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REVIEW ARTICLE

'White Mars' – nearly two decades of biomedical research at the Antarctic Concordia station

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Abstract

Extended stays in isolated, confined and extreme (ICE) environments like Antarctica are associated with a whole set of psychological and physiological challenges for the crew. As such, winter-over stays at Antarctica provide an important opportunity to acquire knowledge into the physiological and psychological changes that ICE environments inevitably bring. The European Space Agency (ESA) is particularly interested in conducting research in such an environment, as it is a unique opportunity to translate these results to space crews experiencing very similar issues. In the past two decades, the ESA has supported a total of 36 biomedical research projects at the Concordia station in collaboration with the French and Italian polar institutes. More specifically, studies in the areas of psychology, neuroscience, sleep physiology, cardiovascular physiology and immunology were performed. The outcomes of these studies are directly relevant for people working in ICE environments, but also help to better understand the biomedical challenges of those environments. Consequently, they can help to better prepare for human space exploration and to identify countermeasures to minimize the adverse effects of space environments on astronaut health. The aim of this review is to provide an overview of the biomedical studies that have taken place in the past two decades at the Antarctic Concordia station and to summarize the results and their implication for human spaceflight.

KEYWORDS
antarctica, cardiovascular physiology, hypobaria, hypoxia, immune response, neuroscience, psychology, sleep

1 | INTRODUCTION

Though the experiences themselves are relatively rare, research into prolonged stays in isolated, confined and extreme (ICE) environments dates as far back as the 1950s and 1960s. It was during this time that human spaceflight first took off, permanent research bases in Antarctica were first established and the human undersea presence was increasing. As such, it has become increasingly important that we understand the impact of such environments on both the functioning and the health of those who are exposed to them for long periods of time. Since that time, an extensive set of research addressing those concerns has been carried out, making use of a variety of platforms, including space stations (ISS, Space Shuttle, Mir), Antarctic research stations (Concordia, Halley VI, Neumayer), analogue stations (Mars 500, HERA, HiSEAS, NEEMO) and subterranean caves. Such investigations have revealed a wide range of potential effects of ICE environments on the different aspects of physical and mental health. These typically include changes in neurocognitive function, misaligned circadian rhythms and sleep disorders, altered stress hormone levels, and immune dysregulation. For an extensive and detailed overview,

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readers are referred to complementary recent review papers (Pagel & Choukèr, 2016; Zuccarelli et al., 2019).

In view of the European Space Agency (ESA)'s plans for future human long-duration exploration missions, Concordia station acts as a powerful, high-fidelity analogue, as it replicates many of the expected conditions of a lunar or Martian base. Such conditions include isolation, confinement, high levels of autonomy and social monotony, living in a small multicultural setting (for Concordia, the average crew size is 12, French and Italian are the most spoken languages, and there are a variety of behavioural customs), daylight/night variations uncommon to most humans, limited resources, restricted access by outside help in case of emergencies, and a hostile external environment.

Concordia station (Figure 1) is a permanent international research facility at high altitude at Dome C on the Eastern Antarctic plateau (Figure 2). The station was built by Institut polaire français Paul-Emile Victor (IPEV, the French Polar Institute) and Consorzio per l'Attuazione del Programma Nazionale di Ricerche in Antartide, Italian Antarctic Programme (PNRA S.C.r.l). The station has been permanently crewed since November 2004. A typical winter-over crew consists of up to 16 people including a technical manager, cook, doctor, plumber and other technicians to ensure safe operations of the station. The remaining crew members are devoted to scientific projects. The overall objective of Concordia station is to operate as an international research facility to conduct science. The main fields of research at Concordia are glaciology, atmospheric sciences, astronomy and astrophysics, Earth sciences, and technology. The area in which Concordia station is located is considered to be one of the most hostile places on Earth. Some characteristics of the extreme environment include an altitude of 3200 m (equal to an altitude of almost 4000 m at the equator), with air pressure of 645 hPa and chronic hypobaric hypoxic stress; no access to the station between mid-February and mid-November (the Antarctic winter season); and an overall mean temperature of −51°C, with temperatures as low as −80°C in winter. Such an extreme external environment means that during the winter season, the crew must take the time to dress in a heavy protective suit to leave the station and are restricted in the length of time they can stay outside when they do venture out (also reminiscent of the potential extravehicular activity (EVA) experiences of future crews at lunar and Martian bases). As a result, some crew members rarely go outside, although one or two of the crew may leave the station on a daily basis. Furthermore, the station is isolated as it is located 950 km from the nearest coast, 1670 km from the South Pole and 560 km from the nearest neighbouring station. This actually makes Concordia station more remote than the International Space Station and also less accessible (at least during winter). Such a reality means the crew are forced into far greater autonomy in cases of emergency than even the ISS, whose astronaut crew members may be returned to Earth relatively quickly in extreme situations. Obviously this real-world factor cannot be replicated by any analogue stations purposefully designed and constructed for ICE experiments.

The combined effect of all these factors is that Concordia is truly unique in its ability to serve as a faithful analogue of spaceflight conditions, especially in the areas of human physiology, behaviour and performance, and may currently well be the station most reflective of future extraterrestrial bases. It has additionally served for use of the testing and validation of telemedical applications.

The aim of this review is to provide an overview of the past two decades of biomedical research that has been conducted at the Concordia polar station, in order to highlight the overall findings in the areas of psychology, neuroscience, sleep physiology, cardiovascular physiology, and immunology. Furthermore, we will discuss the relevance of extreme environments like the Concordia station for preparing astronauts for future long-duration missions.

New Findings

- **What is the topic of this review?**
  Biomedical research at the Antarctic Concordia Station.
- **What advances does it highlight?**
  Overview of findings in psychology, neuroscience, sleep, cardiovascular physiology and immune system, relevant in isolated, confined and extreme environments and spaceflight.

