Otolaryngological and Neuro-Vestibular Considerations for Commercial Spaceflight

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INTRODUCTION: The rapidly expanding commercial spaceflight (CSF) market has fueled increasing interest in spaceflight experiences among individuals without professional astronaut qualifications. Such individuals may present with a range of medical conditions that add uncertainties to medical preparation and risk assessment for spaceflight. As the ear, nose, and throat (ENT) working group of the Aerospace Medical Association Ad Hoc Committee on Commercial Spaceflight, we conducted a scoping review to assess the available biomedical literature for ENT and neuro-vestibular conditions and physiology pertinent to spaceflight for nonprofessional space travelers.

METHODS: The scoping review was conducted in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analyses. The initial database search produced 3232 articles. This set was reduced to 142 relevant publications through a rigorous two-reviewer filtering process using strict inclusion and exclusion criteria.

DISCUSSION: Motion sickness and spatial disorientation were the most common topics of the final set of articles. In contrast, there was limited material on other relevant ENT topics such as hearing loss, sino-nasal dysfunction, and conditions of the pharynx. It becomes clear from this scoping review that the path forward in providing guidance for optimal medical management of CSF passengers will involve the integration of modern biomedical research findings with the accumulated clinical expertise in the civil and military aeromedical communities. We recommend building an industry-wide CSF medical database to address care gaps and improve specialized aerospace medical knowledge.

KEYWORDS: spaceflight, otolaryngology, vestibular, motion sickness, spatial orientation, motor control, hearing, vertigo, mastoid effusion.

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The age of commercial spaceflight (CSF) has arrived. While space has historically been the exclusive domain of professional astronauts, the spacefarers launching on commercial missions come from a variety of backgrounds and levels of preparation for spaceflight.[1] All space travelers are subject to environmental stressors and risks that vary with mission type and duration,[2] but the new generation of space crew and passengers may present with existing medical conditions that predispose them to additional risks during spaceflight. Current U.S. law mandates that commercial space passengers provide written consent after learning about the risks of spaceflight;[1] however, the standards and limitations of medical evaluation in this population are still being developed, and there is relatively little operational experience in managing spaceflight passengers with chronic medical conditions.

Discussions of medical screenings and standards for the CSF community have occurred previously within the Aerospace Medical Association (AsMA), with position papers published in 2002[3] and 2011[4] for suborbital passengers and crew. The AsMA Ad Hoc Committee on Commercial Spaceflight (hereafter the Ad Hoc Committee) was created to review medical physiology and conditions related to CSF passengers across a range of mission types, including suborbital, orbital, and future

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long-duration missions. The primary initial project of the Ad Hoc Committee was to scan the clinical and technical biomedical literature in support of these efforts and to identify gap areas to refine future research strategies. This work was divided among 10 teams. The present report summarizes the work of the ear, nose, and throat (ENT) team.

There is a long history of otolaryngological and neuro-vestibular contributions to flight medicine,[5] particularly relating to spatial disorientation and hearing protection. Medical conditions of the ears, nose, and throat are common in the general population and could easily appear in the medical profiles of CSF passengers. These conditions could create hazards for safe spaceflight through disturbances of sensation (e.g., balance, hearing, smell) and respiration. As an example, advanced hearing loss could prevent an individual from correctly hearing emergency announcements and alarms, potentially jeopardizing the affected individual as well as the flight. As another example, underlying chronic rhinosinusitis would pose a risk factor for barosinusitis pain and barotitis. Special attention will be needed to assess the medical readiness and fitness of individuals who are interested in spaceflight, even if they plan to be a passenger. Since CSF passengers will not undergo the same rigorous selection process as professional astronauts, any available literature developed from primarily nonprofessional astronaut aeromedical research will be useful to incorporate into the preflight medical evaluation.

In this report, we present a scoping review of medical and research literature for otolaryngological and neuro-vestibular information pertinent to the well-being of CSF passengers. Unlike systematic reviews and meta-analyses, scoping reviews seek to broadly survey a topic and map out the range of existing literature sources.[6] Scoping reviews are particularly suitable for initial investigation of topics of complex and heterogeneous nature. The intent is to discover in which areas the knowledge base is well established and in which areas gaps exist. This information can in turn be used to support specific operational objectives, such as safer spaceflight and better preparation for spaceflight passengers. In addition, the scoping review can sharpen further research endeavors and potentially reduce wasted investigative effort.[7]

The present report is the first in a series of 10 planned by the Ad Hoc Committee. The results of the scoping reviews produced by the other teams will be published separately. To our knowledge, this is the first scoping review focusing on ENT and neuro-vestibular physiological issues pertinent to nonprofessional space travelers.

