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Current approaches to mitigate the effect of microgravity on astronauts' nutrition, physical activity and sleep: a narrative review

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ABSTRACT

Introduction: The microgravity exerts enormous changes andimpact on human physiology, specifically on astronauts, such as their food habits, physical activity and awake-sleep cycle. Prolonged exposure to microgravity environments induces a series of adaptations and physiological changes that directly affect body composition, nutrient absorption, and sleep homeostasis. While essential for survival during spacial missions, these changes present significant challenges to the health and well-being of crew members, speciallay in long term missions.
Objectives: To analyze the main effects of microgravity on astronauts regarding their food habits, physical activity, and sleep,and review the contemporary strategies to address them.
Methodology: Scientific articles were searched in PubMed, Web of Science and ScieloPortugal, using the following keywords: "astronaut", "microgravity","food intake", "nutrition", "physical activity", "sleep", combined with the Boolean operators AND or OR.Fifty threescientific publications were selected and analysed.
Results: Literature studies showed that during long-duration spaceflights, astronauts typically consume less energy than needed and presentlow energy availability, which can negatively affect their health with consequences upon body composition, including muscle and bone mass losses. In addition, sleep is also disrupted leading to physical and mental fatigue.
Conclusion: Improved nutritional strategies and sleep hygiene are needed to ensure maintainance of an adequate energy availability during prolonged space missions.

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INFORMAÇÃO DO ARTIGO

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RESUMO

Introdução: A microgravidade exerce enormes alterações e impactos na fisiologia humana, especificamente nos astronautas, nomeadamente nos seus hábitos alimentares, atividade física e ciclo vigília-sono. A exposição prolongada a ambientes de microgravidade induz uma série de adaptações e alterações fisiológicas que afetam diretamente a composição corporal, a absorção de nutrientes e a homeostasia do sono. Embora essenciais para a sobrevivência durante as missões espaciais, estas alterações apresentam desafios significativos para a saúde e o bem-estar dos tripulantes, especialmente em missões de longa duração.
Objetivos: Analisar os principais efeitos da microgravidade nos astronautas em relação aos seus hábitos alimentares, actividade física e sono, e rever as estratégias contemporâneas para os abordar.
Metodologia: Para conduzir esta revisão narrativa, foram pesquisados artigos científicos no PubMed, Web of Science e no ScieloPortugal, utilizando as seguintes palavras-chave: “astronauta”, “microgravidade”, “ingestão alimentar”, “nutrição”, “atividade física”, “sono”, combinadas com os operadores booleanos AND ou OR. Foram selecionadas e analisadas 53 publicações científicas.
Resultados: Os estudos encontrados demonstraram que, durante voos espaciais de longa duração, os astronautas consomem normalmente menos energia do que o necessário e apresentam uma baixa disponibilidade energética, o que pode afetar negativamente a sua saúde, com consequências na composição corporal, incluindo perdas de massa muscular e óssea. Além disso, o sono também é interrompido, levando à fadiga física e mental.
Conclusão: São necessárias estratégias nutricionais e de higiene do sono melhoradas para garantir a manutenção de uma disponibilidade energética adequada durante missões espaciais prolongadas.

Introduction

In recent years, space exploration has been driven by private andinternational initiatives. In 2012, SpaceX successfully docked its Dragon capsule with theInternational Space Station (ISS), and in 2015, NASA's New Horizons mission flew by Pluto, providing unprecedented data about the dwarf planet.[1]

Space exploration has been evolving rapidly, raising important questions abouthuman physiological adaptation to extreme environments.[2]

Microgravity (gravitational forces less than 1×10^{-3}g) one of the main environmental challenges faced during space missions, with significant impactson the health and performance of astronauts.[3] Given the increasing duration of missions, understanding the physiological changes induced by microgravity is essential fordeveloping nutritional strategies that ensure the maintenance of homeostasis and the well-being of crew members during extended missions.[2] In fact, adequate nutrition plays an important role in the “emotional health” of the crew members isolated for long periods. Astronauts often express the natural desirefor familiar, Earth-like foods that provide comfort and a connection to home, so this psychological benefit goes beyond nutrition, facilitating social bonding and maintaining emotional connections.[1]

This study aims to provide an overview of the effect that weightlessness has on astronauts' eating, sleeping, and physical activity habits through a narrative review of the scientific literature.

Methodology

To conduct this narrative review, we followed a structured process, including defining inclusion and exclusion criteria, formulating the search strategy and selecting studies.

The search for published scientific publicationswas conducted across two electronic databases, namely PubMed, Web of Science (WoS) and ScieloPortugal.

The search strategy combined the following keywords: “astronaut”, “microgravity”, “food intake”, “nutrition”, “physical activity”, “sleep”, with the Boolean operators AND or OR.

The inclusion criteria were: publications written in English, Spanish, or Portuguese, published 10 years apart (01 January 2015 to 31 May 2025), involving only human beings with ages between 19 and 65. The exclusion criteria were: studies that did not address the topic and studies without full text available. When relevant for the study scope also manual search was used, and scientific publications before the afore mentioned date were included.

Ethical considerations

Given that this literature review is based exclusively on pre-viously published data, ethical approval was not re-quired. Nevertheless, the study strictly adhered to princi-ples of transparency, scientific integrity, and reproducibil-ity.

Results

The search conducted on 12 June 2025 yielded a total of 116 scientific articles (37 identified in PubMed/25 identified in WoS, 10 in Scielo Portugal, and 44 from manual search), from which, 20 were excluded (31 duplicated, 6 based on title and abstract, and 25 after full-text reading), as shown in Figure 1. Consequently 54 articles were selected for data analysis.

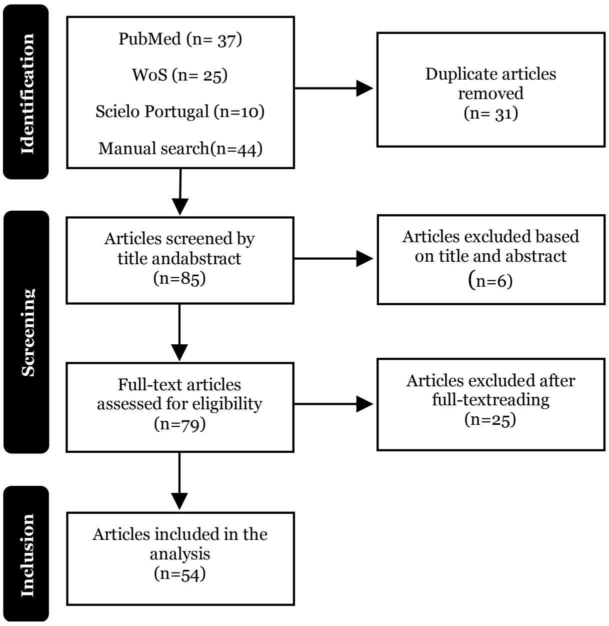

Figure 1. Flowchart of the selected articles (n= 54).