2 | MATERIALS AND METHODS

2.1 | ESA's research selection process

Since the beginning of the ESA/IPEV/PNRA cooperation, six ESA Announcements of Opportunity (AOs) soliciting for biomedical research to be implemented at Concordia have been released (2003, 2007, 2010, 2011, 2013 and 2017). The European science community at a whole is welcome to apply to these AO's. All submitted research proposals undergo peer review by independent experts in the respective fields. Before an experiment is implemented, it needs to pass a science merit score threshold, as well as a technical feasibility assessment. For the first five AOs, approximately 330 investigators and 113 authors have been involved in Concordia experiments, spanning a total of 20 countries. An overview of geographical distribution of scientific involvement can be found in Figure 2.

Once scientific projects are selected and pass both peer review and a technical feasibility assessment, preparations for their implementation begin. This involves the selection of an ESA Research Medical Doctor (MD) for each winterover season to join the crew at Concordia station and collect measurements for the selected experiments. For a clearer perspective of the living conditions and environment of the Concordia crew, a schematic representation of the station is shown in Figure 3.

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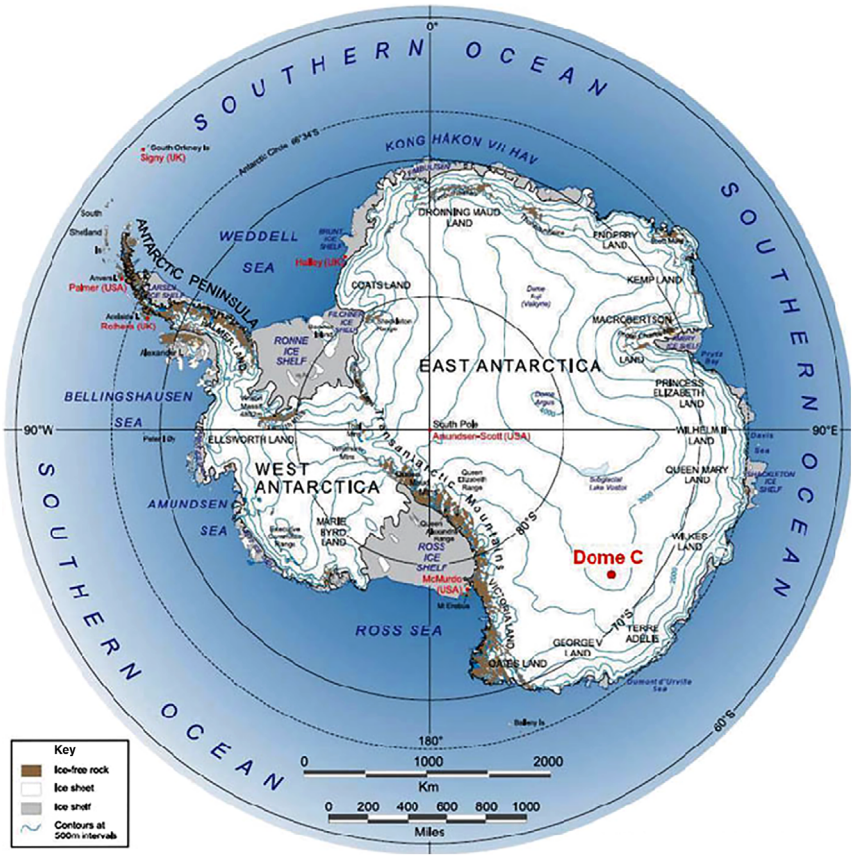

FIGURE 1 The Concordia station (top) and the location of Dome C in Antarctica (bottom) (source: European Space Agency)

2.1.1 | Overview of studies completed and published

For the purposes of this review, only the projects stemming from the first five AOs will be considered. From these, 36 biomedical experiments were selected by the ESA for implementation at Concordia station. As of November 2019, 16 of these projects have resulted in publications. Collectively, the science teams have released 21 publications, of which three publications were excluded because of no availability of the full text or because they were not available in English. In total, 18 publications were included in this review. Broadly, the publications have investigated psychology, neuroscience, sleep, cardiovascular physiology and immunology. A full list of publications included in this article can be found in Table 1. In the following paragraphs, we provide a high-level overview of the results of these studies.

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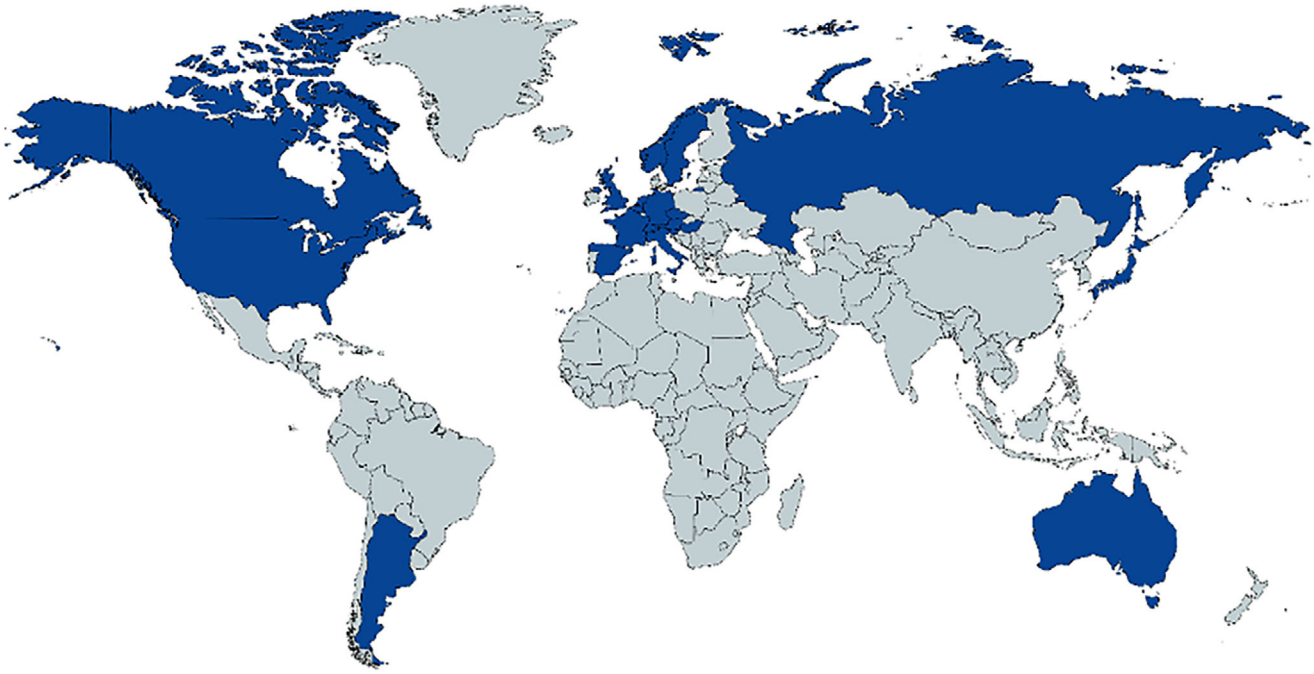

