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► To cite this version:

Barbara Le Roy, Charles Martin-Krumm, Nathalie Pinol, Frédéric Dutheil, Marion Trousselard. Human challenges to adaptation to extreme professional environments: A systematic review. *Neuroscience and Biobehavioral Reviews*, 2023, 146, pp.105054. 10.1016/j.neubiorev.2023.105054. hal-04389117

HAL Id: hal-04389117

<https://hal.science/hal-04389117>

Submitted on 24 Jan 2024

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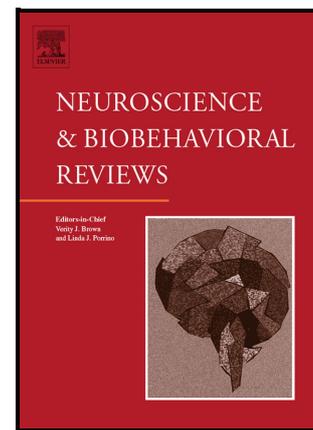
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PII: S0149-7634(23)00023-4

DOI: <https://doi.org/10.1016/j.neubiorev.2023.105054>

Reference: NBR105054

To appear in: *Neuroscience and Biobehavioral Reviews*

Received date: 4 January 2022

Revised date: 16 January 2023

Accepted date: 17 January 2023

Please cite this article as: Barbara Le Roy, Charles Martin-Krumm, Nathalie Pinol, Frédéric Dutheil and Marion Trousselard, Human Challenges to Adaptation to Extreme Professional Environments: A Systematic Review, *Neuroscience and Biobehavioral Reviews*, (2022) doi:<https://doi.org/10.1016/j.neubiorev.2023.105054>

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Human challenges to adaptation to extreme professional environments: a systematic review

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Abstract: 163 words

Manuscript: 18 382 words

Abstract

NASA is planning human exploration of the Moon, while preparations are underway for human missions to Mars, and deeper into the solar system. These missions will expose space travelers to unusual conditions, which they will have to adapt to. Similar conditions are found in several analogous environments on Earth, and studies can provide an initial understanding of the challenges for human adaptation. Such environments can be marked by an extreme climate, danger, limited facilities and supplies, isolation from loved ones, or mandatory interaction with others. They are rarely encountered by most human beings, and mainly concern certain professions in limited missions. This systematic review focuses on professional extreme environments and captures data from papers published since 2005. Our findings provide an insight into their physiological, biological, cognitive, and behavioral impacts for better understand how humans adapt or not to them. This study provides a framework for studying adaptation, which is particularly important in light of upcoming longer space expeditions to more distant destinations.

Keywords:

Adaptation, Extreme and Unusual Environment, Health, Isolated and Confined Environment, Neurosciences, Stress

Acronyms

BDNF: Blood brain Derived Neurotrophic Factor

CELSS: Controlled Ecological Life Support System

EBP: Evidenced Based Practice

EUE: Extreme and Unusual Environments

GRADE: Grading of Recommendations Assessment, Development and Evaluation

HERA: Human Exploration Space Analog

HI-SEAS: Hawaii Space Exploration Analog and Simulation

HF: High Frequency

HRV: Heart Rate Variability

ICE: Isolated and Confined Environments

ISS: International Space Station

LF: Low Frequency

pNN50: Proportion of number of pairs of successive NN intervals that differ by more than 50 ms divided by the total number of NN intervals

NEEMO: NASA Extreme Environment Mission Operations

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

RMSSD: Root Mean Square of Successive Differences

SAD: Subsyndromal seasonal Affective Disorder

SIRIUS: Scientific International Research In a Unique terrestrial Station

SSBN: Sub-Surface Ballistic Nuclear-powered missile submarines

1. Introduction

“At the closing of this century, Homo Sapiens might well be described as an interstitial species. We are not just between two time periods, but between two ways of life. As we make the transition into the 21st century, humankind is being transformed from a terrestrial to an extraterrestrial being. In the process of this transformation, our species will be changed both physically and psychologically. The survival of the species in outer space demands significant adaptation to differing environmental realities”. Harris (1989)

On July 20, 1969, the world held its breath as American astronaut Neil Armstrong became the first man to set foot on the Moon. More than 50 years later, interest in space has been renewed by the exploration of Mars. Although views differ, space missions are vectors

for major technological and scientific advances. A key development, in this new era, is that partnerships with private companies are driving progress. SpaceX became the first private entity to refuel the International Space Station (ISS) and, more recently, transport space travelers (November 16, 2020). Although space agencies were planning a permanent human presence not only onboard the ISS, but also the Moon and Mars (Harrison et al., 1989; National Commission on Space, 1986) in the 1990s, according to NASA Administrator Jim Bridenstine, a return to the Moon is not expected until around 2024, followed by a mission to Mars around 2033. A journey to Mars would require space travelers to spend nearly three years in space and, during this time, they will be confronted with extreme physiological and psychological conditions. Although nearly 600 space travelers have already been in space, fewer than ten have stayed for a significant period of time (i.e., missions usually do not last longer than six months, even though increasingly records are being achieved). It is therefore urgent to evaluate and understand the impact of a long space flight on the physiology and psychology of human beings.

1.1. Beyond the stars: the hazards of space

Space is a naturally hostile environment. Space travelers onboard the ISS are isolated for around six months to one year from the 'normal' world (Collet & Vaernes, 1996), and spend most of their time working. Space is characterized by weaker gravity and various physical and psychological stressors (Borchers et al., 2002). It places high demands on their resources and can compromise performance. Physical stressors include the 90-minute orbit of the ISS, which means that the day is artificially divided into 16 sunrises/sunsets; gravitational forces during launch and landing, vibration, noise, microgravity, radiation, increased microbial load, and malnutrition due to motion space sickness. Psychological stressors include anxiety related to the danger of the mission and the hostile environment, the inability to return

to Earth, the intense workload, isolation from family, friends and normal social settings, and the difficulty of living together as a small group for a long period.

These space stressors have long-term repercussions. Microgravity is cited most often. Effects include physiological changes in vestibular input, and bone and mineral metabolism, a shift of fluids to the upper parts of the body, and disturbed proprioceptive processes (Bettioli et al., 2018; Clément, 1998; Grimm et al., 2017; Hughson, 2018; Nicogossian et al., 1994; Patel, 2020; Van Ombergen et al., 2017a; Van Ombergen et al., 2017b; Vernikos, 1996). However, astronaut Norm Thagard reported that during the Mir-18 mission, psychological stress, isolation, and confinement were the main challenges (Lugg & Shepanek, 1999). Manzey et al. (1998) developed new categories of stressors that include the space habitat and its life support system (e.g., confinement, high levels of ambient CO₂ and noise), workload (both physical and mental), and social aspects (e.g., lack of privacy, distance from loved ones) (Manzey et al., 1998). Furthermore, risk is an integral part of the mission. The inhospitable space environment can quickly become the only sanctuary if there is an equipment malfunction, or a collision with an external object (Connors et al., 2005).

1.2. Extremes on Earth: a challenge for research

Space travelers who travel to another planet or participate in a long-term space mission are confronted with a harsh environment. The multitude of constraints they face are difficult to replicate on Earth. However, there are some terrestrial environments that can be used to study and predict the effects of long-duration space travel on the human body.

Manzey and Lorenz (1998) define extreme environments as, “settings that possess extraordinary physical, psychological, and interpersonal demands that require significant human adaptation for survival and performance” (Manzey & Lorenz, 1998). These

environments share several characteristics – notably constant danger, the need for a high-tech life support system, a lack of space, isolation, discomfort, lack of external visibility, specific clothing, unusual photoperiodicity, lack of intimacy, and possibility of sudden disaster. Often cited as Isolated and Confined Environments (ICE), or Extreme and Unusual Environments (EUE) (Suedfeld & Mocellin, 1987), they have also been named ‘strange’, ‘exotic’, ‘abnormal’, or ‘stressful environments’ (Bachrach, 1982; Harrison & Connors, 1984; Ross, 1974). Suedfeld (2000, 2018) differentiated the characteristics of ICE and EUE. The physical parameters of EUE do not allow humans to survive, giving them an aura of rarity and exoticism, or even fear and wonder. They often require sophisticated, and high-tech survival systems. The failure of which can lead to death. ICE may be a specific category of EUE, which feature physical remoteness or a lack of access to other locations. Whether permanent or temporary, they can be termed ‘extreme’ due to the temperature, altitude, level of danger, lack of access to food, water, shelter, and other resources necessary for safety and comfort. These ICE and EUE environments are extremes.

Extreme environments on Earth include polar stations, Sub-Surface Ballistic Nuclear-powered missile submarines (SSBN), expeditions, and simulations of future space missions (Bishop, 2013; Botella et al., 2016; Feichtinger et al., 2012; Kanas, 1990; Lugg, 2005; Schlacht et al., 2016; Shepanek, 2005; Suedfeld, 2010; Suedfeld & Steel, 2000; Tortello et al., 2018; Ursin, 1991; Van Ombergen et al., 2021; Wharton et al., 1990). They are usually related to the space environment and used as ‘space analogs’. More specifically, analogs are environments that aimed to support or simulate space missions. Thus, they share common characteristics with the space environment and the population target to prepare future space mission (Binsted et al., 2010; Leboeuf, 2008). Individuals who spend time in them require complex support operations to survive and be autonomous. In the context of space exploration, future space travelers must be selected, prepared for, and protected from the

negative effects of the extreme conditions they will encounter (Pagel & Choukèr, 1985). The Antarctic is typically considered a natural laboratory for the study of the effects of isolation and confinement on human behavior (Suedfeld & Weiss, 2000; Shurley, 1974). This ice desert is one of the coldest and most hostile places on the planet, and many scientific studies have been run since its discovery (Bruguera et al., 2021; Gunderson, 1974a; Gunderson, 1974b; Palinkas, 1992; Palinkas & Suedfeld, 2008; Suedfeld, 1991; Taylor, 1987; Van Ombergen et al., 2021). Polar winterers are exposed to around 24 hours of daylight during the austral summer, and around 24 hours of darkness during the austral winter. Like the space environment, time spent in Antarctica is characterized by prolonged isolation, confinement with a small number of individuals, monotony, sensory deprivation, extreme temperatures, and no way to escape, among other factors. More recently, the SSBN is another environment considered as a faithful analog of a space mission (Sauer et al., 1996). Due to their similarities, several parallels can be drawn between an SSBN and a space habitat: (1) autonomous crews, (2) pressurized life capsule, (3) major disasters in case of loss of power, (4) monitored indoor temperatures and radiation levels, (5) distilled and reused water, (6) regenerated and cleaned atmosphere, (7) significant risk of fire and toxic smokes, (8) confined and limited space, (9) significant noise levels, (9) crew members limited, (10) and heavy workload (Earls, 1991; Kanas, 1987; Sandal et al., 2006; Ursin et al., 1991; Vakoch, 1991; Weybrew, 1991; Weybrew & Molish, 1986).

1.3. Exploring analogs: a response to the need for studies in ecological environment

Studies in an ecological environment are a unique opportunity to collect data that a traditional research laboratory cannot provide. Although they require the implementation of advanced technologies to ensure the protection and maintenance of life in a life-threatening environment. Their extreme nature provides valuable information about human adaptive

capabilities. Polar stations and SSBN are examples of ecological environments that have similar requirements in terms of selection procedures, nature of the work, and crew composition. Furthermore, the risks are high, and the costs associated with failure. There are multiple critical interfaces (i.e., human-human, human-technology, and human-environment), and critical requirements regarding coordination, cooperation, and communication within the team (Bishop, 2006; Davis et al., 2021). Polar bases are particularly useful, as they can provide access to more participants. Data are plentiful, meaning that results are more generalizable, and have a greater impact within the scientific community. Cost is another significant factor (Harrison et al., 1991; National Research Council, 1998a; Palinkas, 2003; Rivolier, 1997). Analog environments can lower these costs and facilitate the implementation of long-term experiments. The latter is an essential consideration for future long-duration space missions. Space travelers currently spend an average of six months onboard the ISS, but a journey to Mars would take about two years and a half.

In general, analog environments provide high-fidelity, standardized experimental conditions (Pagel & Choukèr, 2016). They enable in-depth evaluations of the effects of physiological and psychological changes on human health and can help address specific problems related to space missions (Yuan et al., 2019). However, several key aspects of the space environment cannot be replicated. Microgravity and the risk of radiation are difficult to assess on Earth. These risks vary greatly with respect to both the degree, and the nature of the challenges they present to individuals, especially on Mars (Kanas et al., 2007) where distance plays an important role (Retm, 2015). Furthermore, there are clear differences at the individual level, and between analogs. The number of crew members is very different, as their social and demographic characteristics (Palinkas et al., 2000; Suedfeld & Weiss, 2000). Other aspects cannot be replicated, notably the level and source of danger. The distance from Earth is another aspect that is specific to space missions. On the one hand, space travelers do not

necessarily have access to support from the ground. On the other hand, analog studies of physio-psycho-cognitive responses cannot truly reflect the extraordinary reality of space. One example is the impact of the *Earth-out-of-view phenomenon* on the psyche of individuals. Deep in the vacuum of space, Earth will be so far away that it will become a memory. Kanas (2005) suggests that the consequence could be a deep feeling of loneliness and isolation. Effects could range from a restructuring of the conception of humanity's place in the cosmos, to no impact at all. Overall, these issues compromise how faithfully analogs can replicate long-term space missions.

1.4. Extreme stressors and adaptation: similarities with space

Herman and Cullinan (1997) characterized space flight and analogs by the presence of systemic (e.g., hypoxia, noise, isolation) or processive (e.g., lack of privacy, monotony, fatigue) stressors. They represent two different stress pathways that differ in both their temporality, function and cerebral structures involved. Systemic stressors involve immediate physiological threat and thus survival response through a direct pathway to the hypothalamic paraventricular nucleus. Processive stressors have no temporality. They imply a « high-order sensory processing » through the limbic system, using multimodal stimuli that are confronted to previous experiences and labelled « stressful » or « unstressful ». These repeated, multiform, and combined factors can induce high levels of stress, with adverse consequences on health (Cunha et al., 2021; Décamps & Rosnet, 2005; Farrace et al., 1999; Harrison et al., 1989; Orasanu & Lieberman, 2011; Salam, 2020; Stuster, 2010; Stuster et al., 2000; Suedfeld & Weiss, 2000; UK report, 2019) and increased operational risks, as long-term stress tends to degrade human performance (Suedfeld, 2001). While studies of crew members onboard a SSBN report higher levels of cortisone compared to baseline, and higher levels of stress

during the mission (Sandal et al., 2003), we still know little about how stress is experienced by individuals in ICE/EUE.

Sources of stress in ICE/EUE can be divided into five, interacting categories (McPhee & Charles, 2009; Sandal et al., 2006; Smith et al., 2018; Suedfeld & Steel, 2000; Vakoch, 2011, 2013; Vanhove, 2014). (1) *Environmental stressors* relate to the harsh environment. They include microgravity, radiation, extreme temperatures, noise, the atmospheric composition (i.e., helium-oxygen mixtures that increase the risk of fire, CO₂ levels), monotony, isolation, altitude, and light-dark cycles. (2) *Physical and psychological stressors* relate to the confined environment. They include limited space, separation from loved ones, a lack of privacy, psycho-cognitive-emotional challenges, somatic problems, loss of body heat, increased risk of ear infections, the absence of an opportunity to withdraw or escape from the situation, sensory restriction, and overwork. (3) *Social stressors* relate to interpersonal relations. They include conflict, social monotony, communication, leadership, crew size, gender, or culture. (4) *Seasonal stressors* relate to the passage of time. One critical characteristic is the mission length, due to its interaction with physical and psychological stressors. Not only are there critical phases (e.g., after the halfway point), but there are also cumulative effects whose long-term impacts can be significant. In this review, we focus on temporal aspects these seasonal effects are not dependent of these environments. (5) *Post mission stressors* relate to the re-entry shock after a long time away. Experience shows that it can be difficult to readjust to normal life. Problems can be physical, especially for space travelers, who are unable to stand. They can also be familial. Long periods of separation can be difficult for couples. Submariners, for example, experience ‘submariners wives’ syndrome (Glisson et al., 1980; Isay, 1968). Finally, personality changes can occur (Frantzidis et al., 2019; Kanas et al., 2009; Retm, 2015). Table 1 summarizes the major stressors experienced by individuals in ICE and EUE. Analogs are thus spaces close to the space environment

because they challenge the man who settles there to adapt to close or even similar stressors. These analogues challenge the possibilities of human adaptation just as space does.

