Space Motion Sickness - An Overview

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Introduction

Space motion sickness (SMS) is experienced by 60% to 80% of space travellers during their first 2 to 3 days in microgravity and by a similar proportion during their first few days after return to Earth. SMS symptoms are similar to those in other forms of motion sickness; they include: pallor, increased body warmth, cold sweating, and malaise, loss of appetite, nausea, fatigue, vomiting, and anorexia. Unlike motion sickness on Earth, SMS is characterized by a feeling of fullness of the head, a hot face and reduced sweating. In SMS vomiting is episodic, sudden, and brief. Nausea may be present but is more often absent. Because of the high incidence, severity, and duration of SMS, some early flight day activities are limited, and critical tasks such as extravehicular activity (EVA) are delayed and these affect the operational performance of astronauts. Onset ranges from minutes to hours, plateaus, and rapidly resolves in 8-72hrs with 36hrs as an average [1]. The provocative factors include movement of the head in the pitch and roll directions and the unusual visual field. This paper reviews the research that has been carried out to date on space motion sickness, and its counter measures comprehensively.

Mechanism of SMS

Two hypotheses have been proposed to explain space motion sickness: the fluid shift hypothesis and the sensory conflict hypothesis [2]. The fluid shift hypothesis suggests that space motion sickness results from the cranial shifting of body fluids resulting from the loss of hydrostatic pressure gradients in the lower body when entering microgravity. The cranial fluid shifts lead to visible puffiness in the face, and are thought to increase the intracranial pressure, the cerebrospinal-fluid pressure or the inner ear fluid pressures, altering the response properties of the vestibular receptors and inducing space motion sickness.

The sensory conflict hypothesis suggests that loss of tilt-related otolith signals upon entry into microgravity causes a conflict between actual and anticipated signals from sense organs subserving spatial orientation [3]. At 1G, all of the orientation and motion cues, such as vision, proprioceptions, and vestibular inputs, are in agreement, whereas in microgravity these inputs conflict with each other. This lack of agreement between the different sensory inputs leads to a state termed as "sensory-conflict," which is proposed to be the root cause of SMS, vection, and spatial disorientation. Underlying mechanisms have been proposed that further support the sensory-conflict theory, such as otolith-assymetry [4], sensory-compensation [5] and otolith tilt-translation reinterpretation [6]. Such sensory conflicts are thought to induce motion sickness in other environments also.

Spatial disorientation (SD) can be provocative for SMS and may become a dangerous problem in itself if it occurs during an emergency in which it is critical for an astronaut to move through the vehicle quickly. A spatial orientation perceptual-motor system that is inappropriately adapted to the inertial

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environment of microgravity can also result in errors during on-orbit activities, such as switch throws, object location and manipulation tasks.

Management of SMS

The ability to develop techniques to prevent or reduce the occurrence of SMS is important for increasing crew safety and comfort, mission success, and optimizing time and cost factors.

In the Russian space program, countermeasures used in flight have included an antihistaminic drug, pneumatic cuffs applied to the thigh region, application of lower body negative pressure, a head cap that restricted head movement while simultaneously providing force stimulus to the cervical antigravity muscles, and the use of an insole counterpressure device that added pressure to the sole of the foot. Each appeared to have had some limited success in reducing SMS symptoms and disorientation [7]. Other Russian studies have also reported some success in reducing SMS symptoms with preflight stimulation of the vestibular system, primarily involving different types of cross-coupled angular acceleration, and controlled movement strategies in flight [8]. With the of a combination of preflight training and in-flight behavior modification techniques SMS incidence was reduced from ~70% early in the program (without intervention) to ~30% currently.

In the U.S. space program, pre-flight training and medication are currently used both for prevention and treatment of SMS. Besides somewhat limited success, the main drawbacks of using medications are their side effects, such as drowsiness and lack of concentration, which can be more dangerous than the sickness they are employed to remedy. More reliable methods for preventing or minimizing SMS are necessary to ensure the safety and productivity of spaceflight crews. One method that may prove useful in preventing or minimizing SMS is the use of 'Preflight Adaptation Training Techniques'. Related research suggests that training devices, such as those using virtual reality, can partially simulate the sensory rearrangements present in microgravity that lead to SMS and SD [8]. Other investigators are testing different spatial orientation training techniques using virtual environment systems that may also prove useful. The plasticity of the human central nervous system makes it likely that subjects will eventually adapt to the unique sensory conditions present in novel environments and orientations, whether under simulated or actual weightless conditions, and this adaptation can likely be generalized to different situations.

