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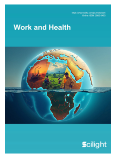

Review

Human Adaptation on 'White Mars': A Narrative Review on the Biopsychosocial Effects of the Isolated, Confined, and Extreme Environment at Concordia Station, Antarctica

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Abstract: This narrative review summarises the current published research from two decades of work at Concordia Station, Antarctica, one of earth's most hostile environments. Its unique location and complete inaccessibility for nine months every year makes it an invaluable long-term analogue for space. Since 2005, the European Space Agency has implemented a biomedical research program to study human adaptation in such an extreme environment. The temperatures, altitude and polar light cycle subject Concordia's inhabitants to chronic physiological and psychological stressors. Twenty years of research on 'White Mars' has informed our understanding of human adaptability and health risks of life in isolated, confined and extreme (ICE) environments like Concordia. Sleep health and human psychology have been the most studied biomedical fields at Concordia. The exposure to such an extreme environment entrains acute and possible long-term health issues affecting every body system that still need to be addressed. Furthermore, as a rapid increase in space travel and use of ICE environments is expected in the upcoming decades, this review highlights the importance of further research to develop robust countermeasures to the challenges faced at Concordia station for ensuring a successful mission in any ICE environment. In particular, more research is required on women's health, especially considering recent findings on sex differences in adaptability to space and work in ICE environments.

Keywords: Antarctica; human physiology; neuroscience; Hypobaria; Hypoxia; psychology

1. Introduction

Isolated, confined and extreme (ICE) environments are domains that induce biological, psychological and social stress on their human inhabitants, challenging the maintenance of physical and mental health, behaviour, and cognitive functioning [1]. Examples of ICE environments include polar research stations, submarines, and outer space.

For the scientific community, isolated, confined and extreme environments offer incredibly unique opportunities for research across a broad range of disciplines on human adaptation when pushed to extreme limits. Antarctica alone houses a changing population of around 1000 year-round on its research facilities (with up to 5000 in the summertime), not counting those on ships [2]. Its bases enable important research on climate and atmospheric sciences, biodiversity, astrophysics, biomedicine and more [3]. Human biomedical studies are important in determining the long and short-term effects of the stressors of ICE environments on their occupants so they can continue to work there safely and for longer periods of time. In aerospace medicine, terrestrial ICE environments are of particular interest as space analogues. Biomedical research in ICE environments can therefore help to predict and overcome future challenges in lunar and Martian missions. This can refine astronaut selection criteria and develop countermeasures to biopsychosocial difficulties expected in long-duration spaceflight. In addition to physical health, the fluctuation of group dynamics when faced with the acute and chronic stressors of ICE environments are a critical point of study for ensuring successful future missions. Due to its likeness to Mars, the European Space Agency has been involved in ongoing biomedical research at the Antarctic base and ICE environment Concordia Station for over two decades. [1].

Concordia Station (see Figure 1) is one of three permanent inland Antarctic research facilities established as a joint venture between the French (Institut Polaire Émile-Victor [IPEV]) and Italian (Programma Nazionale per Ricerche in Antartide [PNRA]) polar institutes [3,4]. Since 2005, it has been permanently crewed. Concordia has been dubbed 'White Mars', owing to its position on the continent, its isolation and the need for crew autonomy, particularly during the Antarctic winter.

Figure 1. Concordia Station at Dome C, entirely isolated in the white Antarctic desert [4].

The following sections detail the magnitude of Concordia's isolation, confinement and extreme terrain and its day-to-day operations. This is to allow readers to better contextualise the research conducted at Concordia and how other environments on earth (and beyond) can be used to further anticipate challenges in human health and adaptability at the station.

1.1. Isolation and Confinement at Concordia

Located at 75.1002° S, 123.3463° E atop Dome C on the East Antarctic Plateau, the station is over 1000 km inland at 3233 m of altitude (equivalent to 3800 m at the equator) and around 600 km away from the nearest other Antarctic base, this being the Russian Station *Vostok*. The altitude exposes the station to extreme weather (with temperatures dropping to −80 °C in winter), which prevents access to and from the base between mid-February to mid-November [1,3]. During these 9 months, the crew is more isolated from human civilisation, including medical aid, than the astronauts on the International Space Station.

The winter-over crew are a group of 12 to 16 individuals of varying ages, educational levels and backgrounds who must spend around 13 months together in this base, isolated in the middle of the Antarctic desert. Although the winter-over cohort is small, in the 3-month summer season the station can host up to 75 people (partly housed in an outdoor summer camp). As part of their selection, crewmembers undergo rigorous medical and psychological testing to optimise interpersonal relationships, conflict resolution, teamwork and adaptation to the isolation and confinement they will face at Concordia. The multinational and diverse group must live and work together in a small, restricted base, uphold each other's safety, maintain the station, troubleshoot and prepare for any possible emergencies. This is akin to a crew of astronauts in space and crucial for mission success [1,3].

On-site (see Figure 2), Concordia Station houses a clinic equipped with a broad range of medications, a small operating theatre, dental chair, an MRI, ultrasound scanner and X-ray [5]. A minimum of two crew members are medically trained, these being the station doctor (usually a French emergency medicine registrar or consultant) and the European Space Agency's sponsored research M.D. The crew are all trained in first aid and basic life support, and are assigned to the fire, search and rescue or medical teams for which they also receive regular training. Concordia's internet system allows for remote psychological support and telemedicine. However, resources and personnel are limited. In case of an emergency, every effort will be made to evacuate personnel, but the crew know that during the winter, they may need to wait months for help to come [1].

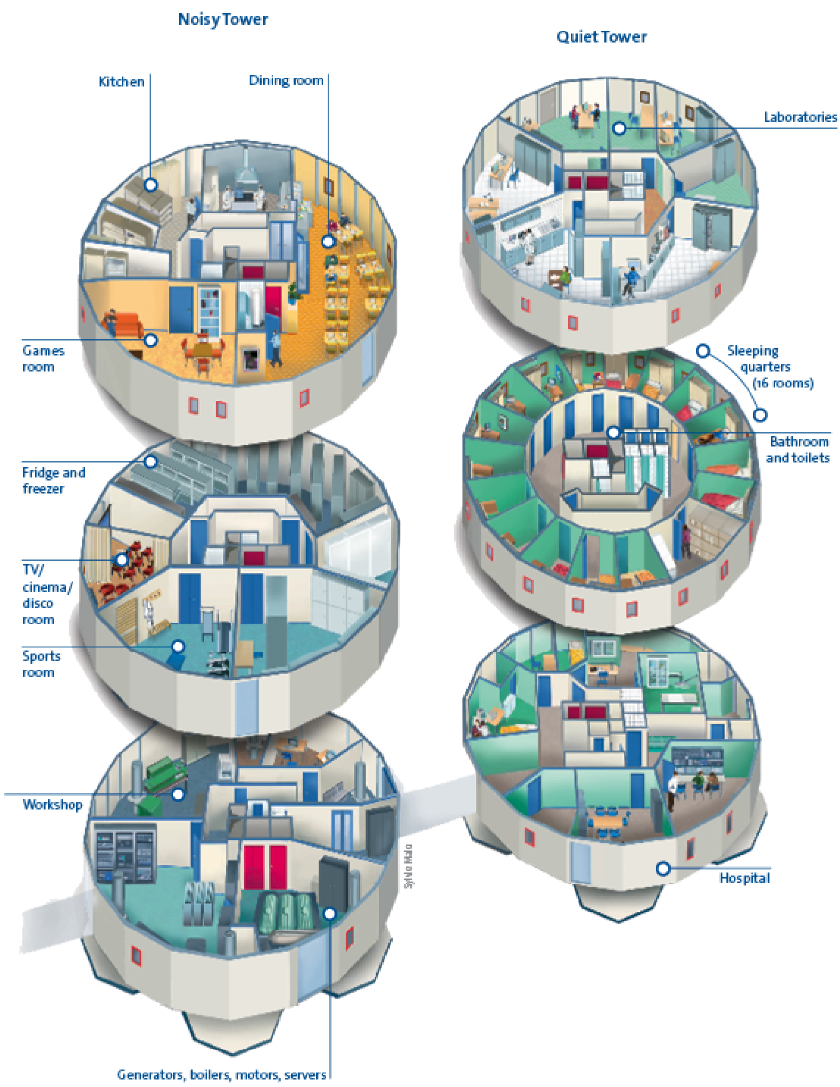

Figure 2. The Concordia Floor Plan [5].

1.2. The Extreme Environment

In addition to the isolated and confined environment, crewmembers face three major environmental challenges: temperature, altitude, and the polar day-night cycles.

As shown by Figure 3, the temperatures at Dome C during the summer months range from −17 °C to −50 °C and are known to drop down to −80 °C during the winter, making it one of the coldest places on earth [6]. The average yearly temperature is −55 °C (−30 °C in summer, −63 °C in winter) [3]. Figure 3 demonstrates the extreme monthly variability in atmospheric temperature. Genthon et al. noted significant 24-h temperature changes, with an almost 30 °C difference depending on the height at which the measurement was taken owing to wind speed and solar radiation [6].

