

Short communication

## Space motion sickness: Incidence, etiology, and countermeasures

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### Abstract

Space motion sickness is experienced by 60% to 80% of space travelers during their first 2 to 3 days in microgravity and by a similar proportion during their first few days after return to Earth. Space motion sickness symptoms are similar to those in other forms of motion sickness; they include: pallor, increased body warmth, cold sweating, malaise, loss of appetite, nausea, fatigue, vomiting, and anorexia. These are important because they may affect the operational performance of astronauts. Two hypotheses have been proposed to explain space motion sickness: the fluid shift hypothesis and the sensory conflict hypothesis. 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. Such sensory conflicts are thought to induce motion sickness in other environments. Space motion sickness is usually treated using pharmaceuticals, most of which have undesirable side effects. Further studies elucidating the underlying mechanism for space motion sickness may be required for developing new treatments.

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Space motion sickness is observed in a large percentage of astronauts beginning within the first hour of transition from Earth gravity to microgravity. It typically persists for 2 to 3 days. The symptoms of space motion sickness are similar to those of other forms of motion sickness, including sea sickness, car sickness, etc., but the environmental factors triggering these symptoms are apparently different because sensitivity to space motion sickness has not been shown to be predicted by levels of sensitivity to other environmental challenges. Indeed, there is also a high incidence of post-space flight readaptation sickness apparently triggered by the transition from microgravity to terrestrial gravity, but the correlation between those experiencing sickness resulting from the transitions into and out of space flight is low.

The cause of motion sickness is unknown, but motion sickness is generally produced by environmental challenges (linear and or angular accelerations) that confuse of the vestibular (balance) system. Subjective symptoms of space

motion sickness include pallor, increased body warmth, cold sweating, malaise, loss of appetite, nausea, fatigue, vomiting and anorexia. Space motion sickness was not reported during the early Mercury and Gemini flights, most likely because of the limited volume for moving around within the small capsules used during these missions (Reschke et al., 1998). The limited opportunity for movement likely minimized exposure to the conflicting visual, motor, and vestibular sensory messages thought to cause motion sickness. However, with larger capsules like in the Apollo and Skylab missions or in the Russian space program, reports of space motion sickness symptoms increased, likely owing to increasing movement of the astronauts within the capsule. In the Shuttle program, up to 80% of the U.S. astronauts felt some symptoms of space motion sickness (Reschke et al., 1998). In a study on 15 Russian cosmonauts, 13 out of 15 showed space motion sickness symptoms; seven of the eight first time fliers and six of the seven repeated fliers experienced space motion sickness (Loeff, 2001). In a larger sample of 72 U.S. astronauts 50% reported various space motion sickness symptoms (Task Group on Life Sciences,

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1988), with the most frequently reported symptoms being: vomiting (86%), anorexia (78%), headache (64%), stomach awareness (61%), and malaise (58%). No gender differences have been found (Oman, 1998), nor have any salutary effects of previous space flight experience been clearly demonstrated (Davis et al., 1988; Loeff, 2001; Reschke et al., 1998). Similar symptoms of motion sickness have been observed after flight. With about 27% of the Russian cosmonauts reporting effects of readaptation syndrome after short-term flights (4–14 days) (Reschke et al., 1998). Bacal et al. (2003) examined neurovestibular symptoms experienced by U.S. astronauts (31 women, 206 men) in the post-flight period. They identified 10 symptoms (clumsiness, difficulty concentrating, persisting sensation aftereffects, nausea, vomiting, vertigo while standing, difficulty walking a straight line, blurred vision, and dry heaves). Most of these astronauts experienced at least three of these symptoms, with the most frequently reported being clumsiness in their movements (69%), difficulty walking a straight line (66%), and persisting sensation aftereffects (60%). The intensity of the symptoms was generally mild and they were thought to pose little risk to the crew during landing and the immediate post-flight period. However, space motion sickness may present a more substantial operational risk to interplanetary travelers since the missions will likely be of much longer duration and there will be no support staff to assist them after landing.

Two hypotheses have been proposed for the causes of space motion sickness: the ‘fluid shift’ hypothesis and the ‘sensory conflict’ hypothesis. The fluid shift hypothesis suggests that space motion sickness results from the headward shifting of body fluids induced by the loss of hydrostatic pressure in the lower part of the body when entering microgravity. This decreased hydrostatic load leads to the cranial shifting of about 2 l of fluid from the lower part of the body, resulting in decreased leg volume and the thinned legs looking like ‘bird legs’. Because the cranial fluid shift leads to visible puffiness in the face, it was suggested that the intracranial pressure, the cerebrospinal fluid pressure or the inner ear fluid pressures might be increased, altering the response properties of the vestibular receptors and inducing space motion sickness (reviewed in Reschke et al., 1998). However, because space motion sickness symptoms were not reported in early flights during which mobility was limited and do not occur in simulation models that produce headward fluid shifts (e.g., head-down tilt bed rest) (Oman, 1998), this hypothesis has been largely discounted.