FIGURE 2 An overview of geographical distribution of scientific involvement in the past five ESA Announcements of Opportunity soliciting for human research activities at Concordia (Countries are: Argentina, Australia, Austria, Belgium, Canada, Czech Republic, France, Germany, Hungary, Italy, Japan, The Netherlands, Norway, Russia, Slovenia, Spain, Sweden, Switzerland, UK and the USA)

2.2 | Psychology and neuroscience

In the domains of psychology and neuroscience, several studies have specifically looked at the psychological consequences of long-term isolation, confinement, monotony and high autonomy during an winter-over season at the Antarctic continent.

A study by Krins and colleagues investigated the role of group processes in ICE environments (Krins, 2009). More specifically, they investigated what the effect is of an individual's identification with the group on group functioning and its relationship with pro-diversity culture. After a 50% drop-out rate after the first data collection point, they were able to analyse only the link between diversity culture and identification through multilevel linear modelling (MLM). The MLM analysis revealed that a pro-diversity culture within the crew significantly increased the likelihood that crew members identified highly with the rest of their group. There were medium to strong correlations between pro-diversity culture and identification with the group, advice seeking, cooperation, friendship and socialization, suggesting that a pro-diversity culture may benefit overall group functioning.

Nicolas and colleagues investigated the impact of a 1-year wintering in Concordia on affective, social, personality and cognitive outcomes (Nicolas, Suedfeld, Weiss, & Gaudino, 2016). More specifically, the Nicolas team wanted to investigate the adaptation process of these domains by studying the time course of stress, recovery and control states, defence mechanisms and lapses of attention. They found a large significant increase in the social dimensions of stress for all participants (Cohen's effect size $d > -0.8$ for all measurement points as compared to the baseline measurement). Any changes in the other stress dimensions were not significant. There were no statistically significant changes in the recovery dimensions. The social stress scale was the only dimension which exhibited a significant and continuous increase throughout the winter-over year, supporting the notion that spending a long time in ICE environments may increase social tension and lead to interpersonal issues. They also found several associations, such as between mean total stress and mean scores on the Perceived Stress Scale (PSS; $r = 0.63$), attention lapses ($r = 0.83$) and immature defence mechanisms (DM; $r = 0.71$). They also found a positive correlation between total recovery and mature DM ($r = 0.68$) and perceived control ($r = 0.77$). This indicates that individuals who feel they have the resources to cope with the environment recover more effectively. Lastly, they found a link, amongst others, between immature DMs and total stress ($r = 0.71$), as well as between mature DMs and total recovery ($r = 0.68$), suggesting that individuals who use more mature defence mechanisms are better suited to adapt to ICE environments.

In parallel, Nicolas et al. also looked at how the occupational and social components of the adaptation process at Concordia changed over time, as well as their mutual relationships with cultural and professional determinants (Nicolas, Bishop, Weiss, & Gaudino, 2016). They found that both occupational and social dimensions were altered throughout the 1-year stay at Concordia. All winterers also showed moderately increased counterproductive activity during the winter period (effect size $\eta š = 0.64$). Interestingly, there were discrepancies between scientists and logistic staff (related to professional occupation), and between the French and Italian

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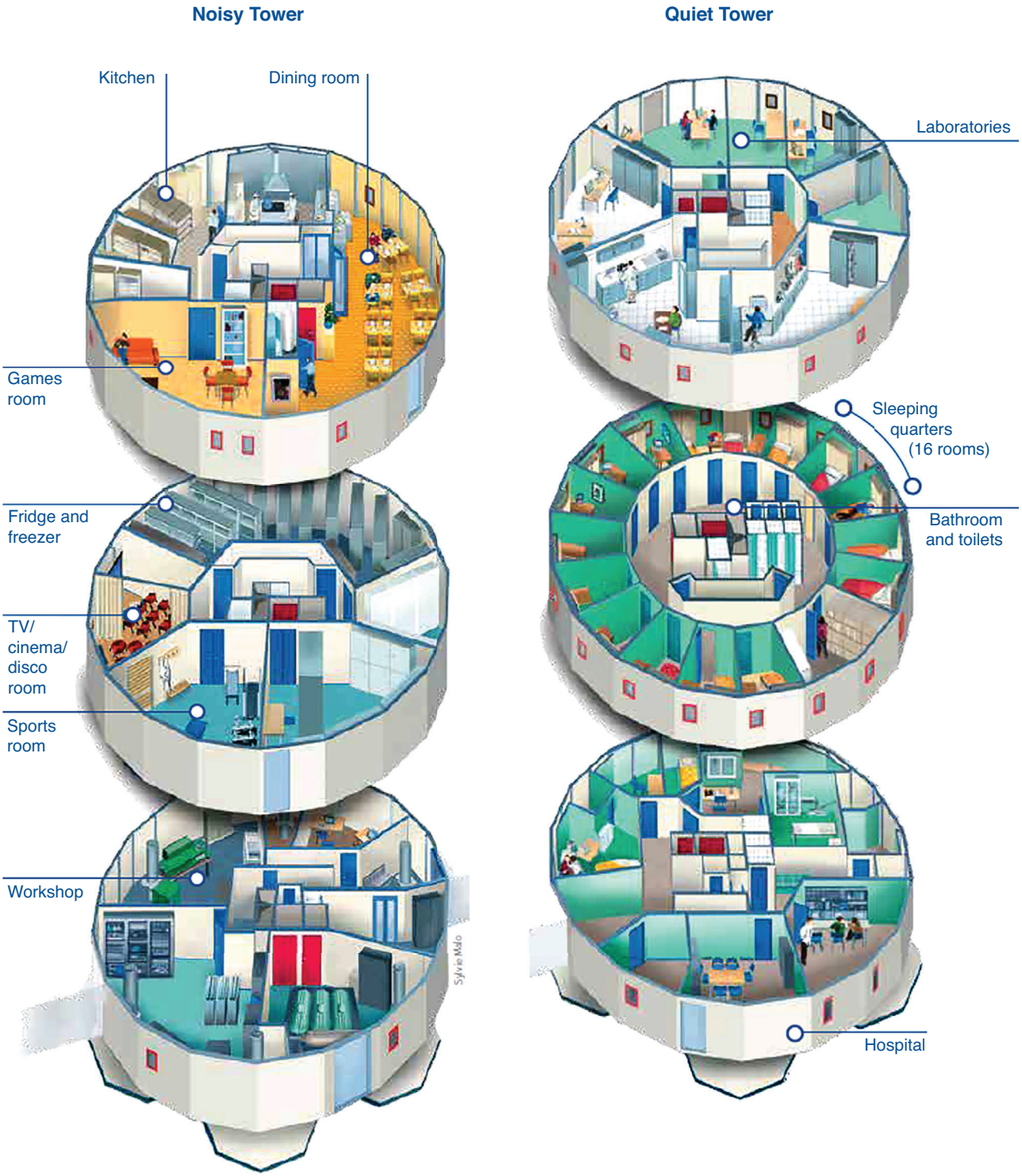