METHODS

Literature Search Strategy

This scoping review was undertaken in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses - Extension for Scoping Reviews.[8] Two lists of search term keywords were developed. The first keyword list (supplemental **Table AI**, found in the online version of this article) included terms related to ENT and neuro-vestibular conditions that could affect the ability of an individual to participate in a spaceflight experience, as well as terms related to associated aspects of physiology or pathophysiology. This list was prepared by the consensus of the ENT team, whose range of expertise included otolaryngology, neurology, audiology, flight nursing, and general medicine. A second list of keywords describing CSF and spaceflight analogs (such as parabolic flight or centrifuge) was developed by the Ad Hoc Committee and was used by all teams (supplemental **Table AII**, found in the online version of this article).

A research librarian used the keyword lists to conduct a systematic search in four bibliographic databases (PubMed, Embase, Web of Science, and Cochrane). Articles were retrieved if they contained at least one keyword each from the ENT and CSF keyword lists and were published within the date range January 1, 2000 through June 9, 2023. The start date was chosen to allow inclusion of references related to the first space tourism flight (Dennis Tito's flight aboard Soyuz in April 2001). The end date was the date of the bibliography search.

Initial Article Review

The list of articles retrieved by the research librarian was reviewed by the team to determine if the paper met predefined inclusion criteria. The criteria were developed by team consensus. As a first pass, the title and abstract were examined and articles that did not meet criteria were discarded. On the second pass, the remaining articles were checked again by examining the full text. During each pass, two team members independently rated the article for inclusion or exclusion. If there was disagreement, a third team member provided the tie-breaking decision. Team teaching sessions were held to ensure a consistent approach to article review. During these teaching sessions team members independently rated a sample article for inclusion or exclusion and discussed with the group their reasoning (**Fig. 1**).

Inclusion Criteria

1. The article must report on an ENT or neuro-vestibular medical condition (or related aspect of physiology) that could have a bearing on the suitability of the individual to safely undertake a spaceflight experience.
2. The article must describe findings from spaceflight or a spaceflight training/analog environment. Relevant analogs are numerous, encompassing both high fidelity simulator environments as well as situations that train or mimic one aspect of spaceflight. Examples include microgravity exposure during parabolic flight, acceleration exposure in a centrifuge, body fluid shifts during head-down bedrest, social isolation enclosures, spatial disorientation by rotating chair or virtual reality, and altitude chambers.
3. The article must describe research on or findings about adult (ages 18 yr or older) human volunteers. This criterion served to exclude studies on tissue samples, nonhuman organisms, and computational models.