Let humans live in space raises the question of adaptation and thus, the preservation of the state of homeostasis retrieved in a new environment of life. Adaptation is a dynamic, polysemic and multidisciplinary concept of evolution of the species and thus of natural selection which attempts to determine the probability of survival of an organism. In order to avoid any confusing aspect regarding the definition of adaptation, we use this term to refer a process that delivers positive and successful health outcomes. Obviously, adaptation does not allow to adjust with the physical requirements of the environment but only acclimatization (i.e., physiological, biochemical, and anatomical changes in an individual after exposure to a new environment from days to months) (Williams et al., 2009). For mammals, acclimatization refers to a coordinated response to single or concomitant stressors (e.g., temperature, gravity, photoperiod). It acts to improve fitness to the environment. Adaptation explicitly recognizes that stressor-strain relationships unfold over time. Health is an inherent state from adaptation/acclimatization, defined by different factors in such extreme environments: temporal, psychiatric, psychological, cognitive, physiological, neurophysiological, sensory, and post-mission. Changes constitute stressors to which everyone's response to adjust and/or recover is interdependent (Selye, 1956). They underline the importance of interactions between humans and their environment. The effectiveness of the response is the key to ensure health (Lazarus & Folkman, 1984). Humans can only remain in a healthy state by trying to minimize the cost of interaction with the environment. Thus, the quality of the interactions plays a fundamental role in acclimatization and adaptation; on which health depends. Nevertheless, it is essential to emphasize that the people involved in these extremes have chosen to work there. It is a commitment and a professional choice that is not undergone, as could be the case in the SARS-COV2 pandemic.

1.5. Ending the challenge: a human confrontation

The first data on human adaptation in ICE/EUE date back to the ‘heroic’ age (Gunderson, 1966; Gunderson & Nelson, 1963; Mocellin & Suedfeld, 1991; Mullin, 1960; Palinkas, 1991; Ursin, 1991). Gunderson (1966, 1968) was one of the first researchers to investigate the response of the organism in a polar environment. Diaries recovered from Scott’s tragic expedition provide valuable information about survival (Halsey & Stroud, 2011; Halsey & Stroud, 2012), notably the role of extreme cold, falling body temperature, loss of weight, and a lack of food (Cherry-Garrard, 2013; Halsey & Stroud, 2011; Huntford, 2007; Rothblum, 1990). Studies aboard nuclear submarines (Earls, 1969; Horowitz, 1964; Weybrew, 1957a), and the first spaceflights (Berry, 1973; Garshnek, 1989; Harris, 1989; Peters et al., 1963; Santy, 1983; Smith, 1990) followed, along with simulations in confined situations (Coburn, 1966; Fraser, 1968). In general, the literature reports psychiatric symptoms such as anxiety and depression (Christensen & Talbot, 1986; Gunderson, 1968; Gunderson & Nelson, 1963; Kanas, 1985; Kanas et al., 1971; Palinkas et al., 1995). Serxner (1968) found that the incidence of anxious, depressive, and psychotic reactions was about 5% during a submarine patrol. Later, Palinkas et al. (2001) reported that, over a four-year period, 5.2% of a crew met the criteria for a DSM-IV disorder after an austral winter in the Antarctic. In space, a review reported two psychiatric events onboard the Mir space station (Shepanek, 2005).

The literature highlights a variety of other psychological and psychosomatic symptoms in ICE/EUE. These include, but are not limited to headaches (Earls, 1969; Mullin, 1960; Natany & Shurley, 1974; Sexner, 1968; Weybrew, 1961), digestive problems (Kanas, 1985; Kanas & Feederson, 1971; Palinkas & Suedfeld, 2008), sleep disturbances (increased sleep latency, decreased sleep efficiency, reduced delta-sleep duration) (Basner et al., 2015;

Frantzidis et al., 2019; Palinkas, 1992; Weybrew, 1957b), thymic variation (Palinkas, 1995; Palinkas et al., 2004; Suedfeld & Weiss, 2000), cognitive impairment (Defayolle et al., 1985; Kanas, 1985; Manzey et al., 1998; Natani et al., 1973; Strage & Yougman, 1971; Vaernes et al., 1993; Ventsenostev, 1973), and poorer sensorimotor performance (Kim et al., 2018; Manzey et al., 1993; Newman & Lathan, 1999; Pagel & Choukèr, 2016; Peters et al., 1963).

Empirical evidence suggests that these symptoms would not be a function of the passage of time (Gunderson, 1968; Kanas & Feddersen, 1971; Le Scanff et al., 1997; Manzey et al., 1993; Strange & Klein, 1974). Palinkas and Suedfeld (2008, 2021) listed three syndromes as: winter-over syndrome (i.e., characterized by sleep disturbance, cognitive impairment, and negative affect which tends to worsen in the third quarter); polar T3 syndrome (i.e., a state of relative hypothyroidism of the central nervous system, accompanied by systemic euthyroidism); and Subsyndromal seasonal Affective Disorder (SAD, i.e., an increase in depressive symptoms related to a change in photoperiodicity). There appear to be specific, crucial periods that occur approximately halfway through, and toward the end of the stay in polar stations (Palinkas et al., 1998), onboard a SSBN (Sandal et al., 2003), or during a space flight (Connors et al., 1985). Strange and Yougman (1971) describe a cluster of symptoms of depression, sleep disturbance, and impaired cognition, which they referred to as *winter-over syndrome*. In some cases, symptoms increase after the midpoint of the mission, with a reduction toward the end, a pattern that has been called the *third-quarter phenomenon* (Bechtel & Berning, 1990). However, many studies have failed to find confirmatory evidence (Gazenko, 1983; Palinkas et al., 1998). Despite a noticeable deterioration in health, there appears to be few long-term, negative effects.

Almost 20 years ago, humans were already trying to find a way to reach Mars. In 2006, Robert Zubrin, President of the Mars Society and advocate of the Mars Direct plan, stated that

humans would definitely be sent to Mars within 10 years (Emurian et al., 2007). The 2004 Garriott-Griffin report on strategy for the American space exploration policy stated that humans could land on the Moon or Mars as early as 2020 (Zubrin, 2000). The technological and human challenges are considerable. Even if the history of manned space missions has shown that humans can endure such conditions for up to a year, few space travelers have spent more than six months in space. In recent years, multiple studies have investigated the question. However, we still do not know enough about the risks of long-duration space missions, nor what can be done to effectively mitigate them. Although most reported problems are relatively minor, they can be mission-threatening. Faced with a hostile event, there is no way to escape.

The principal aim of this systematic review is, therefore, to summarize the literature on the impact of ICE/EUE on human adaptation, from a broader study framework (i.e., physiological, biological, neuroscientific, behavioral/cognitive, and psychological). A secondary aim is to identify the psycho-cognitive processes, and neural mechanisms that professionals develop to adapt to these exceptional environments. A third, exploratory aim is to investigate the differences and similarities between space analogues (i.e., represented by ICE and EUE environments) in terms of their impacts on human adaptability. Finally, these three objectives allow us to discuss the adaptation frameworks for spatial and analogs environment to enrich the knowledge on human adaptation in ICE/EUE environment.

2. Materials and Methods

Our study was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standard (Moher et al., 2010). The protocol was registered with the international prospective register of systematic reviews (PROSPERO) on 24.02.2021 (registration number CRD42021232296). Figure 1 outlines the review process and findings.

2.1. Search strategy

Seven electronic databases were screened (MEDLINE, Embase, PsycINFO, the Cochrane Library, the *Banque de données en santé publique*, the Web of Science, and the NASA Technical Reports Server) for scientific studies examining the impact of ICE/EUE on individuals. A manual search of online resources provided by the Medical Library of Paris Descartes University (France) and Google Scholar identified additional relevant studies. Only studies published between January 2005 and November 2021 were considered, in either English or French. The following search terms were used:

- Group 1: Population studied

Submariner, submarine medicine, medicine submarine, astronaut, cosmonaut, spationaut, spatial exploration, exploratory spatial, medicine space, space medicine, medicine aerospace, aerospace medicine, space simulations, orbital simulations, simulation space, orbital simulation, space simulation, polar expedition, polar base, polar station, polar expeditions, polar bases, polar stations, polar team, polar teams, antarctica, Antarctic, Arctic, Concordia, space environment, space environments, space habitation, space habitations, space travel, space travels, space travelers, space exploration, space explorations, space mission, space missions, spaceflight, spaceflights, space flights, flights, space, space flight, flight, space, space travels, space travel, lunar, Mars, interplanetary, environment, extraterrestrial, extraterrestrial environments, extraterrestrial environment, space crafts, space craft, spacecrafts, spacecraft, HISEAS, human exploration research analog, desert research and technology studies, desert rats, NASA.

- Group 2: Phenomena studied

Confined, confinement, isolated, isolation, extreme, unusual, sensory deprivation, deprivation, sensory, sensory deprivations, perceptual isolation, restricted environmental, enclosed habitat, enclosed habitats, enclosed environment, enclosed environments.

- Group 3: Consequences of the phenomena

Behavior, behaviors, sleep, sleeping, thymia, mood, moods, amnesia, memories, memory, concentrations, attentions, attention, concentration function, concentrate, concentration, concentrating, mental concentration, concentrated, attention function, emotional changes, cognitive, cognitive impairment, impairments cognitive, cognitive impairments, cognitive dysfunction, impairment cognitive, cognition, stresses, stress, sensory perceptions, sensory perception, sense, senses, adaptability, psychologic adaptation, adaptation psychological, behavior coping, behaviors coping, skill coping, behavior adaptive, adaptive behavior, coping behavior, skills coping, coping behaviors, adaptation psychologic, coping skill, coping skills, adaptive behaviors, behaviors adaptive, psychological adaptation, physiological adaptations, physiologic adaptations, physiological adaptation, adaptation physiological, physiologic adaptation, adaptations physiological, biologic adaptation, adaptation biological, adaptation biologic, biological adaptation, interoception, exteroception, position senses, proprioception, position sense, sense position, proprioception, sense of position, alertness, psychological.

2.2. Study selection and eligibility criteria

First, the title and abstract of each publication were checked for relevance. Full-text articles were evaluated for eligibility after this initial verification. The study's authors were contacted, if necessary, to resolve any questions. Any disagreement was resolved through

discussion, and the reasons for excluding studies were recorded. Finally, additional studies were identified by cross-referencing the bibliographies of selected articles. None of the present review's authors were blind to the journal titles, or to the authors or institutions of the selected studies.

Given the lack of research, all study designs were considered. However, those with a high level of evidence were preferred. The following selection criteria were applied. (1) Those that examined a healthy, professional, adult (aged between 18 and 65) human population, working in an ICE/EUE, (2) run in an ICE/EUE or simulation, and (3) addressed the impacts and/or factors that influence individual adaptability to these environments. Factors included biological, physiological, neural, cognitive, and psychological outcomes (e.g., performance, health, emotions, mood, sensoriality, physiology), based on standardized measurements and validated scales. Sleep and fatigue studies were considered if they addressed individual differences in physiological or behavioral outcomes. ICE and EUE included space or space simulations, polar regions, submarine and underwater scenarios, military operations, and, if applicable, cave exploration. Finally, (4) only studies published between January 2005 and November 2021 were considered. The main part of the articles on ICE/EUE were published before this period. Thus, in an effort (1) to have a recent, and representative overview of the latest advances in this field of research, but also (2) to consider the current challenges for long space missions, we thought it is important to provide this selection.

A study was excluded if: (1) it was not run in space or an analog environment, (2) it was not written in French or English, (3) it only considered impacts and adaptability at team or group level, (4) the protocol was not specified; (5) it used animals as subjects, (6) the full-text was not available, (7) it did not focus on active professionals, (8) it focused on pathological

populations, (9) it focused on cellular and molecular levels, (10) it focused on immune function, (11) it focused on microbiome, or (12) it examined missions of less than 15 days.

2.3. Data extraction

Data were extracted by two reviewers (BL, CMK) and checked by another (MT) for accuracy. All potential articles were downloaded as full text and stored in a shared folder. Three of the reviewers (BL, CMK, MT) reviewed each article independently to ensure that only relevant entries were included. Published articles were recorded in a Microsoft Excel (Microsoft Corporation, Redmond, WA, USA) spreadsheet to facilitate visibility. The following data were captured: (1) title, (2) authors, (3) year of publication, (4) citation, (5) type of publication, (6) country of origin, (7) objective, (8) inclusion/exclusion criteria, (9) age of participants, (10) gender, (11) ethnicity, (12) sample size, (13) method, (14) type of environment, (15) environment characteristics, (16) length of time in the environment, (17) measures/tools used, (18) outcomes, (19) limits, and (20) conclusion.

2.4. Methodological quality and level of evidence

Studies were assessed for fidelity/similarity to long-duration space missions using an adapted version of the Palinkas et al. (2011), and Bartone et al. (2018) scales (Table 2). It should be noted that Bartone et al. (2018) modified the initial Palinkas et al. (2011) methodology. Specifically, the former authors added a rating in Category A (*similarity to spaceflight*) to identify studies that included aspects of ICE environments but could not be considered as analogous to spaceflight. The total fidelity score represents the sum across four categories, and our review only considered studies that could be considered as analogous to spaceflight. With respect to Category C (*similarity with respect to the duration of the mission*), we considered missions lasting from 31 to 364 days, divided into two groups of

either up to six months, or up to one year. This decision followed earlier work, which suggests that the impact of the mission differs for these periods. Two of the reviewers (BL, CMK) scored each study. Any disagreements were resolved first by discussion, and, if necessary, by consulting a third author (MT). Scores on the fidelity scale had a theoretical range of 4–13.

Finally, the quality of the evidence for all outcome measures was evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology, based on consistency, directness, precision, and publication bias. Where appropriate, additional domains were considered using the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins & Green, 2008) and criteria taken from Bartone et al. (2018). Quality was categorized as high, medium, or low.

3. Results

3.1. Search results

A total of 3056 publications were initially identified. After screening of titles and abstracts (TI+TB) 561 duplicates were removed, and a further 2258 items were excluded. The remaining 237 full-text articles were assessed for eligibility, which resulted in a further 168 being excluded. Of these: six were not written in French or English; in 15 cases, only the abstract was available; 28 papers were systematic reviews; two studies focused on periods of confinement of less than 15 days; 58 were out of the scope of this review; eight were historical; one focused on space travelers selection; 10 studied interpersonal issues; 13 were run in other extreme environments; seven studied immune function, metabolic and morphologic change, or endocrine response; three validated tools for studying populations in ICE/EUE; three provided insufficient detail; two lacked objective measures; seven were too short (i.e., less than two pages); three contained biases (e.g., methodological shortcomings); one was not found; and one was removed after publication. The final corpus consisted of 69

studies that met the inclusion criteria. Table 3 reported characteristics and results of included studies in this review (supplemented materials).

3.2. Study characteristics

3.2.1. Publication year

Only a few studies were published before 2013 (two in 2005; one in 2007, 2008; and 2009; four in 2010; two in 2011, and two in 2012). From 2010, the number increased, as follows: seven in 2013 and 2014; nine in 2015 and 2016; four in 2017; five in 2018; seven in 2019; six in 2020; three in 2021; one in 2022.