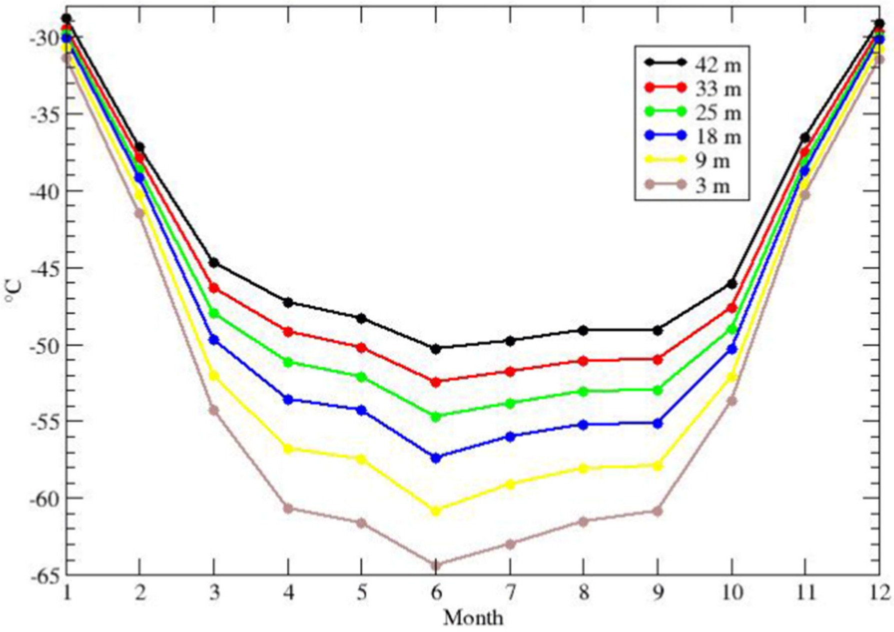

Figure 3. The mean 10-year seasonal cycle of temperature at varying levels of the towers at Dome C (2010–2019) [6].

At 3233 m of altitude, the crew is exposed (through rapid elevation gain) to a chronic hypoxic, hypobaric environment. This atmosphere is equivalent to an equatorial altitude of approximately 3800 m [1,3]. In the initial stages, acute mountain sickness (AMS) is a particular concern at Concordia Station, and during their first week on base, the crew are monitored daily for early signs of AMS by the station doctor. New arrivals to the station are discouraged from over-exerting themselves for the first 48 h, after which they can begin routine activities once cleared by the doctor.

Concordia Station is also subjected to the southern polar light cycle, as illustrated in Figure 4 [7]. Year-round inhabitants experience a minimum of one full 24 h of daytime and 24 h of nighttime in the summer and winter periods, respectively. Dome C has almost 24-h light from November to early February and 24-h darkness from May to August. For four months, the sun does not rise above the horizon, and the crew members experience an almost ‘eternal twilight’ [1,3,7]. Humans are physiologically maladapted to the polar light cycles, and this has significant consequences on crew sleep health. For this reason, sleep is one of the most widely studied physiological parameters at Concordia.

Over 20 years of recorded data at Concordia have advanced our understanding of the human health impact of such an extreme environment and its applications to spaceflight, Mars missions, and terrestrial medicine. This narrative review summarises the currently published literature arising from human biomedical studies at Concordia Station. Furthermore, this review aims to summarise our understanding of the biopsychosocial effects of the conditions at Concordia station and thus draw awareness to short- and long-term health effects that may arise from a prolonged stay there. This review will also comment on considerations for medical selection criteria of over-winterers, countermeasures that may be implicated on-base and identify areas where further research is needed.

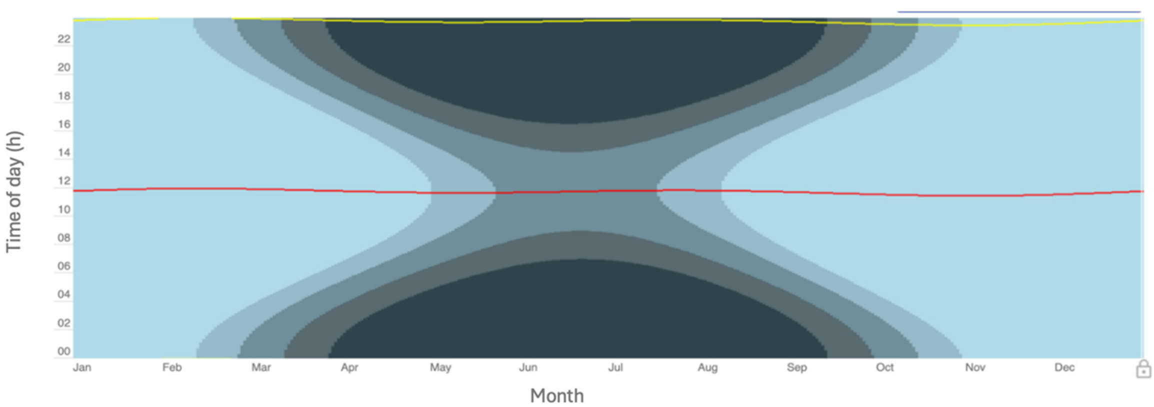

Figure 4. 2025 sun graph for Concordia Station, illustrating a period of total-darkness from early May to early August [7]. Copyright 2025, timeanddate.com.

2. Methods

The following search terms were input into 5 different databases: (Concordia Station) AND ((human physiology) OR (physiology) OR (psychology) OR (occupation*) OR (psychiatry) OR (medication) OR (health) OR (disease)), with a time-period from 2005 (the first winter-over at Concordia Station) to present-day. This yielded a total of 516 results. Exclusion criteria were non-human studies (n = 50), secondary research (n = 55), papers on ecological challenges (n = 1), duplicates (n = 24), and non-English language publications (n = 2). Databases used include: PubMed, Ovid, Google Scholar, and the NASA and ESA HREDA (Human and Robotic Exploration Data Archive) research databases. The remaining 384 papers were screened by title and abstract for relevance. Papers where the full text was not accessible were excluded. 23 papers met the final criteria.

3. Results and Discussion

Long-duration missions in ICE environments like Concordia station can offer valuable insights into expected challenges for future spaceflight. They induce psychological and physiological stress with measurable changes as demonstrated by the biomedical research conducted thus far on Concordia. The published literature ranges from 2009–2025. For a full overview of selected studies conducted at Concordia station, including participant sex split and mean ages, see Table A1 (Appendix A). Studies have been conducted across a range of biomedical fields, including psychology, neuroscience, sleep health, cardiovascular health and immunology. Psychology and sleep health have been the dominating fields of study at Concordia Station and countermeasures to reduce the adverse effects of ICE environments on both have been proposed. However, these countermeasures are yet to be implemented. The demographics of the participants lean towards a middle-age (mean ages between 30–40 years) and significantly male-dominated cohort, as evidenced in Table A1. Many of the studies also comprise small study samples with conclusions that likely need to be corroborated with future research.

Thus, it is important to highlight what we can learn from similar environments to guide future research and countermeasures to improve the health of over-winterers (and other inhabitants of ICE environments). The following section draws information from this pool of data (see Table A1) and other relevant literature to discuss the unique challenges facing human health at Concordia Station.

3.1. Psychology and Neuroscience

The psychological challenge of prolonged stay in an ICE environment is enormous. The outdoor environment is hostile and indoors, life is confined and monotonous. Occupants of Antarctic ICE environments are at risk for dysfunctional stress management and group conflicts as well as cognitive deficits and chronic fatigue [8]. Concordia's isolation, due to its peculiar geographical location compared to other bases, requires the crew to be entirely autonomous during the winter, when evacuation is impossible. Several psychological studies have been conducted there to test how to optimise group cohesion and cooperation, which has important ramifications for long-term space missions. The Concordia crew are effectively strangers who meet only two months prior to departure. Like astronauts, effective crew cohesion and mutual understanding are pivotal for ensuring that operations and research at the base run smoothly throughout the year. All crew members are psychologically screened as part of the selection process to minimise the risks of adverse events, such as a recently reported alleged assault on South African research station Sanae IV [9].

'Winter-over syndrome', also known as 'winter brain', is a term first coined in 1963, which describes the negative psychological disturbances seen in Antarctic expeditioners, more prominently in the winter season. Sixty percent of diagnoses in Antarctica are related to poor sleep, low mood and adaptation problems [10,11]. Many individuals experience a 'third quarter phenomenon'—a propensity to negative psychological adaptation after the halfway point of the mission, when the long polar night starts and Concordia becomes inaccessible [6]. During the winter months at Concordia Station, crew members have been noted to display a flatter affect. This is a form of psychological hibernation, thought to be an adaptive response to the prolonged stress induced by ICE environments [1,10]. Sandal et al. observed this blunting in affect and a reduction in coping strategies from February-October (Antarctic winter) in 27 male participants across two Concordia crews (Crew 1: n = 14, mean age 38.3 ± 10.64 y, Crew 2: n = 13, mean age 34.5 ± 9.17 y) [10]. This was despite a 2-day psychological training course pre-departure to prepare them for mitigating adverse psychological events, such as conflict resolution. The reduction in coping strategies and positive affect followed a statistically significant quadratic trend over time—meaning both were most reduced when conditions were harshest, around midwinter. Sleep quality decreased linearly over time, only slightly increasing towards the end of their stay [10]. Pagnini et al. also commented on the phenomenon of psychological hibernation [12]. They noted decreased creative thinking and increased stress levels over time in both their cohorts of winter-over crews (n = 24 total). Pagnini et al. saw that exercising mindfulness every three months significantly improved crew well-being at Concordia Station over a year-long stay. Higher pre-departure mindfulness disposition scores also predicted lower stress levels.