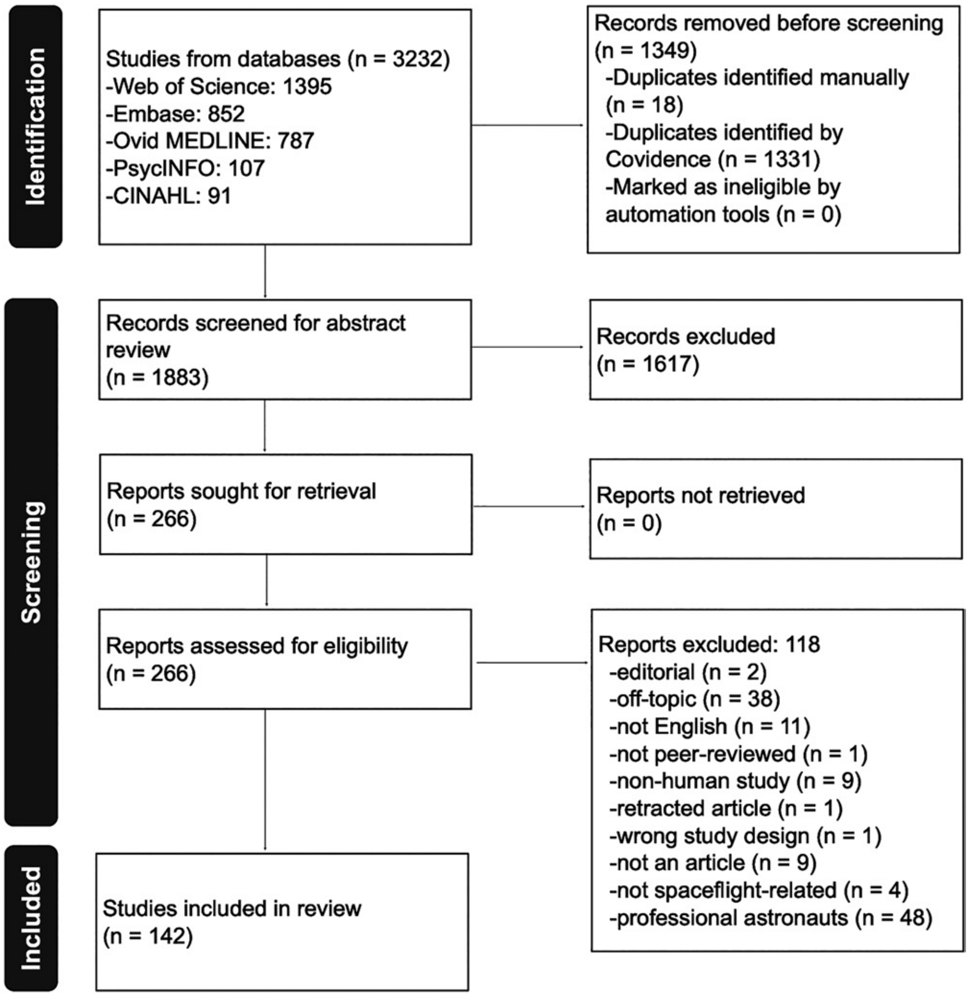

Fig. 1. PRISMA diagram showing the number of articles that were excluded at each stage of screening and the final number of articles included in the review.

4. The article must describe research on individuals other than professional astronauts. Review articles covering both professional astronauts and other research participant groups were accepted. Primary studies on professional astronauts were excluded because individuals within this specialized population have passed stringent medical and physical fitness selection criteria, making them unrepresentative of the typical lay person seeking a CSF experience.
5. The article must have been published under peer review. This criterion excluded editorials and conference posters.
6. The full text of the article must be available in English.
7. The article must be available to public university libraries. This criterion excluded confidential reports such as corporate white papers and military technical reports.

Data Extraction

At the conclusion of the initial article review there were 142 articles that met the inclusion criteria for the scoping review. Each included article was read by two team members who extracted the following data: title, authors, type of article (experiment, case report, or review), environment (spaceflight or analog), and major findings relating to ENT and neuro-vestibular disorders. For experiments, the following information was also collected: experiment type (e.g., randomized controlled trial), number of participants, participant characteristics (e.g., "healthy adults aged 18–30"), and a brief description of the methods used. A quality rating was assigned to the article using the Johns Hopkins Evidence Based Practice – Hierarchy of Evidence.[9] Any disagreement between the two reading team members about the extracted information or the quality rating was resolved by having a third team member provide a final decision. The collected information was entered into a spreadsheet to enable further analysis.

RESULTS

Space Motion Sickness

The scoping review identified 76 articles related to space motion sickness (SMS). Of these, 27 (36%) were review articles (evidence level V) and 23 (30%) were randomized controlled trials (evidence level I). The remaining 26 were quasi-experimental or nonexperimental studies (evidence levels II and III).

General. A consensus of the main points regarding SMS was first assembled from included broad review articles.[10–12] The most distressing features of SMS are nausea and emesis, but drowsiness and lack of motivation (the "sopite syndrome"), as well as cold sweats, may also be present.[13] SMS occurs in roughly 70% of astronauts,[14] with symptoms appearing within minutes to hours of launch.[3] Symptoms typically last up to 3 d,[10] but in extreme cases can continue for more than 1 wk. Re-entry and landing can also lead to substantial nausea and imbalance, particularly after prolonged missions. The exact relationship between SMS and these vestibular readaptation symptoms is unclear, however, both will be covered here.

Etiology. The vestibular system consists of semicircular canals (which detect angular accelerations), otolith organs (which detect linear accelerations and head tilts with respect to gravity), and central processing networks within the brainstem and cerebellum. Vestibular sensory information plays an important role in the control of eye movement and postural balance but has also been shown to affect autonomic functions,[13] certain cognitive abilities, and the development of motion sickness. Individuals with diminished vestibular function exhibit lesser degrees of nausea and emesis during motion sickness.[11]

The sensory conflict theory is the most widely accepted explanation for the development of SMS. This theory proposes that relationships between vestibular, visual, and other sensory inputs[10,15] are learned throughout an individual's life on Earth but are altered by subsequent exposure to the unusual force environment of space. In free fall during orbit or suborbital parabola (hereafter referred to as 0 G), the otolith organs can no longer signal head tilt with respect to gravity but still respond normally to linear accelerations. The brain may react to this change in inputs by deeming the otolith signals to be unreliable and favoring other sensory cues such as vision, or by reinterpreting all otolith signals in 0 G as linear translations. In addition, rotational movements may also be misinterpreted in 0 G since accurate integration of the angular acceleration signal from the semicircular canals appears to depend on gravitational cues.[16,17] Re-entry and landing require sensory readaptation, potentially involving further remapping of vestibular inputs.[18] An altered sense of the vertical direction is a key component of the sensory conflict theory,[12] and head motions in the pitch and roll planes (which provide a tilt with respect to gravity on Earth) are particularly effective in eliciting symptoms.[4] This effect is not limited to microgravity: head movements during the increased-G periods of parabolic flight also stimulate motion sickness.

