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A long trip into the universe: Psychedelics and space travel

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Prolonged periods in space have potentially deleterious physiological and psychological effects. Ensuring the physical health and mental well-being of astronauts will inevitably supersede the need for technological innovation, as the major challenge in long-duration space travel. We propose a role for psychedelics (psychoactive fungal, plant, and animal molecules that cause alterations in perception, mood, behavior, and consciousness) and in particular psychedelic mushrooms to facilitate extended sojourns in space. Psychedelics research is in the midst of a renaissance and psychedelics are being explored not only for their therapeutic potential in psychiatry but also for their ability to promote neuroplasticity, modulate the immune system and reduce inflammation. Psychedelics may be to long-duration space travel in the 21st century, what citrus fruits were to long-distance sea travel in the 18th century—breakthrough and facilitatory. The human intergalactic experience is just beginning and it would be wise to consider the benefits of ensuring that astronauts undertaking potentially perilous space voyages benefit from our planet's rich psychedelic heritage. There is also some justification for considering the application of psychedelics in the processing and integration of the profound and spiritual experience of deep space travel.

KEYWORDS

psychedelics, space travel, neuroplasticity, entheogens, neurobiome

Introduction

In the light of the growing interest in exploring and exploiting the resources of other planets within our solar system (Buchanan, 2017), the success of publicly and privately funded space initiatives (Seedhouse, 2016) and a consensus that long-distance space travel has become technologically feasible (Biswal et al., 2022), the next frontier in space travel is ensuring the health and wellbeing of astronauts on long-duration space missions. Sojourns in space are a source of environmental (radiation and zero-gravity effects) (Young and Sutton, 2021), physiological (energy balance changes, bone mass loss, gut dysbiosis, and micronutrient deficiency) (Bergouignan et al., 2016), and psychological (isolation, confinement, and existential distress) stress (Bergouignan et al., 2016). NASA research highlights over 30 health risks to humans in space (Patel et al., 2020) and the unifying framework that reflects the interaction of all space-related stressors has been defined as the *space exposome* (Czupalla et al., 2004; Wild, 2012).

Extended space station missions have yielded a wealth of data on the effects of sojourns in space on the human organism and raise to date largely only partially answered questions related to the best approach to ensuring the health and wellbeing of long-duration space travelers (Young and Sutton, 2021). Research on polar exploration, submarines, solitary confinement, undersea habitats, and space simulations provides a wealth of evidence that humans are indeed eminently sensitive to isolation and confinement, manifesting neurocognitive changes, fatigue, misaligned circadian rhythms, sleep disorders, altered stress hormone levels, and immune system dysfunction (Cruces et al., 2014; Pagel and Choukèr, 2016; Sandal et al., 2018; Alfano et al., 2021). Space station astronauts have suffered transient, reactive psychological distress causing sometimes critical lapses in attention, sleep disorders, emotional lability, psychosomatic symptoms, irritability towards fellow crew members and mission control staff, a decline in vigor and motivation, and possibly increased risk of anxiety, depression and psychosis, psychosomatic symptoms, emotional problems, and post-mission personality changes (KanasPsychological, 1990; Kanas et al., 2009). Spaceflight also has immune system effects through a range of mechanisms including the action of stress hormones and long sojourns in space suppress general immunity and cause an increase in blood inflammation markers (Crucian et al., 2018).

Until the late 1700s, scurvy (a debilitating condition caused by vitamin C deficiency) was a common and dreaded accompaniment to long-duration sea travel. Scurvy, which resulted in mortality rates of almost 50% among sailors, was attributed to improper diet, poor ventilation, and confinement and was responsible for the failure of numerous exploration and trade expeditions (Carpenter, 1988). In 1747, the Scottish physician James Lind conducted what is regarded as the world's first comparative clinical trial, proving the efficacy of lemons and oranges for the prevention of scurvy (Lind, 1757). While the health impacts of space travel can certainly not be directly compared to scurvy, the search has commenced for solutions that could play a pivotal role not only in the prevention of the negative physical and psychological outcomes related to long sojourns in deep space but also to improve physical and cognitive performance in what is the harshest of environments to which our species has ever been exposed.

NASA, through its various space nutrition programs, is increasingly prioritizing the well-being of astronauts (NASA's Centennial Challenges Program, 2022). There is a general acceptance that functional nutrition can play an important role in ensuring optimal health and wellbeing (Platkin et al., 2020) and NASA's current focus relates to high-potential, but not fully proven terrestrial nutritional technologies such as controlled environment agriculture (CEA) including vertical farming (VF), algae and mushroom culture, cultivation of bio-active or functional foods and cellular agriculture for the production of cultured meat (Benjaminson et al., 2002; Niederwieser et al., 2018; Cortesão et al., 2020; Mortimer and Gilliham, 2022). While there is a growing recognition of the important role that optimized nutrition plays in ensuring the success of long-distance space missions (Zwart et al., 2021), this heartening trend towards prevention should be juxtaposed against the current continued predominance of diagnostic and curative technologies in space medicine and popular space culture (Clément, 2011; Lasbury, 2017).

We present the case for a primary prevention-focused approach to ensuring the health and wellbeing of long-duration space travelers through the potential application of psychedelics (psychoactive substances that induce alterations in perception, mood, consciousness, cognition, or behavior, which when used for the purposes of engendering spiritual development, that in sacred contexts are also called entheogens (Ruck et al., 1979)), and in particular psychedelic mushrooms (mushrooms containing the indoleamine psilocybin molecule). While accepting that there is no direct experimental evidence to support the role of psychedelic mushroom consumption during space missions, our viewpoint is supported by the eminent mycologist Paul Stamets[1]: "I say this with great sincerity: NASA and anyone else working and looking at the settlement of space, you should consider that psilocybin (psychedelic) mushrooms should be an essential part of your psychological tool kit for astronauts to be able to endure the solitude and the challenges of space and isolation" (Scientific American, 2021).

Psychedelics and neuroplasticity—A possible role in facilitating long-duration space travel?