Although individual mindset is important for adaptability to ICE environments, in-group interaction is equally as essential for mission success. Krins and Nicolas et al. both determined that group diversity, in-group self-identification, and the use of mature defence mechanisms support psychological adaptation and better group cohesion throughout the Concordian winter-over period [8,13]. Using questionnaires, Krins showed that a pro-diversity culture and developing a sense of self within a group were important factors in positive group functioning in an isolated, confined environment for 9 over-winterers [13]. Nicolas et al. found a positive correlation between total stress and immature defence mechanisms (such as acting out or withdrawing), attention lapses and perceived stress in 14 individuals [8]. Participants who used mature defence mechanisms (a problem-solving attitude) when faced with conflict recovered better from stress. Those with higher perceived control over mastering their required competences in the environment also showed increased recovery from stress. Nicolas et al. found in a separate study that differences in professional status and cultural background significantly affected social and occupational dimensions throughout the year [14]. Social dimensions were defined as cohesiveness and social support (coworker/peer and hierarchical/leader support). Occupational dimensions were defined as implementation/preparedness, counterproductive activity, decisional latitude, and psychological job demands. Cohesiveness and peer support decreased throughout the year globally. French scientists showed gradually increasing preparedness, whereas the opposite was seen for their Italian counterparts. Scientists were the only occupational group to show significant deterioration in group cohesiveness by month 10, attributed to increased stress related to readying/finishing projects. Caputo et al. showed that individuals with a positive mindset (a positive view of themselves and others, termed secure attachment style [SAS]) reported a higher overall mood and less interpersonal conflict throughout their stay at Concordia [15]. Although subjective results did not reach statistical significance, SAS individuals showed markedly increased biological resilience to the stressors of ICE environments, as suggested by reduced levels of salivary cortisol and genetic dysregulation in pathways involving protein synthesis, circadian rhythm and mitochondrial function. These four studies all highlight preferable traits in individual and group selection for missions in ICE environments to counteract group degradation under long-term stress [8,13–15].

Despite the significant physical and psychological stressors at Concordia, no cognitive decline after prolonged stay has been noted [16,17]. Abeln et al. and Barkaszi et al. assessed cognitive function in over-winterers at Concordia and found no deterioration in cognition [16,18]. However, Bosch Bruguera et al. found that a lack of training led to rapid decay in psychomotor skills and concentration in the Antarctic environment when testing a Soyuz spaceflight simulator in 23 crewmembers at Concordia compared to 21 crewmembers at sea-level British station Halley VI and a matched control group of 25 in Germany [17]. Three-monthly refresher training sessions were not enough to uphold flight and performance standards. The difference in the rapidity of performance decay was attributed to the hypoxic, isolated and confined conditions at Concordia. Interestingly, hippocampal and whole-grey matter volume reduction has been shown in 9 Antarctic expeditioners staying for 14 months at the German Neumayer II and III stations, with associated deficits in spatial processing and elective attention tasks, but no effect on other cognitive post-mission tests [19]. This showed an element of neuroplasticity to the isolated and monotonous environment, also seen in animal models with prolonged sensory deprivation [19]. Bosch Bruguera et al.'s findings highlight the critical importance and challenges of training and upholding standards of competency that, if insufficient, could lead to poorly-managed emergencies [17,20].

Exercise is well-documented to significantly benefit cognitive function and wellbeing in non-ICE environments. However, it has not shown to impact cognitive function at Concordia according to Abeln et al.'s study. They had additionally looked at the impact of exercise on psychological health (n = 8). Exercise exceeding 2500 RPE (validated units of training load) was considered an 'active' lifestyle. At Concordia, crewmembers classed as 'active' (n = 4) showed decreased alpha and beta brainwaves on EEG (proposed to be reflective of better cortical adaptation to the monotonous, isolated environment) and steadier mood in subjective questionnaires, in comparison to 'inactive' participants (n = 4) [16]. However, this study had a very small population. Further research is clearly needed to establish the possible beneficial role of exercise in ICE environments- including on cognition, wellbeing and psychomotor skills.

When considering adaptation to ICE environments, human health should be viewed holistically, with acknowledgement of the bidirectional relationship between physical and psychological well-being. Being confined with effective strangers in a monotonous and unstimulating environment, alongside outdoor conditions incompatible with sustained human life, increases the likelihood of deteriorating psychological and physical well-being in over-winterers at Concordia Station. Overall, mindfulness and traits such as SAS in the pre-departure disposition of crew members have been shown to reduce interpersonal conflicts and increase the psychological resilience of personnel to the multiple stressors encountered during the mission [13,15]. Certain psychological measures have been proposed to build and maintain good interpersonal relationships, such as regular mindfulness sessions [12]. As Sandal et al.'s study showed that a 2-day training session in psychological protection prior to the mission did not affect mood deterioration and psychological hibernation, it seems regular psychological training or exercises during the mission are also essential to maintain group cohesion and individual mental wellbeing throughout a prolonged stay [10].

Psychological testing pre-selection should continue and consider individual candidate mindsets and approaches to challenges as well as their roles or personalities within a group. Monthly hourly mindfulness sessions are ongoing at Concordia station with a goal to maintain their positive impact on the annually changing winter-over group. Mindfulness and other techniques for psychological wellbeing often demand a person to be fully present and not distracted for a given period of time. In ICE environments, where individuals go for the purposes of conducting research and/or supporting science, time is as precious a resource as any. The current research at Concordia aims to develop shorter mindfulness sessions that are easier to implement into regular routines and which are transferrable to space missions.

Although year-long stays at Concordia have not proven to impact cognition, studies on other Antarctic expeditioners have found attention and concentration deficits alongside neuroplasticity. Degeneration of piloting/fine motor skills in Concordia's hypoxic environment has been demonstrated despite regular training. Skill decay in any profession- medical/surgical, piloting, engineering, to name a few- could have serious repercussions in unexpected emergencies during long-term space missions. With the advancements in modern technology, virtual reality and other simulation technologies may play critical roles in mitigating skill degradation in ICE environments in a cost- and time-effective manner. This is certainly a worthwhile avenue to explore in future research.

3.2. Sleep Health

3.2.1. Circadian Rhythm Disruption

Sleep health is widely regarded as one of the most important factors to general physical and psychological health. Chronic sleep deprivation is directly linked to altered behaviour, poor performance and cognition, and directly detriments physical health [21–24]. It is associated with reduced immunity, poorer cardiovascular health, increased risk of breast and prostate cancer and reduced insulin sensitivity [24,25]. The most extensively researched domain in human health on Concordia Station, alongside psychology, is the disruption of sleep-wake habits. ICE environments such as space and the polar regions predispose to chronic sleep loss due to alterations in the light/dark alternation (see Figure 4), considered the strongest factor affecting circadian rhythm [19]. Kawasaki et al. studied the alterations in baseline pupil size, sleep-wake cycles and the melanopsin sensitivity biomarker PIPR (Post-Illumination Pupil Response) in 25 healthy crew members (mean age: 34 ± 11 y; F = 7) at two Antarctic stations (Concordia and Halley VI) during the winter-over period from April to October. A significantly increased pupillary contraction amplitude (CA) during months without direct sunlight (May–July) suggested an adaptive mechanism to increase pupil sizes in low natural daylight. Pupil responses were heightened by cotopic, photopic and blue light, with retinal sensitivity mostly increased under blue light. PIPR reached a maximum point at 10 weeks after the last sunrise in both stations before progressively declining. Increased PIPR levels are directly correlated with changes in light-dependent behaviours in animal and human models, with an inclination towards seasonal affective disorder and depressive disorders [21]. Rod sensitivity was significantly different between the two stations (with peak CA after the last sunrise at 2.3 weeks and 11.9 weeks for Concordia and Halley VI respectively). Kawasaki et al. suggested Concordia's higher altitude may have contributed to this but reflected that participants showed rapid acclimatisation to the altitude, which would not explain the above [21]. Najjar et al. similarly assessed the use of melanopsin-optimised blue-enriched (BE) white light (versus standard fluorescent white [SW] light) as a countermeasure to circadian misalignment on 10 crew members (mean age: 30 ± 2.1 y; F = 2), with exposure to each lasting 2 weeks, in alternation, for a total duration of 9 weeks. Exposure to SW light demonstrated a 30-min delay in the onset of melatonin secretion, which was not noted for BE light. When exposed to BE light, the participants also showed increased alertness and well-being compared to their experience with SW light [26]. Both Najjar et al. and Kawasaki et al. have noted the potential for blue-enriched light to better sleep-wake cycles at Concordia [21,26].

Collet et al. compared sleep patterns in Concordia to the sea-level station Dumont d'Urville (DDU) and noted significantly lesser total sleep times and delayed onsets of wake after sleep at Concordia Station, which they attributed to the local chronic hypoxic hypobaric environment. Sleep fragmentation patterns were significantly raised in both stations during the Antarctic summertime compared to the winter [27]. Furian et al. also compared sleep health at Concordia to DDU. Similarly, they found more prominent sleep disturbances at altitude and additionally noted elevated nocturnal blood pressure in the Concordia group [28].

Sex differences in sleeping habits have been documented in the literature. For example, female shift workers are more prone to suffer from poor sleep quality [29]. In a group of Antarctic over-winterers (n = 54, M = 37, F = 17), Steinach et al. noted that sex may impact sleep health. Their findings demonstrated a linear increase in the number of nighttime arousals in women over time and time spent in bed. They found women had poorer sleep quality compared to their male colleagues. The level of physical activity on the station, which has previously demonstrated to enhance sleep quality, decreased in men but remained unchanged for women. Therefore, Steinach et al. suggested a higher susceptibility of women to the psychosocial stressors aboard the station and a propensity towards seasonal affective disorder (SAD) [25].