The main findings of this narrative review can be found in Table 1. According to the analysed literature, astronaut studies typically involve very few participants (often <20 per mission), which underpowers for detecting subtle physiological or cognitive changes. Variations in measurement protocols, mission duration, and environmental conditions (e.g., ISS *vs.* Lunar missions) complicate comparisons across studies. Many studies are observational or longitudinal rather than randomized controlled trials, which increase susceptibility to bias. Male and female astronauts may respond differently to microgravity. For example, differences in bone density loss, cardiovascular regulation, and hormonal responses can act as confounders, and most studies are conducted in male astronauts. Also, age and baseline fitness, as well as prior mission experience can be other potential confounders. Although extravehicular activity frequency imposes unique physical and psychological stressors (e.g., increased cardiovascular load, radiation exposure, and fatigue), this was not especifically analyzed in this narrative review.

Discussion

Physiological disturbances impared by microgavity

Understanding how microgravity affects human physiology is crucial for developing dietary patterns adapted to astronauts. Microgravity affects fluid redistribution, musculoskeletal and neurological systems, among others.[4,5]

When subjected to Earth's gravity field, the human body experiences a pressure gradient that varies with height: blood pressure is approximately 200 mmHg at the feet, 100 mmHg at the heart, and 70 mmHg at the head.[4] This gradient disappears in microgravity, causing a significant redistribution of body fluids toward the head.[4] The cephalad shift of fluids triggers responses in the baroreceptors and endocrine systems, contributing to a cluster of symptoms known as “space motion sickness”, which includes anorexia, vomiting, nausea, headache, and malaise, symptoms that typically are solved within 48 to 72 hours after exposure to the microgravity environment.[6] Furthermore, research in this field points to a reduction in plasma volume and changes in autonomic regulation, which contribute to orthostatic intolerance, when astronauts return to the Earth's gravitational environment.[4]

Prolonged microgravity exposure induces negative calcium balance, leading to bone loss, muscle atrophy, reduced plasma volume, cardiovascular deconditioning, and orthostatic intolerance.[7] The rate of bone loss significantly exceeds normal aging on Earth, increasing fracture risk and producing a premature osteoporotic phenotype, particularly during long-duration missions.[8] The literature indicates that astronauts can lose 1–1.5% of bone mass per month during spaceflight, substantially increasing the risk of bone fractures and kidney stones.[8] In addition to bone deterioration, the skeletal muscle tissue also undergoes significant atrophy in microgravity, primarily affecting antigravity muscles, which normally work against the Earth's gravity.[9] Without the constant stimulus provided by body weight, antagonist muscles progressively weaken, requiring rigorous exercise countermeasures during spaceflight.[9,10]

Table 1. Main findings of the narrative review on the physiological effects of microgravity and corresponding countermeasures in astronauts.

System domain	Main findings in microgravity	Underlying mechanisms	Consequence for astronaut health	Key countermeasures identified
Fluid distribution & cardiovascular system	Cephalad fluid shift; reduced plasma volume; orthostatic intolerance after return to Earth	Loss of gravitational pressure gradient; altered baroreceptor and endocrine responses	Space motion sickness (nausea, headache, anorexia); dizziness and fainting post-flight	Gradual re-adaptation to gravity; monitoring plasma volume; hydration management
Bone metabolism	Accelerated bone loss (≈1–2% per month); negative calcium balance	Absence of mechanical loading; increased bone resorption; oxidative stress	Increased fracture risk; kidney stones; premature osteoporotic phenotype	Resistance exercise; adequate calcium and vitamin D; antioxidant support
Skeletal muscle	Muscle atrophy (up to 30% in antigravity muscles); fiber-type shift (type I → type II)	Reduced mechanical load; increased protein degradation	Loss of strength and endurance; impaired postural stability	Daily resistance and aerobic exercise; high protein intake; branched-chain amino acids (BCAA) supplementation
Neurologicalsystem	Brain structural changes; altered connectivity; vestibular and motor deficits	Intracranial fluid shifts; sensory reweighting; neural plasticity	Vestibular ataxia; impaired coordination and balance	Sensorimotor adaptation; exercise; nutritional neuroprotection (e.g., omega-3)
Energy balance & metabolism	Energy intake often lower than expenditure; body weight loss	Appetite suppression; altered metabolism in microgravity	Negative energy balance; loss of lean mass	Careful dietary planning; energy intake monitoring
Macro nutrients need	Increased protein requirements; controlled fat and carbohydrate intake	Muscle catabolism; altered cardiovascular and metabolic demands	Muscle and bone deterioration if intake is inadequate	Individualized diets; 1.2–1.8 g/kg/day protein; balanced macronutrient distribution
Oxidative stress	Increased oxidative stress markers (e.g., 8-OHdG, malondialdehyde)	Radiation exposure; mitochondrial dysfunction	Bone loss; muscle atrophy; cellular damage	Antioxidants (vitamins C & E, selenium, polyphenols)
Micronutrients (Ca, Vit D, Vit K)	Reduced vitamin D synthesis; calcium imbalance	Lack of UV exposure; altered hormone regulation	Impaired bone mineralization; increased osteoporosis risk	Vitamin D supplementation (≈1000 IU/day); dietary calcium; exercise
Iron metabolism	Space anemia with paradoxical iron overload	Hemolysis; suppressed erythropoiesis; altered hepcidin activity	Fatigue; worsened muscle and bone loss	Monitoring ferritin; controlled iron intake
B vitamins & vision	Altered folate and B12 metabolism; increased homocysteine	Genetic and biochemical disruption of one-carbon metabolism	Visual impairment (opticdiscedema); neurologicalrisk	B-vitamin supplementation; genetic screening
Electrolytes & trace elements	Reduced magnesium, selenium, zinc post-flight	Fluid shifts; altered absorption and excretion	Neuromuscular dysfunction; metabolicimbalance	Dietarymonitoring; targeted supplementation
Hydration	High risk of dehydration; fluid handling challenges	Fluid redistribution; absence of gravity-driven flow	Reduced cognitive and physical performance	Adequate water intake; advanced drinking systems; water recycling
Physical exercise	Essential for preserving bone, muscle, and cardiovascular health	Mechanicalloadingsubstitutes gravity	Reduced deconditioning during missions	~2 hours/day exercise using advanced resistance exercise devices (ARED), treadmill, cycle ergometer
Sleep & circadian rhythm	Reduced sleep duration and quality; circadian misalignment	Multiple light-dark cycles; confinement; stress	Cognitive impairment; mood changes; operational errors	Light therapy; sleep hygiene; melatonin (when indicated)

