Human Space Exploration: Neurosensory, Perceptual, and Neurocognitive Considerations

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Abstract
Several commercial enterprises and government space agencies are in the process of planning crewed exploration-class space missions to destinations such as the Moon and Mars. Despite the essential protection afforded by spacecraft and life support systems, such missions will expose the nervous system to significant physiological stressors, including microgravity, ionizing radiation, and circadian desynchrony. While the nervous system exhibits a remarkable capacity to adapt to the space environment, much uncertainty remains among space medical researchers regarding the limits of this adaptive capacity, particularly in the context of long-duration missions beyond low Earth orbit. Perturbations to neurosensory, sensorimotor, and perceptual processes associated with changes in the gravitational environment may interfere with the performance of astronauts or cosmonauts during spaceflight and post-flight operations. In terms of potential neurocognitive dysfunction, the available evidence is conflicting, and no definitive conclusions can be drawn as of yet. However, animal data suggests that in the absence of appropriate countermeasures, chronic exposure to the levels of ionizing radiation that will be encountered outside of the Earth’s magnetosphere may compromise neural structures supporting learning and memory. Going forward, research efforts should focus on further evaluating the nervous system’s capability to adapt to hypogravity conditions and how nervous system function will be affected by ionizing radiation encountered outside of the Earth’s magnetosphere. Finally, engineers and scientists alike should continue to work on developing countermeasures that will mitigate the potential nervous system dysfunction associated with exploration-class space missions.

Introduction
With continuing technological advancements and the recent burgeoning of commercial interest in human spaceflight, the possibility for extended space forays, such as a crewed mission to Mars or the establishment of a lunar base, does not loom too far into the future. In addition to addressing significant logistic and technological challenges, we must also consider the potential deleterious effects that exploration-class missions – missions involving travel beyond low-Earth orbit to other terrestrial bodies – could impose on the health and safety of astronauts and cosmonauts (henceforth, simply astronauts). Space is a fundamentally inhospitable environment, and even the vital protection provided by spacecraft and life support systems cannot mitigate all of the health hazards it presents. Microgravity (i.e., weightlessness), radiation exposure, and prolonged isolation and confinement constitute the most prominent threats to the medical safety of space voyagers. Any one or a combination of these environmental stressors may disrupt physiological systems, thereby compromising the health and performance of astronauts.

Nervous system dysfunction has been one of the most widely investigated biomedical issues associated with spaceflight, and is a feature of both short- and long-duration missions. Impairments to neurosensory, neurocognitive, sensorimotor, and postural function have all been commonly observed among astronauts. Circadian desynchronization and sleep deprivation are also frequent. Mood and psychiatric disturbances have also been reported, especially during long-duration spaceflight.

The present review surveys a selection of the biomedical spaceflight literature to provide readers with an overview of what is known regarding the effects of spaceflight on the nervous system, with a particular emphasis placed on neurosensory, perceptual, and neurocognitive functions. These effects are addressed with respect to their implications for long-duration and exploration-class space missions. Due to space limitations, we have omitted a discussion of psychiatric and psychological issues, though we encourage interested readers to consult Kanas and Manzey’s comprehensive examination of this topic. In addition to human studies, we also draw upon animal research in order to highlight potential adverse effects which, to date, have proven either too impractical or too difficult to test using human subjects during spaceflight (e.g., neuronal changes at the cellular and molecular levels). To illustrate the tangibility of the problems addressed, we begin by outlining several long-duration, exploration-class space missions that have been proposed for the decades ahead.
Methods
We searched the Summon™ database compilation through the University of Toronto Libraries website (https://onesearch.library.utoronto.ca/) using the following terms and phrases: ‘spaceflight’ OR ‘space flight’, ‘long-duration’, ‘microgravity’, ‘vestibular system’, ‘otoliths’, ‘ionizing radiation’, ‘astronaut’ OR ‘cosmonaut’, ‘neurosensorial’, ‘neurocognitive’, ‘perception’, ‘dysfunction’, ‘countermeasure’, ‘circadian rhythm’, ‘space motion sickness’, ‘performance’, ‘moon’, and ‘Mars.’ Given the relatively broad scope of the subject-matter examined, implementing separate search strategies in some cases proved more effective at narrowing down relevant results. We also identified other relevant sources from the reference lists of publications acquired through our Summon™ search. Other than a requirement for being peer-reviewed and published in English, no particular inclusion or exclusion criteria were applied, as it was not our intention to conduct an extensive or focused literature review.