Psychedelics are drugs that alter emotions, mood, and perception without generally impairing higher functions such as memory (Nichols, 2016). The paradigmatic "classical" psychedelic is lysergic acid diethylamide (LSD) and to be regarded as a psychedelic, a drug needs to have an "LSD-like" effect (inducing an altered state of consciousness and hallucinogenic manifestations) mediated through activation of the brain's $5HT_{2A}$ receptor system. LSD-like psychedelics include natural products such as the tryptamines, N,N′-dimethyltryptamine (DMT), 4-phosphoryloxy-N,N-dimethyltryptamine (psilocybin or "psychedelic or magic mushrooms"), and 5-methoxy-N,N, dimethyltryptamine (5-MeO-DMT) and the phenethylamine 3,4,5-

1 Paul Stamets also has a popular culture link with space travel. In the Star Trek series, the character Lieutenant Commander Paul Stamets is the astromycologist and Starfleet officer responsible for the Starship Enterprise spore drive propulsion system.

trimethoxyphenethylamine (mescaline) (McClure-Begley and Roth, 2022). Other "non-classical" psychedelics include the dissociative anesthetic ketamine (Bennett et al., 2022) and the entactogens, (psychoactive drugs that result in emotional effects of empathy, sympathy and community such as 3,4-methyl enedioxy methamphetamine (MDMA)) (Vollenweider, 2022). There is evidence that psychedelic mushrooms were used for entheogenic and medicinal purposes across Mesoamerica from the early 16th century (Van Court et al., 2022). From the 1960s, psychedelics were extensively used as recreational drugs and by the early 1970s, global repressive policies and laws largely stifled research in this field (Coppola et al., 2022). Over the past decade, there has been a resurgence of research into the therapeutic applications of psychedelics, particularly in psychiatry (Nutt and Carhart-Harris, 2021; Phelps et al., 2022). A growing number of clinical trials are underway to test psychedelics in the treatment of conditions including depression, PTSD, addiction, eating disorders, and end-of-life care (Siegel et al., 2021). Some American cities are decriminalizing the personal use of psychedelic mushrooms and plants in the light of their low addictive potential and generally benign toxicity profiles (Nutt et al., 2010; Schlag et al., 2022) and positive media coverage is transforming the public perception of psychedelics (Matzopoulos et al., 2022). We recognize that there are still substantial gaps in the biomedical science supporting the generalized preventive and therapeutic application of psychedelics, while noting that psilocybin (for depression) and MDMA (for PTSD) are in advanced clinical development with potential FDA approvals from 2024, and that ketamine (delivered *via* a nasal spray) is already approved for the treatment of depression (An et al., 2021; Carhart-Harris et al., 2021; Mitchell et al., 2021).

There is still considerable debate on the therapeutic mechanism of action of psychedelics. The profound experience or "trip" associated with psychedelics may improve responses to psychotherapeutic interventions and there is a strong placebo effect (Yaden and Griffiths, 2020). Psychedelics also promote neuroplasticity (the capability of the brain to alter its structure or function in response to exposure to new stimuli, insults, or environments) mainly in the prefrontal cortex, possibly repairing neural circuits that are dysfunctional in conditions including depression and PTSD (Olson, 2022).

Deleterious effects of sojourns in space on the brain include changes in motor function and reduction in cognitive reserve, making it important that innovative approaches to enhancing neuroplasticity be developed (Svenska, 2003; Van Ombergen et al., 2017; Roy-O'Reilly et al., 2021). Current research indicates that the action of psychedelics is mainly mediated through effects on the serotonergic (mainly 5-HT_{2A} and 5-HT_{1A}) receptor system enhancing neuroplasticity (including dendritic spine formation, axon branching, and synaptic density) in key brain regions (Ly et al., 2018; Inserra et al., 2021). Psilocybin and other psychedelics increase synaptic density and neurogenesis and these neuroplastic effects are thought to be an important component of their therapeutic mechanism of action (Lima da Cruz et al., 2018; Hutten et al., 2020; Olson, 2020; Raval et al., 2021).

Psychedelics, nutrition, and the microbiome—Maintaining wellness in space

Psychedelic molecules are produced by plants and fungi as secondary metabolites for protection against predators and infections. Animals generally avoid these potentially toxic molecules but in the case of our hominid ancestors it is possible that rather than avoidance they may have elected to consume these secondary metabolites as means of complementing tryptamine levels thereby accelerating the socio-cognitive development of our species (Forbey et al., 2009; Friedman, 2018). Indeed, the so-called "Stoned Ape Theory" was originally proposed by Terence McKenna, who speculated that psilocybin mushrooms were an evolutionary catalyst for the emergence of certain higher cognitive faculties of early hominids (McKenna, 1992).

Psychedelics can form part of a health-promoting diet, as demonstrated by the application of psychoactive plants in Peruvian-Amazonian traditional healing (Berlowitz et al., 2022). These entheogenic wellness practices are largely undertaken with natural products derived from fungi, plants, or animals (mainly amphibians), as opposed to synthetic molecules. A diet that includes psychedelic biomass may not only be healthier but also has the potential to complement strategies to reduce dependence on high protein foods and cell-based animal meat, thereby saving energy and resources on a lengthy space mission. In order to avoid any neurocognitive effects of ingesting psychoactive substances, it may be possible to grow mycelial biomass that contains only trace amounts of psilocybin or grow genetically engineered "psychedelic mushrooms" that do not produce psilocybin. Over the last decade, "microdosing" or sub-psychedelic, small and regular dosing of psychedelics, has attracted a significant amount of public interest with anecdotal reports of positive socio-affective, cognitive, and physical outcomes. However, it should also be noted that the current, peer-reviewed evidence-base does not provide sufficient support for the application of microdosing as a health and wellness promotion strategy in long-duration space travel (Cameron et al., 2020; Cavanna et al., 2022).

To provide a sustainable psychedelic biomass source for long-duration space travel, it may be possible to integrate psychedelics cultivation into a bioregenerative food system using microalgae, fungi, plant, and animal cells (Figure 1) (Hendrickx et al., 2006; Mapstone et al., 2022). Components of such a system include green fractionation, extraction, and purification (Chemat et al., 2012), application of microalgae metabolites for VF (Varia et al., 2022) and the production of

