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Does microgravity effect on oral and maxillofacial region?

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Review Article

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Abstract

Since the beginning of the era of space travel, there have been mentions of related health effects. Various studies have described the effect of space travel and microgravity on health. Some of these studies involved short and extended follow-ups of the effect of microgravity on the head and neck of astronauts. Therefore, we aimed to analyse the oral and maxillofacial health effects associated with this sophisticated mission. It is essential to identify relevant problems and address microgravity complications. Humans have long dreamed of flying and in recent years, the dream has evolved to exploring space and creating new habitats on other planets such as Mars. This led to an increase in the need for dental treatment of the flight crew members, which led to the creation of aviation dentistry for the screening and treatment of the oral cavity of the flight crew. We are moving towards a more conservative approach than before, such as removing pulpless teeth in aircrew patients or extracting roots that had a fracture or incomplete extraction. With all the advancements in aerospace knowledge, the aviation dentistry has rarely or briefly been discussed in dental textbooks. Dentists must screen each flight crew member thoroughly and impose flight restrictions and ground them if necessary; the reasons will be discussed later within this paper. It is the duty of dentists and surgeons to notify their patients (aircrew members) about the postoperative flight consequences and restrictions.

Science background

Recently, missions planned to Mars from 2001 until now have been expected to require 18–24 months of exposure to microgravity conditions, which might have severe effects on human physiology, including that of the oral cavity. The changes were mentioned in previous studies (Ongole, 2009).

Human physiological adaptation to space is challenging in human space flight. Astronauts will encounter physiological and psychological alterations during the journey when they return to the earth. Exposure to microgravity and the space environment, even over a short or long period, affects human health (Anuradha and Grover, 2010).

These effects include neurovestibular problems, involving space motion sickness, disorientation, impaired balance, neuromuscular coordination, fluid retention, orthostatic hypotension, ventricular arrhythmias, reduced cardiac muscle mass, atrophy of muscles, sleep disorders, immune-related problems such as infection and immunodeficiency, psychological effects, temporomandibular joint dysfunction (TMD) and dysfunction of masticatory muscles associated with pain including in the oral cavity. Very few studies have been published on the effect of microgravity on the oral cavity. However, it has been reported that microgravity increases the prevalence of periodontitis, dental caries, periodontal bone loss, fracture of the jawbone, pain, dysesthesia in the teeth and oral cavity tissue, salivary duct stones and oral cancer. The aim of the study was to analyse all the literature regarding microgravity and management of complications of the head and neck among astronauts.

Hypothesis

H1: Microgravity has been shown to alter the function of the tissue and organ systems and microgravity influences the Oral and Maxillofacial region.

H2: There are management options and possible solutions for the influence of microgravity on the oral cavity, sleep and temporomandibular joint disorders.

General methodology

To identify all the records related to the effect of microgravity, we performed a systematic review of articles published in PubMed, EMBASE, Cochrane, SciELO, Google Scholar and NASA about microgravity and oral maxillofacial diseases through 2020. The following search terms were combined in the searches: oral maxillofacial OR head and neck OR oral cavity OR oropharynx AND microgravity AND astronomy AND Nasa AND Mars mission, with no limitation on the year of publication. Additional studies from the reference lists of selected articles were included by manual search. A total of 467 articles were found. EndNote software was used to remove duplicates of the same article in more than one database. Alerts according to the PRISMA guidelines were used to maintain an ongoing list of the literature and after removing duplicate records, 83 articles remained. After the full-text articles were assessed for inclusion eligibility, 47 articles were found to be published in foreign languages and 12 were editorials. Ten scientific documents directly related to microgravity and Oral and Maxillofacial Surgery were assessed. Two reviewers independently screened the titles and abstracts of the identified citations. Full texts of the citations were assessed. Data extraction from individual studies included the name, year of publication and study design.

Results

Eight studies about the missions were included. The studies mentioned and showed that dentists must screen each flight crew member thoroughly and impose flight restrictions and ground them if necessary (Moore and MacDougall, 2010). The reasons will be discussed later within this paper. The average restriction period was 24–72 h until symptoms subside, medication ceases (or at least until it can be verified that there is no diarrhoea), blood clots are stabilized, etc. It is the duty of dentists and surgeons to notify their patients (aircrew members) about the postoperative flight consequences and restrictions (Moore and MacDougall, 2010).