Concerning neurological effects, over the past decade, two concomitant and antagonistic patterns have been observed regarding the effects of spaceflight on brain activity and behavior, such as: dysfunction and adaptive plasticity.[11] Evidence indicates that the spaceflight environment induces adverse effects on the brain, including intracranial fluid shifts, gray matter changes, and white matter decreases.[5] However, studies also suggest that microgravity promotes adaptive neural effects, such as sensory rebalancing and neural compensation.[11] Although studies based on functional neuroimaging during spaceflight are still limited, preliminary results, which are based on a single case study, point to a decreased connectivity of the vestibular and motor systems after six months in space, accompanied by vestibular ataxia and motor coordination deficits,[11] suggesting that prolonged exposure to microgravity may disrupt neural networks critical for movement and balance.

The role of Nutrition

Mission planning necessitates optimal nutritional provision for astronauts, requiring rigorous monitoring of nutritional status throughout the mission duration. To meet this need, a nutritional status assessment is conducted for the clinical purpose of supplementation use, which involves collecting blood and urine samples from astronauts. This assessment aims to identify indicators of bone health, muscle loss, hormonal imbalances, altered gastrointestinal function, cardiovascular health, iron metabolism, ophthalmological changes, and immunological changes that occur during spaceflight under microgravity conditions.[12]

The contribution of macronutrients

Macronutrient recommendations for astronauts are tailored to the specific conditions of space, such as microgravity, radiation, and changes in body physiology.[12] Their diet is planned to maintain muscle mass, bone health, cardiovascular function, immunity, and cognitive performance. The type of diet and its planning are individualized based on assessments of the individual's nutritional status prior to each mission.[12]

Despite the absence of astronaut-specific daily doses, NASA has outlined[7,12] nutritional recommendations (Table 2) for astronauts on space missions of up to 365 days. These guidelines are based on age, body weight and height to ensure adequate calorie consumption and maintenance of a healthy body weight.

The recommended protein intake ranges from 1.2 to 1.8 g per kg of body weight per day, aimed at avoiding nutritional deficiencies, maintaining muscle mass, and minimizing bone loss. Dietary sources include lean meats, soy, dairy, eggs, and protein shakes. Protein should be obtained from both animal and plant sources, with a maximum of 40% plant-based protein and 60% animal-based protein.[12]

Table 2. Nutritional requirements of macronutrients in space missions.[12]

Macronutrients	Daily Dietary Intake (DRI)
Proteins	1.2 – 1.8 g per kg of body weight Vegetable protein: 40% of the daily total Animal protein: 60% of the daily total
Carbohydrates	45-65% of the daily total <10% sugars
Fat	20-35% of the daily total
Saturated fat	ALARA, <10% of total calories
Omega-6	Women: 12 g/day Men: 17g/day
Omega-3	Women: 1.1g/day Men: 1.6g/day
Fibers	Women: 25g/day Men: 38g/day

Astronauts who undergo on physical exercise programs are recommended to consume between 1.3 and 1.6 g of protein per kg of body weight daily.[13] This value, high relative to normal requirements on Earth, reflects the increased degradation of muscle proteins in microgravity. Supplementation with BCAA may be particularly beneficial in this situation, as some studies have shown that the combination of physical exercise and BCAA' supplementation is effective in mitigating muscle atrophy.[14]

For carbohydrates, the total energy intake should be between 45% and 65% of the total daily, as they are intended to provide energy for brain and physical functions. Rice, pasta, dried fruit, and energy bars may be used . Added sugars should be less than 10% of total calories to avoid negative impacts on metabolic health.[12]

The recommended fat intake can vary between 25% and 35% of the total energy value to serve as energy support and the absorption of fat-soluble vitamins (A, D, E, K), whose main dietary forms are nuts, seeds, vegetable oils and fish (omega-3). Saturated fats should be ALARA (*As Low As Reasonably Achievable*), that is, kept at the lowest possible level, without exceeding 10% of total calories.[12]

According to Orwoll,[8] nutritional approaches should also support the neurological function in space focused on neuroprotective compounds and nutrients with anti-inflammatory properties. Omega-3 is one of these micronutrients, as it can partially reduce bone loss and promote neurogenesis, a dual benefit for skeletal and neural tissues.

Fiber aims to maintain intestinal health and prevent constipation (a common problem in space), and therefore, the recommendation is 25g/day for women, and 38g/day for men.[12]

Zwart et al.[15] conducted a study to evaluate the energy balance of 10 astronauts (7 men and 3 women) during long stays in space (approximately 162 days) and compare the caloric intake with total energy expenditure (TEE). Caloric intake was measured by food records and chemical analysis of the food, and TEE was calculated using doubly labeled water, (^2H) and (^{18}O), a high-precision technique for measuring TEE. Measurements were taken at different periods: before, during, and after the mission. The average energy intake during the flight was 2,736 ± 514 kcal/day (13% lower than the TEE), a reduction compared to preflight: ~15% to 25% lower than the usual intake before the mission. The TEE during the flight was 3,117 ± 386 kcal/day, with an average body weight loss during the mission of 2.1 ± 1.4 kg, associated with low energy intake. Thus, the TEE in microgravity was similar or slightly lower than the TEE on Earth, contradicting the idea that basal metabolism would fall substantially in space.[15]