Prospective Long-duration Space Missions
Various organizations, including governmental agencies and private enterprises, have put forth proposals for extended human space missions in the next two decades (see Table 1). Missions involving crewed spaceflights to near-Earth asteroids, the Moon, and Mars have all been suggested. Several commercial companies have presented plans to harvest ice-water located on near-Earth asteroids or at the poles of the Moon. The hydrogen and oxygen contained within molecules of ice water can be utilized to manufacture rocket propellant, which can then be sold in orbit to other private enterprises or government agencies travelling into deep space. Government-led programs are focused on exploration and scientific investigation, though they have also acknowledged a need to collaborate with and support private enterprise.

<table>
<thead>
<tr>
<th>Organization</th>
<th>Headquarters</th>
<th>Type</th>
<th>Destination</th>
<th>Proposed Date</th>
<th>Nature of Mission and Primary Objectives</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNSA¹⁴</td>
<td>China</td>
<td>Gov’t</td>
<td>Moon</td>
<td>2030</td>
<td>Scientific: Explore and study lunar environment</td>
</tr>
<tr>
<td>Deep Space Industries¹⁵</td>
<td>United States</td>
<td>Private</td>
<td>Near-Earth Asteroid</td>
<td>Unstated</td>
<td>Commercial: Harvest H₂O to manufacture rocket propellant and metals to build fuel depots</td>
</tr>
<tr>
<td>ESA¹²</td>
<td>France</td>
<td>Gov’t</td>
<td>Moon</td>
<td>2030s</td>
<td>Scientific/Commercial: Establish lunar outpost; encourage international collaboration and support development of private space sector</td>
</tr>
<tr>
<td>NASA¹⁶</td>
<td>United States</td>
<td>Gov’t</td>
<td>Near-Earth Asteroid</td>
<td>2025</td>
<td>Scientific: Test solar electric propulsion technology; collect geological samples</td>
</tr>
<tr>
<td>NASA¹⁶</td>
<td>United States</td>
<td>Gov’t</td>
<td>Moon</td>
<td>Mid 2030s</td>
<td>Scientific: Further study Martian environment and capability for humans to live and work in it</td>
</tr>
<tr>
<td>Planetary Resources¹⁷</td>
<td>United States</td>
<td>Private</td>
<td>Near-Earth Asteroid</td>
<td>2020s</td>
<td>Commercial: Establish long-term operations for resource extraction</td>
</tr>
<tr>
<td>Roscosmos State Corp¹⁸</td>
<td>Russia</td>
<td>Gov’t</td>
<td>Moon</td>
<td>2030-2031</td>
<td>Scientific: Establish lunar outpost; explore and study environment</td>
</tr>
<tr>
<td>Shackleton Energy Company¹⁹</td>
<td>United States</td>
<td>Private</td>
<td>Moon</td>
<td>2021</td>
<td>Scientific/Commercial: Extract H₂O from poles to manufacture rocket propellant; build fuel hubs in interlunar space to support expansion of space industry and the exploration of the solar system</td>
</tr>
<tr>
<td>SpaceX²⁰</td>
<td>United States</td>
<td>Private</td>
<td>Moon</td>
<td>Unstated</td>
<td>Scientific/Commercial: Study environment and prepare for wide-scale colonization</td>
</tr>
</tbody>
</table>

Abbreviations: CNSA, China National Space Administration; ESA, European Space Agency; Gov’t, Government; NASA, National Aeronautics and Space Administration; SpaceX, Space Exploration Technologies Corporation

Neurosensorial Systems and Perception
Information from the surrounding environment is transmitted to the central nervous system via sensory receptors and afferent nerve fibers, thereby allowing organisms to select and execute appropriate motor outputs in response to changing environmental conditions and demands. Appropriately and flexibly responding to the environment enables successful resource acquisition, reproduction, and survival. Given that the functional organization and structure of the nervous system has evolved in accordance with the enduring environmental features of Earth (such as the presence of gravity), major changes to afferent signals in spaceflight can cause perturbations to neurosensorial and perceptual function. In order to address the neurosensorial and perceptual dysfunction that occurs in space, it is necessary to first discuss the vestibular system.