Microgravity and its effect on bone formation

Bone loss is considered to be one of the most serious and potentially intractable biomedical consequences of human space flight. However, microgravity-induced changes in bone are not uniform along the skeletal axis. For instance, while bone mineral density (BMD) decreases in the lower extremities, it increases in the skull. A similar pattern of region-specific changes in bone properties has been reported to occur with head-down bed rest (Bohra *et al.*, 2019; Nordin *et al.*, 1993; Vermeer, 1997; Zhang *et al.*, 1999).

Studies on the effects of spaceflight on human health are of great importance to develop effective steps to prevent bone loss and other changes induced by microgravity or the spaceflight environment. Bone loss has been mentioned for many years in the metric system, μg (1–2% a month). Increased bone loss and risk of fractures is an identified risk in the bioastronautics critical roadmap for long-term missions to the moon and mars (Bohra *et al.*, 2019; LeBlanc, 1992; Nordin *et al.*, 1993; Vermeer, 1997; Zhang *et al.*, 1999). Exposure to the μ*g* environment of space causes astronauts to lose calcium from bones. This loss occurs because the absence of Earth's gravity disrupts the process of bone maintenance in its primary function of supporting body weight. Exposure to the μ*g* environment of space causes men and women of all ages to lose up to 1% of their bone mass per month due to lack-of-use atrophy, a condition similar to osteoporosis. There are, indeed, four major bone cell types and each of them seems to be influenced by μ*g*. Bone mesenchymal stem cells (MSCs) are able to differentiate into adipocytes, osteoblasts and osteoclasts. Proliferation and differentiation are very sensitive to μ*g* due to the lack of gravity in space (Nordin *et al.*, 1993).

In space, mechanical stress is reduced, leading to a decreased rate of osteogenesis and an increased adipogenesis rate. Osteoblasts are derived from MSCs, but in μ*g* the differentiation process does not occur properly and the resulting bone loss has been attributed to osteoblasts due to their (1) reduced proliferation and activity, (2) reduced differentiation and (3) decreased response to bone-related factors in the microenvironment. Observations have also been made regarding the cytoskeleton of osteoblasts; there is growing evidence that the cytoskeleton is closely connected to nuclear morphology and that the enlarged nuclei observed in flight osteoblasts could be a result of cytoskeletal disruption (LeBlanc, 1992; Paloski *et al.*, 1993; Rai *et al.*, 2012). The osteocytes in cortical bone and periosteum degenerated after a 12.5-day flight in space on the Cosmos Biosatellite [osteocyte apoptosis has been observed after a 2-week flight, increasing the number of functionally active osteoclasts]. Apoptotic osteocytes are essential for the initiation of bone remodelling (LeBlanc, 1992; Paloski *et al.*, 1993; Buckey *et al.*, 1996; Rai *et al.*, 2012), although bone formation was shown to be reduced after 7–19 days of spaceflight; this effect may be mediated in part by the flight-induced increase in glucocorticoid secretion. In different studies, 17 days of spaceflight was associated with reduced osteoblast recruitment in specific weight-bearing rat bone, which occurred independently of endogenous glucocorticoid status (Paloski *et al.*, 1993; Baldwin *et al.*, 1996; Buckey *et al.*, 1996; White and Averner, 2001; Rai and Kaur, 2013*a*). Researchers have predicted that the decrease in blood and plasma volume and flow into the lower extremities of humans during spaceflight would result in a shift in the balance between deposition and resorption of bone such as that bone mass would be reduced (Moore and MacDougall, 2010; Rai *et al.*, 2011*b*; Rai and Kaur, 2013*b*; Goyal *et al.*, 2015; Philippou *et al.*, 2015). Mechanical stress generated by weight-bearing appears to regulate skeletal remodelling. Bassett and Becker suggested that the cell-mediated coupling of bone formation and resorption may be regulated by an electrical signal generated by bearing weight (Hudson, 1969; Hinsenkamp *et al.*, 1981; Simmons *et al.*, 1983; Rai *et al.*, 2011*b*). A cellular uncoupling due to a localized alteration in the surrounding bone appears to be a likely aetiology of site-specific osteopenia and could lead to increased serum calcium and a secondary decrease in PTH secretion and 1,25-(OH)2D production (Hudson, 1969; Hinsenkamp *et al.*, 1981; Simmons *et al.*, 1983; Colleran *et al.*, 2000; Mongini *et al.*, 2000; Korszun *et al.*, 2002; Nishikawa *et al.*, 2005; Moore and MacDougall, 2010; Rai *et al.*, 2011*a*; Rai *et al.*, 2011*b*; Rai and Kaur, 2013*b*; Ulbrich *et al.*, 2014; Goyal *et al.*, 2015; Philippou *et al.*, 2015).

