation.

The translational value is especially strong for sleep medicine, occupational health, neurology, psychiatry, public health, and rehabilitation.

4.8 Strengths

This review integrates evidence across real spaceflight, simulated Mars missions, HERA, HI-SEAS, CELSS, Antarctic overwintering, head-down bed rest, and other ICE settings. It focuses specifically on empirical human data and emphasizes clinically relevant neurobehavioral outcomes.

4.9 Limitations

This review has several limitations. First, the search was conducted through open-access and open-index sources, without direct institutional export from Scopus, Web of Science, Embase, or PsycINFO. Second, screening and extraction were conducted by a single reviewer in this preliminary version. Third, the included studies had small sample sizes, heterogeneous designs, and different assessment tools. Fourth, many studies involved highly selected participants, limiting generalizability. Fifth, no meta-analysis was possible because of heterogeneity in exposures and outcomes.

4.10 Recommendations for future research

Future research should use standardized neurocognitive batteries across missions and analogs; combine cognitive, mood, sleep, behavioral, neuroimaging, endocrine, and biomarker data; and report individual trajectories rather than only group-level averages. Particular attention should be given to mechanisms related to microgravity-induced brain adaptation, intracranial fluid redistribution, neuroplasticity, neuroinflammatory signaling, and microglial activation. Studies should include longer follow-up before, during, and after exposure to determine whether observed changes are transient, adaptive, persistent, or clinically relevant.

Future investigations should also compare multimodal countermeasures, including exercise, sleep protection, circadian lighting, nutrition, psychological support, cognitive training, workload management, and digital health monitoring. Improving sample diversity, reporting sex- and gender-related effects, preregistering protocols, and sharing anonymized datasets when feasible will be essential to improve reproducibility and strengthen causal inference.

CONCLUSION

This PRISMA 2020-informed systematic review indicates that spaceflight, spaceflight analogs, and isolated, confined, and extreme environments are associated with measurable but heterogeneous neurocognitive and mental health effects. The evidence does not support a simple model of generalized cognitive decline or uniform psychological deterioration. Instead, the reviewed studies suggest a more complex pattern in which neurobehavioral outcomes vary according to mission phase, sleep status, workload, environmental monotony, group dynamics, individual resilience, and the availability of structured countermeasures.

Across the included studies, the most consistent effects were observed in sleep regulation, alertness, mood stability, stress response, behavioral adaptation, and selected domains of cognitive efficiency, particularly vigilance, processing speed, sustained attention, and cognitive throughput. These domains are clinically and operationally relevant because even subtle impairments may compromise decision-making, interpersonal functioning, emergency response, and mission safety during long-duration exploration missions. Sleep disruption emerged as a central and potentially modifiable mechanism linking environmental stressors to cognitive and emotional outcomes. Therefore, sleep monitoring and circadian protection should be considered core components of neurobehavioral risk management in future missions.

The findings also highlight the importance of individual variability. Some participants and astronauts maintained stable performance or adapted positively, whereas others showed vulnerability to fatigue, mood changes, stress, or reduced alertness. This variability reinforces the need for individualized monitoring strategies rather than reliance solely on group averages. Longitudinal assessment before, during, and after exposure is essential to identify early signs of maladaptation and to distinguish transient adjustment responses from clinically meaningful impairment.

These findings also suggest that neurobehavioral outcomes in spaceflight should be interpreted through a biological systems perspective. Microgravity, altered vestibular and sensorimotor input, intracranial fluid shifts, disrupted sleep, stress physiology, and neuroimmune signaling may interact to shape cognitive and emotional adaptation. Neuroplasticity may support functional compensation and adaptation to novel gravitational conditions, whereas persistent stress exposure and possible neuroinflammatory signaling may increase vulnerability in selected individuals. This interaction between adaptive plasticity and biological stress responses may explain why neurocognitive and mental health effects are heterogeneous rather than uniform across astronauts and analog participants.

Exercise and structured routines appear to be promising countermeasures, with potential benefits for mood, cortical activity, subjective well-being, and cognitive performance. However, the optimal type, frequency, intensity, and timing of exercise for neurobehavioral protection remain insufficiently defined. Future research should integrate exercise protocols with sleep, light exposure, psychological support, nutrition, workload management, and digital health monitoring to develop multimodal countermeasure packages.

From a translational perspective, this evidence is relevant not only to astronaut health but also to terrestrial clinical and occupational populations exposed to isolation, confinement, circadian disruption, sensory monotony, or prolonged stress. Findings from space medicine and analog environments may inform care strategies for polar expeditioners, submarine crews, military teams, offshore workers, patients in prolonged hospitalization, older adults in institutional settings, and individuals experiencing extended social isolation.

Nevertheless, the current evidence base remains limited by small samples, heterogeneous methods, variable outcome instruments, limited control groups, and incomplete standardization across studies. Future investigations should use harmonized neurocognitive batteries, validated mental health scales, objective sleep measures, biomarkers of stress, and transparent longitudinal protocols. Larger multinational datasets, preregistered protocols, and open science practices will be essential to strengthen causal inference and improve comparability across missions and analog platforms.