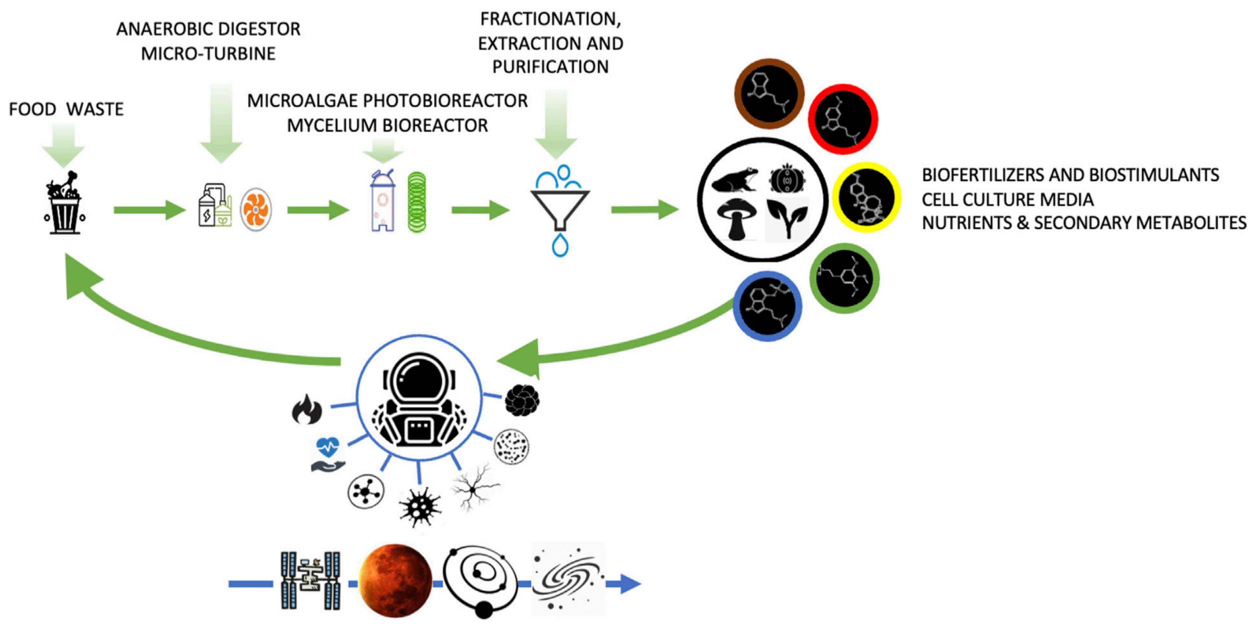

FIGURE 1
A circular and sustainable bioregenerative functional food production model in space.

cultured meat (Tuomisto and Teixeira de Mattos, 2011). Combinations of these technologies would be required to produce functional and psychedelic fungi and psychoactive molecules from animal cells, for example, the cell-based synthesis of 5-MeO-DMT, using immortalized cells of *Incilius alvarius* (Lerer et al., 2021). Moreover, process streams from bacterial anaerobic digestion of food waste (Hendrickx et al., 2006) can be utilized for functional and psychedelic fungi cultivation through submerged culture (Musatti et al., 2017) and for photo-autotrophic algae cultivation (Kisielewska et al., 2022).

Healthy humans exist in a symbiosis with commensal microbes in the nose, mouth, lungs, and epithelial surfaces with microbial concentrations ranging up to 10 (Kanas et al., 2009) in the gastrointestinal tract (Wilson, 2005). This microbiome directly influences our well-being and is our first line of resistance to various diseases (Shreiner et al., 2015). The gut microbiome can produce (and metabolize) neurotransmitters, including dopamine, serotonin, or gamma-aminobutyric acid (GABA) (Strandwitz, 2018) and this could be the mechanism whereby the gut microbiome plays some pathophysiological role in conditions including autism spectrum disorder, anxiety, depression, and chronic pain (Mayer et al., 2014). The gut microbiome of astronauts has been monitored since the 1970s and studies have highlighted that long stays in space impact the microbiome, reducing microbial richness and diversity and increasing levels of pathogenic bacteria (Shreiner et al., 2015; Tesei et al., 2022).

The bidirectional communication between the central and the enteric nervous system links the emotional and cognitive centers of the brain with peripheral intestinal function playing a role in our adaptation to a range of stressors (Kostic et al., 2013). Beyond the effects of cosmic radiation, zero-gravity and psychological stress, sojourns in space expose the gut to a semi-sterile environment limiting both the diversity and density of gut microbiota and it is indeed possible that the reduced prevalence of certain bacteria negatively impacts the cardiovascular and immune systems (Marques et al., 2016; Verhaar et al., 2020). The link between the gut microbiome and nervous system inflammatory pathways provides limited support for considering that psychedelics may exert some of their positive effects through indirect modulation of the gut-brain axis (Kuypers et al., 2019; Cerletti et al., 2021).

Psychedelics to support cognition, empathy, and transcendence in space

The evolution of our species over the past 2.5 million years, has seen a tripling in encephalization and unprecedented intellectual achievements (Whiten and Erdal, 2012). Some believe that the ingestion of psychedelic mushrooms collected from the dung of roaming animals was a key step in the evolution of the early hominid brain, catalyzing the emergence of self-reflection, communal consciousness, and language skills (Rodríguez Arce and Winkelman, 2021). Moreover, the neuroplastic and empathogenic properties of psychedelic mushrooms may have had direct effects on the adaptation of early humans to their environment, enhancing their ability to live in highly social, cooperative communities and participate in collaborative activities with shared goals and intentions (Rodríguez Arce and Winkelman, 2021). The recent renaissance of psychedelic science has advanced our understanding of the phenomenology and physiology of the altered states of consciousness induced by psychedelics and their therapeutic utility in psychiatric conditions (Carhart-Harris and Goodwin, 2017; Millière et al., 2018; Olson, 2021).

In addition to the challenges to individual physical and psychological health, long sojourns in space may result in strained interpersonal relationships and disruptions to group cohesion (Kanas et al., 2009; Sandal and Bye, 2015). Individual behavior adjustment, interpersonal conflict and group performance effectiveness are inevitably difficult to manage in isolated and confined groups and successful long-duration space travel will require that crew members establish and maintain effective, stable interactions between individuals in small groups for prolonged periods (Clément, 2005). Given the psychological pressures of long-duration space travel at an individual and group level, it is useful to consider the potential positive, adaptive effects of the psychedelic experience that include enriched states of consciousness, enhanced cognitive flexibility, heightened creativity, enhanced ability to attribute meaning and value, empathy, enhanced insightfulness, and self-awareness (Rodríguez Arce and Winkelman, 2021). Some astronauts have reported transcendental experiences, religious insights, or a sense of unity with humankind to some extent attributed to viewing the Earth below and the cosmos beyond (Yaden et al., 2016). This profound, personal experience with possible effects on personal beliefs about the universe and consciousness, is largely akin to the experience of many psychedelic users (Timmermann et al., 2021). The feeling of spiritual transcendence and interconnection with fellow humans and the universe, and the depth of the emotional experience linked to the separation from earth mirrors the noetic (a perceived, deeper understanding of space or time), empathogenic and mystical experience associated with psychedelics (Sagan, 1997; Cole-Turner, 2021; Nayak and Griffiths, 2022). The vast majority of psychedelic experiences are indeed regarded as positive and given that there is a strong, positive association between various forms of spirituality and wellbeing, the combination of psychedelics with meditation and group therapy may offer a way to improve psychosocial functioning during long space missions (Móró et al., 2011; Smigielski et al., 2019; Božek et al., 2020).

