Space Motion Sickness

A Common Neurovestibular Dysfunction in Microgravity

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Abstract: This article presents a review of current findings related to neurovestibular physiology, aetiology, and proposed theories on space motion sickness (SMS) during acute and sustained exposure to microgravity. The review discusses available treatment including medication and non-pharmacological countermeasure methods that help prevent the development of SMS in weightlessness. Ground-based simulations using virtual reality, flight simulations and Barany's chairs can be applied to study SMS and demonstrate its signs and symptoms to space crew members. Space motion sickness has been observed in approximately 70% of astronauts within the first 72h in microgravity, having in general an instantaneous onset of signs and symptoms. Stomach discomfort, nausea, vomiting, pallor, cold sweating, salivation, tachypnoea, belching, fatigue, drowsiness and stress hormone release have been documented. This can have detrimental effects on the well-being of astronauts in the initial phase of a space mission. Mental and physical performance may be affected, jeopardizing operational procedures and mission safety.

Keywords: Space neurovestibular physiology, space motion sickness, neurology and microgravity.

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Introduction

Motion sickness is defined as the combination of signs and symptoms, including nausea, vomiting, sweating, lack of well-being, decreased mental and physical performance, disorientation and drowsiness. These symptoms can occur with the introduction of a new type of real or virtual motion environment, as experienced when travelling in a car or on a boat, or when having a ride on an accelerative device, such as found in an entertainment park. When a space traveller exposed to weightlessness during a mission in Earth's orbit experiences this constellation of symptoms, it is referred to as Space Motion Sickness or SMS. The susceptibility of individuals to experiencing motion sickness or SMS depends on several factors. These include initial sensitivity to motion, rate of natural adaptation, and the ability to retain protective adaptation in the longer term[1].

Historically, SMS was first reported as an operational issue in 1962 on board the spacecraft Vostok II, the second manned Soviet mission[2]. After reaching Earth's orbit, Cosmonaut Titov experienced a period in which he felt as if he were flying upside-down,

followed soon after by a period of dizziness associated with movement of his head. Approximately 6h into the spaceflight, he exhibited the signs and symptoms of SMS[3]. Titov's mission lasted only one day, but as flight durations increased with subsequent missions it soon became more apparent that SMS posed a more prominent problem. No incidences of SMS were reported by astronauts in the pioneering NASA Mercury and Gemini manned spaceflight programs, with the first occurrences being described during the subsequent Apollo and Skylab missions[4]. This may be explained by the fact that the spacecraft first used were very small, limiting the movement of astronauts within the cabin and, therefore, decreasing the chances of experiencing SMS, as it would seem to present a close association between rapid head and body movements during microgravity exposure[5].

SMS itself is described as the anomalous perceptual, sensory, sensorimotor, and autonomic reactions that, in general, develop during the very first phase of microgravity exposure[6]. Undoubtedly, there is similarity with the clinical presentation of terrestrial motion sickness, especially with regards to symptoms and time course of clinical development of this neurovestibular condition, in response to an environmental stimulus.

Common symptoms are malaise, anorexia or loss of appetite, reduced initiative, and irritability, stomach awareness, nausea, vomiting, headache, impaired concentration, lack of motivation, cold sweating, fatigue, increased respiratory rate, impaired mental and physical performance, disorientation, drowsiness and lethargy[4;5;7;8;9]. Gastrointestinal symptoms in SMS appear minutes to hours after orbital insertion or in the first set of parabolas of a parabolic flight. The most common symptoms are usually nausea and vomiting, with the onset of vomiting sometimes occurring suddenly and without prodromal nausea. Belching, salivation and flatulence can also accompany, while auscultation of the abdomen during SMS shows that bowel sounds and movement are either decreased or absent[9].

In general, symptoms related to SMS (50% of cases being considered moderate to severe) during a space mission resolve after 3 days in microgravity, and post-flight recovery from this neurovestibular condition appears to occur quickly[9]. SMS is the most common clinical condition experienced by astronauts during the first three days of a spaceflight and can impact significantly on performance, affecting approximately 70% of the men and women who have flown in spacecraft or during the microgravity exposure provided by parabolic flights[10;11;12] .

The detrimental effect of this condition on astronaut functioning, behaviour, well-being and mood can pose additional concerns in relation to astronaut safety, especially if an extra-vehicular activity (EVA) were to be scheduled at the beginning of a space mission. For this reason, unless due to a specific emergency situation, EVAs are not programmed to take place during the first few days of spaceflight, aimed at avoiding the potential negative effects of SMS, with the accompanying reduction in physical and mental performance. Nausea and vomiting in particular could lead to a life-threatening situation should an astronaut vomit whilst wearing an EVA suit[13].Although it is recognised as the one of most frequent neurovestibular disturbances experienced during a spaceflight, the

cause of space motion sickness is an important topic of discussion and is still not fully understood by the space medical and scientific communities[12].