During the winter-over, labile circadian rhythms and later sleep-wake timings reflect a prolonged deprivation from natural light, even in conditions with artificial lighting designed to mimic natural light [18]. Consequent disruptions in melatonin secretion, the primary sleep-wake regulating hormone, may also confer melatonin-induced effects on physical health. Melatonin impacts DNA methylation, although its exact roles are not fully understood [24]. This profound and prolonged circadian alteration remains a significant challenge in long-term missions and may lead to unfavourable epigenetic changes with long-term ramifications. More research is needed to understand the physiological changes in circadian rhythm through shifts in melatonin / cortisol secretion. Further study into the sex differences in sleep habits noted by Steinach et al. may inform more individually tailored countermeasures to improve occupational health standards for sleep in night shift workers and individuals in ICE environments. In addition to simply studying the changes in sleep habits, it would be important to link this to other measurable physiological parameters, such as psychological health, cardiovascular function and immune system function. The epigenetic impact of altered sleep should also be studied to further characterise possible long-term risks of life in ICE environments.

3.2.2. Sleep Apnoea

Beyond the polar light cycle, Concordia's altitude and the consequent chronic hypobaric, hypoxic environment are likely contributors to poor sleep. Collet et al., Furian et al., Tellez et al. and Mairesse et al. all comment on the incidence of nighttime periodic breathing at Concordia, which also disrupts sleep [27,28,30,31]. Its severity and onset appear to vary greatly from one individual to another. Tellez et al. determined that over a year, periodic breathing did not acclimate in 13 healthy male participants (mean age 39.6 ± 9.8 y) at Concordia Station. After three weeks, the apnoea/hypopnoea index (AHI) continued to exceed the clinically severe level of ≥30 (AHI = 65.4 ± 29.1), despite a linear increase in SpO_2. The AHI significantly correlated with the length of each apnoeic episode, suggesting individual physiological variations [30]. This unpredictable individual variability was also demonstrated by Mairesse et al., who studied the effects of sleep on psychomotor function in 13 male over-winterers. They suggested the dry air at Concordia, leading to nasal congestion/inflammation may also have contributed to the development of periodic breathing in some individuals. Decreased psychomotor speed and increased subjective fatigue was noted over time. Mairesse et al. emphasised the use of objective measurements such as polysomnography in documenting sleep health and for candidate selections [31].

Tellez et al.'s findings of sustained severe apnoea (defined by the apnoea/hypopnoea index) despite increasing SpO_2 demonstrate not only wide and unpredictable onset and severity but also important implications for cardiovascular health in prolonged missions [30]. In the literature, high altitude has been linked to sleep apnoea in previously healthy participants. A study conducted by Nussbaumer-Ochsner et al. on healthy mountaineers rapidly ascending to ~4000 m asl showed a reduction in sleep efficiency on the first night at altitude. This inefficiency partially normalised by night 3, correlating to increased nocturnal $sPaO_2$. However, periodic breathing patterns beginning on night 1 worsened by night 3 despite their improved SpO_2, similar to the results seen in Tellez et al.'s study at Concordia. The authors concluded at altitudes exceeding 4500 m, nocturnal apnoeic episodes increase despite other physiologic signs of acclimatisation, whereas other markers of sleep pattern instability improve. Tellez et al.'s findings suggest the former happens at even lower altitudes. Nussbaumer-Ochsner et al. also determined that at altitudes below 3450 m, apnoeic breathing decreases over time [32]. Studies at Concordia, which sits at 3233 m and the equatorial equivalent of 3800 m asl, have demonstrated sustained worsening sleep apnoea over time without the burden of physical exertion mountaineers undergo [30]. The winter period (February-November) is associated with more severe sleep apnoea [31]. The presence and gradual resolution of sleep apnoea appear to be highly variable between individuals, in line with other studies suggesting high individual variability in physiological adaptation to the extreme conditions at Concordia. [27,28,31].

Sleep apnoea is a known major risk factor for future cardiovascular events and metabolic syndrome, and manifests acutely with sleep disruption and excessive daytime somnolence. This can lead to reduced reaction times and poor decision making, which in the context of an ICE environment can lead to serious detriment and harm. Apnoea and poor sleep health can affect and be affected by physical and psychological health changes, notably linked to hypertension, reduced energy secondary to hypoxia and poor psychological well-being. The correlation of sleep apnoea to cardiovascular risk is an area of concern for long-term missions in hypobaric, hypoxic environments—although interestingly, apnoea does not seem to be as great a problem on the ISS, possibly due to microgravity [33]. Maguire et al. noted that apnea may also be linked to separation in submariners, suggesting psychological stress may be a contributing factor [34]. Thus, the onset of sleep apnoea in ICE environments may be multifactorial and not solely attributable to altitude/hypoxia. Nevertheless, further research should be conducted with characterisation of these periodic breathing patterns using the clinically approved AHI. It would also be of interest to compare scores such as quality of life, Q-RISK and clinical depression/anxiety scales in individuals with similar AHIs between ICE environments versus non-ICE environments. This may help to better characterise and evaluate the causes and acute and long-term consequences of periodic breathing in ICE environments in order to tailor selection criteria and identify targetable areas of prevention/treatment.

3.2.3. Countermeasures to Sleep-Wake Disturbances

No robust strategies to combat the effects of the polar light cycle on circadian rhythm have been implemented thus far. On the ISS, sleep-promoting medications are the most frequently used pharmaceuticals [35]. Although pharmaceuticals may present a simple and effective management strategy against dysregulated sleep cycles in ICE environments, they are not feasible long-term countermeasures. Furthermore, the side-effect profile and the impact they may have on the safety of a self-sufficient crew in an uninhabitable environment must be considered.

The use of artificial light as a non-pharmaceutical countermeasure for bettering sleep in over-winterers at Concordia has been proposed. Both Najjar et al. and Kawasaki et al.'s findings on over-winterers at Concordia suggest that appropriate artificial lighting (particularly blue light) is important to mitigate the long-term physical and psychological consequences of natural daylight deprivation, which is also applicable to shift workers, submariners, and astronauts [21,26]. Using blue-enriched light for ambient lighting is a possible cost-effective and simple countermeasure with the added benefit of no noticeable side-effects within a specified wavelength and intensity range, unlike sleep-inducing medication. There is conflicting literature on the 'blue light hazard,' which suggests that prolonged exposure to blue light is a risk factor for age-related macular degeneration [36]. Other sources suggest this is a highly marketed claim, with little evidence of using blue-light blocking spectacles on retinal health [37]. Nevertheless, this should be considered when applying blue light as a countermeasure to circadian disruption, particularly when considering long space missions, such as travel to Mars or lunar habitation.

In addition to lighting measures, crew pre-departure training may also prepare expeditioners for developing long-term adaptation to atypical day-night cycles. Scheer et al. developed a tailored model-based lighting regimen to entrain 5 subjects to the 24.65 h Martian solar day-night cycle (sol) and the 23.5 h cycle experienced by cosmonauts in short-term space missions. Using sleep biomarkers (plasma melatonin and cortisol) and core body temperature, they demonstrated neuroplasticity within the SCN, the body's 'sleep-wake pacemaker' [38]. An effective countermeasure to circadian disruption in extreme environments may therefore also lie in pre-mission training. However, this does not account for seasonal changes in the day-night cycles experienced in polar regions (see Figure 4) but has applicability to space travel and night-shift workers, where year-round changes in daylight/nighttime hours are non-seasonal and less drastic.

The use of CPAP (a common treatment for sleep apnoea) has not been tested in ICE environments- but may not be feasible due to the equipment needs. Sleep apnoea thus remains a challenge that may cause major constraints in prolonged ICE environments (for example on a 5-year Mars mission), particularly for its detrimental long-term effects on cardiovascular health.

3.3. Immunology

ICE environments, such as Concordia and space, have been shown to dampen immune responses. In nine healthy male participants overwintering at Concordia Station, Feuerecker et al. found an initial downregulation of the immune system on initial exposure to the hypoxic conditions at Concordia in summer crew [39,40]. This showed reversibility by 1 month post-exposure. The authors suggested the hypoxic environment to be the main driving factor behind this. Indeed, a follow-up study [40] on 14 Concordia crew members stationed at the base for one year showed that immune response was upregulated from baseline within 3–4 months. This immune activation was reflected by changes in gene transcription affecting hypoxia-driven pathways, demonstrating an epigenetic adaptation to the hypoxic environment at Dome C. In the acute setting, Strewe et al. noted alterations in immune response deemed also secondary to hypoxia [41]. Increased catecholamine secretion causing a downregulation of the endocannabinoid (EC) system was found in over-winterers at Concordia (n = 16). Contrastingly, participants at sea-level Neumayer III station showed a significant increase in EC ($p \leq 0.001$). A hypoxia-driven upregulation of cyclooxygenase-2 (which degrades ECs) was proposed as a mechanism behind this. Participants reported no subjective increases in stress, suggesting this downregulation of the immune system through a physiological stress response to the environment was independent from psychological stress [41]. Further studies are required to understand these immunological changes and how to also best manage crew health pre-departure to prevent catastrophic illness upon return from a mission, particularly given the recent COVID-19 pandemic.

Feuerecker et al. have identified lasting modulations in the immune system that favour a pro-allergenic disposition six months after return to 'normal' life following a year at Concordia. Two of nine male participants reported worsened allergic reactions upon their return. One other participant, who developed new hay fever, had raised IgE levels in post-mission sampling. [42]. Studies with a larger cohort should be conducted to truly assess the correlation between life at Concordia and a pro-allergenic state on return. It is unclear how this might worsen or change following longer missions in Concordia and other ICE environments. Due to the lack of longer-term follow up, it is also unclear whether this pro-allergenic reactivity is temporary or not.