Because microglial activation and neuroinflammatory signaling were not directly assessed in most included human studies, these mechanisms should be considered biologically plausible explanatory pathways rather than primary outcomes of the present synthesis.

In conclusion, neurocognitive and mental health protection should be treated as a mission-critical priority in long-duration space exploration. The available evidence suggests that the main risks are not limited to severe psychiatric events or global cognitive decline, but include subtle, cumulative, and context-dependent changes in sleep, alertness, mood, stress regulation, and cognitive efficiency. Advancing this field will require integrated clinical, neuroscientific, behavioral, and operational approaches capable of supporting both astronaut performance in space and human health in extreme environments on Earth.

ACKNOWLEDGMENTS

The authors have no acknowledgments to declare.

DECLARATION OF INTERESTS

The authors declare that there are no conflicts of interest.

FUNDING STATEMENT

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

DECLARATION OF GENERATIVE AI USE

Generative AI was used to support language organization and manuscript structuring. All scientific claims, references, and interpretations were reviewed and verified by the authors, who retain full responsibility for the accuracy and integrity of the work.

REFERENCES

1. Abeln, V., MacDonald-Nethercott, E., Piacentini, M. F., Meeusen, R., Kleinert, J., Strüder, H. K., & Schneider, S. (2015). Exercise in isolation: A countermeasure for electrocortical, mental and cognitive impairments. *PLOS ONE, 10*(5), Article e0126356. https://doi.org/10.1371/journal.pone.0126356
2. Alfano, C. A., Bower, J. L., Connaboy, C., Agha, N. H., Baker, F. L., Smith, K. A., So, C. J., & Simpson, R. J. (2021). Mental health, physical symptoms and biomarkers of stress during prolonged exposure to Antarctica's extreme environment. *Acta Astronautica, 181*, 405–413. https://doi.org/10.1016/j.actaastro.2021.01.051
3. Barger, L. K., Flynn-Evans, E. E., Kubey, A., Walsh, L., Ronda, J. M., Wang, W., Wright, K. P., Jr., & Czeisler, C. A. (2014). Prevalence of sleep deficiency and use of hypnotic drugs in astronauts before, during, and after spaceflight: An observational study. *The Lancet Neurology, 13*(9), 904–912. https://doi.org/10.1016/S1474-4422(14)70122-X
4. Basner, M., Dinges, D. F., Mollicone, D., Ecker, A., Jones, C. W., Hyder, E. C., Di Antonio, A., Savelev, I., Kan, K., Goel, N., Morukov, B. V., & Sutton, J. P. (2013). Mars 520-d mission simulation reveals protracted crew hypokinesis and alterations of sleep duration and timing. *Proceedings of the National Academy of Sciences, 110*(7), 2635–2640. https://doi.org/10.1073/pnas.1212646110
5. Basner, M., Dinges, D. F., Mollicone, D. J., Savelev, I., Ecker, A. J., Di Antonio, A., Jones, C. W., Hyder, E. C., Kan, K., Goel, N., Morukov, B. V., & Sutton, J. P. (2014). Psychological and behavioral changes during confinement in a 520-day simulated interplanetary mission to Mars. *PLOS ONE, 9(*3), Article e93298. https://doi.org/10.1371/journal.pone.0093298
6. Connaboy, C., Sinnott, A. M., LaGoy, A. D., Krajewski, K. T., Johnson, C. D., Pepping, G.-J., Simpson, R. J., Bower, J. L., & Alfano, C. A. (2020). Cognitive performance during prolonged periods in isolated, confined, and extreme environments. *Acta Astronautica, 177,* 545–551. https://doi.org/10.1016/j.actaastro.2020.08.018
7. Dev, S. I., Khader, A. M., Begerowski, S. R., Anderson, S. R., Clément, G., & Bell, S. T. (2024). Cognitive performance in ISS

astronauts on 6-month low Earth orbit missions. *Frontiers in Physiology, 15*, Article 1451269. https://doi.org/10.3389/fphys.2024.1451269

8. Dunn Rosenberg, J., Jannasch, A., Binsted, K., & Landry, S. J. (2022). Biobehavioral and psychosocial stress changes during three 8–12 month spaceflight analog missions with Mars-like conditions of isolation and confinement. *Frontiers in Physiology, 13,* Article 898841. https://doi.org/10.3389/fphys.2022.898841

9. Hupfeld, K. E., McGregor, H. R., Reuter-Lorenz, P. A., & Seidler, R. D. (2021). Microgravity effects on the human brain and behavior: Dysfunction and adaptive plasticity. *Neuroscience & Biobehavioral Reviews, 122*, 176–189. https://doi.org/10.1016/j.neubiorev.2020.11.017