3.2.2. Country

Sixteen individual countries were identified, broken down as follows: the United States (14), Brazil (1), Argentina (2), France (2), Belgium (5), Netherlands (1), United Kingdom (2), Germany (2), Italy (1), Russia (4), Hungary (1), Ukraine (1), the Czech Republic (2), India (4), China (7), and Japan (1). Thirteen other studies were carried out by international teams, and seven were run by Europe collaborations.

3.2.3. Participants

Sample size and crew composition varied. 69 documents reported the number of participants (mean = 35.79). Of these, the activity was broken down as follows: 113 individuals participated in a spaceflight mission (11 studies); 247 participated in a spaceflight simulation (29 studies); 934 spent several months at a polar station (26 studies) or a polar expedition (1 study); and 163 were studied onboard a submarine (2 studies).

Ages ranged from 20 to 60 years (56 studies). In studies of the polar environment, ages ranged from 20 to 60 (20 studies). In 9 spaceflight studies, subjects ranged from 33 to 63. In

studies of simulated spaceflight to Mars, participants ranged from 24 to 55 (26 studies). Forty studies reported the gender of participants. Most focused-on men (26), some were mixed (24), and only two investigated women. The followed ethnicities were reported: International (17); European (5), of which the majority were French and Italian crews; Russian (1); Ukrainian (1); Indian (3); Chinese (5); Japanese (1); American (3); and Argentinean (1). All studies report sample size, while others did not report demographic factors such as age (13), gender (17), or ethnicity (32).

3.3. Study quality

Most studies were evaluated as medium (51) or low (10) quality. Only six included a control group. Of these, four were rated as high quality, while the others were downgraded due to missing informations. Overall, eight studies were assessed as high quality.

Only two studies specified the design (i.e., a controlled case study, a prospective study), and none of the others clarified this point. This is understandable as most investigations are case studies, with several biases that are inherent to the environment in which the mission takes place. Some studies did not specify the methodology (12), or list inclusion criteria (32). It should be noted, however, that these studies have the benefit that they were run in an ecological environment.

3.4. Impacts of ICE/EUE

Human impacts of ICE/EUE can be categorized into eight groups of factors: temporal, psychiatric, psychological and health, cognitive, physiological, neurophysiological, sensory, and post-mission. These are analyzed in detail in the following sections. For each category of impact, we have endeavored to describe them by systematically organizing them by environment: space, simulation, polar and submarine environments. This organization has the

advantage of highlighting the information gaps (i.e., the environments for which the impact category has not been studied).

3.4.1. Temporal impacts

Steinach et al. (2016) highlight the effect of overwintering time on sleep as a cumulative effect to environment exposure. These effects are particularly worsened during winter, suggesting an additional seasonal aspect to the temporal aspect of the mission. The question of the emergence of a cluster of symptoms around the third quarter of a mission has been discussed for several years. Leon et al. (2011) suggest that it could be related to the harshness of the environment. A study of a polar wintering mission by Décamps and Rosnet (2005) found evidence of a third-quarter phenomenon that was dependent on stress responses (in particular, a significant decrease in the total number of stress responses) and appeared to be consistent with an increase in the number of thymic responses, a decrease in the number of social responses, and a stabilization in the number of somatic responses. However, the same study found no link with occupational reactions. The authors argued that the phenomenon should appear just after the middle of the isolation period, rather than just after the middle of the mission. Also, sleep disturbance, cognitive impairment, and negative affect tend to worsen in the third quarter (Basner et al., 2013; Bhattacharyya et al., 2008; Collet et al., 2015; Folgueira et al., 2019; Sandal et al., 2018; Steinach et al., 2016). Results from other studies are inconclusive. For example, Wang and Wu (2015) found no evidence of an effect on crewmembers' emotional state during a space simulation. Khandelwal et al. (2017) reported similar results for an Antarctic wintering. Individual variability among participants may explain these divergent findings. Environmental factors may also play a role, as the syndrome has not been observed in space and underwater analogs.

3.4.2. Psychiatric impacts

The literature reports symptoms of depression, anxiety, irritability, asthenia, apathy, boredom, decline in initiative, and a decrease in general activity and desire (Basner et al., 2014; Hao et al., 2020; Kanas et al., 2013; Lugg et al., 2005; Nicolas et al., 2021; Palinkas & Suedfeld, 2021; Stuster et al., 2010).

Although no evidence of depression was detected during the Mars 500 simulation, one crewmember reported depressive symptoms in 93% of weeks (Basner et al., 2014). No psychotic disorders seem to have been reported during space missions, notably because of the selection of candidates.

In polar stations, Strewe et al. (2018) investigate the effects of hypoxia. They found higher anxiety level at Neumayer III than at Concordia station, although significance is not met. At the Indian Maitri Antarctic station, Premkumar et al. (2013) report an increase in depression and anxiety, together with increased stress scores during the midwinter compared to summer suggesting a “winter overing” effect. This effect is linked to seasonal effects that are known to be dependent of missions in Antarctica. However, the occurrence of such disorders remains rare. This argument is supported by Tortello et al. (2020), who found that the severity of depressive and anxiety symptoms remained below the criteria for mental disorders throughout a year-long wintering expedition. Moreover, none of the measured scales showed significant variation during this time, indicating stable mood. A recent review by Oluwafemi et al. (2021) assessed the risk of disorders in stressful situations such as ICE/EUE. Although most of the time symptoms did not require psychological support, and were self-limiting, the authors suggest that psychiatric disorders could occur during future long-duration space travel and could challenge the space travelers’ ability to accomplish the mission.

No such symptoms were reported both in space (Garrett-Bakelman et al., 2021) and on SSBN board (Brasher et al., 2012; Trousselard et al., 2015).

3.4.3. Psychological and health impacts (i.e., sleep, mood, emotions, stress, somatization)

Extreme environments impose multiple challenges on crews, both in terms of the environment (e.g., extreme temperatures, confinement, isolation) and the number of stressors (e.g., separation from loved ones). Repercussions on the stress level, sleep, and mood of crews are diverse (Basner et al., 2014; Bhattacharyya et al., 2008). Given the duration of the missions, this is a mood related factor (i.e., effect of duration and no specific cause) whereas a particular event during the mission may generate emotions. These questions were mostly examined in analog studies, aiming to minimize the potentially devastating consequences of psychological disorders for the mission. These studies have highlighted the impact of the environment on the psychology of crews (Hao et al. 2020; Kuwabara et al., 2021; Moraes et al., 2020; Nicolas et al., 2021, 2022; Palinkas & Suedfeld, 2008; Palinkas & Suedfeld, 2021; Rai & Kaur, 2012; Trousselard et al., 2015).

The Mars 500 mission was an opportunity to run several studies on the mood and sleep of the crew. The findings highlighted a variation in mood over time (Basner et al., 2014; Gemignani et al., 2014; Šolcová et al., 2014; Wang et al., 2014), with the most extreme values reported around day 366 (Wang et al., 2014). In this context, mood may be defined as low intensity, diffuse and relatively enduring affective states without a salient antecedent cause and therefore little conscious cognitive content. In contrast, emotions are more intense, short-lived, and usually have de definite cause and conscious cognitive content (Forgas, 1995, 2002). We used inside the review the terms ‘mood’ and ‘emotions’ based on the referencing of the studies mentioned. Although a decrease in positive emotions was observed, there was no change in negative emotions (Šolcová et al., 2014; Yi et al., 2016), while crewmembers tended to evaluate unpleasant stimuli positively (Wang et al., 2014). Several studies report a

significant increase in fatigue (Basner et al., 2013; Basner et al., 2015; Wang & Wu, 2015; Zavalko et al., 2013). Fatigue was found to be significantly higher in the first, compared to the fourth quarter, due to a heavier workload, lack of free time, and greater crew autonomy (Wang & Wu, 2015). An earlier study, run during the Mars 105 mission highlighted difficulty in falling asleep, nocturnal awakening, a decrease in delta activity during sleep, and a lack of rapid eye movement sleep (Kovrov et al., 2012). However, these results were not confirmed by other studies (Chen et al., 2016b; Gemignani et al., 2014; Matsangas et al., 2017; Pattyn et al., 2017; Trousselard et al., 2015; Wang & Wu, 2015; Yi et al., 2014).

A report of overwintering at two Chinese Antarctic stations identified different patterns of mood change depending on the station's location using the profile of moods scale (Chen et al., 2016b). Specifically, no statistically significant differences in indicators were identified for winterers at the Great Wall Station (Chen et al., 2016b). Chen et al. (2016a) found evidence of SAD in two subjects at the Chinese polar station, Zhongshan. The latter authors reported a greater number of depressive symptoms, increased appetite (associated with weight gain), fatigue, and decreased sociability. In contrast, at the Zhongshan Station, negative affect (i.e., fatigue, anger, tension, confusion) significantly increased. Fatigue increased until mid-winter, and peaked at the end of the season, while the other measured variables peaked in mid-winter. A relation between emotions and fatigue was found by (Chen et al., 2016b), who observed that the most severe environmental characteristics were associated with the worst effects. Findings from studies at NASA's Human Exploration Space Analog (HERA) facility are mixed (Weber et al., 2019; Nasrini et al., 2020). In general, crewmembers remain healthy, with mostly positive emotions and good sleep quality – performance degradation appears to be mainly caused by sleep deprivation. However, the average duration of these missions is one month, leaving doubts about their similarity to future long-duration trips in space.

The literature highlights high levels of stress in ICE/EUE, whether during space missions (Barger et al., 2014), simulations of future long-duration space missions (Basner et al., 2014; Jacobowski et al., 2015; Wang et al., 2014; Yi et al., 2014; Yuan et al., 2019), or a stay in a polar environment (Binsted et al., 2010; Moraes, 2020; Nicolas et al., 2015; Nicolas et al., 2021, 2022), with levels peaking at approximately day 500 (Wang et al., 2014; Yi et al., 2014). Social stress appears to have most impact (Nicolas et al., 2014; Nicolas et al., 2015).

Concerning health, most studies highlighted sleep and somatization concerns. The majority of studies on sleep were run during a polar winter. Identified disorders include desynchronization of circadian rhythms, delayed chronotypes, insomnia, sleep latency, decrease in slow-wave sleep, periodic awakening, deeper or shallower sleep and fewer dreams. These effects are ascribed to environmental conditions (e.g., photoperiodicity, cold, altitude), and lead to an increase in subjective fatigue (Bhattacharyya et al., 2008; Binsted et al., 2010; Chen et al., 2016a; Collet et al., 2015; Folgueira et al., 2019; Grófa et al., 2011; Kuwabara et al., 2021; Mairesse et al., 2019; Nicolas et al., 2022; Palinkas & Suedfeld, 2008; Palinkas & Suedfeld, 2021; Pattyn et al., 2017; Sandal et al., 2008; Steinach et al., 2016). Premkumar et al. (2013) investigated sleep both in summer and winter at Maitri station. In five subjects, they found daytime sleepiness during summer, and two of them during midwinter. When exploring the sleep logs, a seasonal difference was highlighted (i.e., decrements in sleep latency, early morning awakenings, sleep recovery, increased sleep time during wintering) in 25% of subjects. Nevertheless, scientists reported a decreased sleep length in summer compared to technical support team in winter. Authors noted that this result was attributed to an increase in napping due to lack of work in winter. Also, a gender difference was found in polar regions leading to sleep quality decrements for woman (Schneider et al., 2016).

Trousselard et al. (2015) did not find a significant effect on sleep, sleepiness, and confusion between days 21 and 51 of a nuclear submarine patrol.

The literature reports several somatic symptoms, such as gastrointestinal complaints (i.e., heartburn, gastric discomfort, gastritis and upset stomach, flatulence, diarrhea, and constipation), digestive disorders, dyspepsia, rheumatic pain, dental pain, headaches, loss of appetite, weight loss, cardiac extrasystoles, and heightened sensitivity to physical and social stimuli (Kanas et al., 2013; Nicolas et al., 2022; Palinkas & Suedfeld, 2008; Yuan et al., 2019). These symptoms appear to be closely associated with stress, without being systematic (Yuan et al., 2019). Although one study found a significant correlation between weight-related phenotypes and psychological factors (Hao et al., 2020), other data do not support this idea. In a four-month study of the Mars 105 crew, Nicolas et al. (2014) found that exposure to an extreme environment did not systematically lead to stress overload or altered psychological states. Similarly, in a study of Antarctic wintering, Strewé et al. (2018) found a distinct modulating effect on the stress response that was not associated with psychological stress. Specifically, at both Concordia (high altitude) and Neumayer III (sea level), stress measures did not significantly change throughout the deployment. However, although overall stress measures did not reach significance, levels were higher at Neumayer III than at Concordia.

Over-commitment and rank lead to increase the level of stress for submariners (Brasher et al., 2012).

Overall, the psychological impact of the mission seems to be related to the length of time spent in the environment and its severity, although here again, there is great inter-individual variability. Most studies identify changes from the first weeks of the mission and note that the stress induced by the environment could lead to subsequent maladjustment (Nicolas et al., 2015).

3.4.4. Cognitive impacts

In space, the literature reports a decrease in cognitive capacities (i.e., under high cognitive load), productivity, vigilance, and collective and individual efficiency, together with an increase in the number of errors (Kanas et al., 2013; Palinkas & Suedfeld, 2021; Patel et al., 2020; Pattyn et al., 2005; Roberts et al., 2019). Cognitive impairment was also reported in the review by Flynn (2005). Effects could be due to microgravity, radiation, stress, or even the tools used (Flynn, 2005; Nasrini et al., 2020; Oluwafemi et al., 2020).

Executive functions seem to be particularly impacted under the non-ecological gravity experienced in space. Studies report a decrease in problem-solving ability, memory (working, short-term, and spatial), learning, attention, and reaction times (Roberts et al., 2019; Moore et al., 2019; Pattyn et al., 2005). These changes appear to be related to a sleep deficit, and the circadian desynchronization problems faced by space travelers, along with stressors inherent in the environment, notably monotony (Kanas et al., 2013; Nasrini et al., 2020; Palinkas & Suedfeld, 2021). Specific white matter regions such as the bilateral optic radiations and the splenium of the corpus callosum were associated with altered reaction time (Roberts et al., 2019).

Many cognitive functions are critical to the mission's success and crew safety. During a 340-day space mission, accuracy and speed scores were found to decrease between the beginning and the end of the flight (Garrett-Bakelman et al., 2019). Surprisingly, cognitive speed was higher in all domains at the beginning of the flight. Other authors underline that it is difficult to evaluate the real impact of the space environment on the cognition of space travelers (Flynn, 2005; Oluwafemi et al., 2020; Roberts et al., 2019). Although some space travelers have reported a subjective decline in cognitive performance, the review by Flynn (2005) highlighted that only minor changes could be recorded using objective measures (i.e.,

increased test response time, reduced accuracy of responses, poorer performance when tracking two tasks, altered visual-spatial recognition ability). In particular, he cites a study of long-duration flights, where these impairments were most problematic during the first 20 days, but then resolved during the mission.

Analog studies have also observed an impact of the environment on cognitive function, whether in polar environments (Palinkas & Suedfeld, 2008; Premkumar et al., 2013; Nicolas et al., 2015; John Paul et al., 2010) or space simulations (Binsted et al., 2010; Cohen et al., 2016; Flynn-Evans et al., 2020; Yi et al., 2016). A recent study at the HERA facility (Nasrini et al., 2020) highlighted a significant impact on psychomotor alertness in terms of speed and accuracy, and cognitive output. Weber et al. (2019) studied a 30-day isolation at the HERA facility and found that it had no significant effect on cortical activity or cognition, despite an increase in cortisol. Other studies have shown no negative impact on cognitive activity while wintering in Antarctica (Barkaszi et al., 2016; Folgueira et al., 2019; Grófa et al., 2011; Palinkas et al., 2007); or in a 105-day simulation (Gemignani et al., 2014). John Paul et al. (2010) studied the Indian Maitri station in Antarctica and observed a positive effect on recognition memory and learning, and a neutral effect on short-term memory during a one-year stay. The latter authors concluded that in extreme situations, individuals can manage their stress and remain cognitively efficient.