Physiological mechanisms associated with space motion sickness

Two major mechanisms have been proposed to explain SMS: the fluid shift and sensory conflict theories. The microgravity of space appears to affect every single organ and body system of astronauts, in different intensities and manner, both during short- and long-term missions. The fluid shift theory suggests there is a progressive displacement of fluid and blood from the lower to upper part of the body that starts with the exposure of an astronaut to microgravity. This process is completed within 7 to 10 days[9;14;15]. Initially, this headward shift increases the central fluid volume, cardiac size (around 20%) and cardiac output. It then leads to a negative fluid balance and reduction of 12-20% in the circulating blood volume[14], which causes a decreased resting stroke volume of 10-20% and a reduced cardiac output, with an average reduction of 1.5L.min^{-1} over pre-flight values[16;17]. These changes are secondary to the reduction in circulating blood volume[18].

This headward fluid shift is also associated with changes in the fluid of the vestibular system, subsequently altering receptor responses in the inner ear. Engorgement of the blood vessels surrounding the endolymphatic duct may restrict the flow of the endolymph sac, resulting in hydrops, or the pressure may act directly on the 8th nerve at the internal auditory meatus. This could then alter the responses of vestibular receptors, inducing the establishment of SMS. Several mechanisms have been proposed to explain how the headward fluid shift associated with microgravity may produce SMS. The headward fluid shift may change angiotensin activity and produce SMS by altering hormonal or neurotransmitter balance in the chemoreceptor trigger zone, or it may alter the biomechanical properties of the vestibular system[6;19].

Sensory conflict theory

The sensory conflict theory has been widely accepted as the primary cause of SMS during two crucial phases of a space mission – at the beginning and the end of an orbital flight. Three-dimensional human spatial orientation under Earth's gravitational conditions is mainly based on sensory inputs that are sent to the central nervous system for interpretation. Therefore, the sensory-conflict theory advocates that space motion sickness must be a consequence of the rearrangement of the terrestrial gravity-related relationship between different inputs that are provided by the eyes, skin, joints, muscles, and especially vestibular receptors in the inner ear, when one is exposed to the microgravity environment of space. The interaction of all body systems, commonly used to orient ourselves in relation to the surrounding environment, become disrupted or compromised to some degree. This causes a sensory-motor disturbance that can lead to sensory conflict, which appears to constitute the basic mechanism underlying SMS, an illusion of self-motion associated with spatial disorientation[10] .

Head movements, however, especially in the pitch and roll planes, could be seen as the dominant provocative stimuli for the occurrence of SMS [20], as they result in discordant cues being transmitted to the central nervous system regions responsible for central

integration of the semi-circular canal (angular acceleration) and otolith (linear acceleration), which are relevant physiological information needed to maintain spatial orientation and promote the stabilisation of eye and body movements[12].

Further possible explanations that suggest some form of anatomical and physiological changes of the vestibular system cause SMS are the otolith asymmetry and the otolith tilt-translation reinterpretation (OTTR) hypotheses. In the first, there is a minor asymmetry between the otolith system on either side of the head, which the brain adapts and compensates to from birth on Earth. However, this asymmetry can be exacerbated when an astronaut experiences the microgravity of space; the central nervous system becomes unable to properly interpret the signals sent by the otolith system and, therefore, the compensatory effect is lost. The latter theory suggests that vestibular signals indicating tilt become unnecessary when in microgravity. This leads to a reinterpretation of these inputs by the brain to indicate translation[19;21].

Fluid shift and sensory conflict, therefore, are the two major theories that attempt to explain why SMS is so prevalent during the first days of a spaceflight. However, many questions remain without answers, including their lack of predictive power, inability to explain those situations in which sensory conflict exists without sickness, or the mechanisms behind the high prevalence of some symptoms of SMS, such as vomiting. Although the fluid-shift theory could be associated with sensory conflict, mechanisms exist whereby the cephalad fluid shift accompanying microgravity could bypass the classic vestibular inputs to induce vomiting[11]. Susceptibility to provocative motion stimulation was not increased during head-down tilt[22].

Managing space motion sickness

Space motion sickness is usually treated using pharmaceuticals, and although the drugs have undesirable side effects, they seem to totally or partially counteract SMS signs and symptoms in parabolic flights or during space missions, especially if the medication is given with other preventive methods. The use of different drugs in isolation or combination has been widely tested, but an ideal treatment for SMS has yet to be found. However, the high prevalence of SMS and the possibility of symptoms interfering with the operational activities required during space missions, has resulted in a general consensus that further research on the development of proper medical treatment and the use of countermeasures are mandatory[23;24] .