Vestibular System
The vestibular system has been perhaps the most thoroughly studied sensory system in the context of spaceflight, as it has long been implicated in the etiology of space motion sickness (discussed in the next section). The vestibular sensory organs form part of the inner ear and are comprised of two otolith organs (the saccule and utricle) and three semi-circular canals (anterior, posterior, and horizontal). The otoliths detect linear acceleration associated with either translational motion or gravity while the semi-circular canals detect angular acceleration associated with rotatory motion (see Figure 1). Head movement in the yaw axis solely involves angular acceleration, whereas head movements in the pitch or roll axes involve a combination of both angular and linear acceleration. In the latter case, communicating this information to the central nervous system (CNS) requires a signal combining input from both the semi-circular canals and the otoliths. The CNS utilizes...
vestibular input to generate reflexive eye and postural movements essential for maintaining gaze stability and balance, respectively. Furthermore, association cortices combine vestibular input with information encoded by the proprioceptive and visual systems to form perceptual representations of spatial orientation and motion.

The mechanosensory receptors of vestibular utricles are activated based on the degree of head tilt relative to gravity. Stimulation of the hair receptors during head tilts generates a signal that is transmitted to the CNS, which in turn contributes to one’s perception of balance and spatial orientation. The absence of apposite gravitational cues (or possible presence of atypical cues) in the space environment undermines the brain’s ability to generate accurate egocentric and allocentric spatial representations. This is believed to result from an asymmetry in neurosensory signals causing disorientation and perceptual aberrations. This notion of afferent asymmetry, or sensory conflict, is the central idea underpinning the most widely accepted theory on the etiology of space motion sickness.

Space Motion Sickness

Space motion sickness (SMS) afflicts 50% to 80% of astronauts and develops within the first hour after reaching orbit. The symptoms resemble other forms of motion sickness and include headache, malaise, anorexia, nausea, and vomiting. While there is relevant individual variation in susceptibility to SMS and the duration for which symptoms persist, most astronauts experience a resolution in their symptoms by the third or fourth day of spaceflight. The dissipation of symptoms is a consequence of neural adaptation and/or plasticity in response to microgravity. Microgravity alone, however, does not seem to be the cause of SMS. The astronauts who participated in the earlier Mercury and Gemini space programs did not report having experienced symptoms of SMS. The spacecraft in these projects were much smaller than those introduced later in the Apollo and Space Shuttle programs, and did not allow astronauts to engage in any significant amount of movement. As the volume of spacecraft increased, so did the incidence of SMS. Evidently, this was associated with an increase in locomotion prompted by a greater availability of space within which to move. As cited by Clement and Reschke, astronauts noted that excessive movements soon after reaching orbit tended to exacerbate symptoms of SMS. Indeed, experimental studies later verified that movement, particularly head pitch and roll, aggravated symptoms. This may be related to gaze instability resulting from microgravity-induced abnormalities in vertical and torsional vestibular-ocular reflex gain.