Probably it is possible for astronauts to encode and learn their visual environment from multiple points of view independent of a "normal upright" (1 g) orientation. Also they develop an increased ability to identify visual forms independent of their retinal orientation when those forms are seen daily in a "visually poor" space cabin environment. Experimental data support the assumption that, with novel stimuli, recognition is mediated by a normalization process and, with repeated exposures to the same visual stimulus, recognition is derived from an orientation-free mental representation [9]. These findings suggest that it is possible to train preflight and to adapt some individuals to the stimulus rearrangement produced by microgravity. There are some training methods for supporting skill acquisition, retention and transfer of training, which are discussed below:-

Part-task preflight adaptation trainers (PATs)

Two PATs are being used at the NASA Johnson Space Centre to pre-adapt astronauts to novel sensory stimulus conditions similar to those present in microgravity to facilitate adaptation to microgravity and re-adaptation to Earth [10]. This activity is a major component of a general effort to develop countermeasures aimed at minimizing sensory and sensorimotor disturbances and SMS associated with adaptation to microgravity and re-adaptation to Earth.

Preflight Virtual Reality Training

It is hypothesized that exposing subjects preflight to variable virtual orientations, similar to those encountered during spaceflight, would reduce the incidence and/or severity of SMS and SD. So, cosmonauts trained to perform a simple task in multiple orientations in a virtual environment during one session to see its influence on the subjects' ability to perform the task in a novel orientation at a later time. It was expected that subjects would retain the skills acquired in the initial session for use in a future session, i.e., skills acquired in variable orientation training would transfer to a new orientation. Subjects were assigned to either a variable training (VT) or non-variable training (NVT) condition to perform a simple navigation and switch activation task in a virtual space station. VT subjects performed the task starting in several different orientations, whereas NVT subjects always performed the task starting in the same orientation. On a separate day, all subjects then performed the same task in a transfer of training session starting from a novel orientation. It was found that when exposed to the novel test orientation, VT subjects performed the tasks more quickly (12%) and with fewer nausea symptoms (53%) than during the training session, compared with NVT subjects who performed more slowly (6%) and with more nausea symptoms (28%). These results demonstrated the effectiveness of using variable training in a virtual environment for reducing nausea and improving task performance in potentially disorienting surroundings, and suggested that such training may be developed into an effective countermeasure for SMS, SD, and associated performance decrements that occur in spaceflight [11].

Autogenic-Feedback Training Exercises (AFTE)

These are psycho physiological countermeasures, which use cognitive images to produce certain effects in autonomic activity while the subject receives immediate sensory feedback with instrumentation. It involves training subjects to voluntarily control several of their own physiological responses [12]. AFTE is a self-regulatory technique that has been shown to have wide effects on autonomic reactivity by the use of self-suggestion exercises designed to induce bodily sensations (e.g warmth in the hands) that are highly correlated with specific physiological responses such as peripheral vasodilatation. When these exercises are practiced in series, the result is a relaxed (i.e parasympathetic like) physiological profile within the subject that prevents the emergence of behavioral and physiological reactions to stress. Biofeedback consists of providing the subject with augmented sensory information about ongoing activity levels of some physiological responses (e.g heart rate on digital panel meter) and rewarding him whenever such levels fluctuate in a direction selected by the trainer (i.e heart rate fluctuates above baseline). The result is an enhanced ability by the subject to maintain the changed level for increasing periods of time. Only repetition and practice are required before physiological control is achieved. Because AFTE involves training subjects to voluntarily control both increase and decrease of specific physiological response levels, it constitutes a learned skill, which can be quantified over time. Unlike relaxation training, subjects learn to recognize physiological changes associated with motion stimulation (i.e rotating chair tests) and to voluntarily "mimic" their own resting level. The training program requires a baseline exposure in a rotating chair and three subsequent exposures after 2, 4 and 6 hours of training.

Pharmacotherapy

Various drugs and drug combinations are used for management of SMS [13]. These are -

(a) Antihistaminic agents - Meclizine 50mg / Cyclizine 50 mg

(b) Anticholinergic agents - Scopolamine

(c) Antihistaminic with additional anticholinergic effect agents - Promethazine, Diphenhydramine, Dimenhydrinate

Besides somewhat limited success, the main drawbacks of using these medications was their side effects, such as drowsiness, lack of concentration, and effect on cognitive performance, which can be more dangerous than the sickness they are employed to remedy. This creates a dilemma for astronauts because cognitive skills are particularly important during gravity transitions (e.g., take-off and landing).