Sensory conflict is now widely accepted as the primary cause of space motion sickness at the beginning and end of space missions (Oman, 1987; Reschke et al., 1998; Stroud et al., 2005). Sensory conflict is thought to arise from a mismatch between expected and actual sensory inputs from the vestibular system, particularly when coupled with discordant inputs from the visual, haptic, and/or proprioceptive senses. This mismatch causes a loss of environmental ‘calibration’ resulting in disorientation and, when persistent, development of motion sickness. Head movements, espe-

cially in the pitch and roll planes, may be the dominant provocative stimuli for inducing space motion sickness (Young and Sinha, 1998) because they result in discordant cues being transmitted to the CNS regions responsible for central integration of semi-circular canal (angular acceleration) and otolith (linear acceleration and gravity) information required to maintain spatial orientation and stabilize eye and body movements.

The underlying mechanisms responsible for inducing the symptoms of space motion sickness have not yet been clearly elucidated. In a search for the mechanism, Serrador et al. (2005) examined cerebral blood flow in 15 test subjects exposed to nauseogenic stimuli generated by a rotating chair. Five of the fifteen volunteers developed nausea preceded by significant increases in blood pressure and decreases in cerebral blood flow during last 2 min prior to reporting symptoms. The authors concluded that a vestibular mediated cerebral vasoconstriction might precede nausea. Should these results be supported by further studies using larger populations, future preventive strategies such as use of inspired CO<sub>2</sub> or cerebral vasodilators might be used to prevent the development of nausea (Serrador et al., 2005).

Although gastrointestinal function is affected by space motion sickness, there are few published experiments examining the mechanisms of these functional changes. Some extant data suggest a relationship between the release of gastroenteropancreatic peptides and exposure to microgravity. For example, Drummer et al. (1990) examined vasoactive intestinal polypeptide (VIP) and pancreatic polypeptide in 20 healthy volunteers during extremely short microgravity exposures (20–30 s) experienced during 45 min of a parabolic flight. They found VIP, which acts as a neurotransmitter in the gastrointestinal system and increases intestinal secretion, to be significantly increased in the subjects affected by motion-sickness when compared to the subjects that were not affected. Pancreatic polypeptide, which is a gastrointestinal hormone that decreases pancreatic and biliary secretion, was significantly decreased. The same investigators also studied an astronaut during the Euromir 94 mission, and found that VIP was significantly increased on the fourth day in flight and remained elevated through flight day 29 (Riepl et al., 2002). Pancreatic polypeptide was also significantly increased in microgravity. VIP and pancreatic polypeptide have also been analyzed in Russian cosmonauts subjected to nauseogenic stimulation paradigms including rotating chairs and centrifuges (Loeff, 2001). Plasma VIP levels were unaffected by either of these stimuli (Loeff, 2001), while pancreatic polypeptide secretion significantly decreased during both (Loeff, 2001). Although these data need further confirmation in more subjects, this is at least a hint that gastroenteropancreatic peptides are correlated with changes in gastrointestinal functions in microgravity and other nauseogenic stimuli.

Because space motion sickness symptoms could interfere with operational activities required of space travelers at the beginning and end of space flight, research on the development of countermeasures is mandatory. Pharmacological

countermeasures have been well-studied (Jennings, 1998; Paule et al., 2004). Putcha et al. (1999) showed on the basis of 219 astronaut logs that 47% took anti-space motion sickness medications. Although metaclopramide, as well as oral and transdermal application of scopolamine, have been used in space by US astronauts, intramuscular application of promethazine has been the pharmacological countermeasure of choice since the STS (Space Transportation System)-29 mission launched in March 1989 (Davis et al., 1992, 1993; Bagian and Ward, 1994; Jennings, 1998). Because of the concurrent side effects of promethazine (drowsiness, sedation), it is usually given in the pre-sleep period so that any drowsiness can be masked by sleep (Jennings, 1998). Examinations of the effects of drug countermeasures for space motion sickness on working memory in humans suggest that, at clinically useful doses, the rank order of the drugs with best cognitive profiles is meclizine ( $H_1$  antihistamine) > scopolamine (muscarinic anticholinergic agent) > promethazine ( $H_1$  antihistamine) > lorazepam (GABAergic) (Paule et al., 2004).

Very recent research suggests that virtual reality training can simulate specific effects of microgravity and may prove to be an effective countermeasure against space motion sickness. Stroud et al. (2005) studied 30 volunteers (17 men and 13 women) using the NASA Device for Orientation and Motion Environments (DOME) virtual reality system to examine the effects of simple navigation and switch activation tasks in a virtual space station. They showed that the DOME creates sensory-conflicts similar to those that occur in space and that preflight training in a virtual environment can be an effective countermeasure, likely through a process of habituation, which has been long-used as a treatment for other forms of motion sickness (Clemens and Howarth, 2003).

In summary, the status of space motion sickness has not changed much in the past decade: it is still experienced, at least to some degree, by a large proportion of space travelers; its symptoms are generally treated by drugs having undesirable side effects; and it is hard to predict who will experience space motion sickness and to what extent it will affect their abilities to perform their assigned operational activities. As we move into a new era of space exploration, which may include sending humans to Mars, the potential risks associated with space motion sickness become a greater concern to mission planners. To develop new approaches to preventing or treating space motion sickness, however, further work must be done to elucidate the underlying mechanisms of the disorder. Such work will insure safer future missions.

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