Furthermore, when a dampened or altered immune system is coupled with limited access to healthcare services and medication, (opportunistic) pathogens pose a serious health risk both on base and on return from a mission. The relative confinement indoors and communal lifestyle (room sharing, communal meals) provides the optimal conditions for rapid pathogenic dissemination throughout the station. This is particularly true during the summer period, when new illnesses are easily brought to Concordia from the rapid influx of new arrivals. Pathogens isolated in ICE environments are brought there by the crew, but microbial overgrowth and the development of antibiotic resistance *a*re anticipated and significant problems of long-term missions. In space, fewer competition, radiation exposure and microgravity are thought to play a role [43–45]. Fewer competition is certainly a risk in confined environments like Concordia and over time can lead to altered human and environmental microbiomes with consequent effects on acute and chronic health. Changes in human microbiomes compared to the environment, have been assessed in other polar bases. Wang et al. [46] showed that a year-long stay at the Chinese Great Wall Station in Antarctica resulted in significantly increased proportions of *Citrobacter*, *Akkermansia* and conditional pathogens such as *Escherichia-Shigella* in the gut microbiota of 12 expeditioners. The authors suggest stress and fatigue, a reduced biodiversity, and dietary changes are contributors to these changes. Gut microbiota and rates of antibiotic resistance are yet to be studied at Concordia.

In terms of the environmental microbiome, Van Houdt et al. noted the presence of several airborne opportunistic pathogens during a 12-month sampling period at Concordia Station. These included *S. aureus* (with one sample resistant to erythromycin and fosfomycin), *Klebsiella pneumoniae*, and *Alloiococcus otitis*. These were more commonly isolated from sampling during the winter period, when the station was 'closed', with limited human movement in and out of the station and no physical contact to the 'normal' world. The airborne microbial population largely originated from the crew and was thought to likely be disseminated by aerosol formation after flushing the toilet. No significant infectious illnesses were reported by the station doctor at the time [47]. Schiwon et al. compared Staphylococcus and Enterococcus isolates from the ISS and Concordia Station. ISS isolates demonstrated almost twofold incidence of resistance to one or more antibiotics compared to Concordia isolates possibly due to microgravity, which enhances microbial resistance through enabling more efficient horizontal gene transfer on a species-dependent basis. However, biofilm was more present in Concordia strains, which may cause technical and equipment problems. Previously, biofilm on MIR station has corroded metal and caused polymer deterioration. This highlights an important added risk of antimicrobial-resistant organisms in ICE environments beyond the direct threat to human health [48]. Stoppiello et al. and Napoli et al. have additionally isolated heterogeneous bacterial and fungal species in the snow and ice within a 1km distance from Concordia Station, reflecting human contamination of the outside environment [49,50]. This has significant applications to space travel and understanding the microbiological human footprint in previously untouched environments, which may also impact the microbial environment on-board stations and the microorganisms subsequent expeditioners may encounter [50,51]. Research is underway at Concordia to study the changes between human and environmental microbiomes coupled with immune response. Results could inform infection control practices in confined environments, crew selection criteria, materials for building stations, and better our understanding of human-environmental microbial transfer. Follow-up research from this with genomic characterisation of any pathogens found is vital for understanding the significance of antimicrobial resistance in ICE environments.

3.4. Cardiovascular Health

Chronic exposure to the altitude and extreme cold at Concordia Station appears to be a cardiovascular risk factor. Several studies across the literature have demonstrated the diverse impact of altitude on short and long-term cardiovascular health, though this is an understudied area at Concordia Station. Blood pressure changes have been noted in over-winterers at Concordia, likely multifactorial. Furian et al.'s prospective cohort study on 12 healthy Concordia crew members (mean age 36.2 ± 10.0 y) compared nighttime blood pressure readings in relation to sleep and to crew members at Dumont d'Urville station. Findings showed overall elevated nocturnal blood pressure readings with a difference of 14 mmHg and 1mmHg in systolic BP and 11 mmHg and 3 mmHg in diastolic BP at 1 and 12 months, respectively, from baseline BP [28]. Rapid ascent to altitudes above 2500 m is associated with an increased BP. A meta-analysis of Tibetan populations at 3000–4300 m asl showed that chronic hypertension is positively correlated with altitude, with blood pressure increases of 2% for every 100m increase in elevation [52,53]. Hypoxia-induced sympathetic stimulation of the chemoreceptors at the carotid body is thought to be the primary driver for the BP increase with altitude [53]. At Concordia, these findings may also be compounded by the effects of sleep disruptions and temperature on blood pressure (as discussed in Section 3.2). A large Chinese survey observed an inverse correlation between blood pressure and temperature [53,54]. Other general factors that may contribute to higher blood pressure during winter months include dietary changes, reduced physical activity, and reduced vitamin D levels [37]. To mitigate the risk of hypertension, close monitoring of blood pressure is recommended at altitude and gradual ascent to allow for acclimatisation. Angiotensin receptor blockers have demonstrated a preserved blood pressure-lowering efficacy at 3500 m but not 5400 m asl [55]. No convincing pharmaceutical management for lowering altitude-induced hypertension has been established [53].

Changes in adipokine levels (such as leptin) at altitude have also been noted. Harrison et al.'s study on the effects of contraception use at altitude noted significantly lower leptin in the group taking oral contraceptives, who also developed a higher incidence of AMS [56]. Anorexia, a symptom of AMS, was suggested as a mechanism for the differences in leptin levels. In ICE environments, appetite may be reduced owing to a multitude of factors, which can further impact adipokine levels [56,57]. Wang et al. demonstrated a significant decrease in human plasma leptin, alongside imbalanced levels of other adipokines in experimental rat models exposed to hypoxia. Their results showed evidence of cardiac remodelling and effects on cardiovascular gene expression, suggesting a targetable biochemical pathway for mitigating cardiovascular disease in chronic hypoxic environments [58]. It is unknown the extent to which these results from animal models could apply to humans. Changes in leptin levels in ICE environments may thus be multifactorial. This dysregulation of adipokine secretion has been linked to an increased risk of cardiovascular events.

Several studies have demonstrated the effects of altitude on pulmonary physiology, though this has not been extensively studied at Concordia. Chronic exposure to the hypoxia at Concordia has shown some changes in gas exchange and oxygen-carrying capacities. Porcelli et al. studied the adaptive effects of the chronic hypoxic environment at Concordia Station on 13 healthy individuals (mean age 34.1 ± 3.1 y). Erythropoietin levels rose rapidly and returned to baseline within the first days, while haemoglobin concentration rose after day 7. This increase was sustained throughout the mission. Reduced pCO_2 (through increased loss) and a consequently elevated arterial pH remained as such throughout the 300-day study. This sustained rise in blood pH suggested a poor renal compensatory mechanism to the altitude. Porcelli et al. thus concluded that human adaptation under moderate hypoxia is poor [59].

Studies on other Antarctic expeditioners have shown alterations in pulmonary physiology. In addition to raised BP, Wang et al. noted significant alterations in cardiopulmonary function, including an elevated heart rate (HR), prolonged corrected QT interval, reduced pump function and reductions in forced vital capacity (FVC) and expiratory flow in 23 healthy male participants (mean age 31.5 ± 6.45 y) located at Kunlun Station (Dome A, 4087 m asl) for 20 days [58]. Contrastingly, O'Brien's study on Antarctic expeditioners undertaking a 40-week crossing of Antarctica (with 24 weeks at 2500 m asl) exhibited a reduced FEV1/FVC ratio and increased VO_2-max post-expedition compared to pre-expedition, demonstrating increased respiratory exchange efficacy [60]. The differences in respiratory function in both groups may be attributed to the milder altitude experienced by the cohort studied by O'Brien, as well as their likely increased physical activity (undertaking the first attempted winter crossing of Antarctica rather than being relatively stationary at a base) [60].

Altitude is also a risk factor to developing pulmonary artery hypertension (PAH). PAH is known to cause right heart strain and cardiac remodelling in the lay population, which can lead to pump dysfunction and right heart failure over time. This has not yet been studied at Concordia. Lalande et al. showed an overall increase in forced expiratory flow in 102 participants rapidly ascending from sea level to the Amundsen-Scott base (2835 m). Those with reduced FEF showed six-fold increased adrenaline and endothelin-1 levels, consistent with pulmonary artery hypertension and upregulated adrenaline production meant to help clear pulmonary fluid. The respiratory response to rapid ascent showed large individual variability, a consistent finding in most studies assessing the effects of altitude on physiology [61].

ICE environments like Concordia may also induce a more sedentary lifestyle to inhabitants, which also contributes to poor cardiovascular health. Virchow's triad of immobility, endothelial damage (which can be induced by physiological stress) and hypercoagulability lists the risks leading to the development of (potentially fatal) venous thromboembolic (VTE) events. In space, this is a particular concern, with hypoxia cited as a possible contributor. Venemans-Jellema et al. studied the separate roles of hypoxia and immobilization on venous thrombosis in 25 male participants at Concordia compared to a bed-rest study at normoxia. Hypoxia without immobilization at Concordia did not demonstrate an increased risk of venous thromboses with no increase in prothrombotic biomarkers [62].

Although few studies have looked at cardiopulmonary health at Concordia, the literature highlights a multitude of environmental factors (altitude/hypoxia and low temperatures) that can significantly affect acute and long-term cardiovascular health. Physiological adaptation to these conditions appears to be highly individual, but chronic hypoxia can consequently affect cognitive function and overall well-being in the longer term [1]. The reports of raised blood pressure and pulmonary arterial hypertension warrant further investigation as to their severity and associated risks (such as right heart strain) during long-term stays in ICE environments. The indication and effectiveness of antihypertensives in such environments is also a question that remains to be answered.