The contribution of micronutrients

The need for additional supplementation with antioxidant substances appears to be related to the increased exposure to radiation, oxidative stress and loss of bone and muscle mass to which astronauts are subject.[12] They are exposed to elevated levels of ionizing radiation during spaceflight due to the absence of atmospheric shielding and reduced geomagnetic protection. Ionizing radiation interacts with cellular water and biomolecules, leading to the increased generation of reactive oxygen species (ROS), including superoxide radicals, hydrogen peroxide, and hydroxyl radicals. Concurrently, microgravity induces alterations in mitochondrial function and cellular metabolism, further enhancing ROS production and disrupting redox homeostasis.[16] Under physiological conditions, ROS are tightly regulated by endogenous antioxidant defense systems, comprising enzymatic antioxidants (e.g., superoxide dismutase, catalase, glutathione peroxidase) and non-enzymatic antioxidants derived from the diet. During spaceflight, however, excessive ROS generation overwhelms these protective mechanisms, resulting in chronic oxidative stress.[16]

Oxidative stress plays a critical role in microgravity-induced musculoskeletal deterioration. In bone tissue, elevated ROS levels stimulate osteoclast differentiation and activity while inhibiting osteoblast function, thereby shifting bone remodeling toward net resorption and accelerating bone mineral loss.[15,17] In skeletal muscle, oxidative stress activates proteolytic pathways, including the ubiquitin–proteasome system, and promotes mitochondrial dysfunction, contributing to increased muscle protein degradation and atrophy.[15,17] These molecular effects act synergistically with the mechanical unloading inherent to microgravity, exacerbating bone and muscle loss during prolonged space missions.[17,18]

Furthermore, long-duration missions are associated with reduced availability and stability of dietary antioxidants, as vitamins degrade during extended storage under spaceflight conditions.[12] Consequently, targeted antioxidant supplementation, including vitamins C and E, selenium, and polyphenolic compounds, is considered a necessary countermeasure to mitigate radiation- and microgravity-induced oxidative stress, preserve musculoskeletal integrity, and maintain cellular homeostasis during extended space missions.[12,17]

The specific nutritional recommendations for vitamins and minerals for astronauts on space missions of up to 365 days are described on Table 3.

Antioxidants against oxidative stress

Reactive oxygen species appear to be among the main contributors to bone mass loss that occurs under microgravity conditions.[18] For example, Rai et al.[19] concluded that prolonged exposure to microgravity may be associated with increased levels of specific markers of oxidative stress, such as 8-OHdG (8-Hydroxy-2´-deoxyguanosine) and malondialdehyde. This effect appears to be even more pronounced during long-duration flights and persists for several weeks after the end of the mission.

Table 3. Nutritional requirements for micronutrients in space missions.[12]

Micronutrients	**Daily Dietary Intake (DRI)**
Vitamin A	Women: 700 µg/day Men: 900 µg/day
Vitamin D	1000 IU (25 µg/day)
Vitamin K	Women: 90 µg/day Men: 120 µg/day
Vitamin E	15 mg/day
Vitamin C	Women: 110 mg/day Men: 125 mg/day
Vitamin B12	2.4 µg/day
Vitamin B6	1.3 mg/day
Calcium	1,000 – 1,200 mg/day
Iron	8 mg/day 18 mg/day for women under 50 years old
Folate	400 µg/day
Sodium	1,500mg – 2,300mg/day
Potassium	Women: 2600 mg/day Men: 3400 mg/day
Magnesium	Women: 320 mg/day Men: 420 mg/day
Selenium	55 µg/day

To mitigate these effects, vitamins such as vitamin C and vitamin E, which are known for their antioxidant effects, are used, as well as trace elements, such as, selenium and other micronutrients.[12] For example, the Morikawa 's study et al.[18] suggests that daily administration of vitamin C significantly attenuates bone loss by preserving trabecular bone volume thickness, number, and separation at optimal values, all indicators of osteoporosis and osteopenia parameters. Similarly, curcumin (1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione),a compound present in the root of Curcuma longa (turmeric),[20] has been investigated in animal models with promising results, increasing osteoblast differentiation and attenuating osteoclastogenesis, having the advantage of acting as a flavor-promoting vehicle and having anti-inflammatory, antioxidant, and antimicrobial properties. To mitigate oxidative stress in muscle atrophy, the administration of antioxidants targeted at mitochondria, such as, superoxide dismutase and catalase mimetics has also been tested.[21] Maecci et al.[22] demonstrated that fat-soluble antioxidant vitamin E improved muscle atrophy by approximately 20%. Despite these studies, the recommended doses of vitamin E and vitamin C in microgravity environments are similar to those on Earth, 15 mg and 110 mg (for women)/125 mg (for men), respectively.[12,22] This intake level is 35 mg/d more than the current Dietary Reference Intake and is in agreement with their recommended intake for individuals exposed to increased oxidative stress. However, these studies highlight that these doses must be actually ingested; the need for supplementation appears to be related to the fact that vitamins degrade during storage in space.[23, 24]

Calcium and Vitamin D against mineral loss

Microgravity environments also dramatically accelerate bone demineralization, leading to a loss of approximately 1–2% of bone mineral density per month (in weight-bearing bones).[25] Increased bone resorption is primarily due to the absence of mechanical loading, which disrupts the balance between bone formation and resorption. As a result, astronauts have a significantly higher risk of osteoporosis and related complications during and after missions, as demonstrated in several studies on the space environment and its effects on the musculoskeletal system.[8,26]

Bone loss in microgravity has traditionally been addressed with calcium and vitamin D supplementation, although their effectiveness is still debated. High doses of calcium and vitamin D through dietary supplements have not been shown to be effective against bone loss, since calcium excretion resulting from bone loss in microgravity can lead to parathyroid hormone suppression, which, in turn, reduces calcium absorption and vitamin D levels.[9] Nevertheless, vitamin D supplementation remains essential due to limited sunlight exposure on spacecraft. During simulated microgravity exposures, oxidative stress and bone metabolism increase. Calcium requirements are elevatedwith recommendations ranging from 1,000 to 1,200 mg per day to support bone health.[12] These values contrast with those needed in a terrestrial environment, which are approximately 1,000mg for adult men under 70 and women under 50.[27] Paradoxically, "space anemia" – the adaptative reduction in blood cells that optimizes oxygen delivery in microgravity coexists with disrupted iron regulation putting astronauts at risk of iron overload.[25] This risk is compounded by spaceflight-induced changes in urine volume, pH, and citrate excretion, which reduce the solubility of calcium salts. Studies have reported that 5–10% of astronauts develop kidney stones during or shortly after missions, often linked to hypercalciuria and high-dose supplementation strategies.[8,25] Therefore, calcium and vitamin D supplementation in astronauts must balance skeletal protection against potential renal complications. Optimizing bone health likely requires a multimodal approach that integrates resistance exercise, sufficient vitamin D status, and careful regulation of calcium intake to maintain plasma and urinary calcium within safe limits. Additional strategies, such as alkalinizing agents or dietary modifications to increase urinary citrate, may further reduce kidney stone risk without compromising the skeletal benefits of supplementation.[12]