Many of the symptoms associated with SMS, such as emesis, are mediated by the autonomic system. This connection may involve a pathway from the vestibular nuclei to the nucleus tractus solitarius and dorsal motor nucleus of the vagus nerve, or alternatively to the reticular formation and caudal ventrolateral medulla.[19,20]

Predictive Factors. No reliable physiological or psychological factors have been identified to predict which individuals will develop SMS during spaceflight,[11] although several have been proposed, including prior spaceflight experience,[10] salivary amylase,[21] vestibular dynamics after rotation,[11] and bias of the subjective vertical reference.[12] Curiously, there does not appear to be a reliable correlation between a history of terrestrial motion sickness (e.g., car or sea sickness) and SMS.[10,22] Ground-based analogs such as rotating chairs, centrifugation, and wide-field visual displays can approximate certain aspects of the sensory mismatch thought to cause SMS,[23] but susceptibility to motion sickness when using these devices does not necessarily lead to SMS during spaceflight.

Prevention. Several forms of preflight training to prevent SMS have been proposed. Preadaptation training based on altered visual cues and orientation illusions[4] has shown some promise in laboratory studies but is time-intensive and has yet not entered widespread use. Chen et al.[24] studied visually induced motion sickness in normal volunteers, finding that training by repeated exposure to rotating visual scenes lowered the subsequent visually induced motion-sickness scores by 40%. They hypothesized that this training allowed the participants to become more reliant on their perceived body axis rather than on visual cues for orientation in space. Autogenic feedback training to increase tolerance of nauseogenic vestibular stimuli has also been suggested[25] but is controversial (see discussion by Lackner and DiZio).[11]

During the mission, strategies to prevent SMS fall into behavioral, pharmacological, and technological categories. Behavioral approaches include increasing attention toward required tasks and limiting head and body movements,[10] although limiting movements may prolong the overall adaptation period. Pharmacological prevention has historically relied on scopolamine, with or without dexamphetamine to limit sedation. Oral, nasal,[26] or subcutaneous[27] scopolamine is preferred over patches due to inconsistent transdermal bioavailability. Protective effects begin within 30–60 min and last for 4 h.[28] Technological prevention can include worn devices or foot straps to enhance directional sensory cues,[10,29] reduced ambient temperature within the vehicle to minimize nausea,[4] or vehicle design to standardize the internal visual orientation of habitable modules.[10]

Treatment. The mainstay of treatment of SMS is pharmacotherapy, however, a recent systematic review of SMS countermeasures found inconsistent data to support any single best approach.[30] The most common SMS treatment medication in the U.S. space program has been intramuscular promethazine, sometimes administered together with dextroamphetamine to help counter the sedative properties of the antiemetic.[11] Chlorpheniramine has also been effective against motion sickness symptoms in ground-based analogs.[31] Meclizine has been proposed as an alternative, given its lower rate of cognitive side-effects.[14] All pharmacotherapeutic options currently available carry the risk of sedation, a concern that must be addressed for anyone engaged in essential mission tasks. Regulations may prevent the spacecraft commander or pilot from taking these medications, and other crew or passengers should preferentially be given these medications before sleep.[4]

Relevance for CSF Passengers. It is likely that SMS will occur at least as frequently in the CSF passenger cohort as in professional astronauts and there are currently no reliable predictive factors for estimating this risk. While ground preparations for spaceflight may include experiences that induce motion sickness, it is not established that such training reduces the subsequent likelihood or severity of SMS. Passengers should discuss the available prophylactic and treatment options with their physician. They should also consider the risk and symptoms of SMS as well as the side-effects of treatment when developing their schedule of activities during the flight.

Spatial Orientation and Vertigo

The scoping review identified 42 articles that included content relevant to spatial orientation and motion perception. Of these, 20 (48%) were review articles (evidence level V) and 16 (38%) were randomized controlled trials (evidence level I). The remainder were quasi-experimental or nonexperimental studies (evidence levels II and III).

General. The human nervous system is adept at combining sensory cues into perceptions about our orientation and movement with respect to our surroundings. This ability is thought to occur through the creation of an internal model describing how actions (such as head turns) lead to changes in sensations.[15] As described in the Motion Sickness section, transitions to and from 0 G lead to alterations of the previously learned action-sensation mapping, and available somatosensory,[32] visual,[33] and motor efference cues become more salient. Full adaptation to changes in the gravito-inertial force environment takes place over a timescale of hours to weeks,[15] so perceptual errors tend to be most pronounced during and shortly after G level transitions (e.g., launch and landing). Erroneous perceptions of orientation and movement have the potential to create safety hazards during critical tasks, potentially endangering both the affected individual and the overall mission. While CSF passengers are unlikely to be directly involved in high-risk launch and landing procedures, they may well be responsible for assisting during emergencies and should be capable of safely egressing from the spacecraft after a contingency landing.