Head and neck barotrauma

Based on the Boyles Law, the surrounding pressure of gas volume varies inversely at a constant temperature and the gas volume in the body's rigid cavities is associated with atmospheric pressure, in which changes in pressure may lead to several adverse effects known as barotrauma (Hodges, 1978). Barotrauma may occur during hyperbaric oxygen therapy, diving or flying; head and face barotrauma include barotitis-media, barosinusitis, barotrauma-related headache, barodontalgia and dental barotrauma. The variation in the volume of the gas inside the body's rigid cavities, which is linked with the variation in atmospheric pressure, causes several harmful effects. This variation may lead to various conditions, such as barotitis media, barosinusitis, barotrauma-related headaches, dental barotrauma and barodontalgia (Moore and MacDougall, 2010).

Head and face barotrauma include external otitic barotrauma, barotitis-media, barosinusitis, barotrauma-related headache, dental barotrauma and barodontalgia. External otitic barotrauma occurs as a result of injury to the lining of the mucosa of the external ear canal; the process of stripping the epithelial layer may be accompanied by pain (Sognnaes, 1946). The rigid cavity of the middle ear space is ventilated by the one-way fluttered auditory (eustachian) tube, which is opened by the simultaneous contraction of the tensor veli palatini and salpingopharyngeus muscles, in a positive air pressure gradient between the outer ear space and the middle ear space, as well as during swallowing or yawning. However, during rapid descent, the negative pressure developed in the middle ear is usually not resolved spontaneously. As a result, a partial vacuum is created and later vascular engorgement, as well as haemorrhage, may occur. The gradient is eventually relieved by the transudation of serum. Some symptoms of barotitis media include ear discomfort, intense pain, vertigo with nausea and tinnitus (Hodges, 1978).

During the descent from high altitudes, a partial vacuum develops, which is manifested by a retracted tympanic membrane leading to barotitis and barosinusitis (Kennebeck *et al.*, 1946). Barosinusitis is an inflammation of the paranasal air sinuses, whereas acute inflammation of the middle ear cavities and inflammation of the sinuses cause barotrauma. The vacuum created due to air pressure difference causes mucosal oedema, dizziness, headache and anoxia (Ingle and Glick, 1994). Pain and numbness can also be sequelae of the pressure exerted on branches of the fifth cranial nerve (Moore and MacDougall, 2010); the dental relevance of non-dental head and face barotraumas is as follows (Rai, 2007). Either barotitis media or barosinusitis can occur and can manifest as toothache (Garges, 1985). Several reports have shown a relationship between eustachian tube dysfunction and dental malocclusion (McDonnell *et al.*, 2001).

Masticatory muscles

Under microgravity conditions, the muscle mass decreases, which results in a small increase in muscle tonicity in difficult situations. Muscles will, in general, become feeble as they are used less often against the power of gravity (Oganov *et al.*, 1991). Therefore, muscle loading is an important factor in maintaining muscle mass; atrophy is unavoidable when the load is removed. Nevertheless, masticatory muscles do not lose mass in clinical conditions such as myopathy requiring critical care. The properties of masticatory muscles can, therefore, be harnessed to conserve mass (Alomar *et al.*, 2007). Mandible elevator muscles that act against gravitational forces, such as the masseter, temporalis and medial pterygoid, are more vulnerable than their counterparts (Smith *et al.*, 1998). Philippou and coworkers performed a 13-day clinical test on two groups of mice; one of them was onboard a space shuttle and the other stayed on Earth. The mice were maintained on a specific nutritional plan, which was mainly a solid base. In the case of the tibialis anterior in the flight group, primary indications of atrophy were detected; they exhibited decreased muscle mass, decreased phosphorylated (P)-act and increased oestrogen expression. On the other hand, a slight alteration was found in the case of the masseter and they had no significant change in mass but an increase in P-focal adhesion kinase, an increase in P-Akt and lower oestrogen production relative to limb muscles that were unaltered in microgravity (44). This proposed constant stacking of the masseter under microgravity conditions was expected to restrict disuse degeneration, as cheek muscles were continuously being used (Smith *et al.*, 1998; Alomar *et al.*, 2007).