As previously mentioned, vitamin D is equally critical, as it facilitates calcium absorption and bone metabolism.[12] The lack of Ultra Violet light exposure in space impairs the endogenous vitamin D synthesis.[28] Not only does vitamin D status decrease after long-duration spaceflight, but vitamin D metabolism or function may also be altered, based on measurements of the differences between the pre- and post-flight ratio of parathyroid hormone to calcidiol.[28] For these reasons, supplementation of 1,000IU daily is recommended as part of strategies to minimize damage caused by oxidative stress during space missions.[12] Studies have shown that these levels are sufficient to maintain vitamin D status and support bone health during long-duration missions.[29] However, vitamin D and C supplementation must be combined with high-intensity resistance exercises in order to significantly attenuate bone loss, hence the importance of ARED that simulate mechanical loads similar to those on Earth.[29]

Other lipossuluble vitamins

Supplementation with vitamin K and resveratrol has been shown to counteract the reduction in bone formation, likely by restoring levels of the decarboxylated protein osteocalcin.[30] This makes vitamin K a promising nutritional countermeasure against bone loss during spaceflight.

Supplementation with antioxidants such as vitamin E and polyphenols can also help protect neural tissues from oxidative damage associated with radiation exposure.[16]

Controlling iron intake to prevent anemia

Microgravity induces profound changes in iron metabolism, and space anemia emerges as a critical health concern for astronauts.[31] In the first 10 days of spaceflight, red blood cell mass decreases by 10–12%, driven by a combination of hemolysis and suppressed erythropoiesis. Nevertheless, this adaptive response, often called "space anemia", that is thought to optimize oxygen delivery relative to reduced plasma volume in microgravity and to minimize metabolic demands under altered circulatory conditions, can coexist with the risk of iron overload, as previously mentioned.

Although the activity of hepcidin, the primary hormone regulating iron metabolism, promotes iron sequestration in splenic macrophages, reducing serum iron levels, and increasing transferrin saturation,[32] the concurrent hemolysis contributes to increased circulating free iron. This hemolysis appears to be evident from a 54% increase in the elimination of carbon monoxide, a byproduct of heme degradation.[33] Therefore, astronauts exhibit elevated serum ferritin levels (70–220%) after flight, indicating iron overload despite anemia. This accumulation is clinically relevant because excess iron catalyzes the formation of reactive oxygen species via Fenton chemistry, contributing to oxidative stress, endothelial dysfunction, and potential exacerbation of bone and muscle catabolism.[33]

Current protocols point to a need for monitoring and mitigating anemia through quantification of serum ferritin to prevent iron overload.[31] Iron intake is 8-10mg/day for men and 15-18mg/day for women.Women's requirements are tailored according to pharmacological menorrhea suppression and genetic or pharmacological modulation of hepcidin production.[34] However, the dual risk of anemia and iron overload presents a unique challenge for nutritional and medical management.

In conclusion, spaceflight challenges the conventional paradigms of iron homeostasis. Astronauts face the unique paradox of concurrent anemia and iron overload, necessitating precise monitoring and tailored interventions. Optimizing iron balance in space requires integrating hematologic assessments, controlled nutrition, and potentially pharmacological measures to prevent the adverse consequences of both iron deficiency and iron excess during long-duration missions.

B vitamins

Folate , vitamin B12 , and vitamin B6 are particularly important for maintaining adequate hematologic function and preventing homocysteine accumulation during spaceflights, with particular relevance for the astronauts' vision accuracy.[35] Literature demonstrates that there are alterations in folate and vitamin B12-dependent metabolism during spaceflight, conditioning changes in astronauts' vision, with complex mechanisms involving biochemical and genetic factors, and approximately 20% of astronauts on ISS missions developed post-flight ophthalmic changes, including optic disc edema.[36] These changes were correlated with elevated levels of homocysteine, cystathionine, and the organic compound 2-methylcitric acid (25-45% higher); astronauts affected by polymorphisms in carbon metabolism enzymes hadincreased susceptibility to these pathologies.[35] Potential countermeasures include supplementation with B vitamins (active folate, B12 and B6) to normalize metabolic markers, genetic screening for polymorphisms associated with carbon metabolism, and monitoring of biomarkers, such as, homocysteine before and during missions.[37]

Electrolytes and trace elements

As already mentioned with regard to vitamins and micronutrients, such as iron, the balance of macrominerals, such as, sodium, potassium and magnesium also undergoes significant changes due to the displacement of fluids in a microgravity environment, and therefore must be measured and monitored before and during missions.[12]

Consuming 1,500 to 2,300mg of sodium and 2,600mg for women and 3,400mg for men of potassium helps maintain physiological homeostasis and prevent dehydration.[12]

Magnesium plays a role in over 300 metabolic reactions and is essential for protein synthesis, nervous system function, and muscle contraction.[12] It minimizes bone and muscle loss during space missions, aiding in neuromuscular regulation and energy production. Due to the high risk of bone and muscle deterioration, magnesium requires a daily intake of 420mg for men and 320mg for women,which should not exceed 350mg/day and should preferably be obtained through food, as absorption may be different from supplements.[12]

According to Smith et al.,[28] astronauts' serum selenium levels also tend to be lower after landing than before launch, as do magnesium and phosphorus (unit values indicate a decrease of approximately 44% and 46%, respectively). Furthermore, they report that 55% of crew members have post-flight urinary magnesium concentrations below the lower limit of the clinical range. Serum zinc concentrations were lower after the flight than before, highlighting the need for careful monitoring and supplementation of these trace elements.