Perceptual Alterations. Numerous studies have demonstrated perceptual errors relevant to spaceflight. Individuals overestimate roll tilt during high G[34] and may underestimate roll tilt during low G.[35] In contrast, during 0 G there can be a complete absence of the ability to perceive yaw[16] or roll[36] rotation unless visual cues are available. Transitions to 0 G can produce compelling visual reorientation or inversion illusions in which the individual suddenly feels upside-down.[12] This phenomenon may be related to the tendency in 0 G to perceive the vertical as aligned with the long body axis, regardless of the person's actual orientation relative to the surrounding space. Proposed explanations for this finding include changes in saliency of visual cues[37] and individual differences between individuals who prioritize vestibular cues and those prioritizing somatosensory cues.[38]

Cognitive Changes. Alterations in G level have been associated with reductions in the ability of individuals to perform a spatial updating or perspective-taking task[39] in parabolic flight. Similar conclusions were reached by another group using galvanic vestibular stimulation to simulate loss of normal vestibular cues.[40] Deficits in shape perception, concentration, memory, and multitasking ability during G transitions have also been linked to altered vestibular function.[2]

Countermeasures and Analogs. Considerable research effort has been expended to develop countermeasures to the sensory alterations and disorientation illusions seen in spaceflight. Preflight training with either virtual reality[24] or galvanic vestibular stimulation[41] may hold promise in decreasing disorientation in novel gravitational environments.[42] During a mission, devices could be worn to increase available somatosensory cues[34] or to display enhanced visual guidance to minimize orientation errors.[43] Novel terrestrial analogs of spatial disorientation have also been developed, such as wheelchair head immobilization,[44] which can replicate some of the illusory perceptions experienced in 0 G.

Spacecraft Design Issues. Multicompartment spacecraft such as the International Space Station (ISS) can be disorienting due to the possibility of rooms being connected in any orientation, including vertically.[12] Some initial research into this problem using virtual reality suggests that the use of colors and clear signage can reduce disorientation in spacecraft, as can limiting the number of turns that an individual must make to traverse between locations.[45]

Intermittent use of a short-arm centrifuge has been proposed for future spacecraft as a means of reducing cardiovascular deconditioning and loss of bone and muscle mass during long-duration missions.[46] Head movements during short-arm centrifugation in 1 G frequently cause motion sickness and illusions of tumbling, head tilt, or body tilt.[47,48] Interestingly, head movements during centerline yaw rotation in 0 G do not lead to these tumbling sensations,[49,50] however, this type of rotation would not provide the same benefits to bone and muscle mass.

Positional Vertigo After G-Loading with Vibration. Liston et al.[51] reported that 3 of 16 participants developed benign paroxysmal positional vertigo (BPPV) following combined, repeated exposure to 3.8-G acceleration and 8–16-Hz vibration along the G_x axis, raising concerns that G-loading could be an exacerbating factor for vibration-induced dislodgement of otoconia. Notably, the affected individuals were older participants (ages 50–52) in the study (age range 21–57). Vibration alone in the 1 G_x condition was not associated with development of BPPV. In two cases, positional vertigo resolved after treatment with Epley maneuvers, and in the third case, symptoms resolved over 1–2 mo without specific treatment.

Relevance for CSF Passengers. All CSF passengers should be informed of the likelihood of perceptual alterations during G level transitions and the associated health and safety implications, including increased chance of SMS, disorientation while navigating through larger spacecraft, and potential difficulties carrying out tasks. Preventive strategies (such as maintaining a similar orientation to other crew/passengers or using straps to increase touch cues) can be discussed or practiced during preflight training. The combined G forces and vibration of launch and landing may increase the chance of subsequent BPPV, particularly in older individuals who are more prone to the condition generally. This disorder may not become noticeable until re-exposure to the gravitational field, at which time it could pose hazards during spacecraft egress or emergency procedures.

Balance, Posture, and Motor Control

The scoping review identified 55 articles with content relevant to balance, posture, and motor control. Of these, 24 (44%) were review articles (evidence level V) and 11 (20%) were randomized controlled trials (evidence level I). The remainder were quasi-experimental or nonexperimental studies (evidence levels II and III).