The symptoms of SMS often reappear following the return to Earth and while re-adapting to the one g environment. This is referred to as post-flight motion sickness. Like SMS, the symptoms of post-flight motion sickness will typically abate within three to four days. It remains unknown to what extent post-flight motion sickness will pose a problem for future missions that see humans return to the Moon (0.16 g) or travel to Mars (0.38 g). Astronauts from the Apollo era who participated in lunar landings reported neither symptoms of post-flight motion sickness following their entry with the lunar module nor SMS after returning to the Apollo spacecraft. Nevertheless, given only a handful of anecdotes, it would be premature to rule out SMS and post-flight motion sickness as potential problems for future lunar expeditions.
Given the clear role of gravity (or more accurately, head motion in the absence of gravity), the vestibular sensory system has long been implicated in the etiology of SMS.\textsuperscript{34,35} In addition, it is well known that the absence of a functional inner ear confers immunity against other forms of motion sickness. Bilaterally severing the vestibular nerve can achieve the same result.\textsuperscript{30} Although perturbations to the vestibular system in microgravity appear to be central, the leading theory on the etiology of SMS (sensory conflict theory) suggests that it is not the vestibular system per se that causes SMS. Sensory conflict theory instead holds that SMS arises due to a mismatch in converging sensory input to the CNS based on what is ordinarily anticipated (i.e., sensory signaling which occurs at one g). As Oman\textsuperscript{3} has described, SMS can arise because “as motor actions are commanded, the brain continuously predicts the corresponding sensory inputs based on a ‘neural store’ of paired sensory and motor ‘memory traces’ learned from previous experience…” Sensory input that is incongruent with the activated paired sensory and motor memory trace may interrupt the motor program and cause disorientation. During spaceflight, the absence of gravitational signals from the vestibular system which, for example, would ordinarily accompany a head pitch, causes the intact proprioceptive or visual signals to be registered as anomalous. The persistence of apparently anomalous sensory information destabilizes the CNS, which can then possibly lead to SMS. Interindividual differences evidently have a large influence on how sensory conflict affects neurophysiological and neurocognitive function, as not all astronauts experience SMS yet remain susceptible to perceptual illusions often associated with it.\textsuperscript{44,45}

Pharmacological countermeasures, namely agents with sympathomimetic, antihistaminic, or anticholinergic properties, can ameliorate the symptoms of SMS and their secondary impacts on performance.\textsuperscript{39} Examples of specific drugs used to prevent or manage symptoms of SMS include d-amphetamine, scopolamine, and promethazine (injected intramuscularly).\textsuperscript{37} A combination of d-amphetamine and scopolamine (“ScopeDex”) is usually taken pre-flight as prophylactic treatment. Promethazine is better suited for administration during spaceflight, given its ideal pharmacokinetic profile under microgravity conditions. Any one or a combination of these drugs can cause side effects that compromise the performance of astronauts.\textsuperscript{30,39} In fact, flight commanders and pilots are prohibited from taking anti-motion sickness drugs prior to missions, given the high performance demands they encounter during launch.\textsuperscript{30} Non-drug countermeasures have also been proposed, an example of which is autogenic feedback training, a technique intended to sensitize astronauts to the bodily sensations associated with SMS (e.g., stomach discomfort).\textsuperscript{38} Studies evaluating the efficacy of autogenic feedback training have thus far yielded conflicting results.\textsuperscript{40-42} Pre-flight virtual reality training, which involves simulated environments with spaceflight modules, has also been considered. Preliminary investigations have yielded encouraging results.\textsuperscript{43}

**Visual Reorientation Illusions**

Visual reorientation illusions are sudden microgravity-induced shifts in the interpretation of one’s orientation relative to the identities of surfaces.\textsuperscript{44} Visual cues such as a fellow crew member floating sideways can, for example, shift the interpretation of a surface from being a wall to being a floor. The main factor is the lack of the gravitational anchor of ‘down’ in microgravity, placing heavier reliance on visual cues for three-dimensional orientation. Existing normal-gravity schemas (top-down processes) of three-dimensional orientation on a largely two-dimensional plane confound orientation interpretation under microgravity conditions. Visual reorientation illusions are a source of disorientation and consequently contribute to SMS, especially during an astronaut’s initial days in space. Other complications include losing one’s sense of direction while performing tasks inside spacecraft and height vertigo experienced during extravehicular activity.\textsuperscript{44,45}

Furthermore, animal studies have demonstrated evidence of vertical reorientation illusions at the single cell level. A rodent experiment conducted over the course of 40 parabolic flights showed that as subjects locomoted on the chamber’s floor in zero g measurements from head-direction cells within the dorsal thalamus displayed a direction-specific discharge pattern consistent with that observed under one g conditions. While an animal locomoted on the chamber’s ceiling or vertical walls, the direction-specific firing properties of the cells were typically absent, with an overall increase in the background firing rate. However, occasional burst firing was observed in a subset of the recorded cells while the animal oriented its head in a way that mirrored the floor’s longitudinal axis, suggesting the occurrence of a vertical reorientation illusion.\textsuperscript{46}