Hydration

Dakkumadugula et al.[38] highlight that adequate water intake is vital for astronauts during spaceflight to prevent dehydration, support blood circulation, regulate body temperature, aid nutrient absorption, maintain muscle function, and promote bone health, cardiovascular health, immune function, and hormonal balance. Eating healthy and safe foods, as well as staying well hydrated by consuming safe drinks during operations is absolutely critical, as dehydration can result in reduced decision-making, concentration, and crew physiology.[39] Hydration in space also presents challenges due to the absence of gravity, requiring specialized equipment and techniques that differ significantly from consumption methods on Earth.[40]

Traditionally, astronauts have consumed beverages by sucking liquid from a bag or container through a straw, but there has been a need to develop more sophisticated approaches that improve the drinking experience,[40] while providing valuable scientific data on fluid dynamics in microgravity.[41] On Earth, gravity causes bubbles to rise and liquids to fall.[12] In a weightless environment, these mechanisms disappear; in microgravity, traditional concepts of floating or sinking, and up or down, are absent. Other forces, such as surface tension, normally suppressed by gravity on Earth, come to dominate the behavior of liquids and must be taken into account.[12] Liquids can be located virtually anywhere within the container, which poses significant challenges for beverage consumption, as any liquid can form floating globules, which can damage sensitive equipment or be inhaled by astronauts.[41] As said, the primary method for drinking in space has been through sealed pouches with straws. However, this method, while functional, deprives astronauts of the sensory experience of drinking from a glass and eliminates much of the pleasure associated with drinking beverages.[42] For hot beverages, like coffee and tea, the pouches can be heated using an electric water heater onboard the spacecraft before consumption.[40] This heating system allows astronauts to enjoy hot beverages despite limitations of the pouch-based system, although the experience remains very different from drinking from a cup on Earth.[40]

Space cups allow astronauts to experience capillary drinking, a process that resembles drinking on Earth.[41] The zero-gravity cup considers the behavior of liquids in a weightless environment and uses the laws of physics to direct the liquid to the rim of the cup, where it can be sipped.[41] Instead of relying on conventional forces to keep the liquid inside the cup, space cups use surface tension, wettability, and the geometry of the cup to prevent the liquid from escaping.[41] The cup design includes a sloped channel along the wall, from the bottom to the rim. In microgravity, the drink is poured into the cup using the spacecraft's galley dispenser. The sloped channel acts as an open passage with only two sides, where capillary forces move the liquid.[40] Touching the lip to the rim of the cup creates a capillary connection, similar to how water is absorbed by a paper napkin, allowing the user to access the entire contents.[43] While the cups allow astronauts to enjoy hot beverages, such as an espresso, they also provide scientific data on how complex liquids (like coffee or tea with sugar) behave in zero gravity.[43]

During space missions, beverages are more limited than on Earth due to storage constraints and challenges of preparation in microgravity.[40] Coffee is a particularly popular beverage among astronauts, providing familiarity and caffeine in an isolated environment.[43] With the arrival of the ISSpresso machine to the ISS in 2015, astronauts were able to prepare fresh expresso in space. The machine was sent along with space cups designed to complement it.

Various types of tea are available, usually in dehydrated blends that can be reconstituted with hot water, and various fruit juices are provided in special pouches or can be consumed from space cups. These beverages help satisfy nutritional needs and offer flavor variety, which helps combat sensory monotony on extended missions.[43]

Water remains the most consumed beverage in space, being recycled and processed through the Environmental Control and Life Support System.[44]

According to NASA,[12] water consumption requirements for astronauts are: 2.81 kg per day for direct consumption and rehydration of food and an additional 0.24 liters per hour during Extra-Vehicular Activity operations, such as, spacewalks. NASA emphasizes that water is a critical resource for the health and safety of the crew during space missions, being essential for maintaining adequate hydration, food rehydration, and personal hygiene.[45] Each ISS crew member requires approximately 5.14 kg per day forin order to meet those requirements. NASA also highlights that a loss of just 2.5% of body weight in water can result in decreased performance, impaired decision-making and concentration, and a 35% reduction in physical performance potential.[12,45]

According to Gaskill,[44] the ISS has achieved a technological milestone of 98% water recycling. The Water Recovery Systemis designed to recycle water from various sources, including sweat, urine, and air condensation and transform it into drinking water, using processes, such as filtration, distillation, and chemical purification to prevent microbial contamination in order to ensure that the water is safe for consumption.[44] This system is essential for the sustainability of long-duration space missions, thus reducing costs and the need for resupply from Earth. If pre-established standards are not met at the end of the process, it is reprocessed.[44]

In addition, the convergence of hydration, water recycling, and nutrition becomes even more pronounced with the incorporation of in-situ food production and supplementation systems. Plant growth platforms based on hydroponic or aeroponic techniques depend directly on reclaimed water for both hydration and nutrient delivery.[46] These systems can provide fresh sources of vitamins, antioxidants, and bioactive compounds that are difficult to preserve in prepackaged foods, while also contributing to dietary variety and crew behavioral health.[46] Similarly, microbial or algal bioreactors utilizing recycled water offer the potential for on-demand production of proteins, essential amino acids, fatty acids, or targeted micronutrients, functioning as a dynamic supplement to stored food inventories.[46] This may be a valuable translational model for sustainable nutrition and water management for long-duration flights in space.

The role of physical exercise

As said before, the development of effective countermeasures to mitigate physiological effects of microgravity is a critical priority to ensure safety on long-duration space missions, as sustained and long-term physiological changes can negatively affect crew health, and thus, compromise mission success and also post-flight recovery.[11,47] Exposure to microgravity during space missions causes significant physiological changes in the musculoskeletal system, such as the loss of bone mineral density, muscle atrophy, decreased strength and tendon stiffness, as well as, alterations in muscle fibers responsible for posture and stability, predominantly in antigravity muscles.[48] Current countermeasures include physical exercise protocols to maintain musculoskeletal health, although their effectiveness on extremely prolonged missions remains questionable.[49]

Effects of weightlessness on physical activity

Since the beginning of space exploration, scientists have recognized that physical exercise is essential for maintaining healthy bones and muscles in space, just as it is on Earth.[48] As early as the 1969 Apollo mission, astronauts simply used elastic bands to perform resistance and weight-bearing exercises.[48]

In fact, the lack of load on the musculoskeletal system causes muscle atrophy and reduced strength, with biochemical and structural changes, including the replacement of type I (slow) muscle fibers by type II (fast) fibers.[48] The muscles responsible for posture, such as antigravity muscles (the quadriceps, gastrocnemius, and spinal extensors) are the most affected, and may show a reduction of up to 30% in volume, and bone mineral density in weight-bearing regions, especially the lumbar spine and femoral neck, can decrease by 1–2% per month in space, after prolonged missions.[48]

Exercise equipment and protocols

To mitigate these effects, the exercise regimen has been strategically designed to target the major physiological systems impacted by microgravity. It includes aerobic conditioning, resistance training, and neuromotor exercises with adaptations to the training system and rigorous, personalized exercise programs, which were created, not only on the ISS, but also on spacecraft.[49]