The investigators explored the topic further, resulting in an intriguing finding. The trial was repeated once again on the same group of mice, only this time, the mice consumed a liquid diet. The masseter muscle remained healthy in the flight group unlike the tibialis anterior. Continuous loading microgravity prevents atrophy, yet masticatory muscles have a different set point that simulates disuse appendicular muscle atrophy (Alomar *et al.*, 2007). This suggests that various muscles have diverse 'set points' for adapting, so it was concluded that masticatory and cheek muscles hold up better in space than leg muscles (Smith *et al.*, 1998; Alomar *et al.*, 2007).

Temporomandibular joint

All procedures and mechanisms beginning from bone formation, new bone deposition and mineralization are reduced or stopped during weightlessness due to the reduced mechanical pressure exerted on bones and joints, which results in porous bones and eventually bone loss (Gibbons, 2003; Nagaraj *et al.*, 2018). In the context of bone loss, the mineral mass of the bone is reduced, leading to bone weakness and predisposition to fracture. In such situations, skeletal muscle support is also not needed to maintain body posture, which weakens these muscles (Nagaraj *et al.*, 2018). The temporomandibular joint (TMJ) is the most perplexing joint in the human body and enables the hinging motion of the mandible in one plane and simultaneously enables sliding movement; consequently, the TMJ is referred to as the ginglymoarthroidal joint (Rai and Kaur, 2013*b*). The TMJ comprises the temporal bone, the mandibular condyle and an articular plate and is classified as a compound joint. It is encompassed by facial musculature, tendons and ligaments, which permit its function (Whedon, 1984). The circadian rhythm of the body is affected by microgravity conditions and is associated with physiological changes; psychological stress also increases, resulting in sleep disturbances (Rambaut and Goode, 1985). This stress legitimately influences the temporomandibular construction as well as the general decrease in bone mineral mass of the complete body (Oganov *et al.*, 1991). Temporomandibular disorders (TMDs) have multifactorial aetiologies and can involve sleep disorders and stress due to microgravity. Higher levels of psychological distress among the TMJ and skeletomuscular muscle groups are prone to being influenced by psychological domains, with lower levels of TMJ pain than muscle pain. Additionally, quality of sleep and stress levels are associated with TMDs. TMDs are a common stress-related condition that are associated with dysregulation of cortisol and melatonin secretion. Increased activation of the stress hormone axis by conscious pain perception is a likely explanation, but the magnitude of the increase could indicate that pain in the facial region acts as a greater stimulus than pain elsewhere in the body. TMDs have multifactorial aetiologies with observed associations with sleep disorders and stress due to extreme conditions during simulated Mars missions (Rambaut and Goode, 1985; Oganov *et al.*, 1991). Regarding masticatory muscles, all the available literature demonstrated higher stiffness in spaceflight. Masticatory muscles, such as temporal muscles and the masseter muscles, are the two main muscles of mastication. The effect of stress directly affects the temporomandibular architecture along with the loss of mineral density of the body (Whedon, 1984; Rambaut and Goode, 1985).