Balance and Posture. The ability to stand upright and walk on Earth depends on our ability to accurately estimate the position of the body relative to gravity and to generate appropriate muscle activations to counteract any postural perturbations. This process involves vestibular, somatosensory, and visual inputs to cortical,[52,53] cerebellar, and brainstem structures. Outgoing vestibulospinal pathway projections control the postural responses.[32] After entry into 0 G, alteration of the vestibulospinal reflexes[54] relevant to the lower limbs occurs over several days,[55] while axial muscles appear to be less affected by gravitational changes.[56]

The major posture-related concern for spaceflight participant safety comes during re-entry and landing. In centrifuge simulations of suborbital vehicle re-entry profiles, approximately half of participants have abnormalities on Romberg testing after their "flight."[23,57] On return to Earth, postural control and balance are typically diminished relative to preflight ability,[10] in a pattern that resembles the deficits seen during the acute vestibular syndrome.[15] These deficiencies may be related to alterations in how the nervous system interprets head rotations.[18] Orthostatic hypotension is also common after 0-G exposure, possibly related to alterations of vestibulo-autonomic activity.[58–60] These deficits could lead to difficulties with egress from the spacecraft in situations where support crew are not available, such as during emergency landings on Earth or during planetary landings in the future. This concern has been noted since the earliest attempts at establishing medical guidelines for CSF participants,[3] and previous recommendations have been made for emergency egress training.[4]

Readaptation to Earth gravity occurs most rapidly during the first 3 d postflight, followed by a slower return to preflight performance levels over the following weeks.[10] Sensorimotor reconditioning can be used to recover satisfactory balance function,[61] and during this time, dynamic head tilts may be useful in uncovering subtle postural instabilities.[62] Walking can produce illusory perceptions during the readaptation period after landing. For example, knee bends can create the illusion that the ground is moving upward toward the torso.[33]

Motor Control. Although most spacecraft control operations will presumably be performed by professional or commercial crewmembers, everyone aboard a spacecraft will likely be expected to perform basic emergency procedures. In addition, passengers may need to carry out experiments or other tasks that require fine motor control. Correlations have been found between vestibular perceptual sensitivity and manual control task precision in 1 G and hypergravity,[63] but not in 0 G.[17] The vibrational characteristics of the spacecraft can also reduce manual task performance,[4] particularly in the 2–16 Hz range. Proprioception[10] and coordination between head, eye, and hand movements are most impaired shortly after orbital insertion and during re-entry,[15] with slow movements affected more than rapid movements. These deficits occur most often in the setting of disorienting flight conditions and increased attentional load,[17] however, some impairments in bimanual control and fine motor control continue after landing.[2]

Vestibular Ocular Motor Control. The control of eye movements by the vestibular system allows for goal-directed movements to fixate on a target of interest and reflexive actions to maintain focus despite movements of the head, body, or environment. Eye misalignments and ocular motor control errors can lead to diplopia (which may be experienced as blurring for smaller errors) and nystagmus. Visual blur has been linked to motion sickness.[64] Nystagmus was noted in 59% of participants after centrifuge simulation of the high-G components of a suborbital flight profile.[23] Two thirds of participants showed reduced nystagmus with further centrifuge runs, while some individuals had worsening nystagmus. Previous research has shown that gaze control and dynamic visual acuity (ability to focus while the head is moving) are impaired during periods of high vibration,[4] shortly after entry into 0 G, and during re-entry.[15] A mild G-dependent vertical skew of up to 2.57° has been found during parabolic flights.[65] The 0-G environment has also been associated with increased vergence of up to 5°, a differential change in torsion between the two eyes,[66] and a reduction or loss of ocular counter-roll in response to head tilts.[54,67] Some of these changes have been seen with short durations of 0 G. Parabolic flight appears to induce vertical and torsional eye misalignments that recur during subsequent flights.[68] Adaptation of the vestibular oculomotor system to 0 G may require months, while full readaptation to Earth gravity requires days to weeks.[66,67]

There is evidence linking the severity of motion sickness with an increased time constant of the vestibulo-ocular reflex (VOR)[20,69] This raises the possibility that training to alter this time constant could reduce motion sickness symptoms. Several experiments have demonstrated that humans are capable of dual adaptation of some types of oculomotor control, meaning that different sensory-motor control strategies can be learned and used for tasks in two different contexts (such as Earth and 0 G). Dual adaptation has been shown for the VOR time constant,[20,70] and there is evidence that gravity can be used as the context cue.[71,72] VOR time constant adaptation has been shown to last for months to years in some cases.[73]

Relevance for CSF Passengers. Passengers should be fully informed about potential difficulties in vehicle egress due to postlanding postural instability or orthostatic hypotension. This is of particular concern when considering spaceflight for individuals with limited mobility. While they may find the 0-G environment freeing, they are likely to be at increased risk during an emergency egress after landing.