Current ISS equipment includes the Treadmill Vibration Isolation and Stabilization System (TVIS), the ARED, a second-generation treadmill called the T2, and the Cycle Ergometer with Vibration Isolation and Stabilization System (CEVIS).[49]

The TVIS enables astronauts to perform weight-bearing aerobic exercise by simulating walking or running. Given the lack of gravity, astronauts wear harnesses tethered to the treadmill with elastic cords to maintain foot contact. This type of exercise helps preserve cardiovascular conditioning and mitigate lower-limb muscle atrophy.[49] The ARED simulates weightlifting in microgravity, using vacuum pistons to generate resistance and allows for a wide range of strength exercises for different muscle groups.[49] This allows astronauts to perform compound resistance exercises, including squats, deadlifts, and bench presses, replicating Earth-like axial loading to maintain bone and muscle strength. The T2 treadmill simulates running or walking, applying load to the lower limbs,despite the absence of weight.[49] The vacuum system creates a downward force on the astronaut's feet, while the elastic straps provide resistance to movement. The CEVIS is an adapted cycle ergometer with adjustable resistance and attachment systems to allow cardiovascular and strength exercises, allowing for moderate to high-intensity aerobic exercisefor the lower limbs in microgravity.[49] This equipment continues to be evaluated and modernized to optimize the intensity and duration of astronauts' training and preparation routines. Currently, astronauts spend on average two hours per day doing these specific physical exercises.

Structured exercise, when combined with appropriate nutritional support, and in some cases, pharmacological intervention, can significantly attenuate microgravity-induced physiological deterioration. As space agencies prepare for longer-duration missions to the Moon and Mars, optimizing exercise protocols and equipment design will be imperative to ensure astronaut health, mission performance, and post-flight rehabilitation.

The impact of microgravity on Astronauts' Sleep

Sleep is an essential physiological process for maintaining physical and mental health, as well as cognitive and motor performance.[50]

However, in the space environment, astronauts are exposed to conditions that profoundly challenge the human body's ability to maintain regular and restorative sleep patterns.[50]

The interaction between the absence of gravity, the disruption of circadian cycles induced by non-terrestrial light and darkness patterns and the conditions of space confinement, culminate in significant disturbances in sleep architecture and quality, and an intrinsic link to the psychophysiological health and cognitive and motor performance capacity of astronauts.[51]

Resting posture

The lack of a defined gravitational orientation allows astronauts to adopt any resting position, but the imperative need for physical restraint to prevent uncontrolled floating and potential collisions with equipment or other crew members is a source of discomfort and sleep fragmentation.[51] This floating sleeping posture, a "neutral" resting posture, without any contact with surfaces, can be uncomfortable and initially disorienting.[52]

Body implications

Microgravity causes a cephalad translocation of body fluids, resulting in facial edema and nasal mucosal congestion, a phenomenon clinically termed "Moon face".[52] This congestion predisposes to upper airway obstruction during sleep, manifesting as snoring and sleep apnea, which can compromise sleep continuity and quality.[51]

Circadian cycles

The space environment presents unique challenges for regulating sleep and circadian rhythms, which is another critical point.

On Earth, the 24-hour day-night cycle, imposed by the planet's rotation, acts as a synchronizer of our biological rhythms, adjusting physiological processes, such as, the sleep-wake cycle, hormonal coordination, body temperature, and metabolism.[53] In space, particularly in low-Earth orbits like that of the ISS, astronauts experience multiple sunrises and sunsets every 24 Earth hours (approximately

16 day-night cycles per day) due to the station's high orbital velocity.[53]

This dissociation of the Earth's day-night cycle, combined with other environmental factors (e.g., noise, confinement, social isolation), operational factors (work schedule, irregular hours), and psychological factors (mission stress, anxiety) contribute to significant disruptions to sleep and circadian rhythms in astronauts.[51]

Extensive research on astronauts' sleep patterns during ISS missions,uses rigorous assessment methodologies, including actigraphy (wearable motion sensors that record rest-activity cycles) and validated sleep questionnaires such as the Pittsburgh Sleep Quality Index and the Epworth Sleepiness Scale.[51] These studies have consistently confirmed the detrimental impact of the absence of a defined day-night cycle and other environmental and psychological factors on the quality, duration, and efficiency of astronauts' sleep.

Data collected on the ISS reveal that most astronauts experience a reduction in total sleep duration, an increase in sleep latency (time to fall asleep), more frequent nighttime awakenings, and a decrease in sleep efficiency (percentage of total time in bed actually spent asleep).[51]

Chronic sleep deprivation, even if seemingly mild, can have significant consequences for health and performance on long-duration space missions. Accurately identifying the factors that most contribute to sleep disruption on the ISS (light-dark cycle, noise, stress, workload) and evaluating the effectiveness of different interventions (pharmacological, behavioral, technological) are crucial to developing optimal strategies to promote sleep and circadian health on future space missions, especially those involving interplanetary exploration.[51]

Dysregulation of circadian rhythms and sleep deprivation can lead to several negative consequences for astronauts' health and daily duties, including insomnia, excessive daytime fatigue, decreased cognitive performance (attention, memory, decision-making), mood swings, irritability, increased risk of operational errors, and compromised immune function.

Therefore, the development and implementation of effective interventions to regulate biological cycles and promote quality sleep are of paramount importance for the safety and success of space missions.[51]

In order to mitigate the harmful effects of microgravity and other environmental factors on our astronauts, several strategies have been implemented and are the subject of ongoing research.