The TMJ is the most complex joint and it provides a hinging movement on one plane. Anomalous facial appearance, loss of pain impression and temperature sensation and diminished tongue and mandibular movement due to microgravity conditions were demonstrated as a result of the fluid shift mechanism. In the microgravity state, along with psychological stress, sleep disturbance also increases, activating the automimic nervous system hypothalamus, which causes fibres of the muscle spindle to contract and increases muscle tonicity. In the case of microgravity, there is a reduction in muscle mass during a stressful period. For this reason, the impact on the TMJ experienced by astronauts is more mental than physiological (44). In longer span space travel, a decrease in the concentration of circling parathormone causes a reduction in vitamin D metabolism. The impact on complete body homeostasis influences disruption of TMJ action. These problems tend to increase with prolonged missions and regular travel (Smith *et al.*, 1998). Space flight-induced bone loss has resulted in health risks among astronauts in recent decades; however, the process is still unclear and it is still a topic that is not well understood. Future study is needed.

Some actions, such as exercise, adequate intake of calcium and vitamin D supplements and appropriate body hydration, are suggested to counteract the danger of metabolic loss caused by space flying (Vermeer, 1997). However, bone resorption and joint dysfunctions occurring during space travel have been revealed as critical health dangers for astronauts in recent decades and these factors have oral and maxillofacial effects; microgravity is also a subject that is not well understood and requires further investigation. Overcoming these issues will empower human investigation missions and enhance crew security (Zhang *et al.*, 1999).

Barodontalgia

Barodontalgia is a kind of oral pain caused by a change in barometric pressure in an otherwise asymptomatic organ. The occurrence of pain as a result of changing pressure depends on the related pathology (Philippou *et al.*, 2015). Barodontalgia is a symptom and not a pathologic condition itself. Normally, barodontalgia is an exacerbation of preexisting subclinical oral disease (Lakshmi, 2014). It occurs due to the entrapment of gases in the closed chamber because it is unable to adjust to the internal pressure (Sognnaes, 1946). Pain occurring on descent is related to facial barotrauma or pulp necrosis and pain occurring on the ascent is related to the vital pulp tissue. Pain occurring on both ascent and descent are related to periapical disease (Lakshmi, 2014). Reduction in atmospheric pressure, in the context of direct barodontalgia, causes an effect on the affected tooth and, in the context of indirect barodontalgia, stimulation of the superior alveolar nerves at the time of maxillary barosinusitis can cause pain. Pain in teeth can occur due to the stimulation of nociceptors in the maxillary sinus (Lakshmi, 2014).

Barodontalgia can occur as a result of defective tooth restorations, pulp necrosis, dental caries, periodontal pockets, mucous-retention cysts, impacted cysts and dental caries (Ongole, 2009). Pulp/periapical conditions and symptoms can classify barodontalgia into 2 types: pulp/periapical-related direct barodontalgia and barotitis/barosinusitis-induced ‘indirect’ barodontalgia (Anuradha and Grover, 2010).

Dental barotrauma; in-flight dental fracture

Several reports, mostly from the WWII period, have addressed restoration fractures during high-altitude flying (Kennebeck *et al.*, 1946; Lakshmi, 2014). The United States Air Force (USAF) symposium, held in 1946, confirmed that the in-flight loss of restorations occurred during the high-altitude flight (Kennebeck *et al.*, 1946). The predisposing factors for in-flight dental fracture, reported in several case reports (Hodges, 1978; Lakshmi, 2014) as well as in an in vitro model (Calder and Ramsey, 1983), are the presence of preexisting leaked restorations and latent secondary caries underneath the restoration in the affected tooth before exposure to the barometric changes.

Odontocrexis

This condition is also known as a barometric tooth explosion. Preexisting leaked restorations or recurrent caries underneath restorations can cause tooth explosion in a high-altitude environment. A common cause of damage is the expansion of gas trapped beneath restorations (Armstrong and Huber, 1937). Calder and Ramsey reported that poor-quality restorations and unrestored teeth result in tooth damage (Calder and Ramsey, 1983). The crowns were poorly positioned because of fractures of PFM restorations and changing pressure in the microtubules of dental cement (Patel and Burke, 1995).