Long-distance space travelers may encounter other forms of life. Experience with DMT may provide some limited familiarity to experiences of transcendence, out-of-body experiences, entry into other realms or dimensions or the afterlife, and meetings with other presences or entities (Bilton, 2018; Timmermann et al., 2018). As we journey farther and farther from the earth and stretch technological limits, it is important to consider that space travelers may be faced with a situation where return to earth is impossible and death in space is inevitable. There is some archaeological data supporting the use of psychedelics to ameliorate mental states at the end of life (Socha et al., 2022) and evidence of the utility of psychedelics in the management of depression and existential distress associated with end-stage cancer and in assisting with the acceptance of death in terminal care (Leung et al., 2006; Zimmermann, 2012; Blinderman, 2016).

A role for psychedelics in long-duration space travel?

There is a growing body of research, mostly from non-human studies indicating that psychedelics enhance neuroplasticity (structural and functional) and have utility in the treatment of psychiatric conditions (Hibicke et al., 2020; Shao et al., 2021; Thomas et al., 2022). Psychedelics exert significant modulatory effects on immune responses by altering signaling pathways involved in inflammation, cellular proliferation, and cell survival with some of this activity being mediated through the 5-HT receptors (Szabo, 2015; Nkadimeng et al., 2020; Meade et al., 2022). Psychedelics, and psychedelic mushrooms in particular, could play a role in supporting human adaption to space through the promotion of neuroplasticity, modulation of inflammatory pathways, and in improving general wellbeing. It is indeed possible that enhanced neuroplasticity may be a potential facilitator of successful long-duration space missions and future human settlement on other planets (Rappaport et al., 2020). The growing public interest in psychedelics can be seen in the context of the search by many in our modern world for mindfulness, spirituality, healing, and meaning. Given the proliferation of retreats and clinics providing psychedelic experiences and therapy, it may indeed be possible that, once space tourism becomes well established, psychedelic space wellness packages will one day be on offer

Even though our understanding of human space physiology has improved substantially, ensuring astronaut wellness, and building medical care capabilities for space exploration remain daunting challenges (Tran et al., 2022). The safe use of psychedelics in a high-risk space environment requires careful consideration, given the duration, intensity and potential negative outcomes of the psychedelic experience or “trip” (e.g., dissociation, paranoia, hallucinogenic phenomena, and confusion). To date, very few adverse events have been reported in clinical trials with psilocybin and other psychedelics (Rossi et al., 2022). Clinical studies and rigorous hazard analysis in controlled environments, including the International Space Station, are required before psychedelics can be used in deep space. Additional risk-reduction technologies, including telemedicine, AI-monitoring, sub-psychedelic dosing schedules, pharmacogenetic identification of susceptibility to adverse events, drugs to “reverse” or neutralize subjective psychedelic effects and non-psychedelic drug analogs, also require testing. Astronauts could also be trained to use safety protocols that have been developed for psychedelics-assisted psychotherapy, benefiting from the growing body experience on the safe and effective deployment of psychedelics in terrestrial therapeutic settings. Ensuring the safety of astronauts who have ingested psychedelics, during emergencies such as an onboard fire, also needs to be seriously considered. By the time psychedelics are indeed deployed for medical and wellbeing purposes on long-duration space missions, it may be possible to avoid the psychedelic experience or trip while still leveraging their neuroplastic benefits. It would also be prudent to consider the first applications of psychedelics in long-duration space travel for the general improvement of wellbeing, rather than the management of serious psychiatric conditions, with a focus on dosing and scheduling to ensure maximum safety and security on the spacecraft.

There is a growing body of evidence that psychedelics are indeed good potential therapeutic options for conditions such as treatment-resistant depression and PTSD, and despite the exuberance related to the “psychedelics renaissance”, it is clear that psychedelic science is at an early stage of development. While there is no empirical evidence to support the application of psychedelics in space exploration, we should be aware that our species has a longstanding history of using psychedelics to explore the fluid interface between our *inner space* (including our consciousness) and the universe or *outer space* (Schultes, 1979; Strassman et al., 2008). Even though the potential preventative and therapeutic role of psychedelics in the advancement of space exploration remains unclear, it is indeed interesting to consider that deep space is a propitious setting for reflection on the nature of consciousness and the enigmas of the cosmos itself (Hartogsohn, 2018; Millière et al., 2018; Smigielski et al., 2019), and that such reflection could be conducted with or without the aid of psychedelics.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

LL and JV contributed equally to the conception, research, and writing of the article.

Conflict of interest

LL and JV were employed by Back of the Yards Algae Sciences and Parow Entheobiosciences. LL holds equity interests in Back of the Yards Algae Sciences and Parow Entheobiosciences.

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References

Alfano, C. A., Bower, J. L., Connaboy, C., Agha, N. H., Baker, F. L., Smith, K. A., et al. (2021). Mental health, physical symptoms and biomarkers of stress during prolonged exposure to Antarctica’s extreme environment. *Acta Astronaut.* 181, 405–413. doi:10.1016/j.actaastro.2021.01.051

An, D., Wei, C., Wang, J., and Wu, A. (2021). Intranasal ketamine for depression in adults: A systematic review and meta-analysis of randomized, double-blind, placebo-controlled trials. *Front. Psychol.* 12, 648691. doi:10.3389/fpsyg.2021.648691

Benjaminson, M. A., Gilchriest, J. A., and Lorenz, M. (2002). *In vitro* edible muscle protein production system (mpps): Stage 1, fish. *Acta Astronaut.* 51 (12), 879–889. doi:10.1016/s0094-5765(02)00033-4

Bennett, R., Yavorsky, C., and Bravo, G. (2022). Ketamine for bipolar depression: Biochemical, psychotherapeutic, and psychedelic approaches. *Front. Psychiatry* 13, 867484. doi:10.3389/fpsyt.2022.867484

Bergouignan, A., Stein, T. P., Habold, C., Coxam, V., O’ Gorman, D., and Blanc, S. (2016). Towards human exploration of space: The THESEUS review series on nutrition and metabolism research priorities. *npj Microgravity* 2 (1), 16029. doi:10.1038/npjmgrav.2016.29

Berlowitz, I., O’Shaughnessy, D. M., Heinrich, M., Wolf, U., Maake, C., and Martin-Soelch, C. (2022). Teacher plants—indigenous Peruvian-amazonian dietary practices as a method for using psychoactives. *J. Ethnopharmacol.* 2021, 114910. doi:10.1016/j.jep.2021.114910

Bilton, A. (2018). *DMT dialogues: Encounters with the spirit molecule*. Rochester: Park Street Press.

