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REVIEW ARTICLE

OPHTHALMIC RISKS DURING SPACE TRAVEL

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Abstract: The aim of the following scientific paper is to address the ophthalmic issues and threats associated with human exposure to microgravity environments and radiation during space flights. We conducted a review of ophthalmic scientific literature related to space flights, focusing primarily on spaceflight-related neuro-ocular syndrome (SANS). NASA (National Aeronautics and Space Administration) considers SANS, along with other vision disorders, to be one of the major medical challenges that can significantly limit human ability for prolonged stays in space and on celestial bodies other than Earth [32]. In this paper, we also present the latest methods for diagnosing and preventing SANS.

Keywords: SANS, ophthalmology, visual disorders, space flights, astronauts, DES, cataract

Table: 1 • **References:** 39 • **Full-text PDF:** http://www.pjambp.com • **Copyright** © 2024 Polish Aviation Medicine Society, ul. Krasińskiego 54/56, 01-755 Warsaw, license WIML • **Indexation:** Index Copernicus, Polish Ministry of Science and Higher Education

INTRODUCTION

The return of humans to the Moon raises many questions within the scientific community regarding their future in space. Unlike the previous space race, this time plans are being considered for a permanent stay on the Moon. This involves greater challenges in many areas—among others, in medicine. There are undoubtedly many medical risks associated with human presence in an environment with different gravity than on Earth and cosmic radiation. It is estimated that the human body ages about 10 times faster in space than on Earth [1].

Given the potential popularization of both professional and tourist space flights in the coming decades, it is essential to familiarize the medical community with the most common complications of these flights. This review work has been created to update and disseminate knowledge about ophthalmic diseases related to human presence in space. Special attention is given to the latest methods of diagnosing and preventing spaceflight-related neuro-ocular syndrome (SANS). Additionally, we present the latest scientific theories regarding the pathophysiology of SANS.

METHODS

To find scientific papers addressing the impact of human presence in space on the visual system, the Google Scholar and PubMed search engines were used. Research papers on the topic were found. It was verified whether the scientific papers were published in journals meeting the standard of rigorous peer review. The focus of the subsequent work was on spaceflight-related neuro-ocular syndrome (SANS). Selected articles were then analyzed, assessing their content for significant information, and a synthesis of the available knowledge was conducted in the following review.

RESULTS

The following review presents a summary of the analysis of selected articles, whose content reliably represents the most important (in the authors' opinion) and the latest reports on ophthalmic diseases occurring in astronauts.

SANS (spaceflight related neuro-ocular syndrome) – symptoms

The first reports on visual disturbances resulting from space flights can be traced back to the Gemini V and Gemini VII missions. In 2011, Mader et al. [14] systematized the knowledge on eye function disorders resulting from prolonged stays of astronauts in space. They conducted eye examinations on 7 astronauts before and after their missions on the International Space Station (ISS). It was at that time that the term VIIP (visual impairment and intracranial pressure syndrome) was first introduced, which was later renamed SANS (spaceflight related neuro-ocular syndrome) due to updates in the knowledge about the pathophysiology of this syndrome. Astronauts suffering from SANS report vision disturbances, which are usually the only symptom. The most common findings in ophthalmic examinations of SANS include: flattening of the eyeball [9], typically manifesting as refractive changes towards hyperopia (23-48%) [10,25], optic nerve swelling characterized by a swollen disc and nerve sheath distension [16], choroidal congestion with visible folds (60%) [1,17], retinal ischemia presenting as soft exudates [11], and retinal folds [11]. There is also an observed increase in intraocular pressure, which resolves a few days after returning to Earth's gravity [1]. SANS occurs in both sexes. Otto diagnosed SANS in as many as 43% of astronauts (n=36) [23]. NASA, on the other hand, reports the presence of SANS in 66% of astronauts, indicating the widespread and serious nature of the issue [22]. Mader et al. [14] categorized the risk of developing SANS based on the duration of stay in a microgravity environment. For stays of 3 to 4 months, the risk was 23%. For stays exceeding 6 months, the risk was 48%. Symptoms of SANS can appear even after 2 weeks in space and persist for years after returning to Earth [14,15] Additionally, there is evidence that the symptoms of SANS worsen with each subsequent stay in a microgravity environment [15].

SANS – Pathophysiology and Differentiation

The exact pathophysiological mechanism responsible for SANS is not yet known. The leading theory involves microgravity-induced fluid redistribution in the human body. An indicator of this redistribution towards the head is the enlargement of the cross-sectional area of the jugular vein (by 30–40%). Jugular vein stasis has been documented both during simulated and actual flights [2,5]. Jugular vein stasis leads to cerebral venous congestion. Enlargement of the dural venous sinuses is a characteristic feature of all astronauts suffering from SANS [29]. Subsequently, cerebral venous congestion is further exacerbated due to the shifting of the brain hemispheres towards the cranial vault and the enlargement of the brain

Tab. 1. Comparison of Spaceflight-Related Neuro-Ocular Syndrome (SANS) to Idiopathic Intracranial Hypertension (IIH) based on Lee et al. [2].