10. Klein, T., Braunsmann, L., Koschate, J., Hoffmann, U., Foitschik, T., Krieger, S., Crucian, B., Schneider, S., & Abeln, V. (2023). Short-term isolation effects on the brain, cognitive performance, and sleep: The role of exercise. *Frontiers in Physiology, 14,* Article 903072. https://doi.org/10.3389/fphys.2023.903072

11. Li, Z., Wu, J., Zhao, T., Wei, Y., Xu, Y., Liu, Z., Li, X., & Chen, X. (2024). Microglial activation in spaceflight and microgravity: Potential risk of cognitive dysfunction and poor neural health. *Frontiers in Cellular Neuroscience, 18*, Article 1296205. https://doi.org/10.3389/fncel.2024.1296205

12. McGregor, H. R., Hupfeld, K. E., Pasternak, O., Beltran, N. E., De Dios, Y. E., Bloomberg, J. J., Wood, S. J., Mulavara, A. P., Riascos, R. F., Reuter-Lorenz, P. A., & Seidler, R. D. (2023). Impacts of spaceflight experience on human brain structure. *Scientific Reports, 13*, Article 7878. https://doi.org/10.1038/s41598-023-33331-8

13. Nasrini, J., Hermosillo, E., Dinges, D. F., Moore, T. M., Gur, R. C., & Basner, M. (2020). Cognitive performance during confinement and sleep restriction in NASA's Human Exploration Research Analog (HERA). *Frontiers in Physiology, 11*, Article 394. https://doi.org/10.3389/fphys.2020.00394

14. Palinkas, L. A., & Houseal, M. (2000). Stages of change in mood and behavior during a winter in Antarctica. *Environment and Behavior, 32*(1), 128–141. https://doi.org/10.1177/00139160021972469

15. Palinkas, L. A., Reed, H. L., Reedy, K. R., Do, N. V., Case, H. S., & Finney, N. S. (2001). Circannual pattern of hypothalamic–pituitary–thyroid function and mood during extended Antarctic residence. *Psychoneuroendocrinology, 26*(4), 421–431. https://doi.org/10.1016/S0306-4530(00)00064-0

16. Schneider, S., Brümmer, V., Carnahan, H., Kleinert, J., Piacentini, M. F., Meeusen, R., & Strüder, H. K. (2010). Exercise as a countermeasure to psycho-physiological deconditioning during long-term confinement. *Behavioural Brain Research, 211*(2), 208–214. https://doi.org/10.1016/j.bbr.2010.03.034

17. Schneider, S., Abeln, V., Popova, J., Fomina, E., Jacubowski, A., Meeusen, R., & Strüder, H. K. (2013). The influence of exercise on prefrontal cortex activity and cognitive performance during a simulated space flight to Mars (MARS500). *Behavioural Brain Research, 236*(1), 1–7. https://doi.org/10.1016/j.bbr.2012.08.022

18. Tafforin, C. (2013). Time effects, cultural influences, and individual differences in crew behavior during the Mars-500 experiment. *Aviation, Space, and Environmental Medicine, 84*(10), 1082–1086. https://doi.org/10.3357/ASEM.3692.2013

19. Tafforin, C. (2015). Confinement vs. isolation as analogue environments for Mars missions from a human ethology viewpoint. *Aerospace Medicine and Human Performance, 86*(2), 131–135. https://doi.org/10.3357/AMHP.4089.2015

20. Tays, G. D., McGregor, H. R., Lee, J. K., Beltran, N., Kofman, I. S., De Dios, Y. E., Bloomberg, J. J., Mulavara, A. P., & Seidler, R. D. (2022). The effects of 30 minutes of artificial gravity on cognitive and sensorimotor performance in a spaceflight analog environment. *Frontiers in Neural Circuits, 16*, Article 784280. https://doi.org/10.3389/fncir.2022.784280

21. Wang, Y., Jing, X., Lv, K., Wu, B., Bai, Y., Luo, Y., Chen, S., & Li, Y. (2014). During the long way to Mars: Effects of 520 days of confinement (Mars500) on the assessment of affective stimuli and stage alteration in mood and plasma hormone levels. *PLOS ONE, 9*(4), Article e87087. https://doi.org/10.1371/journal.pone.0087087

22. Yuan, M., Custaud, M.-A., Xu, Z., Wang, J., Yuan, M., Tafforin, C., Treffel, L., Arbeille, P., Nicolas, M., Gharib, C., Gauquelin-Koch, G., Arnaud, L., Lloret, J.-C., Li, Y., & Navasiolava, N. (2019). Multi-system adaptation to confinement during the 180-day Controlled Ecological Life Support System (CELSS) experiment. *Frontiers in Physiology, 10*, Article 575. https://doi.org/10.3389/fphys.2019.00575

23. Zimmer, M., Cabral, J. C. C. R., Borges, F. C., Côco, K. G., & Hameister, B. R. (2013). Psychological changes arising from an Antarctic stay: Systematic overview. *Estudos de Psicologia (Campinas), 30*(3), 415–423. https://doi.org/10.1590/S0103-166X2013000300011