The complications of the oral cavity can be divided into the following categories:

Periodontal Health

Rai *et al.*, tested periodontal criteria such as probing depth, bleeding on probing and attachment loss in some healthy individuals on a Mars mission (Vermeer, 1997). The measure of all the criteria was fundamentally superior at the end of the mission than at the beginning. During microgravity studies, elevated bone resorption by osteoclasts was observed (Zhang *et al.*, 1999). Mainly, levels of macrophage inflammatory proteins, as a potential indicator of bone loss, were found to be inversely associated with other patterns towards the end of the analysis. On the other hand, in space travel, the reduced oxygen can harm teeth, restorations and gums. Due to a decrease in oxygen level, a common complaint is xerostomia and due to a decrease in saliva content, there is an increase in the risk of periodontal disease (Ongole, 2009). Another reason can be the breathing of dry compressed gases in the aircraft (Fontana and Zero, 2006). Other factors influencing crew member periodontal health include poor oral health, anxiety and flying exhaustion (Nordin *et al.*, 1993). In addition to other variables, stress has been considered a significant determinant of periodontal wellbeing. The periodontal status of individuals on prolonged space missions remains unknown (Smith *et al.*, 1998). Based on research findings, mandibular teeth generally benefit more from saliva, as saliva appears to bathe the mandibular teeth under the influence of gravity. However, research has shown a reversed relation under microgravity conditions. Therefore, caries susceptibility is either the same or slightly greater in mandibular teeth (Smith *et al.*, 1998).

Oral surgery

The main focus of oral surgery in the context of aviation dentistry is the extraction of posterior maxillary teeth, which can lead to oroantral communication and later lead to sinusitis, as flight crews experience a pressure-changing environment; therefore, the dentist must screen for the presence of oroantral communication and when he or she finds it, the patient must be referred to an oral surgeon for the closure of oroantral communication (Susarla *et al.*, 2003; Zadik, 2009; Mandke and Garg, 2015).

Endodontics

From 1940 to now, the chief reason for barodontalgia has been pulpitis. Proper diagnosis of pain should be made to treat barodontalgia at an earlier stage. Barodontalgia often goes unnoticed due to negligence (Anuradha and Grover, 2010). Rossi recommended endodontic treatment in cases of deep dental carries and suspicion of invasion of bacteria into the pulp chamber instead of direct pulp capping (Rossi, 1995). Open, unfilled root canals can cause leakage of the intracanal infected content into the periradicular tissues as well as facial subcutaneous emphysema (Halm and Saghy, 1963; Verunac, 1973; Heymann *et al.*, 2013).

Restorative dentistry

Arrested lesions are associated with minimal risk in our daily life since they are not active, but Sognnaes suggested that such lesions may become active in a pressure-changing environment and should be removed to prevent any problems during the flight (Lakshmi, 2014). We must be careful with amalgam restorations since there is a higher chance of corrosion due to increased exposure to oxygen from pure oxygen inhalation (Heymann *et al.*, 2013).

Hawkey reported that cold temperature is unlikely to be the dominant mechanism underlying dental fracture. This is because of differential thermal contraction of amalgam materials compared with tooth hard tissue in cases of the low temperature in a high-altitude environment (Hawkey, 2005). Additionally, excessive occlusal forces were a factor in dental restoration dislodgement, as seen in aircrew members; Sognnaes suggested that clenching or grinding of teeth was a causative factor for restorative failure (Lakshmi, 2014).

Prosthodontics

Retentions of dentures are based on atmospheric pressure, adhesion and gravity. Reduced barometric pressure can impair the retention of complete dentures, which indicates that implant-supported prostheses favour prosthesis removal.

Lyons stated that the type of cementation is importan, and he says that crowns cemented with resin cement did not have reduced retention, whereas those cemented with glass–ionomer cement or zinc phosphate cement had reduced retention under environmental pressure changes (Lyons *et al.*, 1997). This result is mostly due to micro porosities expanding and contracting upon the pressure changes leading to weakened cement (Jagger *et al.*, 1997) and microleakage may also be one of the factors related to low strength detected in zinc phosphate and glass–ionomer cement (Lyons *et al.*, 1999).

Microgravity effects on cervical and vertebral bone

Since space studies are limited, knowledge of the effects of long-duration space flight and microgravity is limited. Lower extremity skeletal muscle atrophy has been mentioned in the context of long-term spaceflight and gravity-induced muscle degradation; one of the most common spinal injuries is a herniated nucleus pulpous disc. Herniation is 4.3-times more likely in space flight conditions than in normal conditions. The combination of spaceflight-induced loss of muscle strength and sensorimotor impairment reduce postural stability. Bone loss results in a higher likelihood of injury during the dynamic loading encountered in spacecraft landings (Ulbrich *et al.*, 2014).