Biswal, M. M. K., Kumar, R., and Basanta Das, N. (2022). *A review on human interplanetary exploration challenges*. San Diego: American Institute of Aeronautics and Astronautics, Inc., 2585. AIAA-2022-SCITECH.

Blinderman, C. D. (2016). Psycho-existential distress in cancer patients: A return to “entheogens”. *J. Psychopharmacol.* 30 (12), 1205–1206. doi:10.1177/0269881116675761

Bożek, A., Nowak, P. F., and Blukacz, M. (2020). The relationship between spirituality, health-related behavior, and psychological well-being. *Front. Psychol.* 11, 1997. doi:10.3389/fpsyg.2020.01997

Buchanan, M. (2017). Colonizing Mars. *Nat. Phys.* 13 (11), 1035. doi:10.1038/nphys4311

Cameron, L. P., Nazarian, A., and Olson, D. E. (2020). Psychedelic microdosing: Prevalence and subjective effects. *J. Psychoact. drugs* 52, 113–122. doi:10.1080/02791072.2020.1718250

Carhart-Harris, R., Giribaldi, B., Watts, R., Baker-Jones, M., Murphy-Beiner, A., Murphy, R., et al. (2021). Trial of psilocybin versus escitalopram for depression. *N. Engl. J. Med. Overseas. Ed.* 384 (15), 1402–1411. doi:10.1056/nejmoa2032994

Carhart-Harris, R. L., and Goodwin, G. M. (2017). The therapeutic potential of psychedelic drugs: Past, present, and future. *Neuropsychopharmacology* 42 (11), 2105–2113. doi:10.1038/npp.2017.84

Carpenter, K. J. (1988). *The history of scurvy and vitamin C*. New York: Cambridge University Press.

Cavanna, F., Muller, S., de la Fuente, L. A., Zamberlan, F., Palmucci, M., Janeckova, L., et al. (2022). Microdosing with psilocybin mushrooms: A double-blind placebo-controlled study. *Transl. Psychiatry* 12, 307–311. doi:10.1038/s41398-022-02039-0

Cerletti, C., Esposito, S., and Iacoviello, L. (2021). Edible mushrooms, and beta-glucans: Impact on human health. *Nutrients* 13 (7), 2195. doi:10.3390/nu13072195

Chemat, F., Vian, M. A., and Cravotto, G. (2012). Green extraction of natural products: Concept and principles. *Int. J. Mol. Sci.* 13 (7), 8615–8627. doi:10.3390/ijms13078615

Clément, G. (2011). *Fundamentals of space medicine*. New York: Springer Science & Business Media.

Clément, G. (2005). "Psycho-sociological issues of spaceflight," in *Fundamentals of space medicine*, 205–244. doi:10.1007/1-4020-3434-2_6

Cole-Turner, R. (2021). Psychedelic epistemology: William James and the "noetic quality" of mystical experience. *Religions* 12, 1058. doi:10.3390/rel12121058

Coppola, M., Bevione, F., and Mondola, R. (2022). Psilocybin for treating psychiatric disorders: A psychonaut legend or a promising therapeutic perspective. *J. Xenobiot.* 12 (1), 41–52. doi:10.3390/jox12010004

Cortesão, M., Schütze, T., Marx, R., Moeller, R., and Meyer, V. (2020). "Fungal biotechnology in space: Why and how?," in *Grand challenges in fungal biotechnology*. Editor H. Nevalainen (Cham: Springer). Grand Challenges in Biology and Biotechnology.

Cruces, J., Venero, C., Pereda-Peeez, I., and De la Fuente, M. (2014). The effect of psychological stress and social isolation on neuroimmunoendocrine communication. *Curr. Pharm. Des.* 20 (29), 4608–4628. doi:10.2174/1381612820666140130205822

Crucian, B. E., Chouker, A., Simpson, R. J., Mehta, S., Marshall, G., Smith, S. M., et al. (2018). Immune system dysregulation during spaceflight: Potential countermeasures for deep space exploration missions. *Front. Immunol.* 9, 1437. doi:10.3389/fimmu.2018.01437

Czupalla, M., Aponte, V., Chappell, S., and Klaus, D. (2004). Analysis of a spacecraft life support system for a Mars mission. *Acta Astronaut.* 55 (3-9), 537–547. doi:10.1016/j.actaastro.2004.05.008

Forbey, J. S., Harvey, A. L., Huffman, M. A., Provenza, F. D., Sullivan, R., and Tasdemir, D. (2009). Exploitation of secondary metabolites by animals: A response to homeostatic challenges. *Integr. Comp. Biol.* 49 (3), 314–328. doi:10.1093/icb/icp046

Friedman, M. (2018). Analysis, nutrition, and health benefits of tryptophan. *Int. J. Tryptophan Res.* 11, 1–12. 117864691880228. doi:10.1177/1178646918802282

Hartogsohn, I. (2018). The meaning-enhancing properties of psychedelics and their mediator role in psychedelic therapy, spirituality, and creativity. *Front. Neurosci.* 12, 129. doi:10.3389/fnins.2018.00129

Hendrickx, L., De Wever, H., Hermans, V., Mastroleo, F., Morin, N., Wilmotte, A., et al. (2006). Microbial ecology of the closed artificial ecosystem MELiSSA (Micro-Ecological Life Support System Alternative): Reinventing and compartmentalizing the Earth's food and oxygen regeneration system for long-haul space exploration missions. *Res. Microbiol.* 157 (1), 77–86. doi:10.1016/j.resmic.2005.06.014

Hibicke, M., Landry, A. N., Kramer, H. M., Talman, Z. K., and Nichols, C. D. (2020). Psychedelics, but not ketamine, produce persistent antidepressant-like effects in a rodent experimental system for the study of depression. *ACS Chem. Neurosci.* 11 (6), 864–871. doi:10.1021/acschemneuro.9b00493

Hutten, N. R. P. W., Mason, N. L., Dolder, P. C., Theunissen, E. L., Holze, F., Liechti, M. E., et al. (2020). Low doses of LSD acutely increase BDNF blood plasma levels in healthy volunteers. *ACS Pharmacol. Transl. Sci.* 4 (2), 461–466. doi:10.1021/acsptsci.0c00099