Training devices and methods can be applied to familiarize astronauts and future space tourists with spatial disorientation and SMS. This equipment is also widely used for ground-based SMS studies with three main objectives – to have a better understanding of the underlying mechanisms involved, to test medications that can decrease or abolish symptoms, and to develop countermeasures to prevent the establishment of SMS during acute and chronic microgravity exposure[25] . Virtual reality, flight simulators and rotatory chairs (Barany's chair) have been widely used, either in isolation or in combination, to create a real or virtual motion environment capable of triggering the symptoms of SMS.

Figure 1. Volunteer in a *Barany's Chair at the Microgravity Centre, PUCRS, Brazil*. Note that the volunteer is blindfolded to avoid visual inputs during neurovestibular angular acceleration (Source: authors).

Histamine, acetylcholine and noradrenaline are neurotransmitters that seem to be involved in neural processes of motion sickness, which helps with the selection of possible medication, in isolation or in combination, that can be administered to either prevent or treat SMS, by abolishing or decreasing its symptoms. Pharmacological countermeasures have been well studied and many medications have been considered for preventing the occurrence of SMS during space missions or parabolic flights. Although, several drugs have been tested in-flight or during ground-based studies, few have been found to be effective and none can completely prevent the occurrence of signs and symptoms of motion sickness[8]. Two of the many medications evaluated that demonstrate more promise as a prophylactic treatment are Scopolamine and Prometazine[26].

Scopolamine, also known as either hyoscine or 6-p-hydroxy-hyoscyamine, is a tropane alkaloid found in various solanaceous plants, especially in species of *Datura*, *Scopolia*, and *Duboisia*. Scopolamine presents a variety of biological activities and therefore has been used to treat seizures, vomiting and motion sickness. It also has undesirable effects, like drowsiness and performance decrement, particularly in tasks requiring continuous attention and memory storage of new information. This might affect the safety of astronauts during a space mission[24;27].

Oral L-scopolamine hydrobromide (ranging from 0.3mg to 0.6mg) is a drug commonly used to provide short-term protection against SMS, as it begins to act within 30min to 1 hour and provides protection for around 4 hours[28]. The use of a transdermal therapeutic scopolamine patch behind the ear 12 to 16 hours prior to requirement and delivering scopolamine into the blood for 72 hours has been proposed[23;27]. Nonetheless, the transdermal method of delivering scopolamine is inappropriate for use during spaceflight,

as immediate relief of SMS symptoms is required [27, 29]. To counteract known side effects of scopolamine, such as drowsiness, an amphetamine (5mg to 10mg orally) can de added, a combination commonly used pre-flight during the parabolic flight campaigns of the European Space Agency (ESA)[7]. Oral medication often interacts with food, different types of diets or fasting. Scopolamine associated with controlled diet has been shown to ameliorate the intensity and/or number of symptoms experienced by volunteers during a ground-based study, in which rotation of a Barany's chair was used to induce SMS[30]. Although the scopolamine/amphetamine combination protocol has been used by ESA, oral administration of scopolamine is known to have variable absorption rates and low oral bioavailability. These characteristics can become worse in the microgravity environment of space, which can cause alterations in the gastrointestinal system[29]. Considerable numbers of studies have recently been performed to find a solution for overcoming these problems, through the development of a new form of scopolamine dosage[27;29]. Researchers have identified that intranasal scopolamine can provide an improved method of administration, as it is a quick-acting (15min), non-invasive route of delivery. First-passage metabolism is avoided, signifying the potential for enhanced efficacy at a lower dose, thus minimizing side-effects[27;29;31]. Nowadays, an aqueous intranasal scopolamine spray (INSCOP) is available and is likely to be used by astronauts to prevent SMS[31].

In 2007, NASA advocated the use of 25 or 50mg of intramuscular promethazine to prevent or decrease symptoms of SMS. The pharmacodynamics of both medications have shown that scopolamine is a selective vestibular suppressor while promethazine is a global vestibular suppressor, resulting in a greater number of promethazine mediated-secondary effects, which can cause more pronounced sedation and orthostatic hypotension[9;10;29;32,33].

Conclusion

The main functions of the neurovestibular system are spatial orientation, maintenance of balance, and stabilising of vision through vestibular–ocular reflexes. Motion sickness is a syndrome that occurs when an individual is placed in a real or virtual moving environment, being called space motion sickness when it occurs during microgravity exposure. It is an extremely prevalent clinical condition seen during parabolic flights or space missions and can cause important detrimental effects on the well-being and performance of individuals, and, therefore, it is essential that the underlying neurovestibular mechanisms are better studied and understood on the ground and in space. There remains the need to further prevent or reduce the symptoms of SMS. Further research should aim to develop better non-pharmacological and pharmacological treatments.

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