Place cells are hippocampal neurons that fire when an animal occupies a circumscribed region of space within its environment.\textsuperscript{47} Using a rodent cage rotation model during long-duration spaceflight, investigators found that two of three subjects had established near-identical place cell firing fields in each rotation orientation. The experiment required the rats to navigate an Escher staircase track involving three 90-degree turns in the yaw and pitch planes. The place cell activity seemed to reflect the occurrence of a vertical reorientation illusion, reinterpreting each surface as the same “floor surface” despite having moved onto the next surface. This was likely due to the similar visual cues that were visible ahead, accompanying each orientation shift. Over time, however, the place cells fields encompassed the entire cage, likely suggesting the rats had learned the allocentric orientation of the cage in its entirety.\textsuperscript{48,49}

The complications of vertical reorientation illusions can pose problems in the event of an emergency when a rapid undertaking of remedial actions is required, as was the case with several incidents involving Mir in 1997.\textsuperscript{44} More benignly, performance during day to day tasks and extravehicular activity can be hindered, resulting in a loss of productivity. Countermeasures have primarily involved distinguishing surfaces by patterns and colours, or installing orientation-specific landmarks, such as a chair on the actual floor. Although vertical reorientation illusions gradually subside as adaptation to microgravity occurs, spontaneous reoccurrences have been noted to occur well after adaptation.\textsuperscript{44}
Inversion Illusion

Related to vertical reorientation illusions, an inversion illusion describes a sudden feeling of being upside down, despite the absence of any inherent ‘up’ or ‘down’ in space. This most often occurs directly following orbital insertion and for a few days thereafter.\textsuperscript{34} Inversion illusions are also accompanied by a tumbler or somersaulting sensation.\textsuperscript{34,44} A possible cause of this perception in microgravity is headward hydrocephalic pressure due to fluid shift in the absence of gravity, thereby producing the same sensation as being upside down in one g.\textsuperscript{44,56} Another explanation or contributing factor is the absence of gravity acting on trunci gravireceptors[51]. Although inversion illusions are readily adapted to by astronauts, they can sporadically reoccur in later phases of the mission.\textsuperscript{54} Countermeasures used have included Adeli suits utilizing elastic cords to place an axial load on the body, as well as other load-adding equipment to simulate gravity.\textsuperscript{30}

Depth, Distance, and Size Perception

Prolonged exposure to microgravity in long-duration spaceflight has been shown to affect astronauts’ depth perception. In normal gravity, people are biased to perceive objects from above due to our gravity-tied vertical orientation and use of the visual horizon as a projection plane to indicate depth. However, this is no longer applicable in microgravity and astronauts are free to navigate through the spacecraft in many orientations. In normal gravity conditions, individuals are predisposed to interpreting ambiguous three-dimensional images (e.g., a Necker Cube) in one orientation more than the other, usually as viewed from above.\textsuperscript{52} Clement and colleagues\textsuperscript{55} reported that this bias steadily diminished over a three-month period that astronauts spent in microgravity. However, the perceptual bias returned to pre-flight levels over the course of nine days after returning to Earth. Floating in many orientations during long-duration spaceflight rather than maintaining an upright posture may also potentiate ambiguity in geometric depth interpretation. The perceptual schema integrating eye-ground elevation for depth perception accommodates such that objects in the lower visual field may no longer indicate nearness, as would be the case in normal gravity.\textsuperscript{35} These effects on depth perception may potentially affect performance during initial ground operations on Mars or the Moon.

Visual perception of size, shape, and distance has also been found to be distorted in microgravity, with astronauts perceiving a perfect cube as being shallower and taller than in one g.\textsuperscript{54} This phenomenon may also be due to the lack of normal eye-ground elevation for scaling distance. A related experiment saw astronauts in microgravity attempt to catch a falling ball, but they would often miss the target due to premature arm movements.\textsuperscript{56} It is possible that this is due to a misinterpretation of distance to the ball, or because motor programs remain calibrated to Earth-based gravitational acceleration.\textsuperscript{56} In summary, perceptual distortions due to the effects of microgravity have been a source of concern for NASA, particularly with respect to the safety of vehicle control during future space missions.\textsuperscript{45}