Inserra, A., De Gregorio, D., and Gobbi, G. (2021). Psychedelics in psychiatry: Neuroplastic, immunomodulatory, and neurotransmitter mechanisms. *Pharmacol. Rev.* 73 (1), 202–277. doi:10.1124/pharmrev.120.000056

Kanas, N., Sandal, G., Boyd, J., Gushin, V., Manzey, D., North, R., et al. (2009). Psychology and culture during long-duration space missions. *Acta Astronaut.* 64 (7-8), 659–677. doi:10.1016/j.actaastro.2008.12.005

KanasPsychological, N. (1990). Psychological, psychiatric, and interpersonal aspects of long-duration space missions. *J. Spacecr. Rockets* 27 (5), 457–463. doi:10.2514/3.26165

Kisielewska, M., Debowski, M., Zielinski, M., Kazimierowicz, J., Quattrocelli, P., and Bordiean, A. (2022). Effects of liquid digestate treatment on sustainable microalgae biomass production. *Bioenergy Res.* 15 (1), 357–370. doi:10.1007/s12155-021-10251-x

Kostic, A. D., Howitt, M. R., and Garrett, W. S. (2013). Exploring host–microbiota interactions in animal models and humans. *Genes Dev.* 27 (7), 701–718. doi:10.1101/gad.212522.112

Kuypers, K. P. C., Ng, L., Erritzoe, D., Knudsen, G. M., Nichols, C. D., Nichols, D. E., et al. (2019). Microdosing psychedelics: More questions than answers? An overview and suggestions for future research. *J. Psychopharmacol.* 33 (9), 1039–1057. doi:10.1177/0269881119857204

Lasbury, M. E. (2017). *The realization of star Trek technologies*. Cham: Springer International Publishing.

Lerer, L. R. E., Ojeda-Torres, G., and Lerer, B. (2021). *Incilius alvarius cell-based synthesis of 5-MeO-DMT*. San Juan: American College of Neuropsychopharmacology. ACNP Annual Meeting.

Lerer, L., and Varia, J. (2022). *A long trip into the universe: Psychedelics and space travel*. SSRN.

Leung, K.-K., Chiu, T.-Y., and Chen, C.-Y. (2006). The influence of awareness of terminal condition on spiritual well-being in terminal cancer patients. *J. Pain Symptom Manag.* 31 (5), 449–456. doi:10.1016/j.jpainsymman.2006.02.001

Lima da Cruz, R. V., Moulin, T. C., Petiz, L. L., and Leão, R. N. (2018). A single dose of 5-MeO-DMT stimulates cell proliferation, neuronal survivability, morphological and functional changes in adult mice ventral dentate gyrus. *Front. Mol. Neurosci.* 11, 312. doi:10.3389/fnmol.2018.00312

Lind, J. A. (1757). *Treatise on the scurvy*. London: A. Millar.

Ly, C., Greb, A. C., Cameron, L. P., Wong, J. M., Barragan, E. V., Wilson, P. C., et al. (2018). Psychedelics promote structural and functional neural plasticity. *Cell Rep.* 23 (11), 3170–3182. doi:10.1016/j.celrep.2018.05.022

Mapstone, L. J., Leite, M. N., Purton, S., Crawford, I. A., and Dartnell, L. (2022). Cyanobacteria and microalgae in supporting human habitation on Mars. *Biotechnol. Adv.* 59, 107946. doi:10.1016/j.biotechadv.2022.107946

Marques, R. E., Marques, P. E., Guabiraba, R., and Teixeira, M. M. (2016). Exploring the homeostatic and sensory roles of the immune system. *Front. Immunol.* 7, 125. doi:10.3389/fimmu.2016.00125

Matzopoulos, R., Morlock, R., Morlock, A., Lerer, B., and Lerer, L. (2022). Psychedelic mushrooms in the USA: Knowledge, patterns of use, and association with health outcomes. *Front. Psychiatry* 12, 780696. doi:10.3389/fpsyt.2021.780696

Mayer, E. A., Knight, R., Mazmanian, S. K., Cryan, J. F., and Tillisch, K. (2014). Gut microbes and the brain: Paradigm shift in neuroscience. *J. Neurosci.* 34 (46), 15490–15496. doi:10.1523/jneurosci.3299-14.2014

McClure-Begley, T. D., and Roth, B. L. (2022). The promises and perils of psychedelic pharmacology for psychiatry. *Nat. Rev. Drug Discov.* 21, 463–473. doi:10.1038/s41573-022-00421-7

McKenna, T. (1992). *Food of the gods: A radical history of plants, drugs and human evolution*. Rider.

Meade, E., Hehir, S., Rowan, N., and Garvey, M. (2022). Mycotherapy: Potential of fungal bioactives for the treatment of mental health disorders and morbidities of chronic pain. *J. Fungi (Basel).* 8 (3), 290. doi:10.3390/jof8030290

Millière, R., Carhart-Harris, R. L., Roseman, L., Trautwein, F.-M., and Berkovich-Ohana, A. (2018). Psychedelics, meditation, and self-consciousness. *Front. Psychol.* 9, 1475. doi:10.3389/fpsyg.2018.01475

Mitchell, J. M., Bogenschutz, M., Lilienstein, A., Harrison, C., Kleiman, S., Parker-Guilbert, K., et al. (2021). MDMA-assisted therapy for severe PTSD: A randomized, double-blind, placebo-controlled phase 3 study. *Nat. Med.* 27 (6), 1025–1033. doi:10.1038/s41591-021-01336-3

Móró, L., Simon, K., Bárd, I., and Rácz, J. (2011). Voice of the psychonauts: Coping, life purpose, and spirituality in psychedelic drug users. *J. Psychoact. Drugs* 43 (3), 188–198. doi:10.1080/02791072.2011.605661

Mortimer, J. C., and Gilliham, M. (2022). SpaceHort: Redesigning plants to support space exploration and on-earth sustainability. *Curr. Opin. Biotechnol.* 73, 246–252. doi:10.1016/j.copbio.2021.08.018

Musatti, A., Ficara, E., Mapelli, C., Sambusiti, C., and Rollini, M. (2017). Use of solid digestate for lignocellulolytic enzymes production through submerged fungal fermentation. *J. Environ. Manag.* 199, 1–6. doi:10.1016/j.jenvman.2017.05.022

NASA's Centennial Challenges Program (2022). The deep space food challenge: Food for the next frontier. Available at: https://www.deepspacefoodchallenge.org/challenge (Accessed March 1, 2020).