Auditory and Tympanomastoid Effects

Hearing. Abel et al.[74] studied the effects of noise at 72 dBA on auditory and psychometric measures during a 70-h ground-based ISS simulation. In this level I evidence study, 25 healthy volunteers with normal hearing were randomly assigned to one of 3 conditions: quiet, continuous noise, or noise only during each 14-h workday. The noise was spectrally shaped to match typical ISS noise and was kept within ±2.5 dB of the target intensity. There were no significant decrements in auditory function or in auditory performance tests, including cognitive and communications tasks. Post-study audiometry revealed mean hearing thresholds were maintained within ±10 dB. The authors noted that this contrasted with the hearing problems previously reported in professional astronauts. While the results were favorable, this study was not able to simulate certain relevant aspects of long-duration missions such as intermittent high noise exposure and vibration. Pre-existing hearing loss, which could be important to the CSF passenger population, was also not evaluated. We note there is a professional astronaut NASA Technical Report indicating that unexpected low-frequency hearing loss occurs variably in a substantial number of astronauts during prolonged space missions. That analysis is as yet unfinished and remains unpublished.

Fluid Shifts and Effusions. Lecheler et al.[75] present evidence level II data on mastoid effusions occurring during a spaceflight analog study. The 24 healthy participants undergoing 60 d of head-down tilt bed rest were assigned to one of three groups: no intervention, 30 min $\cdot$ d^{-1} artificial gravity by short-arm centrifugation, or six 5-min sessions per day of short-arm centrifugation. Prior to the study, all head MRIs were clear of mastoid effusion, but by Day 14, 25% showed mastoid fluid and this increased to 67% by Day 52. In roughly half the cases, the effusions were bilateral. These results were comparable to those previously reported in professional astronauts. Centrifugation did not change the incidence of mastoid effusion development during the study. A single participant developed otitis media, but none developed clinical mastoiditis. There was, unfortunately, no audiometric data or tympanometric data to correlate the presence of mastoid fluid to changes in middle ear ventilation and hearing.

It is assumed that tympanomastoid changes in pressure and aeration during microgravity are related to the increased intracranial pressure (ICP) arising from cephalad fluid shifts. Watkins et al.[76] studied ICP (estimated noninvasively using tympanic membrane displacement) in 15 healthy volunteers during 15° head-down tilt, which served as a spaceflight analog. Use of a lower body negative pressure device was associated with lower estimated ICP. While the possible significance of this study in relation to spaceflight-associated neuro-ocular syndrome (SANS) was discussed, the potential benefits in relieving sinus pressure and mastoid congestion were not addressed.

Relevance for CSF Passengers. Although the noise level inherent to short-duration spaceflight appears to produce little decrease in auditory acuity in individuals with normal hearing, crew and passengers should have access to ear protection until further studies can be performed. Prolonged exposure to 0 G appears to also be associated with MRI signal enhancements suggestive of mastoid effusions, although the clinical and auditory significance of this finding remains unclear.

Other ENT Issues

Chemosensory. Olabi et al.[77] reviewed the literature on the chemosensory functions of taste and smell. They found no definitive evidence for spaceflight-related decrements in taste and smell, however, it should be noted that the subjective experience of flavor involves multisensory integration and may not be captured by studies focusing on a single sense. The role of head-congestion in flattening taste via diminished olfactory function was not clarified in this review.

Wound Healing and Infections. The immune system is undoubtedly affected by the stresses of spaceflight and other extreme environments,[78,79] and this has been studied in a variety of spaceflight analogs. Changes have been found in the amount and distribution of oral and nasal organisms over the course of a 6-mo sealed habitat experiment, including an increase in nasal *Staphylococcus* organisms.[80] Increased rates of herpes zoster reactivation were found in individuals inhabiting the Antarctic research station compared to historical controls[81] (level II evidence). Increased Epstein-Barr virus and varicella zoster virus were found in a head-down tilt bed rest plus centrifugation protocol,[82] although no clear signs of immunocompromise were seen (level III evidence). Stress biomarkers have been detected during parabolic flight[33] as well as during a Mars analog mission.[83] Notably, oral wound-healing was also delayed in that study (level III evidence).