Phototherapeutic exposure to light

On the ISS, advanced lighting systems are available that can modulate the spectrum and intensity of light to simulate the Earth's natural light and dark cycle.[52]

Controlled exposure to blue-spectrum white light at specific times of the day can be used to simulate sunlight exposure and resynchronize the circadian rhythm by suppressing the secretion of melatonin (the sleep-inducing pineal hormone) and promoting alertness, while reducing blue light exposure before rest promotes melatonin synthesis and sleep induction.[51] Dawn simulators and sleep monitoring devices (actigraphy) may also be useful.[51]

Sleep hygiene

Astronauts follow strict sleep hygiene protocols, which include maintaining consistent sleep schedules, creating an optimized resting environment (controlling light, temperature, noise, ventilation), abstaining from substances such as caffeine before sleep, restricting the use of screens and electronic devices before bed, and practicing relaxation techniques to reduce stress and anxiety.[51]

Pharmacological intervention

The pharmacological intervention involves the use of sleep-inducing drugs, such as melatonin (a hormone naturally produced by the body that regulates the sleep-wake cycle), and, in more severe cases and under medical supervision, short-acting benzodiazepine or non-benzodiazepine hypnotics.[51]

Melatonin, in particular, has been widely studied and used in spaceflight due to its safety profile and relative efficacy in resynchronizing circadian rhythms. The results of these studies indicate that melatonin may be effective in reducing sleep latency and improving subjective sleep quality in some astronauts, particularly in situations of acute circadian desynchronization (e.g., rapid shift shifts).[51]

However, the effectiveness of melatonin may vary between individuals and at different stages of the mission. New research is being tested with a focus on improving melatonin administration protocols (dose, timing, formulation), identifying the subgroups of astronauts who benefit most from this intervention, and exploring other promising pharmacological approaches, such as, more selective melatonin receptor agonists and drugs with complementary mechanisms of action.[54]

It is important to emphasize that the use of any drug in space missions must be carefully evaluated, considering potential side effects, drug interactions, and the need for stable formulations suitable for the space environment.

The integration of the astronaut's physiology, systems and operations

Considering the complex integration of the astronaut's physiological systems on the mission operations along with all crew members' needs and the mission's success, some recommendations related with nutrition, sleep and light exposure are suggested in Figure 2, such as:

i) Energy Intake - adjust meal portion sizes based on daily energy expenditure (measured via wearable monitors);

ii) Protein Distribution - ensure from 20 to 30g of protein per meal/snack, spread evenly across 3 to 5 feeding times;

iii) Light Exposure - blue-enriched light in the morning promotes alertness, and dim/red light in the evening facilitates sleep;

iv) Sleep Flexibility -allow approximately 30 - 60 min adjustment for operational demands; include short naps as recovery tools and;

v) Monitoring - daily logging of meals, sleep, exercise, and subjective alertness allows for adaptive adjustments.

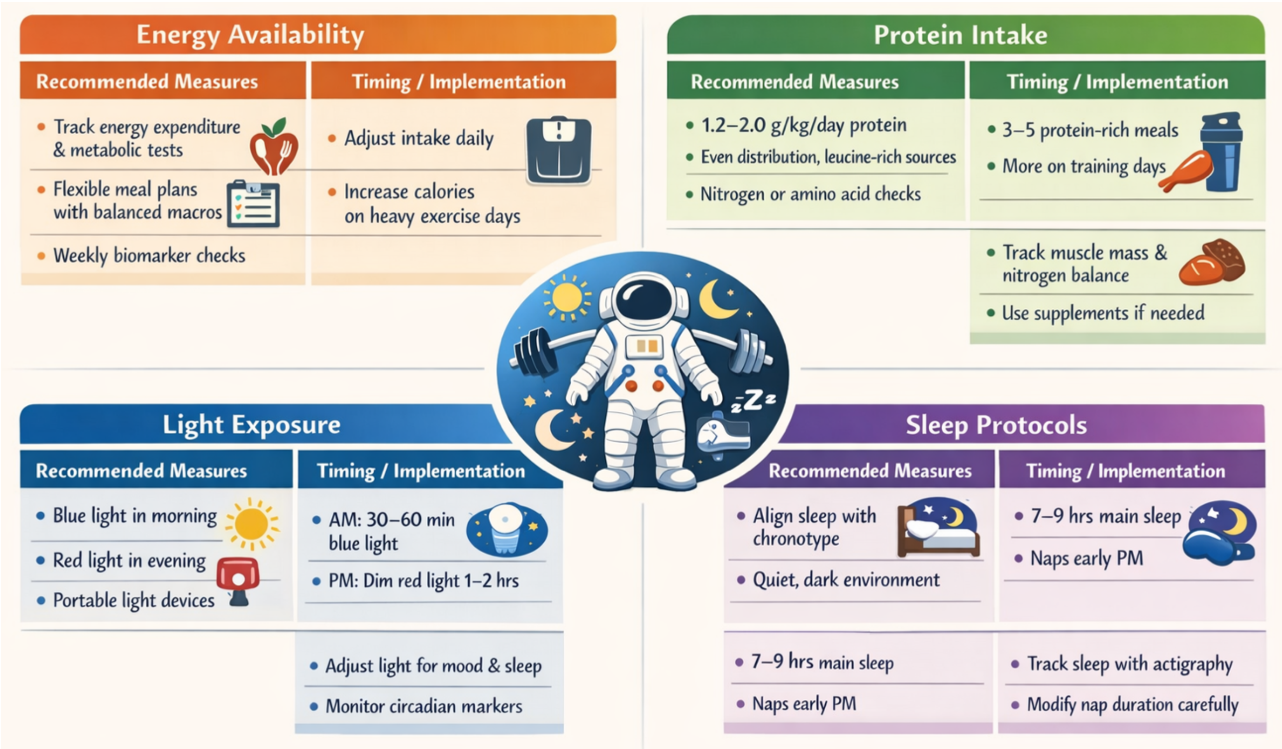

Figure 2. A mission-action plan for astronaut's health management, integrating energy, light, and sleep measures with practical adjustment guidelines.

Conclusion

Long-term space exploration poses a unique challenge to human mental health and physiology, with significant impacts on astronauts'nutrition, physical exercise and sleep. Pharmaceutical science, in collaboration with other disciplines such as nutrition, physical therapy, biomedical engineering, and space psychology, plays a key role in developing innovative and multifaceted strategies to mitigate the adverse effects of microgravity and ensure the health, well-being, and physical performance of astronauts.

The future of human space exploration depends largely on our ability to overcome the physiological challenges posed by the space environment. Continuous research, technological innovation, and interdisciplinary collaboration are essential to making long-duration space missions safer, more viable, and more productive, paving the way for humanity's expansion beyond Earth's orbit and the conquest of new worlds.

Astronauts consume less energy than they need during long-duration spaceflights, resulting in an energy imbalance that can have negative health consequences, such as loss of muscle and bone mass. Improved nutritional and sleep hygiene strategies are needed to ensure astronauts maintain adequate energy availability and sleep qualityand a healthy body composition during prolonged space missions.

Conflict of interest

No conflicts of interest were declared by the authors.

Data supporting the results will be provided on request.

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