FIGURE 3 Schematic representation of the Concordia station (European Space Agency)

crew members (multicultural factors). These results highlight and give further insight into the role of social (cohesiveness, social support) and occupational (implementation/preparedness, counterproductive activity, decision latitude and psychological job demands) dimensions of adaptation to ICEs. Furthermore, these psychosocial aspects could have important implications for pre-mission selection, monitoring and support in Concordia and re-adaptation post-mission.

The same group also constructed and developed a standardized and integrated tool for evaluation of psychological adaptation processes: the Isolated and Confined Extreme Environments Questionnaire (ICE-Q) (Nicolas, Martinent, Suedfeld, & Gaudino, 2019). With this aim, they included data from a total of 140 French winterers. This first version of the ICE-Q consisted of 90 items covering social, emotional, occupational and physical variables that were reported in

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previous literature from ICE environments. Validation of the ICE-Q was performed and it was shown to be a robust tool to assess in particular the psychological state of adaptation to ICE environments, as well as to assess the effect of psychological support techniques and countermeasures.

Abeln et al. (2015) studied the effect of a long stay in ICE on the interaction of brain activity, mood and cognition. Secondly, they also investigated whether levels of physical activity had an effect on these factors. Based on an activity log, participants were divided into an active (G_{act}; $n = 4$) and inactive (G_{inact}; $n = 4$) group. Findings showed that the active group experienced a steady mood throughout the stay, as well as a decrease in alpha activity (decreasing progressively over time, with maximum decrease of 46% when comparing interval 7 to 1), beta activity (decreasing progressively over time, with maximum decrease of 40% when comparing interval 7 to 1) and concurrent decrease in brain cortical activity. In comparison, inactive people experienced a deterioration in their mood: a negative progression over intervals for perceived psychological strain (decreasing up to 43% at interval 5) and a negative trend for perceived motivational state was seen over time (falling to 28% lower at intervals 5 and 6). The inactive group also exhibited an increase in alpha activity (with an increase of about 44% from interval 1 to 2, then remaining high through intervals 2–7). Cognitive tasks, however, showed no significant influence of isolation or exercise. The results support the notion that exercise may be an important countermeasure against the mood deteriorations that normally result from the chronic stressors of ICE environments.

Also looking at cognitive function in ICEs were Barkaszi, Takács, Czigler, & Balázs (2016). They postulated that ICEs would have a negative effect on cognitive function. Using two cognitive tasks (auditory distraction and attention-based) whilst conducting electroencephalography (EEG) recordings, they did not find any statistically significant deterioration in the cognitive domain, in contrast to their hypothesis and despite the numerous stressors present. These results are in accordance to the study of Abeln et al. (2015).

Gro Sandal and her team monitored how the different coping strategies of Concordia personnel changed over time and investigated the extent to which these changes were linked with changes in mood and sleep (Sandal et al. 2018). They found that at midwinter, when conditions were harshest, resources were more depleted, participants were less involved in any form of coping, and reported less positive affect (effect sizes between 0.32 and 0.82 for coping strategies, depending on use of linear or quadratic time-based models; effect size of 0.43 for positive affect). Reports of negative affect, however, stayed low. There was a reduction in all of the observed coping strategies during the midwinter period, contradicting the idea that chronic stress results in increased use of emotional strategies and avoidance and decreased use of active strategies. Participants seemed to become more indifferent or emotionally flat during winter months, a term the authors called 'psychological hibernation'. The latter has also been described as a symptom of burnout after prolonged stress exposure at work. However, the authors suggested that such a state could possibly be an adaptive response to the prolonged stress of extreme environments, particularly if it disappears once the conditions become less extreme.