Nayak, S. M., and Griffiths, R. R. (2022). A single belief-changing psychedelic experience is associated with increased attribution of consciousness to living and non-living entities. *Front. Psychol.* 13, 852248. doi:10.3389/fpsyg.2022.852248

Nichols, D. E. (2016). Psychedelics. *Pharmacol. Rev.* 68 (2), 264–355. doi:10.1124/pr.115.011478

Niederwieser, T., Kociolek, P., and Klaus, D. (2018). A review of algal research in space. *Acta Astronaut.* 146, 359–367. doi:10.1016/j.actaastro.2018.03.026

Nkadimeng, S. M., Nabatanzi, A., Steinmann, C. M. L., and Eloff, J. N. (2020). Phytochemical, cytotoxicity, antioxidant and anti-inflammatory effects of Psilocybe natalensis magic mushroom. *Plants* 9, 1127. doi:10.3390/plants9091127

Nutt, D., and Carhart-Harris, R. (2021). The current status of psychedelics in psychiatry. *JAMA Psychiatry* 78 (2), 121–122. doi:10.1001/jamapsychiatry.2020.2171

Nutt, D. J., King, L. A., and Phillips, L. D. (2010). Drug harms in the UK: A multicriteria decision analysis. *Lancet* 376 (9752), 1558–1565. doi:10.1016/s0140-6736(10)61462-6

Olson, D. E. (2022). Biochemical mechanisms underlying psychedelic-induced neuroplasticity. *Biochemistry* 61 (3), 127–136. doi:10.1021/acs.biochem.1c00812

Olson, D. E. (2021). The promise of psychedelic science. *ACS Pharmacol. Transl. Sci.* 4 (2), 413–415. doi:10.1021/acsptsci.1c00071

Olson, D. E. (2020). The subjective effects of psychedelics may not be necessary for their enduring therapeutic effects. *ACS Pharmacol. Transl. Sci.* 4 (2), 563–567. doi:10.1021/acsptsci.0c00192

Pagel, J. I., and Choukèr, A. (2016). Effects of isolation and confinement on humans-implications for manned space explorations. *J. Appl. Physiology* 120, 1449–1457. doi:10.1152/japplphysiol.00928.2015

Patel, Z. S., Brunstetter, T. J., Tarver, W. J., Whitmire, A. M., Zwart, S. R., Smith, S. M., et al. (2020). Red risks for a journey to the red planet: The highest priority human health risks for a mission to Mars. *npj Microgravity* 6 (1), 33–13. doi:10.1038/s41526-020-00124-6

Phelps, J., Shah, R. N., and Lieberman, J. A. (2022). The rapid rise in investment in psychedelics - cart before the horse. *JAMA Psychiatry* 79 (3), 189–190. doi:10.1001/jamapsychiatry.2021.3972

Platkin, C., Cather, A., Butz, L., Garcia, I., Gallanter, M., and Leung, M. M. (2020). *Food as medicine: Overview and report: How food and diet impact the treatment of disease and disease management*. New York: Center for Food as Medicine and Hunter College NYC Food Policy Center.

Rappaport, M. B., Szocik, K., and Corbally, C. (2020). Neuroplasticity as a foundation for human enhancements in space. *Acta Astronaut.* 175, 438–446. doi:10.1016/j.actaastro.2020.06.011

Raval, N. R., Johansen, A., Donovan, L. L., Ros, N. F., Ozenne, B., Hansen, H. D., et al. (2021). A single dose of psilocybin increases synaptic density and decreases 5-HT2a receptor density in the pig brain. *Int. J. Mol. Sci.* 22 (2), 835. doi:10.3390/ijms22020835

Rodríguez Arce, J. M., and Winkelman, M. J. (2021). Psychedelics, sociality, and human evolution. *Front. Psychol.* 12, 4333. doi:10.3389/fpsyg.2021.729425

Rossi, G. N., Hallak, J. E. C., Bouso Saiz, J. C., and Dos Santos, R. G. (2022). Safety issues of psilocybin and LSD as potential rapid acting antidepressants and potential challenges. *Expert Opin. Drug Saf.* 21, 761–776. doi:10.1080/14740338.2022.2066650

Roy-O'Reilly, M., Mulavara, A., and Williams, T. (2021). A review of alterations to the brain during spaceflight and the potential relevance to crew in long-duration space exploration. *npj Microgravity* 7 (1), 5–9. doi:10.1038/s41526-021-00133-z

Ruck, C. A., Bigwood, J., Staples, D., Ott, J., and Wasson, R. G. (1979). Entheogens. *J. Psychedelic Drugs* 11 (1-2), 145–146. doi:10.1080/02791072.1979.10472098

Sagan, C. (1997). *Pale blue dot: A vision of the human future in space*. New York: Random House Digital, Inc.

Sandal, G. M., and Bye, H. H. (2015). Value diversity and crew relationships during a simulated space flight to Mars. *Acta Astronaut.* 114, 164–173. doi:10.1016/j.actaastro.2015.05.004

Sandal, G. M., van deVijver, F. J. R., and Smith, N. (2018). Psychological hibernation in Antarctica. *Front. Psychol.* 9, 2235. doi:10.3389/fpsyg.2018.02235

Schlag, A. K., Aday, J., Salam, I., Neill, J. C., and Nutt, D. J. (2022). Adverse effects of psychedelics: From anecdotes and misinformation to systematic science. *J. Psychopharmacol.* 36 (3), 258–272. doi:10.1177/02698811211069100

Schultes, R. E. (1979). Hallucinogenic plants: Their earliest botanical descriptions. *J. Psychedelic Drugs* 11, 13–24. doi:10.1080/02791072.1979.10472087

Scientific American (2021). Future space travel might require mushrooms. Available at: https://www.scientificamerican.com/article/space-travels-most-surprising-future-ingredient-mushrooms (Accessed March 1, 2022).

Seedhouse, E. (2016). *SpaceX's dragon: America's next-generation spacecraft 1-9*. New York: Springer.