Finally, it should be noted that no studies have been run onboard SSBN.

3.4.5. Physiological impacts

Most studies examine Heart Rate Variability (HRV) and cardiovascular and breathing adaptation. In a study that investigated the impact of isolation and confinement on cardiovascular and brain function, Garrett-Bakelman et al. (2021) showed that, during a 340-

day space mission, the environment increased internal jugular vein cross-sectional area, frontal tissue thickness, cardiac filling, stroke volume, and cardiac output. The latter authors also found a decrease in these changes during a long-duration space flight on the ISS.

Several studies have highlighted that the Mars 105 mission, which laid the foundations for the Mars 500 mission, was not as stressful as the latter. In particular, the literature has identified the effects of the two missions on HRV. Studies carried out during the Mars 500 mission used HRV to assess the functional status of a human being in an extreme environment (Bersenev et al., 2013; Šolcová & Vinokhodova, 2013). A 2013 evaluation of the vegetative regulation of blood circulation and individual health risks during the 520-day Mars 500 mission reported changes in HRV parameters (Bersenev et al., 2013). The most noticeable changes occurred during the simulation of the return trip: a decrease in heart rate; an increase in sympathetic regulation; an increase in parasympathetic regulation; and sympathetic and neurohumoral regulation. On waking, the following observations were recorded: greater amplitude oscillations, mainly at high and low frequencies; an increase in HRV; and a decrease in heart rate that contrasted with a decrease in the high frequency component during sleep (Vigo et al., 2013), along with increased parasympathetic activity (Vigo et al., 2012; Vigo et al. 2013). These changes seemed to be more pronounced during the second month of isolation (Vigo et al., 2012).

In their study of the Mars 105 mission, Wan et al. (2011) found that the autonomic nervous system was altered through a decrease in blood pressure regulation. A reduced cardiovascular response to mental stress was particularly evident during the first month of confinement but did not persist after leaving. Similarly, confinement did not affect the cardiovascular response to slow-paced breathing. The Chinese Controlled Ecological Life Support System experiment (Yuan et al., 2019) found that individuals' morning heart rate and

blood pressure remained normal, and HRV frequency markers (Low Frequency, LF and High Frequency, HF) along with baroreflex sensitivity, were not pathologically altered. Furthermore, carotid intima-media thickness and masseter tone increased, and endothelium- and paravertebral muscle-dependent vasodilation decreased. A space simulation onboard the Lunar Palace (Hao et al., 2020) examined the correlation between blood pressure and heart rate, and psychological changes. The study found that the lower the morning diastolic blood pressure, the more anxious individuals were. The lower the bedtime diastolic blood pressure, the more prone they were to fatigue-inertia, obsessive-compulsiveness, anxiety, and phobic anxiety. Finally, the lower the bedtime heart rate, the more anxious they were.

Results seem more mixed for polar stations. Moraes et al. (2020) evaluated the physiological effects of an Antarctic expedition, consisting of a 26-day trip onboard a ship, followed by a 24-day summer camp in the Antarctic field. The study found changes in the cardiac autonomic regulation of HRV parameters during the trip onboard the ship. Biphasic changes were found in the Root Mean Square of Successive Differences (RMSSD) and the Proportion of number of pairs of successive NN intervals that differ by more than 50 ms divided by the total number of NN intervals (pNN50). Parasympathetic activity, assessed from the HF band, decreased on day 16, then moderately increased, before returning to pre-mission values. No differences were observed between initial and final measurements. Fluctuation in the HF band, and the unchanged LF band resulted in a biphasic response of the LF/HF ratio. In contrast, no changes were observed for resting heart rate, or any of the HRV parameters during the summer camp. Similarly, a 2019 study by Folgueira et al. found no significant changes in blood pressure during wintering at the Antarctic Belgrano II station, while Gríofa et al. (2011) found no significant cardiopulmonary changes during a 37-day polar wintering.

3.4.6. Neurophysiological impacts

Several studies highlight neurophysiological responses during long-duration space missions. There appear to be major structural changes at the cerebral level, including a redistribution of cerebrospinal fluid, decreased ventricular volume, and a generalized decrease in gray matter volume (Lee et al., 2019; Stahn & Kühn, 2019; Roberts et al., 2019). Roberts et al. (2019) have shown significant global and local (i.e., crowding of the brain parenchyma, displacement of the brain parenchyma as the ventricles dilate) changes in brain structure after a space mission on board the ISS. Lee et al. (2019) reported a shift of cerebral spinal fluid upwards in the brain after all long (but not short) space flights, along with a narrowing of the cerebral spinal fluid spaces in the vertex after all long flights (but in only one crew member after short flights). Combined changes are observed in somatosensory, visual, vestibular, and cardiovascular function (Demertzi et al., 2016; Kanas et al., 2013; Liu et al., 2015; Moore et al., 2019; Verheyden et al., 2009). Liu et al. (2015) report that microgravity leads to change in blood circulation, which becomes more efficient due to the redistribution of cephalic blood. Alterations in cerebellar and motor connectivity, as well as a decrease in vestibular connectivity, particularly in the right insula, have been observed (Demertzi et al., 2016). Sensory conflicts between visual and tactile inputs, and the vestibular organs can lead to a syndrome of adaptation to space (Kanas et al., 2013; Moore et al., 2019; Vam Ombergen et al., 2017).

During the Mars 500 mission, Yi et al. (2016) examined the impact of chronic exposure to isolation and confinement on brain cortical activity and identified a reduction. Similar results were found in a study of neural activity during 120 days of isolation in a spatially confined, space-analog environment (Weber et al., 2020). Jacobowski et al. (2015) reached similar conclusions. In particular, the authors found that a decrease in neurotrophicity,

assessed by Blood brain Derived Neurotrophic Factor (BDNF) concentrations, was linked to a decrease in dentate gyrus volume, the latter being associated with decreased cognitive performance in spatial processing and selective attention tests.

In the polar environment, Stahn et al. (2019) evaluated the effects of physical and social deprivation on the hippocampus, based on MRI scans of eight members of a polar expedition. Their results highlighted a reduction in hippocampal volume in the dentate gyrus compared to controls. A significant reduction in gray matter volume in the left parahippocampal gyrus and left orbitofrontal cortex was also reported. Finally, a decrease in cortisol concentration is reported to be consistent with adaptation to confinement during a summer camp in Antarctica (Moraes et al., 2020).

Any results are reported on SSBN patrol.

3.4.7. Sensory impacts

In space, sensory input is limited, and space travelers' sensory responses are altered. The neurovestibular system is one of the first to be affected during spaceflight (Kim et al., 2018).

3.4.7.1. Vestibular system

Demertzi et al. (2016) reported the results of a 44-year-old cosmonaut who spent 169 days on board the ISS. Alterations were observed in the vestibular and motor regions. The observed dysfunctions were correlated with vestibular ataxia and reduced motor control abilities. Results from space missions show significant decreases in postural stability, oculomotor control, eye-hand coordination, eye-neck coordination, and proprioception during the flight (Bloomberg et al., 2015; Wood et al., 2015). These effects become more pronounced as the mission length increases (Roberts et al., 2019). Overall, there are several acute and chronic sensorimotor events during space flight that may affect operational

proficiency (Moore et al., 2019). These include space motion sickness, spatial disorientation, proprioception changes, or the ability to track visual targets. Also, Roberts et al. (2019) highlighted an association between decreased postural control recorded after the space mission and changes of the left caudate nucleus in case of a task requiring dynamic control of postural balance. More specifically, the decrease in motor function performance was predicted by structural change of the left caudate nucleus and the right lower extremity primary motor area/midcingulate. These events are driven by vestibular modifications.

A study run in the context of the NASA Extreme Environment Mission Operations project (NEEMO) in the underwater Aquarius module (Kim et al., 2018) found that measurements of upper body balance and gait regularity during open and closed eye tandem walking revealed anomalies, due to changes in sensorimotor performance during the 15-day mission. The variability and amplitude of gait regularity for left-handed steps, along with trunk displacement, were correlated with the duration of time crew members spent in the habitat. Although gait regularity for right-handed steps was not significantly different, wide variability in performance was noted.

3.4.7.2. Spatial navigation system

Sensors used in spatial navigation could be impaired during long-duration spaceflight (Moore et al., 2008; Wood et al., 2015).

Perceptual distortion has been reported in space travelers onboard the ISS (Wood et al., 2015) and during the Mars 500 simulation mission (Sikl & Simeček, 2014). Similarly, although crew members' 3D perception was not found to change significantly during the Mars 500 mission (Sikl & Simeček, 2014), the relative length of 2D lines was consistently misperceived. Parallel line lengths were generally judged more accurately than perpendicular

line lengths, and the magnitude of under and overestimations was lower among the crew than in a control group.

No such results were reported in other analog environments.

3.4.7.3. Vision system

The literature has, for many years, highlighted the cerebrospinal displacement of fluids during stays in space. This phenomenon has major impacts on the body, notably the visual function (Lee et al., 2018; Strangman et al., 2014). This shift results in an elevated intracranial pressure that causes visual alterations. These changes occur during a timeframe of three weeks to three months after arrival in the space environment (Demontis et al., 2017). Radiation exposure can also damage vision. An innovative study of twins, one in space, the other on Earth, found that a stay of 340 days led to ocular modifications in the astronaut that were not present in their twin on Earth (Garrett-Bakelman et al., 2019). More specifically, the authors identified an increase in the thickness of the sub foveal choroid, and the total thickness of the peripapillary retina (i.e., retinal edema). Moreover, the severity of the astronaut's choroidal folds, present before the mission, increased during spaceflight.

In contrast, an ophthalmological study of the first trans-Antarctic winter expedition (Stahl et al., 2018), which examined explorers who overwintered in Antarctica, did not identify any pathological changes in visual acuity, contrast sensitivity, color vision, auto-refraction, subjective refraction, retinal examination, retinal autofluorescence and retinal thickness, or intraocular pressure.

No such results were reported in other analog environments.

3.4.7.4. Gustatory system

Gustatory alterations were reported during a 15-day confinement onboard an analog reproduction of the Martian desert (Rai & Kaur, 2012). In the latter study, subjects completed both mental and physical tasks, and tastes were found to be more pronounced after physical than mental tasks. After mental tasks, decreases were found for bitter, sour, and sweet tastes with respect to peak intensity, duration of aftertaste, and total amount of taste (i.e., summation every 5 seconds). After physical tasks, peak intensity changed, as did the duration of aftertaste, and total amount of aftertaste for bitter and sweet taste, while sour tended to decrease. The authors also reported a relationship between the time-averaged intensity of sweetness, bitterness and sourness, and stress (measured as cortisol levels).

No such results were reported in analog environments.

3.4.8. Post-mission impacts

Return to Earth is a particularly stressful event. Gravity, and readjustment to life in society make it one of the greatest physiological challenges of spaceflight. In the period immediately following landing, stress manifests as cardiovascular and musculoskeletal problems, and inflammatory reactions. Liu et al. (2015) reported a lack of rhythmicity of body trunk 4 to 6 days after the end of the spaceflight. Impacts on mood and performance include drug addiction, major depressive symptoms, and anxiety that may require psychotherapy and psychoactive medication (Kanas et al., 2013). Coming home after a long period away can be difficult for families; jealousy and marital problems can end in divorce (Kanas et al., 2013).

Garrett-Bakelman et al. (2021) observed a decline in the cognitive functions (speed, accuracy) of an astronaut who spent 340 days in space, compared to their twin who remained on Earth. This decline persisted for six months after the return. However, Moore et al. (2019) highlighted that fatigue alone is not responsible for the decrease in performance. Nicolas and

Gushin (2014) reported lowest levels of perceived stress upon return from the Mars 105 simulation, while fatigue increased. Stahn et al. (2019) also concluded that BDNF levels had not recovered one and a half months after the end of a polar expedition, suggesting an impact on key cognitive functions. Recovery from ocular changes that occur during a space mission remains a concern. While recovery is possible in some cases (e.g., choroidal congestion), others persist or worsen. Choroidal folds have been found to remain following a stay in space (Garrett-Bakelman et al., 2021).

Nicolas et al. (2022) highlights that recovery was inversely proportional to the severity of polar environment. While no decrease was observed at Kerguelen station, recovery responses decreased at Dumont d'Urville.

Six months after leaving the 520-day Mars 500 simulation, crew members participated in a parabolic flight campaign during which they were subjected to acute stress (Yi et al., 2015). Cortisol levels increased compared to the control group, indicating marked chronic stress.

Postural stability and walking speed are deeply impacted during the first twelve hours following the return from a space mission, and several weeks after landing, space travelers continue to have difficulty standing when performing dynamic head tilts (Wood et al., 2015). Anatomical changes and visual problems have been found to persist for several months, or even years after the return to Earth (Strangman et al., 2014). Furthermore, the absence of the usual gravitational force in space has been shown to affect various brain mechanisms, including the efficiency of cognitive and perceptual-motor skills (Kanas et al., 2013). Once out of the environment, the NEEMO analog crew had not recovered their pre-mission sensorimotor performance. Improvements to postural stability after landing can be divided into two phases: an initial rapid improvement, followed by a gradual recovery.

No post-mission factors are reported in the reviewed studies of submariners. Overall, the reviewed studies confirm, and provide some additional insight into the role of recovery and stress in adaptation to ICE/EUE. Finally, an important insight that emerges from these studies is the role of inter-individual differences among crew members. Further investigations of adaptation mechanisms are needed to better-understand how individuals cope with extreme conditions.

3.5. Psychological mechanisms and adaptation to ICE/EUE

The literature refers to several types of adaptation, mainly drawing upon the coping framework (Lazarus & Folkman, 1984; Lazarus & Folkman, 1985; Lazarus, 1986). The selected studies highlight the importance of different coping strategies for understanding positive adaptability. Most focus on space simulation and polar environments, while none address submarine patrols.

3.5.1. Coping and defense strategies

A review by Leon et al. (2011) argues that problem-solving strategies are an effective way to overcome decreased motivation, especially towards the middle of the mission. However, the authors also highlight the importance of engaging in emotion-oriented strategies, as they appear to be an effective way to cope with stressful situations via emotional regulation and sharing one's emotional state. As early as the Mars 105 simulation, it was concluded that task-oriented adaptation was associated with positive adaptation, while withdrawal or disengagement was associated with depression and poor adaptation (Palinkas & Suedfeld, 2021). Nicolas et al. (2013, 2014) provided further insights into crew adaptation. They found a link between defense mechanisms (i.e., mature defenses, intermediate defenses, immature defenses), coping (i.e., task-oriented coping, disengagement-oriented coping), and emotional state (i.e., positive emotions, depressive symptoms) (Nicolas et al., 2013). Tortello

et al. (2021) found similar results among Antarctic winterers, notably a relationship between task-oriented coping and defense mechanisms (i.e., immature, mature). Nicolas et al. (2015) also found a link between stress, mature defenses, and recovery during a one-year wintering at the Concordia station. Individuals who used mature defense mechanisms appeared to be better-able to adapt to the stressful environment, and their recovery was efficient (Tortello et al., 2021; Van Ombergen, 2021), regardless of season or isolation (Tortello et al., 2021). Recently, Nicolas et al. (2021, 2022) show that both perceived control and environmental mastery are involved in adaptation processes. They found that level of perceived control is associated with emotional, social, and physical adaptation at both Concordia and Amsterdam station, and that this indicator predict emotional adaptation for winterers at Concordia (Nicolas et al., 2021). Also, they reported that the level of environmental mastery correlates with the evolution of success (Nicolas et al., 2022). Those with a low level of environmental mastery experienced more success through the wintering instead of those with high levels remains stable (Nicolas et al., 2022). Moreover, coping appears to be a function of gender, with men using more avoidant coping, and females using more active strategies (Binsted et al., 2010). It seems that women are better-able to cope with stressors and, thus, adapt to ICE/EUE (Palinkas & Suedfeld, 2021).