A more recent study by Bosch Bruguera et al. (2019) focused on the impact of ICE environments on piloting skills. Indeed, an important factor to understand in preparing for long-duration deep space missions is how it will affect the ability of astronauts to engage in complex skills of which piloting performance is an example. A high-fidelity Soyuz-TMA spacecraft docking simulator was used to recreate a docking manoeuvre to the ISS, one that requires a high level of skill performance in order to control a 6-degrees-of-freedom spacecraft while monitoring other spaceflight parameters in the cockpit. Different flight scenarios were designed to measure performance under different conditions and crew were divided into 'frequent' flyers (FF, once a month) and 'infrequent' flyers (IF, every 3 months). FF pilots improved their success rate up to approximately 97% during the final months of the experiment. IF pilots exhibited an increase in cockpit activation duration over time (100 s in later sessions as compared to median of 40 s in first check flight), compared to a decrease and then maintenance of duration for the FF pilots. The results indicate that training frequency is essential for retaining high concentration and psychomotor skills. Without it, pilots or astronauts may experience increased cockpit activation duration and increases in steering errors. They also suggest that isolation, confinement and hypoxia can increase the decay of piloting performance and other activities requiring high levels of cognitive and psychomotor skills.

2.3 | Sleep

Several studies on sleep and alertness in ICE environments have been performed. The lack of a regular day–night photoperiod has been linked to disrupted sleep in both space and Antarctic stations. Peak circadian sensitivity to light is found in the blue region of the spectrum (460–480 nm), and blue-enriched light in the workplace has been found to enhance subjective sleep quality, subjective alertness and subjective performance compared to regular white light. One study by Najjar and colleagues aimed to investigate the chronic effect of blue-enriched light *versus* white light on circadian entrainment, the rest–activity cycle, mood, and neuro-behavioural responses at Concordia (Najjar et al., 2014). Indoor light was adjusted throughout the 9 weeks of the study. During the starting week, participants were in standard white (SW) light as a baseline. Lighting alternated every 2 weeks after this: during weeks 2, 3, 6 and 7, participants were exposed to blue-enriched (BE) light during the day, and the other weeks they were exposed to SW light. Overall, a significant delay in bedtime and time of lights off was found under SW light compared to BE light weeks (average of 1 h 43 min for SW *versus* average of 1 h 21 min for bedtime; average of 1 h 20 min for SW *versus* average of 0 h 54 min for BW for lights off time). Wake-up time, however, was not different, resulting in a significant decrease in sleep duration during the SW light weeks compared to the BE light weeks (on average 6 h 45 min for SW, 7 h 27 min for BW). No circadian phase delay of melatonin was detected during BE light weeks. In contrast, a significant circadian phase delay was observed

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TABLE 1 Synthesis of the different studies

Study	No. of participants	Sex of participants	Age of participants	Main conclusions
Psychology and neuroscience				
Krins (2009)	9[a]	2♀, 7♂	Not given	• Pro-diversity culture increased likelihood that crew members identified highly with rest of the group • Pro-diversity culture may benefit overall group functioning
Nicolas et al. (2016)	14	1♀, 13♂	Mean ± SD 38.14 ± 11.90 years	• Spending a long time in ICE environments may increase social tension and lead to interpersonal issues • Individuals who feel they have the resources to cope with the environment recover more effectively • Individuals who use more mature defence mechanisms are better suited to adapt to ICE environments
Nicolas et al. (2016)	13	1♀, 12♂	Mean ± SD 37.14 ± 11.90 years	• Social, cultural and occupational factors play a role in the adaptation process during long winter-over stays • These psychosocial aspects could have important implications for pre-mission selection, monitoring and support in Concordia and re-adaptation post-mission
Nicolas et al. (2019)	Overall: 140; Concordia only: 39[c]	25♀, 115♂; Not given[c]	Mean ± SD 34.42 ± 13.34 years Not given[c]	• The ICE-Q is a robust tool to assess psychological state of adaptation, as well as preventative countermeasures and psychological support techniques during and after missions
Abeln et al. (2015)	8 (G_{act} = 4; G_{inact} = 4)	0♀, 8♂	G_{act}: mean ± SD 42.3 ± 8.8 years G_{inact}: mean ± SD 37 ± 5.6 years	• Exercise may be an important countermeasure against the mood deteriorations that normally result from the chronic stressors of ICE environments • No significant deterioration in cognitive function was found
Barkaszi et al. (2016)	13	0♀, 13♂	Age range: 20–55 years	• No significant deterioration in cognitive function was found
Sandal et al. (2018)	27	3♀, 24♂	Mean ± SD 38.3 ± 10.64 years	• Coping strategies change throughout the year, indicating an influence of seasonal factors • 'Psychological hibernation', i.e. detachment and emotional flattening, could possibly be an adaptive response to prolonged stress in ICE environments
Bosch Bruguera et al. (2019)	Overall: 69; Concordia only: 23[c]	13♀, 56♂; 3♀, 20♂[c]	Age range: 20–70 years Not given[c]	• Training frequency is essential for retaining high concentration and psychomotor skills. Fewer training sessions showed increased cockpit activation duration and increases in steering errors • Isolation, confinement and hypoxia can increase the decay of piloting performance and other activities requiring high levels of cognitive and psychomotor skills
Sleep				
Najjar et al. (2014)	10	2♀, 8♂	Mean ± SD 30 ± 2.1 years	• A significant decrease in sleep duration was found during the SW light weeks compared to the BE light weeks • BE could be used as a countermeasure to circadian disorders, and well-being and alertness decrements
Tellez et al. (2014)	13[b]	0♀, 13♂	Mean ± SD 39 ± 9.8 years	• Periodic breathing prevailed for the major part of sleeping time in most of the crew. This could impair sleep quality, leading to fatigue, a reduction in productivity and a higher error probability • Significant and stable inter-individual differences suggest that some people respond to hypoxia with severe period breathing and others do not
Collet et al. (2015)	Overall: 26; Concordia only: 8[c]	5♀, 13♂; 0♀, 8♂[c]	Not given Median ± SD 36 ± 9.8 years[c]	• Constant daylight in summer leads to higher sleep fragmentation and night-time energy expenditure • Hypoxia has a negative effect on sleep, probably due to periodic breathing

(Continues)

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TABLE 1 (Continued)