Anomalous Light Flashes

During the final seven Apollo missions, subtle light flashes experienced by astronauts (generally while dark-adapted) were attributed to cosmic ray nuclei (high-Z and energy particles; HZE) penetrating the head and visual system.\textsuperscript{37} As a result, the potential for ionizing radiation to adversely affect brain function in space became a more salient concern for space medical researchers. Subsequent experimental studies verified that similar visual phenomena could be elicited by exposing subjects to fast neutron and positive pion beams, as well as Cerenkov radiation.\textsuperscript{59,58} More recently, project ALTEA (Anomalous Long Term Effects of Astronauts) and its precursor Alteino were launched specifically to investigate these ‘light flash’ phenomena and their potential impacts on brain function.\textsuperscript{60} Studies performed by the ALTEA group found that subjective reports of observing the ‘light flash’ phenomena coincided with significant amplitude shifts in the electrical activity of the occipital cortex (as measured with electroencephalography) and the detection of HZE.\textsuperscript{2,61} The ALTEA project is still ongoing and the ‘light flash’ phenomena await further characterization.

Neurocognition

Many of the tasks and problems encountered during exploration-class space missions will demand a high or exceptional level of cognitive ability. Thus, understanding how neurocognition is affected by long-duration spaceflight will be essential for ensuring the success of exploration-class missions and the safety of their crew. However, there have been a limited number of studies done in this area to date and sample sizes have also been limited. A series of relatively early investigations – mostly involving single case studies – conducted on the Russian Mir assessed cognitive performance in the domains of attention, logical reasoning, memory, and visuomotor tracking. These studies yielded mixed results, with some astronauts showing performance deficits compared to pre-flight levels while others showed either no change or, surprisingly, improvement.\textsuperscript{61} Moreover, many performance impairments that were observed during spaceflight were restricted to the initial days following launch, thereby complicating the ability to investigate them as independent of SMS or other space adaptation-related phenomena.\textsuperscript{5}

A more consistent finding from the Mir studies, however, was a noted decline in visuomotor and dual-task performance compared to pre- and post-flight levels.\textsuperscript{6,62,63} However, it has been difficult to isolate these impairments from the experiences of stress and fatigue associated with the high workloads that astronauts frequently undertake. Indeed, the most notable declines in visuomotor and dual-task performance have occurred during periods in which astronauts perceive to have unusually high workloads, high fatigue, or both.\textsuperscript{64} Thus, it is unclear if these performance deficits are attributable to unique elements of the space environment itself. Nevertheless, some researchers have maintained that at least some of the variability in dual-task impairment can be linked to microgravity.\textsuperscript{65} It should also be noted that visuomotor function is not strictly a cognitive process. Deficits in this area are more likely to reflect abnormalities in muscle force calibration and
A circadian rhythm is an endogenous, free-running clock that coordinates changes in our physiology and behaviour in an approximately 24 hour cycle. In mammals, circadian rhythms are largely governed by the suprachiasmatic nucleus (SCN), or central pacemaker, located within the hypothalamus. The SCN central oscillators are entrained by the Earth’s 24 hour light/dark cycles via photic input from specialized ganglion cells within the retina. The lack of normal light/dark cycles during spaceflight and untimely work schedules can cause phase and amplitude shifts in astronauts’ circadian rhythms. Insomnia experienced during scheduled rest periods is a common result of this, as evidenced by the fact that hypnotics are the drugs most commonly taken by astronauts.

A recent study comparing astronaut sleep quality during periods of sleep that were aligned or misaligned with circadian rhythms (as determined via fluctuations in core body temperature) demonstrated that sleep misaligned with the phase of an astronaut’s circadian rhythm is reduced in duration and quality (see Table 2). Sleep can further be impacted by other factors including noise, psychosocial stress, and microgravity-related effects (such as a lack of proprioceptive cues). Additionally, astronauts have reported that the radiation-related ‘light flash’ phenomena described above can also significantly interfere with sleep. Importantly, fatigue related to disrupted sleep can cause performance deficits that may jeopardize the success of the mission, as well as the crew’s safety. Indeed, fatigue is known to be a leading cause of accidents in spaceflight.