3.5. Musculoskeletal Health

The decline in musculoskeletal health characterised by muscle loss and reduction in bone density has been extensively researched in the space environment. Musculoskeletal degeneration, manifesting as conditions such as sarcopenia and osteoporosis are common age-associated pathologies inciting huge injury burdens, healthcare costs and reduced quality of life. Poor musculoskeletal health is associated with short and mid-term consequences [63]. In space, this decline is attributed to the lack of gravity-induced muscle/bone stress required for bone remodelling and strengthening, but at Concordia station other factors can impact musculoskeletal health. The 3–4 month absence of sunlight during the polar winter, resulting in a lack of vitamin D, poses a major risk to mineral bone density. Collomp et al. studied the effects of overwintering at Concordia on awakening and evening concentrations of cortisol and testosterone, body composition and physical aptitude on 23 male participants from two Concordia crews. Group 1 ($n = 10$, mean age 36.1 ± 3.6 y) defined by a loss of muscle mass >2%, demonstrated unchanged evening/waking cortisol and testosterone levels and a preserved physical aptitude compared to Group 2. Group 2 ($n = 13$, mean age 42.9 ± 2.8 y) had preserved muscle mass but a significant increase in body and fat mass from August onwards. A significant relationship was found between body mass and fat mass, and between body mass and muscle mass in both groups. However, when compared to Group 2, Group 1 had statistically significantly higher end-exercise heart rate and reduced fluctuation in waking versus evening testosterone levels [63]. This showed alterations in muscle mass are independent from evening/waking cortisol and testosterone levels and physical aptitude [63]. Further studies are needed to understand the musculoskeletal changes at Concordia Station and their underlying pathophysiological pathways. Appropriate countermeasures such as dietary changes or exercise regimens could then be developed to help maintain the fitness, quality of life and overall health of crew members in ICE environments.

3.6. The Chemosensory System

Our sense of smell and taste significantly impact our appetite, dietary choices, and mood. Klos et al. observed changes in olfactory and gustatory function in 2 groups of over-winterers at Concordia station ($n = 19$, $f = 3$). 84.2% of participants were non-smokers at baseline [57]. They found an overall reduction in smell throughout the winter period and a reduction particularly in the perception of salty flavours, followed by sour flavours. BMI decreased overall by 1.09 units over the winter period but increased by 1.66 units 6 months post-mission. There was high individual variability in these changes and although gustatory changes returned to baseline 6 months post-isolation, olfactory alterations did not. During their stay at Concordia, it is likely the chemosensory system was partly affected because of the dry air [57]. Changes in the chemosensory system can lead to anorexia and a poor diet with obvious consequences for general physical health. Psychological wellbeing can also strongly be affected by and affect food intake. An improved understanding of how the chemosensory system reacts in isolation and confinement is key to tailoring nutrition in ICE environments to help maintain physical and psychological crew health, particularly important for missions lasting several years (i.e., Mars).

3.7. Women's Health

Although women make up approximately 50% of the global population, there is a stark lack of female representation in the biomedical research conducted in ICE environments. Expedition into extreme environments is historically and culturally a male-dominated field, but it is something more and more women are stepping into, which should be encouraged. Both Krins and Nicolas et al. (2016) make note of the importance of women in groups to improve social support and group cohesion [13,14]. In a recent publication, Mark et al. [45] highlight major differences in the impacts of the space environment on male and female astronauts, including differences in radiation-associated risks and immunological and physiological stress responses. None but one of the studies conducted at Concordia thus far made remarks on the differences in adaptation noted within the studies between men and women. This is a firm reminder that women's physiology, psychology and capability to adapt in extreme environments remains significantly understudied.

Over 150 million women use oral contraception (OC) worldwide [64]. Pregnancy is an absolute contraindication for travel to Concordia; it is screened for in pre-departure testing and both oral and physical contraceptives are available on station to avoid it. Women travelling to Concordia are not obliged to be established on any form of contraception pre-departure. Although some may take oral contraception at baseline, OC medication is also prescribed to manage other conditions, such as endometriosis, polycystic ovarian syndrome, premenstrual syndrome and non-gynaecological conditions such as acne vulgaris. Women who go to ICE environments may thus do so while already taking an OC or be prescribed it as medical management were they to develop the aforementioned conditions during their stay. It is therefore important to discuss the implications of oral contraceptive use on human physiology in ICE environments such as Concordia. The particular concern in Concordia is the altitude. Through their mechanisms of action, OCs reduce circulating progesterone (and, in some forms, oestrogen), which is a natural anti-inflammatory. AMS is thought to be related to a hypoxia-induced inflammatory response, supported by the effective use of steroids such as dexamethasone to treat it. Harrison et al. hypothesised that individuals on oral contraception would be more susceptible to developing AMS. Harrison et al. assessed the AMS incidence in a group of 50 women who experienced a rapid ascent of <4 h to the Scott-Amundsen station from the sea level McMurdo station and stayed at altitude for at least 1 week. There was a statistically significant increase in the AMS incidence in the group taking OC medication ($n = 13$, incidence 85%) versus those not ($n = 37$, incidence 51%). In Harrison et al.'s study, participants could elect whether to take acetazolamide prior to ascent to mitigate AMS. Interestingly, 100% of OC participants also taking acetazolamide experienced AMS, double the amount of those taking solely acetazolamide. Furthermore, circulating progesterone ($ng \cdot ml^{-1}$) was almost fourfold lower in non-OC versus the OC group at altitude and sea level (non-OC group: 0.7 ± 0.5 and 0.7 ± 0.7, respectively; OC group: 3.2 ± 4.6 and 3.1 ± 4.6, respectively), supporting the hypothesis that lower circulating progesterone increases susceptibility to AMS [56].

Progesterone and aldosterone are competitors for human mineralocorticoid receptors, but progesterone has a higher affinity and is a weaker agonist. Lower progesterone thus reduces the competition for aldosterone to rise. Higher levels of angiotensin II, a product of aldosterone metabolism, have previously been linked to increased risk of AMS and increased cerebrospinal fluid (CSF) pressures in animal models [56]. While no cases of AMS studied by Harrison et al. developed high-altitude cerebral oedema (HACE) or high-altitude pulmonary oedema (HAPE), this suggests an increased risk of HACE in OC users, which requires further study. The effects of circulating oestrogen levels on the risk of AMS are still unknown.

Unfortunately, there remains an enormous gap in our understanding of women's adaptability to ICE environments compared to men. Like many other studies conducted in space or at other Antarctic bases, there is minimal information on the way Concordia Station affects women. Diverse crew groups (including mixed gender groups) perform better in isolated, confined and extreme environments and this should always be considered during crew selection, particularly for long-term missions. Although the maximum number of women in the Concordia winter-over crew is 4 (in a group of 12–16) to date, only one study across any medical discipline comments on the differences observed between male and female participants. This is crucial to lay the groundwork for future research in understanding sex-differences in adaptability to ICE environments. In space, recent data from female astronauts has served to highlight important differences in health and adaptation between male and female astronauts, such as women being able to mount a more significant immune response on the ISS than their male counterparts. However, this is an area in the literature that needs extensive developing. The impact of ICE environment stressors on women's health specifically; the menstrual cycle, fertility and female hormones; is still not well understood. Oral contraceptive use at high altitude in Antarctic regions has been shown to increase the risk of developing AMS. Though pregnancy is a contraindication to work in most ICE environments, the safety of other medical contraceptive methods has not been explored extensively enough. Every effort should be exerted by the scientific community to ensure women can also go to ICE environments, including Antarctica and space, safely.

3.8. Medication use and Pharmaceutical Constraints

The most frequently used pharmaceuticals in the International Space Station are sleep medications, closely followed by painkillers for both acute and chronic treatment. Wotring conducted a comprehensive analysis of the type of medications most used by cosmonauts aboard the ISS [35]. No such study currently exists on Concordia Station. Nevertheless, given its similarities to the space environment, it is important to understand the implications (both positive and negative) of medication use and efficacy at Concordia.

The intended drowsiness of sleep medications, for example, is a side-effect of other drugs, particularly stronger painkillers such as opioids. In Concordia, such medications may compound the negative effects of the environment on cognition, posing an additional risk for irrational decision-making, inefficiency, and poor conflict resolution. Prescription medications should thus always be taken as directed and as recommended by the station's chief medical officer.

The effects of sleep-promoting medications zolpidem, zaleplon and temazepam have been assessed for their efficacy at varying altitudes above 3500 m in small size studies. Of the three medications, temazepam (10 mg) was shown to increase subjective sleep quality and oxygenation levels at 5300m of altitude. However, it did not improve actigraphic indexes of sleep. Acetazolamide has been historically used by Concordia crews to mitigate AMS. The use of such medication has been noted to disrupt sleep due to the need for excessive urination. Furthermore, Acetazolamide used in combination with oral contraception has been shown to be ineffective, deemed possibly due to the inhibition of progesterone, which is a natural anti-inflammatory [56]. Dexamethasone is a steroid (thus with anti-inflammatory properties) which is licensed for use to treat AMS and HAPE/HACE. It has shown improved oxygen saturations and subjective and objective markers of sleep efficacy in HAPE-susceptible individuals [65]. The value of dexamethasone for acute mountain sickness in individuals taking oral contraception has yet to be studied.

Hypoxia has been shown to significantly affect the in-vivo metabolism of pharmaceuticals and alter the activity of drug-metabolising enzyme cytochrome P450, and the metabolism of cardiovascular drugs in rodent models [66]. No studies have explored this in human models at altitude but drug metabolism is one of the key factors that determines drug efficacy. This may be a worthwhile avenue for future research.