Study	No. of participants	Sex of participants	Age of participants	Main conclusions
Kawasaki et al. (2018)	Overall: 25; Concordia only: 13[c]	7♀, 18♂; 3♀, 10♂[c]	Not given Mean ± SD 34.6 ± 11.0 years[c]	• During long-term daylight deprivation, retinal sensitivity to blue light increases, whereas circadian rhythm stability decreases and sleep–wake timing is delayed
Mairesse et al. (2019)	13	0♀, 13♂	Mean ± SD 4.54 ± 9.46 years	• Increased sleep latencies and severe periodic breathing throughout the winter; gradual decrease in psychomotor speed and increase in fatigue over time in crew with variable schedules • Overall large inter-individual variability and responses remain relatively stable under prolonged exposure, indicating trait-like characteristics of sleep • Pre-departure performance and polysomnographic monitoring can be important for the selection of candidates for (extra)terrestrial missions
Cardiovascular physiology				
Venemans-Jellema et al. (2014)	Overall: 49; Concordia only: 25[c]	24♀, 25♂; 0♀, 25♂[c]	Not given Mean 38.0 years[c]; SD not given[c]	• Long-term hypoxia exposure without immobilization does not increase the risk of venous thrombosis
Immune system				
Crucian et al. (2011), Feuerecker et al. (2012, 20142014)	9	0♀, 9♂	Mean ± SD 39.1 ± 11.8 years	• Oxygen saturation and heart rate changes in line with the expected physiological changes accompanying high altitude exposure • Lowered innate immune response found was not due to acute psychological stress
Strewe et al. (2018a, b)	Overall: 31; Concordia only: 15[c]	0♀, 31♂; 0♀, 15♂[c]	Not given Mean ± SD 39.1 ± 2.8 years[c]	• Exposure to an extreme environment enhances the endocannibinoid response, but exposure to hypobaric hypoxia may downregulate this response • High inter-individual variability in acclimatization responses to high altitude

[a]50% drop-out in $n = 9$ after first measurement. [b]Two subjects dropped out resulting in $n = 11$ at the end of the study. [c]The sample size and female distribution from the Concordia part of the overall experiment. ♀: number of females in the study and ♂: number of males in the study. BE, blue-enriched light; G_{act}, active subgroup; G_{inact}, inactive subgroup; ICE, isolation, confinement and extreme environments; SW, standard white light.

during weeks SW5 and SW9 under SW light. Subjectively assessed motivation significantly increased generally over the course of the study. Subjective well-being (average of +9.7% and +14.5% on week 3 and week 7 of BE, respectively) was significantly increased under BE light compared to SW light (−2.96% and +3.2% during week 5 and week 9 of SW light, respectively). Subjective alertness was marginally increased on weeks 3 and 7 under BE light compared to SW light weeks 5 and 9 (not significant). In conclusion, the authors suggested that BE is capable of correcting, or avoiding, circadian phase delay and sleep loss during polar winter that would otherwise occur under regular daytime SW light. BE light could be used as a countermeasure to circadian disorders, and well-being and alertness decrements in conditions where light levels are chronically low or moderate during the daytime, and solar light not available for extended periods of time.

Another study by Tellez et al. (2014) investigated periodic breathing under long-term exposure to hypoxia. The participants' acclimatization to the conditions at Concordia were monitored, as well as nocturnal breathing patterns. Symptoms of acute mountain sickness (AMS) were below clinical significance within the first 3 weeks after arrival. Due to periodic breathing, the average number of apnoeic/hypnoeic events per hour was above the level clinically considered severe and persisted throughout the stay, despite AMS absence. Their most important finding was that during the entire 13-month campaign, for most of the participants, periodic breathing prevailed for the major part of sleeping time. Marked inter-individual differences in the results suggest the existence of responders and non-responders in terms of periodic breathing.

A follow-up study by the same group also investigated how sleep is affected by a hypobaric hypoxic environment and by irregular photoperiods by collecting data from Concordia and Dumont d'Urville (DDU, a sea-level station at Antarctica) (Collet et al., 2015). No differences for daylight parameters were found. For night-time parameters, total sleep time (TTS) was significantly longer and sleep efficiency (SE) significantly higher at DDU than at Concordia (TTS: mean ± SD 427.4 ± 42.4 min at DDU *versus* 382.9 ± 57.5 min at Concordia; SE: 90 ± 4.8% at DDU *versus* 83.2 ± 8% at Concordia . Analyses also revealed a significantly longer wake after sleep onset for Concordia participants than for DDU (85.7 ± 44.6 min for Concordia *versus* 42.2 ± 28.7 min for DDU). Sleep fragmentation (Fr) and night-time energy expenditure (EEn) were significantly higher in the summer than

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in the winter on both stations (Fr: mean ± SD of 10 ± 7 episodes in summer *versus* 7 ± 5 episodes in winter; EEn: 2814.5 ± 559.7 J) in summer *versus* 2501.5 ± 559.7 J in winter). The authors suggest this may be due to circadian desynchronization caused by melatonin secretion delay due to constant daylight in summer. The paper also concluded that hypoxia has a significant effect on sleep, likely due to periodic breathing.

Kawasaki et al. (2018) studied the effect of long-term daylight deprivation on retinal sensitivity, sleep and circadian rest–activity. Since artificial light is quantitatively and qualitatively different from natural light, it is important to understand its impact on human health, particularly in places like Concordia where it is the primary source of light during long winter periods. Overall, there was an increased retinal sensitivity after the disappearance of natural daylight. This was determined from pupil responses to stimulus protocols and was also clearly observed from post-illumination pupil response, the biomarker that was used for melanopsin sensitivity. Circadian rhythm analysis revealed a significant decay of intra-daily stability, indicating more fragmented rest–activity rhythms during the dark period. Sleep and wake were significantly delayed after the first month without sunlight. These results suggest that during long-term daylight deprivation, retinal sensitivity to blue light increases, whereas circadian rhythm stability decreases and sleep–wake timing is delayed.