Upper Airways. Microgravity may alter the characteristics of the upper airway structures, and there are reports of reduced sleep apnea, hypopnea, and snoring in 0 G.[84] Airway emergencies may require intubation, possibly by nonphysicians, and several studies have investigated this in a space analog setting. Experts and novices were equally successful at intubation of a mannequin during parabolic flight,[85] despite the experts showing higher proficiency in Earth gravity. In both groups, videolaryngoscopy was more successful than conventional laryngoscopy (level II evidence). A simplified rapid sequence induction of general anesthesia with oro-tracheal intubation was successfully performed by five crewmembers with limited medical training on a simulated injured astronaut at the Mars Desert Research Station.[86]

Relevance for CSF Passengers. CSF passengers with baseline immunological disorders may be at elevated risk during a mission due to immunological stress, however, the impact in terms of increased rates of clinical illnesses or diminished wound-healing is largely unknown. While this topic is very important in the ENT domain (e.g., mucositis, oral ulcers, head and neck infections), the topic is very broad and will be covered in more detail in the report of the Immunology team of the Ad Hoc Committee. In terms of upper airways, cephalad fluid shifts during microgravity aggravate mucosal swelling in upper respiratory passages and increase respiratory resistance. Given that 50% of the total respiratory tract resistance is attributed to the nasal airways, even mild airway constrictions at baseline should be optimized preflight to minimize excessive work of breathing during spaceflight.

DISCUSSION

Our scoping review indicates that within the ENT and neuro-vestibular fields, most of the research relevant to CSF passengers has been focused on the problems of SMS and spatial disorientation. Additionally, it is clear from the review that studies on prophylaxis and treatment of these conditions lag behind basic research on relevant physiology. For example, it is still not possible to predict which individuals will experience SMS, although it will likely affect most CSF passengers on all but the shortest (suborbital) missions. Given the gradual recovery time course from SMS, severe cases could interfere substantially with the spaceflight experience for a significant portion of the mission. Pharmacotherapy remains the mainstay of treatment but is not free of sedative side-effects. Further efforts are required to identify improvements in prevention and treatment, with an increased focus on treatments that minimize cognitive side-effects. Further research on spatial disorientation is also needed given the hazards it can present during emergency procedures and spacecraft egress. Few studies were found covering medical issues related to other areas of otolaryngology.

Historically, astronaut candidates with significant ENT conditions were screened out by the rigorous astronaut selection process. Flight surgeons have accumulated decades of experience with assessing and managing common ENT conditions in this healthy astronaut population. What is less certain is how existing aerospace medical standards (both military and civilian) should be applied to commercial space passengers, who may have a wider range of medical disorders that would previously have been disqualifying. This scoping review provides an initial overview of the literature, but medical evaluations will also need to draw upon the expertise of aerospace medicine specialists within the civilian and military aviation and spaceflight communities. An example of this sort of collaborative endeavor may be found in a standard published by the American Society for Testing and Materials: ASTM F3568-23, Standard Guide for Medical Qualifications for Suborbital Vehicle Passengers.[87] The ASTM is preparing a separate document on space passenger medical guidance for orbital spaceflight.

One prominent finding in this scoping review is the emphasis on outcomes in healthy volunteers within various analog environments. While the scientific rationale for this emphasis is understandable, it sets limits on how the results can be applied. All analog space paradigms are imperfect simulations of spaceflight conditions, often with isolated variables under study. The analog results may not remain valid in the actual spaceflight setting with multiple concurrent stressors. This is especially true when applied to individuals already predisposed to disorders due to chronic ailments. It would be highly impractical to conduct systematic laboratory investigations covering the multitude of infrequent medical disorders. We support the development of an industry-wide collaborative effort to pool spaceflight-related medical knowledge for the benefit of all stakeholders. CSF medical databases can be designed to safeguard crew and passenger privacy. The goal would be to build case-study knowledge of medical conditions affecting or arising in spaceflight, with an eye toward enhancing flight safety. This was previously recommended by the AsMA working group on suborbital crew medical recommendations.[4]

A limitation of this scoping review is the exclusion of studies based entirely on professional astronauts. The rationale was that professionally trained astronauts would have careful medical selection and intensive training for spaceflight that will be lacking in CSF passengers. The scoping review did include numerous review articles, many of which incorporated important knowledge from professional astronaut cohorts. On specific topic investigations, the full range of professional resources should be evaluated. For example, in addition to the analog study of ISS noise and hearing assessments described above,[74] extensive research on noise during spaceflight and on-orbit hearing assessments in professional astronauts is summarized by Danielson et al.[88] and references therein. Another review, by Alford et al.[89] addresses spaceflight-related hearing loss as well as general ENT problems during Space Shuttle flights.

In summary, this ENT and neuro-vestibular scoping review identified strong research efforts undertaken to understand SMS and spatial orientation in healthy, non-astronaut volunteers. Other medical conditions received less attention, with a distinct paucity of data on pre-existing medical conditions that would have previously been disqualifying for professional astronaut crews but which may now need reconsideration for the CSF passenger population. We suspect that similar problems will be encountered in the other medical specialty scoping reviews. This scoping review highlights several areas for further research and the need for an industry-wide, anonymized database of medical findings to further the goal of CSF passenger safety.

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