To counter this potentially dangerous side effect, drug combinations are used. Various drug combinations currently used are-

(a) Promethazine 25 mg + Dexamphetamine 10 mg

(b) Promethazine 25 mg + Caffeine 200 mg

(c) Scopolamine 0.8 mg + Dexamphetamine 5 mg

(d) Chlorpheniramine 12 mg + Ephedrine 50 mg (Chlorphedra)

With the use of drug combinations, no decrements in any objective performance task are seen. The drugs did not affect performance on addition or memory tests. Most of the drugs used have an optimal effect 2 hours after ingestion and lasting 8-12 hours with the exception of scopolamine (optimal effect about 30-60 min after ingestion, lasting for 4 hours) and chlorpheniramine (optimal effect about 3 hours after ingestion, lasting for about 5 hours). Some Subjects did report mild side effects, such as feeling jittery or that their heart rate was fast, after taking medications.

Newer Modalities

Intranasal mode of drug administration is being developed, as it has various advantages enumerated below:-

(a) Rapid onset of action

(b) Highly vascular nasal mucosa provides a more direct pathway to the central nervous system

(c) Eliminates gut wall metabolism and hepatic first pass effect

(d) Enhanced absorption, efficacy, and bioavailability

(e) Fewer negative systemic side effects

(f) Well tolerated

(g) Absence of cognitive decrement or increasing symptomatology.

Various intranasal formulations are:-

<u>Intranasal Chlorphedra (chlorpheniramine 12 mg + ephedrine 50 mg)</u>- Intranasal combination of chlorphedra used against motion sickness in the form of an aerosol spray has a rapid onset ofaction and is without negative effects on cognitive performance [14].

<u>Intranasal encapsulated microcapsule Promethazine Hydrochloride (PMZ HCl)</u> **-** After oral administration, the bioavailability of Promethazine is very variable and intravenous administration is both inconvenient in the operational environment and involves risks. Also the injection site can become irritated. Nasal delivery provides benefits including convenience, rapid onset of action, and good bioavailability. However, intranasal PMZ HCl

caused severe nasal irritation. This nasal irritation could be eliminated (only) by encapsulating PMZ HCl to provide controlled release which helps in maintaining the PMZ HCl concentration below the cytotoxic limit. Also this provided controlled release of PMZ HCl over a 6-h period. Furthermore, the microcapsules did not deteriorate after being stored for 1 yr at 37°C or after exposure to 9.18 kGy gamma radiation. This medication could be valuable for spaceflight crewmembers and for individuals on Earth [15].

<u>Intranasal scopolamine</u> **-** Majority of studies conclude that scopolamine, an anticholinergic, is the most effective single medication for preventing SMS, however, successful treatment is directly related to the speed of medication onset, optimum dosing, and the ability to limit unwarranted side effects. Oral administration of scopolamine results in plasma peak concentration at 1-2 hours with the therapeutic effect diminishing in 4-6 hours with a significant side effect of sedation. Transdermal administration of scopolamine is easy, but absorption time is slow (average of 8 hours) and side effects associated with treatment over multiple days can be severe resulting in significant detrimental effects on physiological and cognitive function.

Intranasal administration of scopolamine has various advantages [16]-The dose required for intranasal administration of scopolamine is 0.4 mg. It is absorbed rapidly, with elevated concentrations in the blood within 15-30 min post-dose. Intranasal Scopolamine gel formulation (INSCOP) will be more suited than liquid dosage forms for prophylaxis and treatment of SMS. INSCOP (at dosages of 0.2 and 0.4 mg) was found to be effective for the treatment of motion sickness.Thus intranasal scopolamine is efficacious, safe, non-invasive route of medication administration in diverse operational environments.

Conclusion

Over the past two decades, extensive experimental research has been conducted on humans to better understand how the space environment affects the control of posture and movement in astronauts. Because of this, considerable information is now available regarding space motion sickness in microgravity. In future work, it will be important to extend the research to basic mechanisms operating at the cellular and molecular levels in the control of posture and movement in microgravity.We know that compensatory mechanisms function effectively in the vestibulomotor pathways on Earth and that compensatory mechanisms also occur in space. So further experiments to determine the basis for the compensation on Earth and in space, and to evaluate whether the mechanisms are the same, need to be conducted, since these compensatory mechanisms operate in astronauts entering and returning from space and may have a profound effect on their performance in space and their postflight recovery on Earth. Also in-flight recordings of signal processing following otolith afferent stimulation need to be made, to determine how exposure to microgravity affects central and peripheral vestibular function and development.

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