In the most recent study, Mairesse and colleagues (2019) studied the effect of sleep problems on psychomotor problems. Participant acclimatization was monitored upon arrival and sleep and psychomotor measures were conducted throughout the winter season. Overall, results revealed increased sleep latencies and severe periodic breathing throughout the winter. There was an increase in obstructive respiratory events towards the end of the stay. Crew members had frequent cases of dry nose, nasal obstruction and sore throat, likely caused by inflammation resulting from chronic exposure to extremely dry air. Such inflammation may have increased pharyngeal collapse and increased the occurrence of obstructive sleep apnoea by the end of the winter period. Findings also indicated that though most people develop changes in their circadian rhythmicity due to extreme photoperiods, those who maintain steady sleep schedules experience fewer subjective sleep difficulties. Crew with variable schedules also showed a gradual decrease in psychomotor speed and an increase in subjective fatigue over time. One important finding from this study was that most of the affected sleep, vigilance and performance parameters exhibit inter-individual differences with at least moderate degrees of stability and robustness, implying that person-specific characteristics play a considerable role in how humans respond to extreme conditions. As such, these results emphasize the importance of performance and polysomnographic monitoring for the selection of candidates for such missions.

2.4 | Cardiovascular physiology

The team of Venemans-Jellema investigated the separate effects of immobilization and hypoxia on markers of coagulation and thrombosis in healthy subjects (Venemans-Jellema et al., 2014), using both Concordia participants and participants in a bed rest study. Their main aim was to investigate the role of hypoxia in the development of venous thrombosis (VT). A case of VT has recently also been described in an astronaut in spaceflight (Auñón-Chancellor, Pattarini, Moll, & Sargsyan, 2020). There are many risk factors for VT, but one risk factor is long-distance air travel (found to increase the risk by two- to fourfold). A possible explanation for this has been immobilization. However, previous studies have indicated that immobilization is not a sufficient explanation for thrombosis in flights. As such, hypoxia was proposed as a possible contributing factor. At Concordia, no increase in coagulation markers was found, suggesting that long-term hypoxia exposure without immobilization does not increase the risk of venous thrombosis.

2.5 | Immunology

Feuerecker et al. investigated the effects of confinement and hypobaric hypoxia on the human immune system by studying the role of the hypoxia–adenosine–immune modulation pathway (Crucian et al., 2011; Feuerecker et al., 2012, 2014). In addition, they studied changes in hormonal and psychological stress levels during early adaptation at Concordia (Crucian et al., 2011; Feuerecker et al., 2012, 2014). Oxygen saturation levels decreased significantly from 98–100% at baseline to 85.7% at week 1 and 88.7% after 1 month. Resting heart rate also increased significantly from 71 bpm at baseline to 79 bpm (1 week) and 80 bpm (1 month). Such changes are in line with the expected physiological changes accompanying high altitude exposure. It was found that the cytotoxic function of granulocytes was mitigated in the first week despite a significant increase from baseline levels. Plasma adenosine concentrations increased slightly at week 1, with a return to baseline after 1 month at Antarctica, likely as a response to the hypoxia. Night-time urinary noradrenaline levels increased significantly in the first month. This, combined with the granulocytosis indicated an early stress response to lowered oxygen tension. No changes in the stress questionnaires was found and salivary cortisol concentrations remained within normal ranges showing no significant changes over time, indicating that the lowered innate immune response found was not due to acute psychological stress.

In another study from the same team it was investigated how chronic hypobaric hypoxia affects the stress-related endocannabinoid system (ECS) (Strewe et al., 2018b), which plays an important role in coping with stress reactions. Results revealed a significant increase (up to 10-fold) of stress-related metabolites under normoxic conditions at Neumayer, a German Antarctic station at sea-level. In contrast, in the Concordia crew, levels of stress metabolites stayed low until the end of the isolation period when an increase was observed. Urine noradrenaline, however, increased significantly at the start of the stay only for the Concordia crew and then returned to baseline over time (baseline data collected 2–4 months before departure to Antarctica yielded an average of 19.07 ± 1.88 mg up to an average of 42.18 ± 7.87 mg in February of the winter-over season) and

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stayed on a significantly elevated level until April. Peak values were already reached in February before levels decreased slowly and constantly till July. Cortisol levels showed no changes. The authors suggest that exposure to an extreme environment enhances the EC response, but that exposure to hypobaric hypoxia may downregulate this response. They propose a potential mechanism (not investigated in the study) behind this downregulation: a hypoxia-induced upregulation of an enzyme (cyclooxygenase 2) that oxidizes ECs. No significant changes were found regarding subjective stress levels.

3 | DISCUSSION

Because of the currently limited possibilities for access to space in general, the ability to study individual and group functioning in the actual space environment has been, and will continue to be, severely limited. In addition, the psychology of space travel remains a sensitive subject. Therefore, studying groups in such extreme ground-based analogues is an excellent opportunity to look into the many factors that impact group performance, health and well-being under challenging environments.

Long-duration winter-over missions at the Concordia station induce alterations in various physiological systems and psychological function: a plethora of biomedical studies implemented at Concordia station have reported changes in psychological measures, mood parameters, sleep quality, cardiovascular and immunological responses, to name but a few.

One important area of research in these studies is coping strategies, because they help us to better understand how exactly crew in long winter-over stays deal with the ICE environment, and in addition, they may help to select those crew members that are better suited to cope, which in its turn has a positive impact on mission success. Perceived control has been shown to be linked to a better total recovery, an overarching dimension including success, social relaxation, somatic relaxation, general well-being and sleep quality (Nicolas et al., 2016). Furthermore, mature defence mechanisms, using problem-solving strategies, has been shown to be more beneficial than immature defence mechanisms (based on behavioural withdrawal of acting out) for coping purposes (Nicolas et al., 2016). Coping has also been shown to be influenced by the time of the year (seasonal effects), up to the extent that during winter months, winterers became more indifferent (Sandal, van de Vijver, & Smith, 2018). This sort of 'psychological hibernation' has been suggested to be a coping strategy in itself. This is an important finding, as it indicates that this psychological detachment can be beneficial in coping, and as such, could have implications for countermeasures, i.e. that stress amelioration techniques like yoga, meditation and self-hypnosis could be beneficial (Sandal et al., 2018). The importance of adaptation and coping mechanisms, as well as supporting techniques in-mission, is underpinned by the need for and development of a specific questionnaire to assess this: the ICE-Questionnaire (ICE-Q) (Nicolas et al., 2019). In parallel to psychological coping, physiological coping is also necessary. It has been shown that exposure to a physically challenging and physiologically new and unknown environment with extreme conditions, like Concordia, generates a neuroendocrine reaction pattern of interacting physiological systems (Strewe et al., 2018b).