3.5.2. Behavioral strategies

Other authors note different coping strategies in extreme environments. These include redirecting negative affect to the control center rather than to crew members (i.e., displacement) (Kanas et al., 2013), self-sufficiency and autonomy (Kanas et al., 2013), and strategies derived from the individual's personality (Bersenev et al., 2013; Wang et al., 2014), functions assigned during the mission (Bersenev et al., 2013; Palinkas & Suedfeld, 2008), and resilience (Sandal et al., 2018). The role of interpersonal relationships in adaptation is also highlighted (Kuwabara et al., 2021; Tortello et al., 2021). A wintering at the Japanese

Antarctic station revealed four types of coping strategies: the use of instrumental social support, denial, acceptance, and planning (Kuwabara et al., 2021). The results of the Baum test on 172 Japanese winterers (i.e., only 11 women were in the sample) over a period of 5 years at the Syowa polar station showed two types of behavior to cope with the extreme environment. Some of them clung to the memories of the life they had before and tried to copy this old life to the new one in Antarctica. Others adjusted by adopting a new way of life. These are both types of behaviors that allow for maintaining mental states during the mission. However, having a flexible adaptive behavior, as highlighted by the second case, implies having sufficient resources to fit with the demands of the new environment. Thus, this type of behavioral coping allows for quality adaptation.

3.5.3. Impacts of the timeline on strategies

Some authors suggest that coping is nonlinear over time. The mission itself has a psycho-physiological impact that evolves as it progresses. Many note that coping occurs in stages (Demertzi et al., 2016; Kanas et al., 2013; Khandelwal et al., 2017; Moiseyenko et al., 2016; Wang et al., 2014). Psychological and cognitive changes seem to reflect strategies that individuals use to cope with the environment. These changes evolve during the mission (Kanas et al., 2013; Moiseyenko et al., 2016; Palinkas & Suedfeld, 2021; Tortello et al., 2021; Demertzi et al., 2016; Wang et al., 2014), with a decrease by the third quarter, regardless of the environment (i.e., space or analogs) (Kanas et al., 2013; Tortello et al., 2021; Wang et al., 2014). Gushin et al. (1993) highlighted an accommodation over time in space travelers' adaptation. The authors developed a four-stage model of emotional change during a space flight: (1) psychological and physical discomfort at the beginning of the flight; (2) six weeks into the flight, psychological and physical adaptation began, but the space travelers were not yet impacted by the isolation and confinement; (3) between the sixth and twelfth weeks, the space travelers became less stable; (4) a feeling of euphoria developed during the last phase.

Adaptation has been investigated in analogs. Studies have identified three stages, with minimal effectiveness at the beginning, some increase in effectiveness in the middle, and a decrease at the end of the mission (Khandelwal et al., 2017; Moiseyenko et al., 2016; Nicolas et al., 2013). A specific pattern has been noted in the polar environment, namely an acute phase of adaptation, functional stress, relative stabilization, and depression (Moiseyenko et al., 2016). Khandelwal et al. (2017) found that externalized psychological responses peaked in mid-winter, anxiety and insomnia peaked during the coldest period, and cognition was at its poorest during the last phase of an Antarctic wintering. More recently, a new type of adaptation has emerged during wintering in Antarctica – polar wintering (Palinkas & Suedfeld, 2021; Sandal et al., 2018). Individuals appear to enter a state of psychological hibernation as an adaptation to stress, which takes the form of a depletion of resources as the cold period approaches, and the reconstitution of resources in the second half of the stay. This strategy seems, therefore, to be influenced by environmental conditions, and involves a long period of isolation and confinement.

3.5.4. Salutogenic strategies

Other authors compare coping to salutogenic phenomena. The latter term is derived from positive psychology, which supports learning to cope with stressful situations. The term *salutogenic*, developed by Antonovsky (Antonovsky, 1987), proposes that under certain circumstances, stress does not only have harmful, but also beneficial consequences for health, notably because humans like to engage in flow experiences (Csikszentmihalyi, 2000). *Salutogenic* appears to be associated with the ability of individuals to overcome the stressors inherent in these environments. Extreme environments can have long-term beneficial effects throughout life. Outcomes include successful stress management, increased strength, better relationships with others, greater autonomy, improved health, personal growth, greater self-

confidence, greater belief in human values, and a sense of meaning in life (Palinkas & Suedfeld, 2008; Palinkas & Suedfeld, 2021; Nicolas et al., 2022).

Others go so far as to suggest a combination of psychological, emotional, and cognitive adaptation (Nicolas et al., 2013; Nicolas et al., 2015; Šolcová et al., 2014). It should be emphasized that negative emotions never reached a critical stage during the Mars 500 mission (Nicolas et al., 2013). A study by Šolcová et al. (2014) of the Mars 500 crew suggests that during the simulation, crew members changed how they felt, and regulated their emotions. Each individual favored a different regulation strategy. Three participants preferred to express their emotions as they felt them, while two others preferred to hide their emotions. Crew members preferred to suppress and neutralize their negative emotions, and only openly expressed positively valenced emotions. The authors suggest that changes in the expression of positive and negative emotions are a manifestation of the individual's experience in the ICE/EUE and, thus, a sign of adaptation (Nicolas et al., 2013; Šolcová et al., 2014). Furthermore, Yuan et al. (2019) highlighted an increase of emotional adaptation of the crew towards the mission. In this context, Solcova et al. (2013) showed that the individuals who are best adapted to a 520-day mission should be those with a higher level of stress resistance, and a greater capacity to self-regulate their emotional state. Individual adaptation in ICE/EUE thus appears to be a multifactorial, flexible, and real process. However, understanding psychological strategies for positive adaptation remains a challenge for longer missions, where the data are insufficient to draw any conclusions.

3.6. ICE/EUE and preparing for future long-duration space missions

Table 4 summarizes the characteristics of the space and analogs environment studied in the reviewed corpus.

3.6.3. Types

All the 69 publications were quantitative studies. Experiments in the space environment were, however, under-represented – only eleven studies took place during a spaceflight. Twenty-seven focused on polar environments: two expeditions, two in the Arctic polar desert, four at the Concordia station; one at both Concordia and the Dumont d'Urville station (DDU), one at both Concordia and the German Neumayer III station, one at both Concordia and Amsterdam station, one at the DDU, one at both DDU and Kerguelen station, one at the Syowa Station, one at the Akademik Vernadsky station, four at the Maitri station, two at the Belgrano II station, one at the Belgian station, one study at both the Mc Murdo and the South Pole stations, one study at the Zhongshan station, one study at both the Chinese Great Wall and Zhongshan stations, one study at both the German Neumayer II and III stations, and one study at the German Neumayer III station. Twenty-nine investigated spaceflight simulation, broken down as follows: the Russian Academy of Sciences' Institute of Biomedical Problems (21 studies), the HERA facility (two studies), the Mars desert research station (one study), the Lunar Palace (two studies), the NASA Extreme Environment Mission Operations (NEEMO) (one study), the Hawaii Space Exploration Analog and Simulation (HI-SEAS) (one study), and the Controlled Ecological Life Support System (CELSS) (one study). The activities carried out during space simulations have the will to reproduce the typical days of the astronauts on board the ISS as well as the living conditions. Also, they have an important margin of maneuver allowing to challenge the mission (e.g., extension of the mission duration) (Hao et al., 2020).

Two studies were run in a submarine environment (Brasher et al., 2012; Trousselard et al., 2015). Analogs such as bed-rest, dry immersion, parabolic flights, and OPEX studies were considered as out of scope and excluded from this review.

3.6.4. Time spent in the environment

The length of the study in the ICE/EUE varied from 15 days to 17 months, broken down as follows: four studies lasted about two weeks, 12 between one to four months, nine studies lasted approximately six months, three lasted one month, 23 lasted around one year, and 12 studies extended over 18 months. In other cases, either the duration was not reported (two studies), or several studies were run over different periods of time (4 studies).

3.6.5. Fidelity of analogs to the vacuum of space

Studies were evaluated with respect to their fidelity to the space environment. Ratings ranged from five to 13 (i.e., see Methodological quality and level of evidence in Methods section for further details). Thirty-three were rated as High (10–13), twenty-seven as Medium (7–9), and nine as Low (4–6) fidelity. The high-fidelity studies were broken down as follows: spaceflight (eleven studies), spaceflight simulation (13 studies were dedicated to the Mars 500 experiment), one from the CELSS platform, one from the HERA facility, one from the Lunar Palace, one from the Scientific International Research In a Unique terrestrial Station program (SIRIUS); one from the HI-SEAS facility; and four from Antarctica.

Medium fidelity studies were broken down into: spaceflight simulation (seven were dedicated to the Mars 105 experiment), one study at the Lunar Palace, one study at the HERA facility, one at the Mars desert research station, one at the NEEMO facility, and various Antarctic stations (16 studies). Low fidelity studies examined submarine patrols (three), and Antarctic stations (six).

Space studies are complex to implement. They are very expensive to run, require a high degree of technology, and space agencies receive many requests, but only select a few research teams. Pagel and Choukèr (2016) underline that analogs offer a standardized, high-fidelity experimental framework, and a real expedition environment. They make it possible to simultaneously collect data from more subjects, using a wider range of methods, for variable durations, and in controlled environmental conditions. These experiments offer unique ecological conditions to explore the nature of human adaptation in a clinical context. Most analog studies ran for about one year in ICE/EUE in Antarctica. Other representative studies were run in a spaceflight simulation; however, it should be noted that there is a high degree of heterogeneity between these environments.

4. Discussion

Humanity is one step closer to returning to the Moon and embarking on a journey to Mars. The progress that has taken place over the past decade is unprecedented. Advanced life-support technology has allowed us to explore places where we could not have survived before. The three objectives of this systematic review enriches knowledge in the field of human adaptation to the challenges of space missions and travel by (1) summarizing the existing literature on the impact of professional ICE/EUE on human adaptation from a broader studied framework (i.e., physiological, biological, neuroscience, cognitive, and psychological), (2) describing the identified psycho-cognitive processes and neural mechanisms developed by professionals to cope in these exceptional environments, and (3) exploring the differences and similarities between space analogs (i.e., represented by ICE and EUE environments), in terms of their impacts on human adaptability. Humanity is one step closer to returning to the Moon and embarking on a journey to Mars. The progress that has taken place over the past decade is unprecedented. Advanced life-support technology has

allowed us to explore places where we could not have survived before. The need to sustain life in space has presented many unique challenges to research, since the dawn of the space age more than 60 years ago. However, many challenges remain before we can preserve life beyond Earth.

4.5. What analogs?

Our analysis of the environments included in this review reveals that studies in space are underrepresented. Analog environments are, thus, a real pathway to carrying out research that is complex to undertake during a space flight. Our review also highlights that simulation studies appear to be most faithful to the conditions found in long-duration missions, followed by Antarctic wintering. However, although simulations can closely model the conditions that crews on future exploratory missions might experience, evacuation is still possible. Thus, the crew can keep a level of control over the environment. It is always possible to be extracted from the mission within a very reasonable time. On the other hand, polar environments provide similar conditions to establishing a base on Mars or the Moon. Rescue and evacuation are very complicated, if not impossible, during the winter months, and dependent on the station's location. Antarctica cannot be accessed every month of the year due to the formation of ice blocks. The rotations to bring equipment and overwinterers take place between October and March of each year. On site, the access to the different stations can quickly become perilous if the weather conditions are not favorable. Thus, the crews are entirely autonomous. Emergencies cannot be rescued before several hours, days, or even no one can be rescued. Characteristics of polar stations are very different, depending on their geographical position and altitude, which ranges from 100 m to 3 233 m. Different studies reported results from polar stations at sea level (Bhattacharyya et al., 2008; Khandelwal et al., 2017; Strewe et al., 2018; Tortello et al., 2020). Thus, in terms of mission length, space simulations have lasted

the longest with the Mars 500 mission (Basner et al., 2013; Basner et al., 2014; Bersenev et al., 2013; Cohen et al., 2016; Jacobowski et al., 2015; Sikl et al., 2013; Šolcová et al., 2014; Vigo et al., 2013; Yi et al., 2014; Yi et al., 2016; Wang et al., 2014; Zavalko et al., 2013). Polar environments are predominantly described by day and night periods, as well as frequent station isolation during winter months, making crews fully self-sufficient even in emergencies. In this, they are perfect analogues to future long space missions. For all that a station does not experience polar day (Chen et al., 2016b).

Another consideration is that the population included in such studies is mostly older than other ICE/EUE, and crew selection methods differ. Finally, although some parallels can be drawn, Antarctica does not replicate the weightlessness and radiation that space travelers may experience in space. This heterogeneity necessarily impacts the variables studied and raises questions about the generalizability of results. It is essential to be able to homogenize all the measurements collected within these environments. This work has already begun in the Antarctic research bases (Van Ombergen et al., 2021). As space travel continues to expand, crews will face new, and increasing challenges (Binsted et al., 2010; Engel, 2019; Orasanu & Lieberman, 2011; Palinkas, 2000; Shepanek, 2005). Given the impossibility of being evacuated or of receiving material assistance from outside, the crew can only rely on its own resources, hence the issues related to crews' selection and training.

Drawing upon the work of Bartone et al. (2018), our analysis shows that studies onboard submarines are least representative of the space environment these last years, notably because of the shorter mission duration and larger crew size. However, the stressors encountered during a patrol are the most similar to those encountered during space missions (Crosnier, 2013; Ferragu, 2019; Lafontaine, 2019; Lefranc et al., 2021; UK report, 2019). In this respect, they may be considered as the best analog (Orasanu & Libierman, 2011). To provide clear guidelines, it is necessary to define a list of environments suitable for studying

stressors involved for future space missions. Initially, space analog missions were developed based on the methodology applied for orbital spaceflights. Consequently, it seems necessary to re-categorize analogs according to new criterias that consider environmental constraints (e.g., environmental factors, characteristics specific to space), operational constraints (e.g., workload, crew composition, size, mission duration, specific tasks performed during the mission), and stressors (e.g., temporal, physico-psychological, social, and post-mission factors). The most complex constraints to measure are the temporal aspect of the mission, the distance from planet Earth, the confinement in a restricted space, the crew life and the management of the permanent danger of death. It is difficult to find a place where all these characteristics can be combined with the impact of the space environment on the human body. Today, analogue environments allow some of these characteristics to be studied separately. Nevertheless, there remain questions on the cumulative effect of all these elements. This should not be ignored, as it is precisely this cumulative effect that can lead to the individual's resources being exceeded and to a slide towards a state of chronic stress that is deleterious to health. In addition to these aspects, it also raises the question of crew selection. As long as we will be unable to define the real impact (i.e., in its global perspective) of future missions, it will not be possible to highlight the type of profile to be recruited (i.e., depending on the type of resources to be deployed to adapt). A necessary and valuable part of the development of future space missions would be long-term spatial simulations that consider the full range of cumulative effects found in ecological environments. Analogs make it possible to work with larger sample sizes, identify characteristics specific to each environment, and observe their impacts on behavior and performance (Palinkas, 2000; Shepanek, 2005). Future space exploration will be very different to current ISS missions, and professionals will need to adapt to these new objectives. A reflexive work on these issues seems essential to identify the future space analogues. A summary of the results is highlight Figure 2.