All medications licensed for use are marked with expiration dates and have specific storage requirements in terms of humidity and temperature. One challenge in the space environment is that the lifespan of medications is shortened due to degradation from radiation and drug repackaging prior to transport [67]. Priston et al.'s pilot study concluded that hydrocortisone cream and various eye medications should not be stored in 'field medical boxes' in Antarctica (kept at −15 °C and undergoing 5 freeze-thaw cycles) due to the freeze-thaw mechanisms interfering with drug stability. Of particular concern was the production of potentially cornea-damaging tetracaine crystals and hydrocortisone degradation to sub-therapeutic doses. This is the only study conducted on medication stability in Antarctica [68].

Overall, medication use by over-winterers at Concordia Station remains an area of study. Research conducted on the ISS and other ICE environments draw attention to the significant use of sleep and pain medications by otherwise healthy crew and their potential impact on performance. More research is also required to understand the effects of the Antarctic environment on drug metabolism and efficacy in relation to handling and storage, as this is of particular concern for emergency management in longer-term missions and may help to make more cost-effective decisions when making choices for medical supply in ICE environments.

3.9. The Challenging Environment at Dome C

3.9.1. Temperature

Physiologically, cold temperatures have demonstrated a detrimental effect on cardiorespiratory and sleep function, as described in Section 4. With outdoor temperatures at uninhabitable levels, frostbite requiring limb amputation and death due to over-exposure are obvious risks that are addressed through safety protocols at Concordia and appropriate cold weather gear [1]. The crew are free to exit the station during the summer season but must do so in pairs during the winter. Inside the station, the temperature is maintained at 21–23 °C [6]. Frostbite, historically a significant injury burden in Antarctic expeditions, is now a lesser concern thanks to the development of appropriate clothing [69]. Nevertheless, mild frostbite has occurred at Concordia due to inadequate wear; one such example was frostnip of the ears due to a crewmember forgetting to wear a hat when going outdoors to work. Holes in boots from wear and tear can also cause frostbite if unnoticed.

Windspeeds and temperature can also affect skin integrity. A 33-year-old female Antarctic ski expeditioner developed a rash which ulcerated secondary to overexposure (attempting an Antarctic crossing for 70 days) and required a skin graft [69]. However, this sort of exposure is extremely unlikely to affect the crew at Concordia. Furthermore, outposts in the perimeter of the station provide temporary shelter for workers (such as glaciologists) spending extended periods of time outside for research purposes. A minor effect of the dry, cold air results in frequent nosebleeds on initial arrival to the station, which tend to self-resolve. There is no current accessible detailed data on the incidence of cold exposure injuries or outdoor emergencies at Concordia Station. The risk of serious injury remains but can be mitigated by reasonable adherence to safety protocols.

3.9.2. Altitude

Altitude is likely a significant contributor to physiological health changes at Concordia. Its effects (chronic hypoxia and hypobaric conditions) on almost all body systems, from sleep to cardiovascular health, have been described in Sections 4 and 5. Although human survival is clearly possible at Concordia's altitude (3233 m asl, 3800 m equatorial equivalent), and indeed at higher altitudes still (i.e., Kunlun station, 4087 m asl), Porcelli et al.'s study suggests poor human adaptability to the altitude, noting increased blood pH levels over time which indicate a renal inability to compensate metabolically for CO_2 loss [57,58].

The largest immediate concern at high altitude is altitude sickness, an umbrella term encompassing a series of symptoms and syndromes seen in individuals subjected to altitudes beyond 1500 m above sea level. AMS is the mildest form of altitude sickness, and often a precursor for its more severe forms, high altitude pulmonary oedema (HAPE) and cerebral oedema (HACE). Reportedly, AMS occurs more frequently at Concordia Station than in other places at the same altitude [59]. Its development is influenced by rate of ascent, peak altitude, altitude at sleep, and individual susceptibility [56].

High altitude pulmonary oedema and cerebral oedema are potentially fatal conditions which have previously occurred at Concordia and have been detailed in other Antarctic stations [70,71]. Rose et al. documented 3 cases of serious altitude sickness (2 HAPE, 1 HACE) in individuals aged 23–52 years at the Amundsen-Scott station, located at 2835 m above sea level (asl) [72]. All were treated on-site; for 2 individuals, symptoms fully resolved during their evacuation flight. The third individual, who presented with symptoms consistent with HAPE and a SpO_2 of 41%, had a full resolution of symptoms 4 days after returning to sea level. Rose et al. suggested that miseducation on the use of prophylactic medication was a significant contributor. All cases developed within 4 days of arrival during the Antarctic summer, meaning they could be evacuated, but this may not be the case for Concordia or other regions of the pole, as evacuation is often significantly dependent on weather conditions [72]. Given Concordia's altitude is higher than the Amundsen-Scott station, these events pose a serious hazard despite the advanced medical treatment, pre-departure screening and prophylactic medication available.

3.9.3. The Polar Light Cycle

Finally, the polar light cycle particularly affects sleep and psychological wellbeing, with prolonged periods of up to 24-h darkness and light during the winter and summer months respectively. In the polar regions, an important consideration of the prolonged and direct sunlight is the highly reflective nature of snow and ice. Both substances reflect up to 80–90% of UV rays, which can increase the risk of radiation-exposure injury, particularly in individuals who must spend prolonged periods of time outdoors. This includes photokeratitis (including 'snow blindness'), non-melanoma skin cancers, and solar keratosis (with possible malignant transformation in later life), particularly for exposed skin (most often the face). This has potential implications for the long-term health of crew members [73]. To mitigate this, crewmembers at Concordia are equipped with full-body protective gear (including balaclavas and snow goggles), as well as 50+ SPF sunscreen for the face and lips. An eye exam is also required pre-mission.

4. Occupation and Role-Specific Issues at Concordia Station

As an incoming crewmember, the author has compiled this section on information made available during logistic and training weeks with IPEV, ESA and PNRA and experience at the station itself. Concordia Station is an exclusive research facility, not open to Antarctic tourists. There is a large variety of occupational roles at Concordia Station (split between research and maintenance), and their associated risks should be considered. The crew includes a station doctor, a chef and technical workers who ensure proper maintenance of the station. The remaining members (approximately 30%) perform research in fields including but not limited to human biomedicine and psychology, astrophysics, astronomy, glaciology and earth sciences.

Crew are appropriately fitted with safety gear prior to arrival. The winter gear for all members comprises of the following, from head to toe: hat, polarised goggles, sunglasses, thick and thin balaclavas, mouth-nose cover, neck warmer, long-sleeve thermal, thermal leggings, fleece, waterproof polar jacket and trousers, waterproof jumpsuit, mittens, thermal gloves, long socks and slippers. Lined boots, larger outdoor boots and separate boot-liners are also provided. For the technical crew, five-fingered leather and thermal/waterproof pairs of gloves are also provided, with an indoor work jumpsuit. The scientific crew have the option of a ski-jumpsuit for outdoor wear and are also supplied with leather boots for outdoor work. The kitchen staff are provided with an appropriate apron.

All crew members undergo a rigorous selection process to ensure their competency and medico-psychological capacity to work and live in such an environment and are thus expected to perform their roles professionally and safely. All station members are also given a personal GPS-fitted radio which they must always carry, especially when leaving the station. The winter-over crew are also assigned to one or two emergency teams; fire, search and rescue and medical, led by the head mechanic, ESA research M.D. and station doctor respectively. The groups are trained with weekly theory/practical sessions and simulation training throughout the entire year.

There is a lack of published information on the detailed risks pertaining to each role at the station. Each role within the crew poses its own physical and psychological risks, with differing occupational hazards. For example, the station chef is more likely to be at risk of a burn injury and adversely affected by confinement due to the nature of the role being primarily indoors. The physicians (station doctor and ESA biomedical doctor) are at higher risk of needlestick injury. Electricians and mechanics may be at risk of electrical burns or traumatic injury, given the manual labour involved in their work. For the crew members whose occupation requires them to work outdoors year-long (such as the glaciologists and technical engineers), they are more at risk of exposure injuries including frostbite, ice rashes, and traumatic injury.

Aside from the extreme cold, Concordia has two specificities that are a focus for search and rescue training; the seismology cave and the American tower. The seismology cave is a series of stacked underground shipping containers that serve as icy shelters and workspaces for the seismologists. However, access is through a steep set of stairs that can be a risk for traumatic injury and make for a difficult extraction, which is usually executed using a winch and a tripod. The American tower is equipped with sensors that must be cleaned weekly by the French glaciologist, year-round. It is 45m high and must only be climbed with a harness and appropriate safety equipment. However, this presents a particular risk for traumatic injury. Access alone is forbidden. Weather is constantly monitored and beyond certain windspeeds outdoor operations (including access to the American tower) are disabled for crew safety.

To the author's knowledge, there is no publicly available data on the frequency of medical events at Concordia station, which may help to quantitatively assess the medical impact of the conditions on over-winterers and summer visitors, such as the frequency of altitude sickness, traumatic injury and medical evacuations. What is known in terms of medical events comes from cases mentioned in the ESA doctor's blog, or through other publicly available sources, such as media interviews and articles. A published audit outlining the frequency of such events or the number of medical consultations required by crew members during the year would help to gauge the medical burden imposed on the station doctor, as well as aid identification of risk factors, common errors and assess any potential long-term effects.

5. Conclusions

The European Space Agency's involvement in biomedical research at Concordia Station was established with an aim to understanding human adaptability in extreme environments mirroring missions to the moon and Mars. The harsh conditions at Concordia predispose its occupants to acute and chronic biopsychosocial health stressors. Results have demonstrated the detrimental effects of the polar light cycle on circadian rhythm and helped to identify crew mindsets that are better equipped to withstand the psychological stressors of ICE environments. While some countermeasures have been proposed (such as blue-enhanced light for circadian rhythm regulation) these have yet to be tested in the field. There are still many unknowns as to the adaptability of human beings to this ICE environment and how this may apply to space missions, particularly concerning long-term effects.