Astronauts are prone to sarcopenia, increased fatigue levels and decreased muscle strength. Research has shown that microgravity results in a decrease in type I and II myofibres. Further studies should include assessments of changes in vertebral disc height, cervical curvature, vertebral bone density and cortical thickness (Oberholzer *et al.*, 2019).

Exercise plays a key role in maintaining astronaut health and fitness while in space. Protein and its components (amino acids) are essential for all body chemical reactions, structure and muscles. In spaceflight, total body protein turnover increases, as measured by the loss of the orally ingested stable isotope. Glycine is an amino acid that is found abundantly in proteins, so changes in blood levels indicate the amount of glycine moved to the tissues for protein synthesis. Some of the changes may be due to the catabolic state of weight loss found in many astronauts due to lower-than-needed energy intakes. The stress of spaceflight found in astronauts may increase protein breakdown. Increased stress was reflected by increased levels of blood and urinary cortisol. Dietary protein levels are already high during spaceflight. Protein recommendations are the same as those of ground-based dietary recommendations (Oberholzer *et al.*, 2019).

Sleep disorders

It has been reported that a heavy workload, international environs (different traditions, languages and habits), restricted internet access, poor diet and insufficient supplies result in stress in the simulated Mars mission (Nordin *et al.*, 1993). The human physiological status will change in response to microgravity and certain parameters, as mentioned earlier, result in extreme conditions (Vermeer, 1997; Zhang *et al.*, 1999; Alomar *et al.*, 2007). The evaluation of crew members in simulated Mars missions shows that quality of sleep and level of stress induced by extreme conditions may be related to TMD (Bohra *et al.*, 2019). TMD is a stress-related state related to the deregulation of cortical and melatonin discharge. Simple muscle pain (SM) and TMD were reported in the test groups. A nonsignificant difference was recorded among the TMD and control groups in regard to psychological indications, including depression, obsessive-compulsive disorder, anxiety and somatization. Additionally, daytime dysfunction has been reported to be significantly more common in the TMD and SM groups than in the control group. Considerably lower sleep durations were also observed in the SM group than in the TMD group (Bohra *et al.*, 2019). In the examination, more significant levels of psychological suffering in most psychological domains were found in people with temporomandibular joint pain. The findings of the studies have shown various degrees of psychological suffering in individuals with TMJ pain compared with the effects of muscle pain in crew members (LeBlanc, 1992). The modality of sleep and feelings of anxiety have been related to TMD in investigations and a relationship was found between the pressure scores, salivary cortisol and melatonin levels and the existence or nonexistence of sleep disorders (Bohra *et al.*, 2019). Enhanced stimulation of the stress hormone axis by cognizant agony discernment is a possible clarification. In any case, the extent of the enhancement could demonstrate that pain in the facial area is a more significant stimulus than pain elsewhere in the body (LeBlanc, 1992). TMDs comprise multifactorial aetiologies with a pragmatic relationship with sleep disorders and anxiety because of extraordinary situations within the simulated Mars mission (Rai *et al.*, 2012; Rai and Kaur, 2013*a*). Investigations have revealed a relationship between sleep disorders and specific types of stress (LeBlanc, 1992; Rai *et al.*, 2012). Sleep disorders enhance the measure of common indicators of stress and other factors, including salivary cortisol, melatonin and heart rate, which aggravate the impacts of stress (LeBlanc, 1992; Paloski *et al.*, 1993; Rai *et al.*, 2012). It has been reported that an increased cortisol awakening reaction is related to an enhanced degree of stress (LeBlanc, 1992; Rai *et al.*, 2012).

This information increases the probability that objective factors thought to drive primary sleep disorders, such as psychophysiological stimulation, as well as improvement in sleep duration and melatonin regulation, may improve the medications for TMD and other idiopathic pain issues, conceivably resulting in prophylactic advantages. Melatonin treatment may help in easing sleep, stress and TMD issues on earth, in space and in extreme situations. However, the existence or nonexistence and level of TMD have not yet been confirmed and the kind of TMD has not been identified in investigations (Bohra *et al.*, 2019).

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