4.6. Impact of extremes on the human being

Our review highlighted significant inter-individual variability. Regardless of the field of study, results are mixed (Basner et al., 2014; Clément et al., 2020; Flynn, 2005; Kanas et al., 2013; Kim et al., 2018; Oluwafemi et al., 2021; Pagel & Choukèr, 2016; Palinkas et al., 2000; Strangman et al., 2014; Zimmer et al., 2013). Some find an alteration in performance, psychological disorders, and sensory and physiological changes, while others find no change, or even improvements. These modifications are not systematically independent of the phase of the mission, illustrated by the so-called ‘wintering’ syndrome, or the third-quarter phenomenon. Palinkas and Suedfeld (2008) argue that this is due to psychosocial, rather than environmental factors, and that it is independent of the duration of the expedition. There is no evidence of a temporal effect because results are inconclusive. They highlight a cumulative effect to environment exposure involving both temporal and seasonal aspects. A review by Patel et al. (2020) evaluated the evidence regarding a third-quarter phenomenon. They only identified a significant effect for *Adjustment*, which reflects individual morale. Also, some of the reactions appear to be related to prolonged isolation in extreme environments (Cunha et al., 2021). Although these symptoms are frequently reported, they are rarely treated. Palinkas et al. (2008) related them to the cold and psychological stressors of living in the environment. Mullin (1960) argued that cold, danger, and hardship are not major stressors. Overall, the third-quarter phenomenon appears to be associated to emotional, fatigue, social, cognitive concerns and dependent of the isolation period rather than mission timeline. Nevertheless, most of studies do not report any sign of third-quarter phenomenon. This appears to be due to environmental factors (i.e., third-quarter phenomenon reported most frequently in Antractic bases) and interindividual variability. Thus, there is a need to conduct studies that explore the *in situ* impact of the evolution of the different measures through different specific times (e.g., weekly, monthly, semester, quarterly). This depends on the specificities of the mission and

must be adapted to these needs. Isolation and confinement are both of far greater concern (Palinkas, 1991), and tend to increase over time (Bhargava, 2000).

Results of this review suggests that the individuals in tomorrow's missions will have the necessary background to carry out the mission they are given. Professionals in the ICE/EUE environment are adjusting to survive the first few weeks in the new environment to potentially acclimatize to the new time and environmental space they are dealing with. There are no major events to report. Nothing that directly jeopardizes an individual's life. According to the transactional model of the stress episode established by Lassarre (2002), a stress episode is structured according to three concepts: the *situation* (i.e., a state of stress arises when an individual is faced with an issue for which he or she must estimate gains and losses), the *transactional process* (i.e., the emotional and cognitive evaluation of a situation), and the stressor (i.e., emotional and cognitive evaluation of a situation in relation to its constraints and resources, the issue at stake, the magnitude and difficulty of the task to be accomplished) and the action (i.e., responding to the issue at stake in the situation in order to put an end to the stress episode through action or inaction). A stress episode is delimited by a temporal space during which individuals sometimes anticipate and sometimes feedback. Acclimatization to the environment and ultimately adaptation in the broad sense is the result of a process of negotiation leading to a compromise between individual needs and environmental demands. Depending on what is at stake in the situation, the response may differ. Thus, each individual in an ICE/EUE environment goes through a set of specific processes to respond to environmental signals. The latter induce phenotypic changes that can last for a long or short time. This will depend on the resource capacity of the individuals. In this context, it seems difficult to influence the level of environmental demands. Neither is their level of severity flexible. The environment, due to the nature of the risks to which it exposes crews, is very demanding, especially in the space environment. Consequently, it seems relevant to operate

on the resources to an individual with a quintuple temporality (i.e., long before, pre *in situ*, *in situ*, post *in situ* and long after). The targets are both inter-individual (e.g. emotional regulation strategies, sleep management, physical activity) and intra-individual (e.g. group cohesion, strengthening the link with the Earth). The *demand-resource model* developed by a research team (Bakker & Demerouti, 2007; Demerouti et al., 2019) highlights the relationship between the demand inherent in work activities and the perceived resources available for them. While environmental demand affects the health of individuals, resources are dependent on the level of motivation predictive of engagement and performance. This is where the challenge of selection arises, with profiles that can endure the challenges arising from the mission and the environment, but also from the values attached to the mission they have to accomplish, and which give meaning to their lives. This is less apparent in polar environments, with more frequent reports of psychological disorders. In the other environments, variations in mood and sleep are observed instead. A review by Zimmer et al. (2013) highlights that the psychological and physical health of crews can be significantly affected in both space and analog environments. Psychological factors may have played a role in three evacuations from the Russian space station (Flynn, 2005). Also, astronauts seem to experience psychological issues throughout a spaceflight (Bettioli et al., 2018; Nicogossian et al., 2016). Both environments' and internal' stressors are reported to be at the root of psychological problems experienced both during and after long-duration space travel (Marazziti et al., 2021). Depressive and anxious symptoms were reported in Mars 500 simulation mission (Basner et al., 2014), as well as in polar stations (Premkumar et al., 2013; Strewe et al., 2018). Palinkas and Suedfeld (2008) reported that insomnia, irritability and distraction were the most common symptoms. Also, mood disorders were highlighted in Mars 500 mission, with specific time report (Basner et al., 2014; Gemignani et al., 2014; Šolcová et al., 2014; Wang et al., 2014) and a decrease in emotional regulation (Šolcová et al., 2014; Yi

et al., 2016). Stress levels were mitigated. Studies reported high levels of stress in space (Barger et al., 2014), simulations space missions (Basner et al., 2014; Jacobowski et al., 2015; Wang et al., 2014; Yi et al., 2014; Yuan et al., 2019), or in polar stations (Binsted et al., 2010; Moraes, 2020; Nicolas et al., 2015). Others tend to reach casual rates (Nicolas et al., 2014; Strewe et al., 2018). During a simulated Mars expedition, crew reported subjective stress rating, despite no significance on cortisol level (Groemer et al., 2010). Nevertheless, several somatic symptoms associated with stress were reported (Kanas et al., 2013; Palinkas & Suedfeld, 2008; Yuan et al., 2019). Most of the findings were reported by space simulation missions and polar winterers. Astronauts and submariners are populations trained and selected for their stress management. This may be one reason why this issue is not highlighted in the literature.

Sleep disorders appear to have the most negative impact. Among space travelers, restricted sleep is associated with abrupt changes in the sleep/wake schedule, lack of a 24-hour light–dark cycle, high workload, and physical stress (Flynn-Evans et al., 2015). Poor sleep has been found to be one of the main factors influencing neuropsychological changes (Kanas, 1997), although hypnotics may help (Barger et al., 2014; Basner et al., 2015). Space travelers sleep, on average, six hours per night, a level that is considered as chronic deprivation (Orasanu & Lieberman, 2011). However, sleep alone may not constitute a factor that decreases performance (Moore et al., 2019). Sleep is also impacted in space analogs in which fatigue was found to be significantly higher (Basner et al., 2013; Basner et al., 2015; Wang & Wu, 2015; Zavalko et al., 2013), but not necessarily consistent toward the literature (Chen et al., 2016b; Gemignani et al., 2014; Groemer et al., 2010; Matsangas et al., 2017; Pattyn et al., 2017; Trousselard et al., 2015; Wang & Wu, 2015; Yi et al., 2014). The latter has major implications for its close links with cognitive performance. The results are mixed and seem to be specific to the environments and potentially the tests used. The results are

mixed and appear to be environment and potentially test specific. Both the spaceflight and analog literature report mixed results regarding cognitive performance in ICE/EUE (Pagel & Choukèr, 2016; Strangman et al., 2016). Negative impacts have been identified for high-level cognitive functions, which, along with reduced productivity and alertness, can have catastrophic repercussions for the survival of the crew. A study of a 340-day mission on the ISS found negative effects on post-flight cognitive performance (Garrett-Bakelman, 2019). While some studies find alterations in performance in perceptual-motor and attentional tasks, others do not report a decrease in executive functions (e.g., memory, reasoning, mental arithmetic) (Kanas et al., 2013; Strangman et al., 2014). Thus, least consensus is found (Basner et al., 2015; Derayapa, 1971; Rivolier, 1997). For example, Newman (1999) found, using the Fittsberg experimental paradigm, a significant decrement in motor, but not cognitive performance. Manzey et al. (1993) reported similar results. One hypothesis regarding these mixed results is the use of inappropriate tools to detect changes (Barkaszi, 2016). In this context, Basner et al. (2015) developed a battery of 10 cognitive tests to meet NASA's needs. However, literature point out a significant learning effect on cognitive tasks during spaceflight (Basner et al., 2015; Roberts et al., 2019; Strangman et al., 2014). Another factor underlying this disparity in outcomes could be the adaptation process itself. Strategies and resources for coping with stress are not equally distributed in a social group and identifying successful adaptation will have benefits for future experiments, regardless of the environment (Palinkas, 1992).

Physiological, vestibular and somatosensory impact seem to be inherent to space or confined environments. Physiological (Farrace et al., 2003; Demontis et al., 2017; Garrett-Bakelman et al., 2021; Hughson et al., 2018; Kim et al., 2018; Moraes et al., 2020; Otsuka et al., 2016; Patel, 2020; Wan et al., 2011) and brain (Angeloni & Demontis, 2020; Schneider et al., 2012; Stahn & Kühn, 2019; Van Ombergen et al., 2017a; Van Ombergen et al., 2017b)

modifications have also been observed. Specific cardiovascular reactions occur in long space mission (Garrett-Bakelman et al., 2021), long space mission simulations (Bersenev et al., 2013) and ice desert (Gríofa et al., 2011; Moraes et al., 2020). A review by Van Ombergen et al. (2021) examined the results of several years of research at the Antarctic Concordia station. These studies showed a periodic breathing pattern during wintering among the crew. This pattern dominated for most of the night and was associated with an increase in apneic or hyperventilating events, which continuously exceeded the acceptable clinical threshold. During one mission, an increase in obstructive breathing events was also noted toward the end of the stay. However, oxygen deficiency did not induce a clinical increase in acute mountain sickness symptoms during the first three weeks after arrival, nor did it induce venous thrombosis. These results suggest that any effects are heavily influenced by, and dependent on the characteristics and severity of the environment. Moreover, a link between anxiety and vestibular disturbances is suggest via the vestibulocortical hemisphere (Clément et al., 2019). Specifically, anxiety levels during the mission appear to be lower among right hemisphere-dominant individuals (Clément et al., 2019).

During a prolonged stay in space, vestibular and somatosensory systems are also modified (Bock et al., 2001; Demontis et al., 2017; Hallgren et al., 2016; Harris et al., 2010; Lackner, 1993; Roberts et al., 2019; Stahn & Kühn, 2021; Wood et al., 2015). Sensory inputs are affected by the linear acceleration of stimuli reaching the otolith receptors, which are essential to spatial orientation on Earth. This, in turn, impacts balance, walking speed, and head-trunk coordination (Black, 1995; Glasauer et al., 1995; Reschke, 1994). Black (1995) identified a change in somatosensory and visual orientation upon return to Earth. A review by Clément et al. (2020) reports that space travelers have altered assessments of the volume, depth, and height of the habitat in which they are operating, along with distances. Pagel and Choukèr (2016) also cite a study which reports that the Hoffman reflex, considered as a

measure of changes in otolith-spinal reflexes, decreased during the mission, without being significant compared to pre-mission measures. More recently, Stahn and Kühn (2021) identified neurovestibular impairment in, for example, manual dexterity, motion perception, orientation, distance estimation, rotational sensation, head-trunk coordination, along with ataxia, hypo or hypertonia, excessive body weight, and motion sickness. They suggest that complex tasks involving the encoding, processing, storage, and retrieval of visuospatial information may be particularly vulnerable. The authors highlight the essential role of the entorhinal cortex when exploring unknown terrain, navigating new planets, and performing complex operational visuospatial tasks. The hippocampus, which is vulnerable to environmental stressors, is also thought to play a fundamental role in complex spatial navigation. Few information is available on the sensory impact of ICE/EUE, where the monotony is profound. Moderate, reversible changes in visual function have been shown both in studies in the polar environment, due to altitude (Barabasz & Barabasz, 1986; Bosch et al., 2010; Guly, 2012; Leach, 2016; Salam, 2020; Varyvonchyk et al., 2014) and in space, due to the movement of fluids to the upper part of the body (Lee et al., 2018; Mader et al., 2011; Patel et al., 2020; Zhang & Hargens, 2018). Olfactory and gustatory senses can also be disturbed during a stay in space (Leach, 2016; Newberg, 1994; Olabi et al., 2002), and increased sensitivity to sound was reported during the Russian Salyut 6 and 7 missions (Kelly & Kanas, 2012).

Moreover, an important component of the future space missions relates to the return. Some authors underline that post-mission impacts are an important risk in future space missions (Stahn & Kühn, 2021). A few studies in ICE/EUE have reported a link between performance and a lack of recovery (Nicolas et al., 2015; Pagel & Choukèr, 2016). Nevertheless, this is a crucial time point to truly assess, understand the impact of these stays on humans and their interactions with the milieu at all levels (i.e., temporal, psychiatric,

psychologic, cognitive, physiologic, neurophysiologic, and somatosensory factors). The literature report various impact from several weeks to years after the end of the mission (Garrett-Bakelman et al., 2021; Liu et al., 2015; Nicogossian et al., 2016; Strangman et al., 2014; Yi et al., 2015). These ones include psychiatric and psychological disorders, physiological modifications, proprioceptive and sensory decrements, familial issues (Bloomberg et al., 2015; Garrett-Bakelman et al., 2021; Kanas et al., 2013; Stahn & Kühn, 2021; Strangman et al., 2014; Yi et al., 2015; Wood et al., 2015). Preparing the return from the mission will thus be a crucial point to ensure that it goes as well as possible both psychologically and physically. The plastic capacity of the brain has been widely demonstrated and allows adaptation to a new environment. However, the process of returning can be complex and confronts the individual with a new foreign environment. The quality of the feedback depends on the state of health in which the individual leaves the ICE/EUE environment. Each study conducted in these environments should systematically evaluate the recovery of the crews. This fact constitutes a major concern for future long space missions. Lack of recovery can lead to psychological and behavioral disorders and compromise an individual's ability to adapt to environmental stress.

4.7. Adaptation in space and analogs

At present, our results do not allow us to highlight the psycho-cognitive mechanisms underlying adaptation. One of the crucial points is that the difference between the analogues being so important between certain studies, it is not possible to generalize the results and clearly discriminate responses in terms adaptation (i.e., evidenced through acclimatization process). Further studies need to better describe the human responses in the time of the mission; this will be relevant for identify physiological, biological and/or psychocognitive variables of interest for health monitoring during long mission. Indeed, the studies are often heterogeneous, and the observed phenomena mixed or even contradictory. There are as many

possible strategies as there are environments and individuals. Adaptation involves multidimensional, complex, and several dynamic processes (Nicolas et al., 2021). Nevertheless, some categories appear: coping and defense mechanism toward a cognitive regulation; behavioral toward crewmembers, or auto directed; nonlinear over time with stages (e.g., beginning, middle, several weeks before the end, return) as the mission progress; and salutogenic strategies toward positive outcomes. Individuals in space and analogs are an unusual population. They are resourceful, able to manage stress, and adapt (Antonovsky, 1987; Barkaszi et al., 2016; Sandal et al., 2006; Nicolas et al., 2022). Palinkas (1990) reported that people who have spent time in these extreme environments have fewer pathologies than the general population: 73% fewer admissions for neoplasms, 60% fewer for endocrine, nutritional, and metabolic diseases, and 44% fewer for musculoskeletal diseases. Such individuals were generally highly stress-resistant and predisposed to adaptation (Weiss et al., 2000). Another aspect is mindful disposition, where a recent study highlighted its benefits on submariners' ability to cope with confinement during a nuclear submarine patrol (Aufauvre-Poupon et al., 2021). Rohrer (1961) highlighted three stages of adjustment among individuals in ICE/EUE: (1) initial anxiety at the beginning of the mission; (2) mid-mission monotony and depression as the routine is established; and (3) late-mission euphoria or hostility as the end is anticipated. These modifications are particularly apparent during the third quarter, even if the existence of the third-quarter phenomenon remains disputed.