**Discussion and Conclusions**

As we enter into a new space era and humans begin to move further out into the space frontier, it is essential that we understand how nervous system function will be impacted by the space environment and that of the extraterrestrial bodies we intend to explore. Although many of the adverse effects of space on nervous system function are only evident during the initial period of spaceflight and dissipate as the nervous system adapts to microgravity, this adaptation later undermines neurologic and neurocognitive function during the post-flight stage. Therefore, a process of physical deconditioning will be required when returning to Earth or landing on another terrestrial body. Moreover, many uncertainties remain regarding the extent to which the nervous system can adapt to novel environmental conditions during space exploration, as well as the irreversibility of these adaptations (neural plasticity).

**Table 2. Characteristics of astronaut sleep during periods of circadian alignment versus circadian misalignment**

<table>
<thead>
<tr>
<th></th>
<th>Aligned</th>
<th>Misaligned</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep Duration (hours)</td>
<td>6.4 (1.2)</td>
<td>5.4 (1.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Latency (minutes)</td>
<td>10.3 (15.0)</td>
<td>13.2 (25.2)</td>
<td>0.26</td>
</tr>
<tr>
<td>Number of Awakenings</td>
<td>1.7 (1.9)</td>
<td>1.7 (1.7)</td>
<td>0.38</td>
</tr>
<tr>
<td>Sleep Efficiency</td>
<td>89% (7%)</td>
<td>90% (7%)</td>
<td>0.26</td>
</tr>
<tr>
<td>Sleep Quality</td>
<td>66.8 (17.7)</td>
<td>60.2 (21.1)</td>
<td>0.01</td>
</tr>
<tr>
<td>Alertness</td>
<td>57.9 (21.7)</td>
<td>53.6 (21.5)</td>
<td>0.13</td>
</tr>
</tbody>
</table>

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Crew members participating in future exploration-class missions, such as a mission to Mars, will not have the same supports that are available when returning to Earth. Therefore, astronauts participating in high-stakes exploration-class missions should be selected from a pool of candidates who have demonstrated a low susceptibility to space and post-flight motion sickness, and the ability to effectively cope with perceptual anomalies related to sensory conflict. Future research should focus on adaptation to hypogravity environments (such as Mars and the Moon) following prolonged periods of zero g. Additional and more effective countermeasures for dealing with space and post-flight motion sickness should also be investigated. Artificial gravity is a particularly attractive area of research. This is because the capability to efficiently generate various gravitational forces could significantly mitigate many of the problems associated with non-Earth gravitational environments.88

Further research investigating neurocognitive function during long-duration spaceflight is also required. Although perception has drawn much attention from investigators, research on memory, learning, and executive functions has been comparatively limited. As others have also pointed out,61 the evidence that is currently available neither proves nor disproves that spaceflight in low Earth orbit negatively impacts cognitive function. Many of the experiments performed in this domain have had limited sample sizes (a common problem with human space research) and show high levels of interindividual variability, which may confound results. It is possible that neurogenetic variation exerts a high degree of influence on the susceptibility of neurocognition to the adverse effects of spaceflight. In support of this notion, it has recently been shown that long-duration spaceflight produces abnormalities in the genetic expression profiles of the serotonergic and dopaminergic neurotransmitter systems, both of which are important for cognition.78

Before extensive exploration-class missions are launched, it is also necessary to further evaluate the effects of ionizing radiation on the CNS in comparatively larger doses than those characterizing spaceflight in low Earth orbit. Recent animal data suggests that exposure to radiation in doses more comparable to those that will be encountered outside of Earth’s magnetosphere will significantly affect neural systems that support learning and memory.70,71,80 More effective shielding materials should be considered for future spacecraft design. Furthermore, antioxidants appear promising as potential countermeasures for mitigating the harmful effects of radiation.72,73 In closing, there are many medical challenges that remain to be addressed before humans can begin to establish a long-term presence on the Moon or launch crewed missions to Mars. Nevertheless, we remain confident that these challenges can and will be overcome.

References
30. Kornilova LN, Naumov IA, Azarov KA, Sagalovitch VN. Gaze control and post-flight motion sickness should also be investigated. Artificial gravity is a particularly attractive area of research. This is because the capability to efficiently generate various gravitational forces could significantly mitigate many of the problems associated with non-Earth gravitational environments.