Shao, L.-X., Liao, C., Gregg, I., Davoudian, P. A., Savalia, N. K., Delagarza, K., et al. (2021). Psilocybin induces rapid and persistent growth of dendritic spines in frontal cortex *in-vivo*. *Neuron* 109 (16), 2535–2544.e4. e4. doi:10.1016/j.neuron.2021.06.008

Shreiner, A. B., Kao, J. Y., and Young, V. B. (2015). The gut microbiome in health and in disease. *Curr. Opin. Gastroenterology* 1 (31), 69–75. doi:10.1097/mog.0000000000000139

Siegel, A. N., Meshkat, S., Benitah, K., Lipsitz, O., Gill, H., Lui, L. M., et al. (2021). Registered clinical studies investigating psychedelic drugs for psychiatric disorders. *J. Psychiatric Res.* 139, 71–81. doi:10.1016/j.jpsychires.2021.05.019

Smigielski, L., Kometer, M., Scheidegger, M., Krahenmann, R., Huber, T., and Vollenweider, F. X. (2019). Characterization and prediction of acute and sustained response to psychedelic psilocybin in a mindfulness group retreat. *Sci. Rep.* 9 (1), 14914. doi:10.1038/s41598-019-50612-3

Socha, D. M., Sykutera, M., Reinhard, J., and Perea, R. C. (2022). Ritual drug use during Inca human sacrifices on Ampato mountain (Peru): Results of a toxicological analysis. *J. Archaeol. Sci. Rep.* 43, 103415. doi:10.1016/j.jasrep.2022.103415

Strandwitz, P. (2018). Neurotransmitter modulation by the gut microbiota. *Brain Res.* 1693, 128–133. doi:10.1016/j.brainres.2018.03.015

Strassman, R., Wojtowicz, S., Luna, L. E., and Frecska, E. (2008). *Inner paths to outer space: Journeys to alien worlds through psychedelics and other spiritual technologies*. Rochester: Park Street Press.

Svenska, K. (2003). Neuroplasticity changes during space flight. *Adv. Space Res.* 31 (6), 1595–1604. doi:10.1016/s0273-1177(03)00011-5

Szabo, A. (2015). Psychedelics and immunomodulation: Novel approaches and therapeutic opportunities. *Front. Immunol.* 6, 358. doi:10.3389/fimmu.2015.00358

Tesei, D., Jewczynko, A., Lynch, A. M., and Urbaniak, C. (2022). Understanding the complexities and changes of the astronaut microbiome for successful long-duration space missions. *Life* 12 (4), 495. doi:10.3390/life12040495

Thomas, C. W., Blanco-Duque, C., Breant, B. J., Goodwin, G. M., Sharp, T., Bannerman, D. M., et al. (2022). Psilocin acutely alters sleep-wake architecture and cortical brain activity in laboratory mice. *Transl. Psychiatry* 12 (1), 77–13. doi:10.1038/s41398-022-01846-9

Timmermann, C., Kettner, H., Letheby, C., Roseman, L., Rosas, F. E., and Carhart-Harris, R. L. (2021). Psychedelics alter metaphysical beliefs. *Sci. Rep.* 11 (1), 22166. doi:10.1038/s41598-021-01209-2

Timmermann, C., Roseman, L., Williams, L., Erritzoe, D., Martial, C., Cassol, H., et al. (2018). DMT models the near-death experience. *Front. Psychol.* 9, 1424. doi:10.3389/fpsyg.2018.01424

Tran, Q. D., Tran, V., Toh, L. S., Williams, P. M., Tran, N. N., and Hessel, V. (2022). Space medicines for space health. *ACS Med. Chem. Lett.* 13, 1231–1247. doi:10.1021/acsmedchemlett.1c00681

Tuomisto, H. L., and Teixeira de Mattos, M. J. (2011). Environmental impacts of cultured meat production. *Environ. Sci. Technol.* 45 (4), 6117–6123. doi:10.1021/es200130u

Van Court, R. C., Wiseman, M., Meyer, K., Ballhorn, D., Amses, K., Slot, J., et al. (2022). Diversity, biology, and history of psilocybin-containing fungi: Suggestions for research and technological development. *Fungal Biol.* 126 (4), 308–319. doi:10.1016/j.funbio.2022.01.003

Van Ombergen, A., Laureys, S., Sunaert, S., Tomilovskaya, E., Parizel, P. M., and Wuyts, F. L. (2017). Spaceflight-induced neuroplasticity in humans as measured by MRI: What do we know so far. *npj Microgravity* 3 (1), 2–12. doi:10.1038/s41526-016-0010-8

Varia, J., Kamaleson, C., and Lerer, L. (2022). Biostimulation with phycocyanin-rich Spirulina extract in hydroponic vertical farming. *Sci. Hortic.* 299, 111042. doi:10.1016/j.scienta.2022.111042

Verhaar, B. J. H., Prodan, A., Nieuwdorp, M., and Muller, M. (2020). Gut microbiota in hypertension and atherosclerosis: A review. *Nutrients* 12 (10), 2982. doi:10.3390/nu12102982

Vollenweider, F. X. (2022). Brain mechanisms of hallucinogens and entactogens. *Dialogues Clin. Neurosci.* 4 (3), 265–279. doi:10.31887/dcns.2001.3.4/fxvollenweider

Whiten, A., and Erdal, D. (2012). The human socio-cognitive niche and its evolutionary origins. *Phil. Trans. R. Soc. B* 367 (1599), 2119–2129. doi:10.1098/rstb.2012.0114

Wild, C. P. (2012). The exposome: From concept to utility. *Int. J. Epidemiol.* 41 (1), 24–32. doi:10.1093/ije/dyr236

Wilson, M. (2005). *Microbial inhabitants of humans: Their ecology and role in health and disease*. Cambridge University Press.

Yaden, D. B., and Griffiths, R. R. (2020). The subjective effects of psychedelics are necessary for their enduring therapeutic effects. *ACS Pharmacol. Transl. Sci.* 4 (2), 568–572. doi:10.1021/acsptsci.0c00194

Yaden, D. B., Iwry, J., Slack, K. J., Eichstaedt, J. C., Zhao, Y., Vaillant, G. E., et al. (2016). The overview effect: Awe and self-transcendent experience in space flight. *Psychol. Conscious. Theory, Res. Pract.* 3 (1), 1–11. doi:10.1037/cns0000086

Young, L. R., and Sutton, J. P. (2021). *Handbook of bioastronautics*. Cham: Springer.

Zimmermann, C. (2012). Acceptance of dying: A discourse analysis of palliative care literature. *Soc. Sci. Med.* 75 (1), 217–224. doi:10.1016/j.socscimed.2012.02.047

Zwart, S. R., Mulavara, A. P., Williams, T. J., George, K., and Smith, S. M. (2021). The role of nutrition in space exploration: Implications for sensorimotor, cognition, behavior and the cerebral changes due to the exposure to radiation, altered gravity, and isolation/confinement hazards of spaceflight. *Neurosci. Biobehav. Rev.* 127, 307–331. doi:10.1016/j.neubiorev.2021.04.026