The strategies employed to cope with environmental stress are highly individual. Each person finds a way to balance the demands of the environment, and the resources available to maintain their ability to operate. This model is similar to the stress-adaptation paradigm developed by Selye, in which the capacity to adapt successfully decreases as time passes (Selye, 1956). In a review, Zimmer et al. (2013) showed that the impact of stress factors could affect individual performance during Antarctic missions (i.e., cognitive impairment, hormonal

alterations, stress, fatigue, adaptation difficulties). On the contrary, Palinkas and Suedfeld (2008) suggests that rates of stress may decrease, giving a way to adaptation. In another study, Palinkas and Suedfeld (2021) argue that the characteristic symptoms of polar T3 syndrome are merely a physiological adaptation to prolonged exposure to the extreme temperatures and the lack of light that occur during winter. Finally, four factors have been identified as key to successfully maintaining space travelers' performance during long missions: psychological adaptation; the human-system interface; sleep and circadian function; and behavioral health (Flynn, 2005). Studies of space missions have highlighted strained relations between the crew and the control center. Kanas et al. (2009) argue that this strategy of transferring conflict to the outside world is a way to vent negative emotions. They point out that it is undesirable because of an increased risk of blocked emotions, territorial behavior, and poor group cohesion, which are crucial factors for the success of the mission. Rohrer (1961) described three stages in an individual's reaction to conditions in ICE/EUE. The first stage, initial anxiety (related to the perceived danger), occurs at the beginning of the mission. The second, depression and boredom (due to the routine), increase gradually as the mission progresses. The final stage, terminal euphoria (i.e., childlike, hypomanic and aggressive behavior), is a period of anticipation as the end of the mission approaches (Kanas, 1987). At the same time, the mechanisms that individuals use to cope with these stressors can have a significant influence on their ability to maintain their health and professional activities during the mission. In this context, the coping framework (Lazarus & Folkman, 1984) identifies two, well-known strategies: problem-focused and emotion-oriented. Both are observed in extreme environments (Palinkas & Suedfeld, 2008; Suedfeld, 2001; Suedfeld, 2005), and tend to evolve as time passes (Nicolas et al., 2013; Palinkas, 1989). More recently, Nicolas et al. (2021) highlighted that perceived control towards the environment constraint impact adaptation processes with an increase of emotional and physical component. Both stress and

recovery responses seem correlated with the latitude of the polar station, and thus with the harsh of the environment (Nicolas et al., 2022).

Therefore, dynamic interpersonal, biological, and psychocognitive systems interact with contextual and environmental factors to shape acclimatization and adaptation over the mission span (Lehman et al., 2017). It seems interesting to consider a dynamic biopsychosocial model that views human health in ICE/EUE as the product of reciprocal influences of biological, psychological, cognitive. To these influences should be added the social dynamics that are divided into interpersonal factors and broader contextual dynamics of the mission. All these dynamics unfold over personal and group time. Moreover, the importance, or centrality, of these influences may vary within a person over time. The multilevel in responses to constraints may explained the difficulties to offer a consensual model of acclimatization and adaptation to ICE/EUE. Furthermore, it is necessary to take into account that self-reported psychological measures, cognitive performances and biological outcomes imply different dynamics of responses (Epel et al., 2018). Self-questionnaires use limited Likert-type scaling including interval responses, cognitive performances are based on quantification of errors and/or reaction time for an overview of the cognitive impacts whereas biological outcomes are most often not linear (Epel et al., 2018). Lastly, the use of different variables across multiple studies makes an integrative approach to adaptation in ICE/EUE more difficult. Concerning the main psychological recorded variables, for example, it should be noted that the use of the concepts of emotion and mood is not taken into account. In view of the differences proposed for these affective states, notably in their temporal inscription, it can be suggested that the variations of emotions inform on the adaptation processes and that the variations of mood inform on the adaptation processes.

In order to advance our understanding of how space's and analogs' constraints influences trajectories of health, the recursive and multilevel processes that link ICE/EUE to human responses must be considered in an integrative dynamic approach (Figure 3). Such an approach conceptualizes health as a system where interpersonal, biological, and psychocognitive systems interact with each other and do so differently in different social contexts. Consequently, a unified roadmap using shared interpersonal, biological, and psychocognitive variables between researchers of this field would be useful. This would allow comparison of data across studies to better understand the processes of acclimatization and adaptation to ICE/EUE and to better consider countermeasures in relation to mission contexts.

4.8. Tomorrow's challenges

Tomorrow's space exploration will impose additional stressors on crews that will be consubstantial to any space life. The latter include the *Earth-out-of-view* phenomenon, technological aspects (duration/ distance, communication delays), the use of free time, autonomy, and responsibility. Mars is much further from Earth than any other place we have ever been, and this distance significantly changes the mission profile. Although some individuals have been in orbit for more than a year, no human being has spent two years in space with the same crew. Isolation, confinement, monotony, and distance from loved ones is expected to have unprecedented consequences on the health of crew members. Moreover, no individual has ever experienced the Earth-out-of-view phenomenon (Kanas & Manzey, 2008). This phenomenon considers that the fact of no longer seeing and thus feeling the Earth will cause psychic disorders. However, no human being currently experienced it because no one has ventured far enough from Earth. Its consequences can only be imagined and reflexive. Only the first crew on a trip to Mars will be able to answer this question as Earth dwindles in the window. While authors assume that it will result in a profound sense of loneliness (Kanas,

2005; Launius, 2010; Palinkas & Suedfeld, 2021), there is no way to assess the consequences in advance. Kanas (2005) raises the question of a reorganization of the human species in new colonies.

Over time, ICE/EUE living conditions have improved considerably to minimize stressors, and many authors have argued that the community focuses too much on the pathogenic experience of individuals in these extremes (Palinkas, 2003; Shea et al., 2009; Suedfeld, 2005; Vanhove et al., 2014; Zimmer et al., 2013). Due to the nature of ICE/EUE environments, it has been considered for many years that humans cannot adapt. The literature has repeatedly reported the negative effects of exposure to these environments without considering that the lack of result could ultimately be a result. Progressively, salutogenic effects are being describe, but it will take some time to replace the literature focusing only on negative effects and to get a more realistic view of the mechanisms that are really at work. ICE/EUE could also have beneficial and positive consequences (Leach, 2016; Suedfeld, 2001; Suedfeld & Mocellin, 1989; Vakoch, 2012) – some space travelers dream of returning to space, Antarctic winterers go back, and submariners carry out multiple missions. Cherry-Garrard (2013) underlines this ambiguity, noting that an Antarctic expedition is “the worst way to have the best time of your life”. Since the first space missions, space travelers have reported feelings of adventure and accomplishment, pleasure, fulfillment, humility, humanity, and a restructuration of their values (Collins, 1974; Kanas, 1987; Suedfeld & Weiszbeck, 2004). Some compare this to the ‘break-off’ experienced by fighter pilots, which is a feeling of separation from Earth (Clark & Graybiel, 1957). Similarly, many space travelers have experienced the *overview* effect. Defined by White (1987), this refers to a profound reaction to viewing Earth from beyond the limits of its atmosphere – an awe-inspiring and self-transcendent experience (Yaden et al., 2016). Several studies report personal growth, increased self-awareness, resilience, self-esteem, self-confidence, and a better ability to cope

with stress in the ICE/EUE (Bhargava et al., 2000; Palinkas, 2003; Šolcová & Vinokhodova, 2013; Vakoch, 2012; Zimmer et al., 2013). Palinkas (2003) found that depressed mood was inversely associated with the severity of the physical environment, and that the wintering experience was related to reduced rates of later hospital admissions. This impact of the severity of stressors has also recently been described by Nicolas and collaborators (2021, 2022). Altogether, the literature supports the idea that something happens in these environments that transcends anything these professionals may have experienced before.

Tomorrow's spaceflight will pose challenges that are quite different from those we have already faced. Further work may have practical implications for understanding human behavior in extreme situations (Nicolas et al., 2018). Although the literature reports mixed results on the impact of ICE/EUE on humans, little is known about individual adaptation to such extreme conditions (Figure 2). If studies on Earth are any indication, future missions involving large crews, more spacious environments, and more sophisticated communications with the outside world should result in fewer psychosomatic complaints, and fewer psychological and cognitive disorders. However, the heterogeneity of existing results means that we cannot draw firm conclusions, and current studies are carried out in environments that do not resemble a trip deeper into the solar system. Finally, targeted countermeasures that help to maintain space travelers' health need to be established (Palinkas & Suedfeld, 2021; Salam, 2012; Stahn & Kühn, 2021). Countermeasures before, during and after space flight are essential. Committee on Space Biology and Medicine (1998b) shed light on countermeasures classified by stages. At the pre-flight stage, learning and training coping strategies is important, especially in males regarding our findings. During in-flight stage, measures include real time monitoring, interventions with the ground and aerospace medical team, facilitation to specific medical specialties, communication with families. Post flight stage include debriefing, and health evaluation. Manier et al. (2016) went further by specifying the

implementation of a 'psychological seal' before and upon the return from mission. They also specify the issue of habitats able to meet the challenges of the space environment and mission needs. Currently, countermeasures are being investigated and implemented to overcome spaceflight-associated health risks. The Evidence Based Practice (EBP) perspective is a framework that guides research and intervention practices (Sackett et al., 1996). Originating in medicine, EBP suggests that intervention design rests on three foundational pillars: (1) scientific research knowledge about how interventions work, (2) experiential knowledge of populations and professionals, and (3) consideration of the specific preferences, values, and contexts of target populations (Sackett et al., 1996). Thus, it seems important to conduct studies in line of the EBP perspective. Some papers investigating the potential of noninvasive brain stimulation to modify brain activity (Badran et al., 2020; Romanella et al., 2020). Among them, various techniques are studied including transcranial magnetic stimulation, transcranial electric stimulation. These techniques should lead to maintain cognitive performance, increase neuroplasticity, motor system, increase psychological states, decrease psychiatric disorders, and prevent ocular issues during the mission (Romanella et al., 2020). Thus, they are promising tools to maintain health and prevent risks at all levels (i.e., pre-in flight-post) for future long space missions. Botella et al. (2016) explored a psychological strategies program learning to increase positive emotions during mission. However, there are concerns about the assessment of mood and emotions in the literature. Depending on whether one uses the term 'mood' or 'emotions', tools and resources to be developed and applied in individuals may differ. Mood, given its long-term temporal nature, implies practices with beneficial consequences (e.g., diet, physical activity, sleep quality). Emotions arising from a particular event and thus in a sudden and short temporal context suggest a different regulation (e.g., conflict resolution, recontextualization to cope with the situation). These considerations should be taken into account when researchers develop and design countermeasures to

improve emotions and mood. Benefits of being mindful have also been investigated to maintain health during a submarine patrol (Aufauvre-Poupon et al., 2021). Also, regular activity and exercise appear beneficial in limiting the effect of isolation and confinement that crew may have (Martin-Krumm et al., 2021; Nicogossian et al., 2016; Petersen et al., 2016; Schneider et al., 2010; Schneider et al., 2013). Furthermore, engagement in these activities is likely to maintain people's perceptions of control over their environment. Nicolas et al. (2021) highlighted the role of perceived control on adaptation processes. Thus, they potentially have feedback effects on the stress level of crews (Gabriel et al., 2020; Lazarus, 1991). Lefranc et al. (2021, *submitted*) investigates the association between virtual reality and physical activity to and highlight its benefits to overcome health risks in ICE/EUE environments. Technological advances open the way to new possibilities. The use of virtual reality and digital health are the future of space medicine (Salamon et al., 2018), especially the use of natural virtual scenes (Anderson et al., 2017; Anderson et al., 2018; Anderson et al., 2022). Artificial gravity is under evaluation to prevent the cardiovascular deconditioning as well as ocular alterations during spaceflight (Anderson et al., 2018; Evans et al., 2018; Nicogossian et al., 2016). Bloomberg et al. (2015) developed a sensorimotor training to increase proprioception and decrease cognitive load of visually dependent subjects. Finally, NASA investigates a lighting countermeasure to synchronize circadian rhythms during Phoenix Mars Lander mission (Barger et al., 2012). This countermeasure has shown its implication to improve sleep and its potential in ISS (Brainard et al., 2016). Also, the research team highlighted the benefits of a blue-enriched light associated with physical activity to improve operability (Barger et al., 2014; Barger et al., 2021). Nevertheless, countermeasures must be seen as a dynamic structure that can be adjusted to the individual needs identified before the mission, but also in function of the duration and the type of the mission. Thus, countermeasures tailored to each individual and therefore personalized are essentials. This

finding underscores that it is fundamental to use an integrative approach with several methodological approaches to better health monitoring and adapt countermeasures. A better understanding of adaptation to ICE/EUE will allow a relevant crew monitoring with a panel of tools sufficiently flexible to be suitable for the crew profiles.

Highlights of this systematic review suggest practical results overview breaking down several disciplines together and proposes some approaches in terms of countermeasures to the main results of this review (Figure 2).

4.9. Limitations

Our systematic review has several limitations. Firstly, there are few randomized controlled studies (i.e., studies involving a randomly assignment of subjects between an experimental group and a control group). Most of the corpus of articles reports case studies or observational studies, with a medium to low level of evidence, and a risk of bias that is inherent to the environmental conditions. These studies deal with the challenges of conducting studies in extreme environments in which a significant number of constraints must be considered (e.g., high costs, few subjects, permanent adaptability, danger, mission demands). Thus, it is complex to conduct randomized controlled studies under operational and environmental constraints. Nevertheless, they are currently the most reliable means of studying human adaptation to ICE/EUE. Although studies conducted under laboratory conditions are more methodologically reliable, they clearly lack ecological validity. In extreme conditions, cognitive-psycho-physiological factors must be studied with realistic environmental, operational, and time constraints. At the present time, we still cannot say what the impacts of a long trip outside the low Earth orbit will be. Secondly, the reviewed studies are relatively heterogeneous, which is one reason why we could not conduct a meta-analysis. Different methodologies, and the multitude of environments prevent any firm conclusions. In

recent years, space agencies have been more willing to collect similar data from research bases in Antarctica. However, the lack of harmonization limits comparisons. Further international collaborations could help to overcome this problem. Third, most reported sample sizes are very small, leading to two issues: a lack of statistical power, and unrepresentative outcomes. Finally, although crews are carefully selected, depending on the country and the environment, the population can be very heterogeneous. Men make up most of the population, and gender differences have not really been taken into account. Implementing selection criteria that reflect those of space travelers would give a better insight and reduce bias. While, overall, these limitations are unavoidable, they contribute greatly to the lack of clarity in the results reported in the literature.

4.10. Conclusion

Space, characterized by reduced gravity, and environmental and operational stressors, is a hostile environment for the human species. Nevertheless, since the beginning of the space conquest, studies have shown that humans are able to adapt. While NASA's mission to Mars is expected to last 1,100 days, missions to more distant places may be even longer, and will expose crew members to unprecedented risks. Therefore, understanding the impact of the extreme on the individual, and adaptation mechanisms is more necessary than ever to ensure the success of future human space exploration. Analog environments are a valuable way to study the risks. Our results highlight that there has been a slowdown in research since the 1980s, and there is a need to reconsider how analogs are chosen and used to predict future long-duration space travel. This systematic review covers many disciplinary fields that may not necessarily share the same discourse but are complementary in that they address concepts such as stress, stressors and the framework of adaptation in atypical environments. This integrative approach is the strength of this review. The mixed results reported in the literature

underline the fundamental need to harmonize methodologies and report non-changes that could be signs of adaptation. We also need to develop countermeasures to mitigate the harmful effects of ICE/EUE and improve individual performance. We need clear answers to the following questions: Is a human being capable of surviving in such an extreme environment? If so, at what cost? The door to future human space exploration is opening, it is only waiting to take flight.

4.11. Acknowledgements

The authors would like to thank the *Centre National d'Etudes Spatiales* (the French Space Agency) and the *Agence de l'Innovation de Défense* of the *Direction Générale de l'Armement* (the French Government Defense Agency), for their support.

4.12. Author contributions

BL, CMK, MT drafted the manuscript. All authors contributed to the development of the selection criteria, the risk of bias assessment strategy, and data extraction criteria. BL developed the search strategy and the implementation of the PRISMA-P protocol. BL, FD and NP developed the equation for databases. All authors read, provided feedback, and approved the final manuscript.