Related to coping mechanism are countermeasures. Identifying suitable countermeasures is key for risk mitigation and minimizing the changes acquired in ICE environments. One study looked at exercise and found it to have a positive effect on mood, i.e. keeping it more stable throughout the winter-over period (Abeln et al., 2015). Regularly performed and voluntary exercise can support (subjective) well-being of people in ICE environments, which is also relevant directly for spaceflight and even terrestrial groups related to an increasing inactive and ageing population. In another study, blue-enhanced light was found to be an effective countermeasure for circadian disorders (Najjar et al., 2014). In addition, it also enhanced alertness and general well-being (Najjar et al., 2014). This is also relevant for conditions in which light levels are chronically low, such as in polar base stations, power plants, submarines, workspaces lit with solely artificial light and space missions due to the lack of sunlight.

Some of the described studies have also suggested considering some of their findings for selection of winterers. Nicolas et al., for example, put forward that social, cultural and occupational components should be considered during selection of the crew as these factors can directly influence adaptation to ICE environments (Nicolas et al., 2016). They also suggested pre-mission training at a group and individual level. On a more physiological level, it was suggested taking into account pre-departure performance and polysomnographic monitoring as it has been shown that there might be certain sleep phenotypes similar to trait-like characteristics (Mairesse et al., 2019). Just like for pre-mission, some studies also suggested focusing on offering (psychological) support techniques or facilitating the re-adaptation process post-return.

Some limitations are inherent to the Antarctic environment. Sample sizes are usually limited and in addition, there is a strong dominance of males for the crew (see Table 1 for an overview). As such, there are very little data on female winterers. Furthermore, there are operational constraints that make it difficult to conduct certain studies or limit measurement procedures to a stripped-down version. Furthermore, the pre- and post-mission time window to test crew is relatively limited. Lastly, it is not always possible to differentiate which of the specific effects (hypoxia *vs.* confinement, etc.) are responsible for specific changes. However, it can be argued that space environments also result in the interaction of different factors (radiation, microgravity and confinement) and such interactions are an important consideration. Additionally, by comparing different stations or analogues, some of these complex interactions may be better understood. Indeed, studies at Concordia are also often implemented at other Antarctic stations such as Neumayer-Station III or Durmont d'Urville for the very purpose of exploring hypoxic *vs.* confinement effects. However, the challenges at Concordia are still only a fraction of those that are present in human spaceflight and astronaut studies. Higher sample sizes can usually be achieved in a shorter time frame, crew time and accessibility are less

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restricted (allowing multiple measurement points in-mission and as such increasing statistical validity of the data) and operational and hardware constraints are less.

Overall, the Concordia station provides a high-fidelity environment to test the impact of long stays in ICE environments on physiological and psychological function in humans. As such, it is a very important testbed to advance crewed space missions, especially with an eye on future interplanetary missions. Missions to, for example, Mars will require a high autonomy, crew will be isolated and confined for a very long period, interpersonal issues may arise, and monotony and boredom will highly likely show, especially *en route* to and from Mars. Furthermore, environmental aspects will play an important role.

As indicated earlier, the location of the Concordia station continuously exposes its crew members to hypobaric and hypoxic conditions. This is especially relevant for human exploration missions because future planetary vehicles and habitats will most likely be hypobaric and hypoxic, therefore a better understanding of the effects of altered atmospheric conditions is important and exploration-relevant. Unsurprisingly, these environmental stressors can have an impact on various physiological and even psychological functions, such as sleep (Collet et al., 2015; Mairesse et al., 2019; Tellez et al., 2014), immune responses (Crucian et al., 2011; Feuerecker et al., 2012, 2014; Strewe et al., 2018b) and cognitive skills like piloting performance (Bosch Bruguera et al., 2019). Furthermore, there seems to be a high individual variability in acclimatization to these high altitudes (Mairesse et al., 2019; Strewe et al., 2018b; Tellez et al., 2014). Other ground-based platforms have also specifically looked at physiological and psychological alterations induced by a changing environment, e.g. by conducting bedrest studies in hypoxic environments (PlanHab and Lunhab studies; Ciuha, Eiken, & Mekjavic, 2015; Keramidas, Mekjavic, & Eiken, 2017; McDonnell, Eiken, Frings-Meuthen, Rittweger, & Mekjavic, 2019; Rullman, Mekjavic, Fischer, & Eiken, 2016; Salvadego et al., 2018; Šket et al., 2017; Strewe et al., 2017, 2018a). The ESA aims to further build upon this in the future and has initiated preparations for a 60-day head down tilt bedrest study at the Planica Nordic Centre in Slovenia, allowing environmental pressure and oxygen parameters to be altered. The unique feature of the Concordia station is that it can offer the combination of the ICE environment and chronic hypobaric and hypoxic exposure.

Last but not least, apart from all those physiological and psychological topics addressed in this review, Concordia station also serves ideally for testing, validating and preparing technologies for future interplanetary missions. As a matter of fact, the dependence on technology for survival is an important parallel to the dependence astronauts have on advanced technology for environmental control, communication and general survival.

In conclusion, Concordia and Antarctic stations in general are without doubt a very valuable and well-suited ground-based platform to get a better understanding of the challenges we face to prepare humans for the tremendous task of long-duration spaceflight further into our solar system and in particular, to test countermeasures to mitigate the risks associated with it.

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COMPETING INTERESTS

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

A.R. performed the literature review. A.R., A.V.O. and T.J.N wrote the main manuscript. All authors reviewed the final version of the manuscript. All authors have read and approved the final version of this manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All persons designated as authors qualify for authorship, and all those who qualify for authorship are listed.

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