Stays at Concordia are for a maximum of 13 months, significantly shorter than an expedition to Mars, and post-mission data collection occurs some 5–6 months after crew leave. Long-term consequences (such as cardiovascular events and cancer) are unlikely to be detected so soon after return. In the future, a retrospective study looking at long-term effects decades after return in winter-over crews may be beneficial to identify any patterns in long-term health consequences of exposure to Concordia's stressors, if any. Furthermore, biomedical research at Concordia is conducted on a very small pool of participants (maximum 16). Larger-scale studies would be necessary to solidify many of the study findings thus far. Historically, there have been no more than 4 women in the winter-over team. While research has emerged to show the stark differences in adaptability to the space environment between men and women, our knowledge of women's health in ICE environments is significantly limited. With clear evidence that mixed groups withstand the stressors of ICE environments better, future research in ICE environments should comment on the presence or absence of sex differences when interpreting results.

Two decades' worth of human biomedical research at Concordia Station in Antarctica has improved our understanding of human adaptability and resilience to isolated, confined and extreme environments. It is the multitude of effects exerted upon the human body and psyche by the environment of Dome C that has earned it the nickname 'White Mars.' Concordia Station is, and remains, one of the closest spaceflight analogues on Earth and one of its most hostile environments. As the space sector grows and humanity's eye turns to the moon and beyond, the biomedical research conducted at Concordia continues to help us reflect on terrestrial medicine and take a step further into outer space- as securely and as informed as possible.

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Conflicts of Interest

The authors declare no conflict of interest.

Use of AI and AI-Assisted Technologies

No AI tools were utilized for this paper.

List of Abbreviations

AMS	Acute mountain sickness
Asl	above sea level
BP	Blood pressure
BE	Blue-enriched light
CA	Pupillary contraception amplitude
CSF	Cerebrospinal fluid
DDU	Dumont d'Urville
DM	Defence mechanisms
ESA	European Space Agency
FEF	Forced expiratory flow
FEV1/FVC ratio	The ratio of forced expiratory volume (in 1 s) to forced vital capacity
HACE	High altitude cerebral oedema
HAPE	High altitude pulmonary oedema
HR	Heart rate
ICE	Isolated, confined and extreme
IPEV	Institut Paul-Émile Victor
ISS	International space station
OC	Oral contraception
M.D.	Medical doctor
MRI	Magnetic resonance imaging
NASA	National Aeronautics and Space Administration
pCO_2	Partial pressure of CO_2
$sPaO_2$	partial pressure of arterial oxygen
PIPR	Post-illumination pupil response
PNRA	Programma Nazionale per Ricerche in Antartide
SAD	Seasonal affective disorder
SCN	Suprachiasmatic nucleus
SAS	Secure attachment style
SW	Standard fluorescent white light
UV	Ultraviolet

Appendix A

Table A1. A summary of the published available literature on studies conducted at Concordia station, organized by field of study and date.

Reference	Field of Study	Participants, (of Which Female (F), Male (M)) Mean Age (Years)	Results/Proposed Countermeasures
Krins, 2009 [13]	Psychology	n = 9 (F = 2, M = 7) Age not given	Group diversity and ingroup self-identification reduces crew alienation and interpersonal conflicts.
Abeln et al., 2015 [16]	Psychology	n = 8 (F = 0, M = 8) (4 = active, 4 = inactive) * G_A: 42.3 ± 8.8 y G_I: 37 ± 5.6 y	Exercise is an effective countermeasure against psychological strain. Prolonged stays at Concordia do not demonstrate cognitive deterioration.
Nicolas et al., 2015 [8]	Psychology	n = 14 (F = 1, M = 13) 38.14 ± 11.90 y	Individuals with mature defense mechanisms and higher self-confidence in their competencies adapt better to the stressors of ICE environments.
Nicolas et al., 2016 [14]	Psychology	n = 13 (F = 1, M = 12) 37.14 ± 11.90 y	Sociocultural and occupational factors can impact group dynamics and adaptation throughout a year-long stay and should be considered in selection, monitoring and post-mission support.
Sandal et al., 2018 [10]	Psychology	n = 27 (F = 3, M = 24) 38.3 ± 10.64 y	Psychological hibernation is an adaptive response to the stressors of ICE environments and is not mitigated by a 2-day pre-mission preparative psychological training course.
Bosch Bruguera et al., 2019 [17]	Psychology	n =69 (F = 13, M = 56) Age range: 20–70 y Concordia: n = 23 (F = 3, M = 20)	A lack of regular training results in rapid decay of psychomotor skills.
Caputo et al., 2020 [15]	Psychology	n = 13 (F = 3, M = 10) 34.1 ± 3.1 y	Secure attachment style is a protective trait against deterioration in mood and interpersonal conflicts in ICE environments.
Pagnini et al., 2024 [12]	Psychology	n = 24 (F = 5, M = 19) 39.96 ± 11.42 y	Psychological assessments showed decreased creative thinking and increased stress throughout the mission. Mindfulness is a protective factor against the stressors of ICE environments.
Barkaszi et al., 2016 [18]	Neurology	n = 13 (F = 0, M = 13) Age range: 20–55 y	No deterioration in cognitive function was found.
Najjar et al., 2014 [26]	Sleep health	n = 10 (F = 2, M = 8) 30 ± 2.1 y	Blue-enriched (BE) white light does not delay melatonin secretion and improves alertness and wellbeing compared to standard fluorescent light. BE may mitigate circadian misalignment.
Tellez et al., 2014 [30]	Sleep health	n = 13 (F = 0, M = 13) 39.6 ± 9.8 y	Periodic breathing did not acclimatize at Concordia Station. Participants' apnoea/hypopnoea index was clinically severe despite a linear increase in SpO_2. Individual variability in adaptation is significant.
Collet et al., 2015 [27]	Sleep health	n = 26 (F = 5, M = 21) Concordia: n = 8 (F = 0, M = 8) 36 ± 9.8 y	onstant daylight in summer causes sleep disruption. Hypoxia also contributes to sleep fragmentation, likely secondary to apneic episodes.
Kawasaki et al., 2018 [21]	Sleep health	n = 13 (F = 3, M = 10) 34.6 ± 11.0 y	Pupil responses were heightened by cotopic, photopic and blue light, with retinal sensitivity mostly increased under blue light. Blue light may be an efficient countermeasure to enhance adaptation to the polar light cycle.
Mairesse et al., 2019 [31]	Sleep health	n = 13 (F = 0, M = 13) 4.54 ± 9.46 y	There is a large inter-individual variability in sleep adaptation. Fatigue, reduced psychomotor skill and severe apnea were more prominent during winter. Polysomnography and pre-departure performance may be important for candidate selection in Antarctic and space missions.
Furian et al., 2023 [28]	Sleep health, Cardiovascular health	n = 25 Concordia: n = 11 (F = 4, M = 7) 36.2 ± 10.0 y	Persistent elevated nocturnal blood pressure and sleep disturbances are more prominent at Concordia compared to low-altitude settings.
Feuerecker et al., 2015 [39]	Immunology	n = 9 (F = 0, M = 9) 39.1 ± 11.8 y	Exposure to hypoxia in early stages induces a reversible downregulation of immune function.

Table A1. *Cont.*

Reference	Field of Study	Participants, (of Which Female (F), Male (M)) Mean Age (Years)	Results/Proposed Countermeasures
Strewe et al., 2018 [41]	Immunology	n = 31 (F = 0, M = 31) Concordia n = 15 (F = 0, M = 15) 39.1 ± 2.8 y	Acute exposure to altitude/hypoxia triggers catecholamine release which downregulates the endocannabinoid system. This is not associated with psychological stress.
Feuerecker et al., 2019 [40]	Immunology	n = 14 Age not given	Epigenetic changes in response to the hypoxic conditions at Concordia station cause modulations of the immune response.
Feuerecker et al., 2022 [27]	Immunology	n = 39 (F = 7, M = 32) Age not given Concordia n = 23 (F = 2, M = 21) Age not given	Long-term confinement causes immune system alterations that can result in pronounced responses to allergens upon return.
Venemans-Jellema et al., 2014 [62]	Cardiovascular health	n = 49 (F = 24, M = 25) Concordia n = 25 (F = 0, M = 25) 38.0 y (SD not given)	Prolonged hypoxia without immobilisation is not associated with an increased risk of venous thrombosis
Porcelli et al., 2017 [59]	Pulmunology, Haematology	n = 13 34.1 ± 3.1 y	Exposure for 10 months to the altitude at Concordia Station reduces pCO_2 and increases Hb concentration. Overall increased blood pH suggests humans have poor capacity to acclimatize under these conditions.
Collomp et al., 2025 [63]	Musculoskeletal health	n = 23 (F = 0, M = 23) ** G_{MM}: 36.1 ± 3.6 y G_{PM} 42.9 ± 2.8 y	Loss of over 2% of muscle mass was noted to be significantly associated with higher end-exercise heart rate and lower testosterone fluctuations between waking and evening.
Klos et al., 2025 [57]	The Chemosensory system	n = 19 (F = 3, M = 16) 39.2 ± 10.9 y	Prolonged isolation and confinement at Concordia causes a reduction in objective olfactory and gustatory functions.

* G_A: Active group (n = 4). G_I: Inactive group (n = 4). ** G_{MM}: group that experienced muscle mass loss > 2% (n = 10). G_{PM}: group that had preserved muscle mass (n = 13).

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