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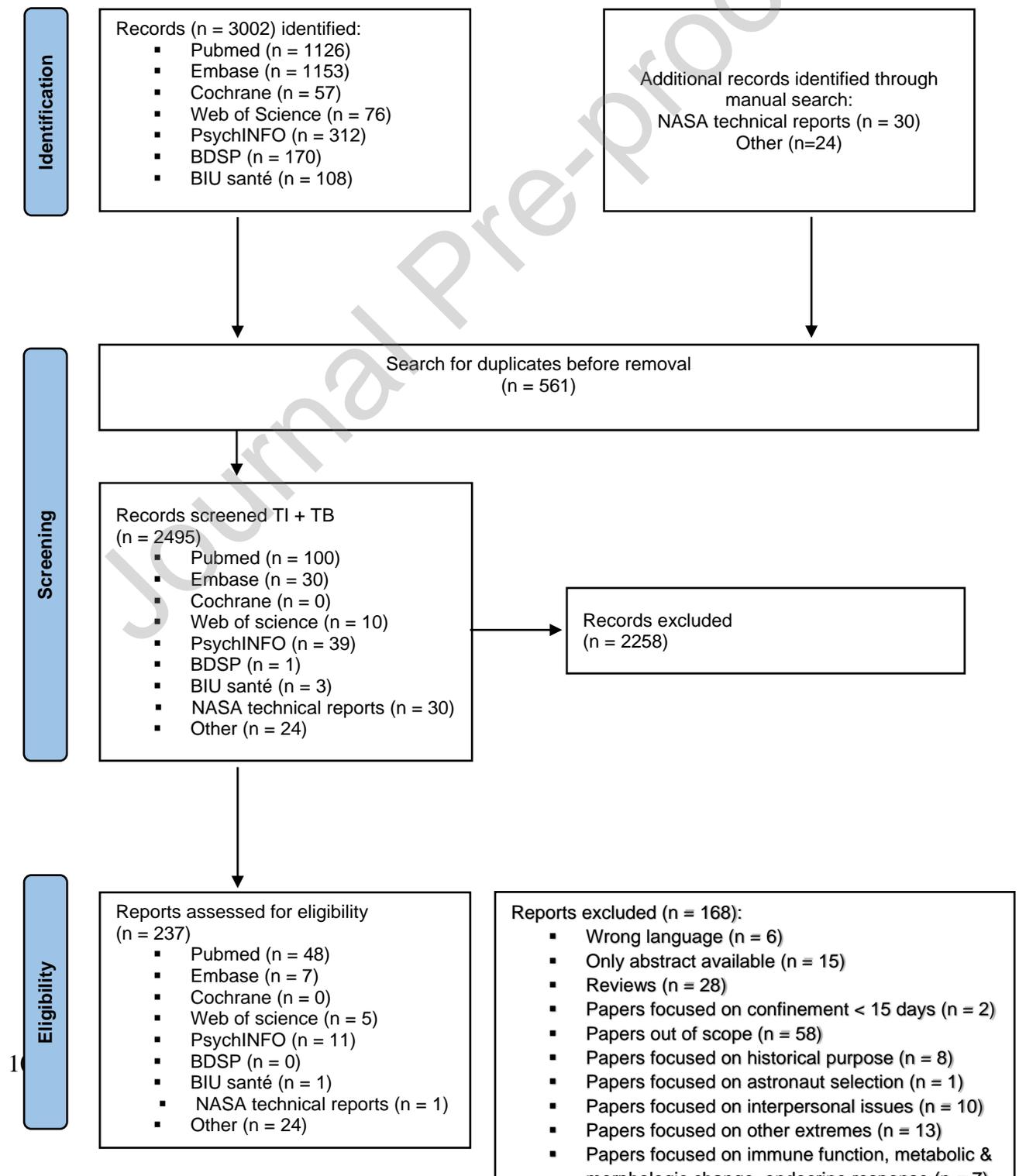
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6. Figure

Figure 1

PRISMA flow chart



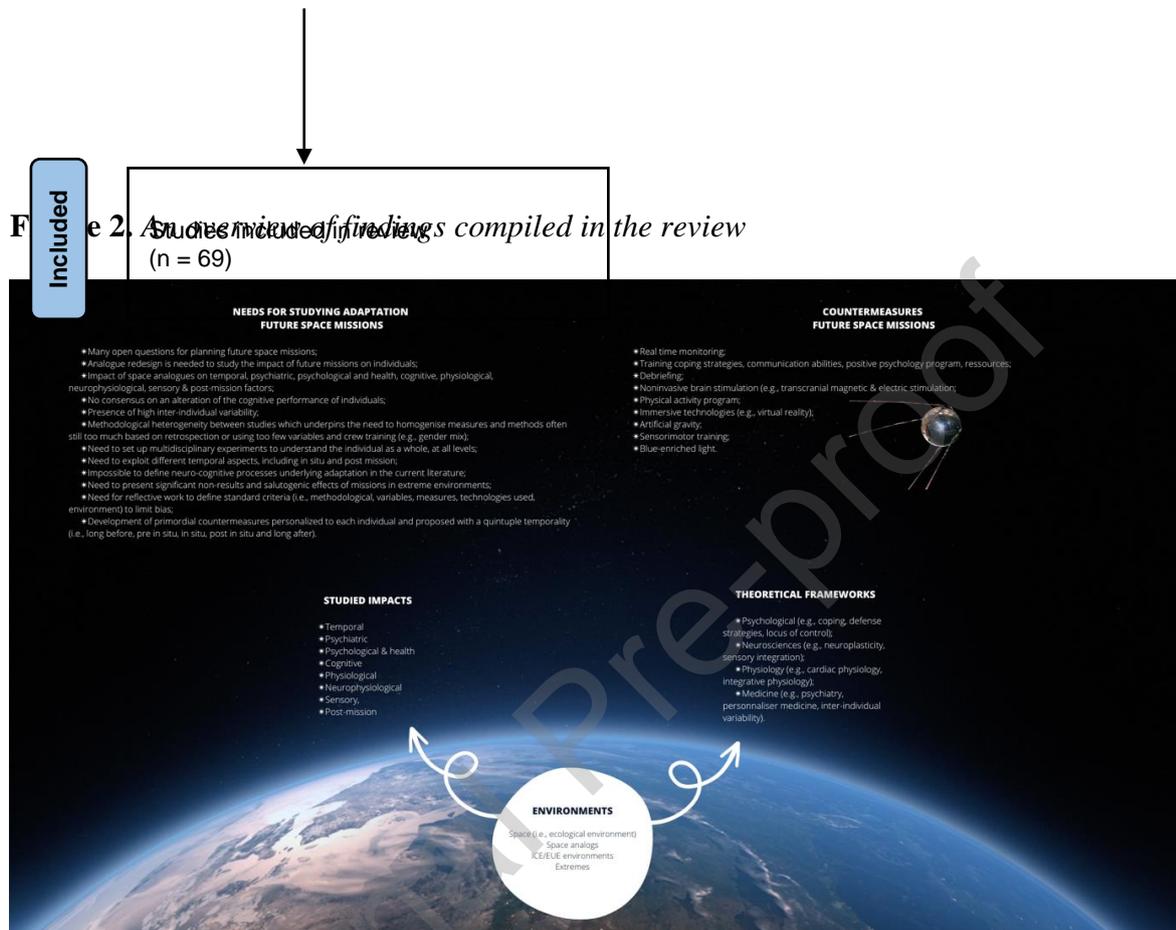
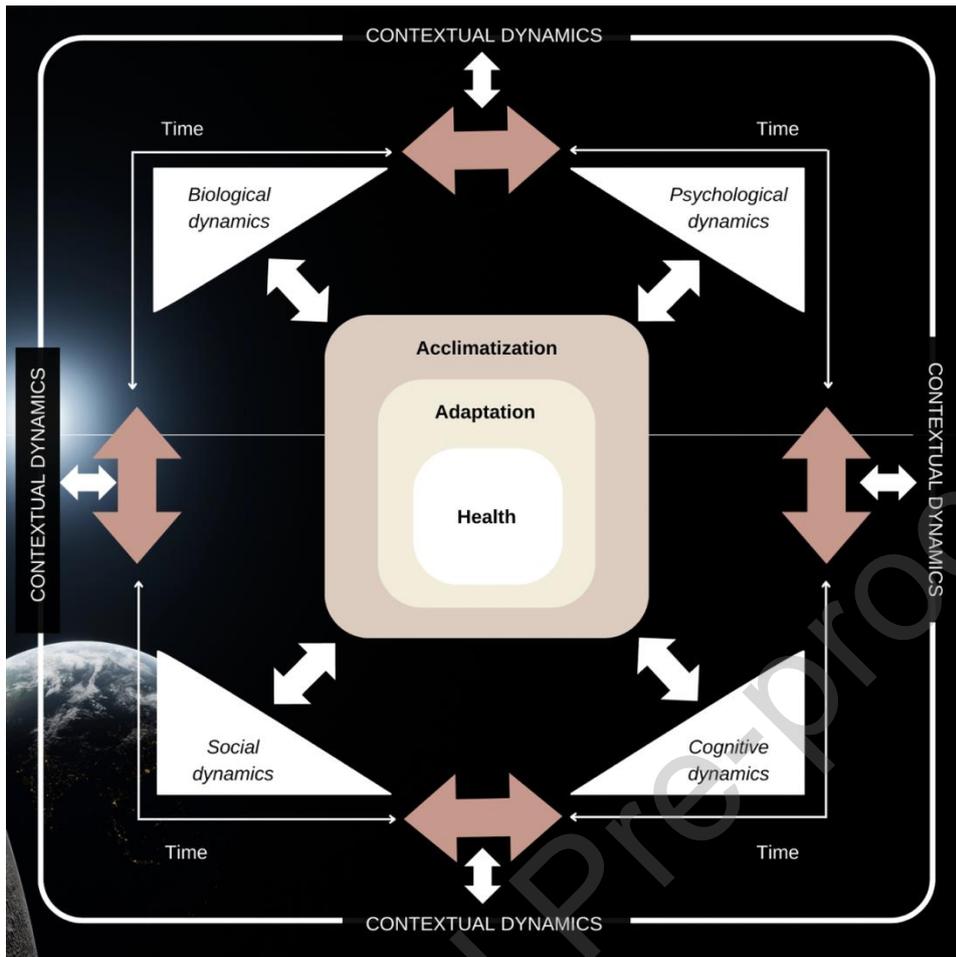


Figure 3. A dynamic biopsychosocial model of relevant factors organizing the complexities of acclimatization and adaptation of human to ICE/EUE. Acclimatization refers to a coordinated response to several simultaneous stressors to improve fitness to the environment whereas adaptation explicitly recognizes that stressor-strain relationships unfold over time



7. Table

Table 1

The major stressors in ICE/EUE

Stressor	Environments
Perpetual danger	Spacecraft, polar station, submarine, expeditions
High-tech life support system	Spacecraft, polar station, submarine
Confinement	Spacecraft, polar station, submarine, caves
Isolation	Spacecraft, polar station, submarine
Physical discomfort	Spacecraft, polar station, submarine, caves, expedition
Protective clothing	Spacecraft, polar station, submarine
Photoperiodicity	Spacecraft, polar station, submarine, simulation, caves
Lack of intimacy	Spacecraft, polar station, submarine, simulation, caves
Possibility of sudden disaster	Spacecraft, polar station, submarine, expeditions
Cross-cultural differences	Spacecraft, polar station, expeditions, simulation
Demanding work	Spacecraft, submarine, simulation
Dream time	Polar station, expedition, caves
Unusual circadian rhythms	Spacecraft, polar station, submarine

Limited communication	Spacecraft, polar station, submarine, expedition, caves
Sensory deprivation	Spacecraft, polar station, submarine, simulation, caves
Monotony	Spacecraft, polar station, submarine, simulation, caves
Radiation	Spacecraft, submarine
Microgravity	Spacecraft
Noise	Spacecraft, polar station, submarine
CO ₂	Spacecraft, submarine, simulation
Temperature	Spacecraft, polar station, submarine
High altitude	Polar station, expeditions
Humidity	Spacecraft, submarine, expeditions, caves
Similar duty rotation	Spaceflight, polar station, simulation
Limited supplies and equipment	Spacecraft, polar station, submarine, simulation

This list is not exhaustive. Only the most frequently mentioned stressors are reported.

Table 2

Fidelity of studies compared to long-duration space missions

Category	Scoring			
	Similarity to spaceflight		<i>Spaceflight</i> (3)	<i>Space simulation</i> (2)
Similarity to long-duration expedition astronauts		<i>Similar with respect to age, sex, and education, and possibly cultural diversity</i> (3)	<i>Similar with respect to age and education, but not sex or cultural diversity</i> (2)	<i>Possibly similar with respect to age, but not sex, education or cultural diversity</i> (1)
Similarity with respect to duration of mission	<i>Over 12 months</i> (4)	<i>6–12 months</i> (3)	<i>1–6 months</i> (2)	<i>Less than 1 month</i> (1)
Similarity to crew size		<i>Small (1 to 8)</i> (3)	<i>Moderately small (9 to 15)</i> (2)	<i>Large (>16)</i> (1)

Overall fidelity: High: 10–13 (21 studies); Medium: 7–9 (24 studies); Low 4–6 (5 studies).

Table 3

Characteristics of the included studies

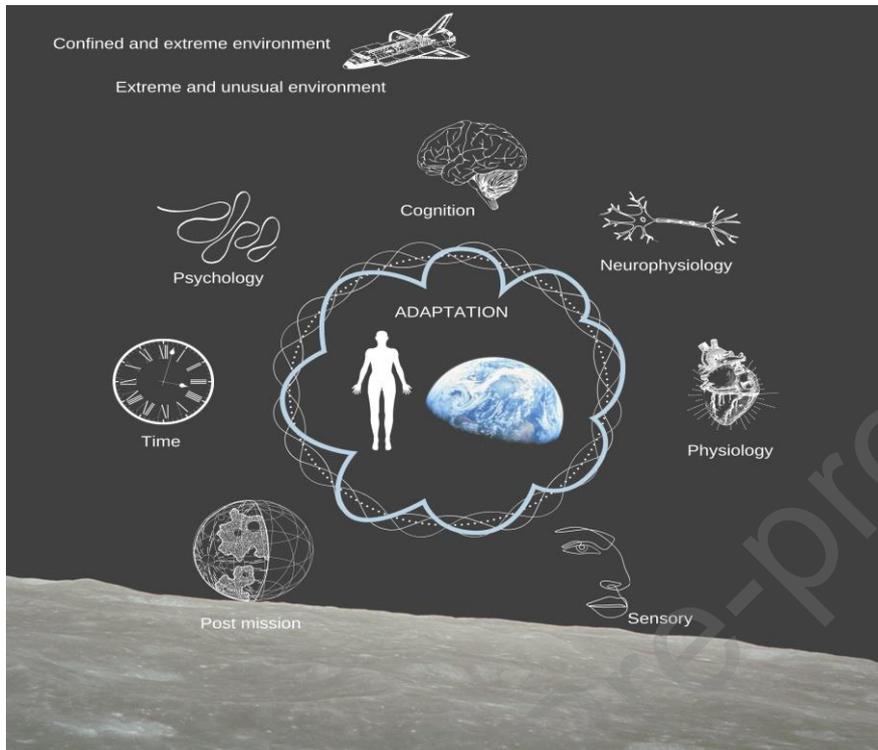
cf. excel file (file's size). This table will be placed in the supplementary materials file.

Table 4

Specificities of the environments studied

cf. excel file (file's size).

Graphical abstract



Highlights

- Space analogues should be rethought for the next long space missions
- Significant inter-individual variability and mixed results in extreme environments
- Positives and non-changes results could be signs of adaptation
- Post-mission recovery needs to be studied