Similarities and differences	IIH	SANS
Optic disc swelling	Yes	Yes
Symptoms	Chronic headaches (94%); Transient visual disturbance (68%); Pulsatile noise in the ears	Usually no symptoms other than complaints concerning vision
Is there bilateral swelling?	Approx. 96% bilateral	Differential image, usually right-sided
Intracranial pressure (ICP)	Increased	Some elevated intracranial pressure in post-flight LP, but no convincing evidence that increased ICP is the main etiology
Body structure	Obesity in more than 90%	From standard to athletic
Radiological results	Distinct fluid shift forward in the subarachnoid space, optic nerve sheath, eyeball flattening, empty sella, venous sinus narrowing without thrombosis	Increased fluid in the orbital subarachnoid space and optic nerve sheath, eyeball flattening, brain shift towards the cranial vault, limited evidence of venous sinus abnormalities
Features of the retina	Anterior displacement of Bruch's membrane opening. 5:1; Retinal folds appear first	Posterior displacement of Bruch's membrane opening. 1:5; Choroidal folds appear first
Fold pattern	Typically concentric around the optic nerve head	Typically linear

ventricles [1]. Since the absorption of cerebrospinal fluid (CSF) depends on the pressure gradient between the cerebrospinal and venous compartments, cerebral venous congestion reduces CSF flow, thereby increasing intracranial pressure (ICP). SANS should not be considered a variant of idiopathic intracranial hypertension (IIH). First, SANS does not present with the headaches, tinnitus, or double vision characteristic of IIH [10]. Secondly, in SANS, choroidal folds are much more frequent than in IIH (60% compared to 1-10%), and changes in refraction are also more common [1]. Thirdly, the soft exudates—"cotton wool spots"—visible on the retina in SANS, do not occur in IIH [10]. Fourthly, the optic disc swelling in IIH is usually bilateral and symmetrical (90-97%) [11]. Fifthly, the subarachnoid space (SAS) of the optic nerve is more expanded in SANS than in IIH, and the eyeball is more flattened [10]. While the optic disc swelling in IIH may primarily result from increased ICP, in SANS, increased ICP and changes in the CSF outflow pathways within the optic nerve likely interact to cause optic disc swelling [10]. Anatomically, the SAS of the optic nerve becomes a cul-de-sac at the back of the eye. Due to the microgravity-induced displacement of CSF volume towards the head, it is unlikely that the CSF already in the orbital space can reverse its flow direction from the optic nerve SAS towards the intracranial SAS. Additionally, the microgravity-induced fluid shift towards the head may disrupt the function of the optic nerve's orbital lymphatic drainage systems, potentially resulting in lymphatic stasis [14]. Both factors can impede CSF outflow from the optic nerve SAS. An alternative outflow pathway could be the expulsion of CSF from the optic nerve SAS into the paravascular glymphatic pathway within the optic nerve [21,38]. In astronauts, the decrease or inversion of the typical transluminal pressure gradient (calculated by subtracting ICP from intraocular pressure (IOP)), resulting from increased ICP, may further promote paravascular CSF flow into the eye, while inhibiting the posterior paravascular fluid outflow from the eye [37]. Table 1 shows the key differences between SANS and IIH.

Reilly et al. [27] suggest another element of the pathomechanism that may lead to SANS. They argue that the primary cause of SANS in astronauts is orbital fat edema, which arises from the non-physiological distribution of body fluids in a microgravity environment. This edema leads to compression of blood vessels, lymphatics, the optic nerve, and the eyeball, resulting in the characteristic SANS features: eyeball flattening, optic nerve swelling, choroidal congestion, and retinal ischemia [27]. Additionally, the computer model used by the authors showed slight exophthalmos, which has not been reported in patients with SANS. According to the authors, it may have been easily overlooked during a physical examination [27]. They do not entirely rule out the role of elevated ICP, which they believe may synergistically contribute to the occurrence of SANS.

Furthermore, ICP measured in six ISS crew members, according to Lee et al. [12], was too low to solely explain the visible symptoms of SANS. This may support another local mechanism suggested by Zwart et al. [39]. They claim that SANS is partly caused by genetic predispositions to one-carbon pathway dysfunctions, resulting in local vitamin B deficiencies and oxidative stress leading to endothelial dysfunction [39]. Malfunctioning endothelium leads to blocked CSF drainage, causing local compartmentalization and elevated ICP, leading to SANS. Additionally, they highlight the possible role of elevated CO2 levels in the air, high-sodium diets, cosmic radiation, and non-physiological cellular responses to testosterone and insulin. Their hypothesis that local processes cause SANS is supported by reports of CSF com-

partmentalization in the SAS of the intraorbital part of the optic nerve [6–8,11]. This would explain the possibility of SANS occurring even in individuals with ICP within the normal range and the absence of symptoms characteristic of IIH. Differences in the degree of optic disc swelling between the eyes of the same person could then be explained by the different spatial structures of the SAS, leading to greater or lesser patency of the SAS. In summary, the pathophysiology of SANS is undoubtedly complex, and further research is necessary to determine the specific cause. It is highly unlikely that elevated ICP is the sole etiological factor.

SANS – Diagnosis and Prevention

To diagnose SANS, the following methods are used: magnetic resonance imaging (MRI) of the skull, orbital ultrasonography (USG), optical coherence tomography (OCT) of the fundus, fundus photography, visual field testing, and refraction testing [10,11,13]. Attempts to correlate CSF pressure measured by lumbar puncture with SANS symptoms have produced inconclusive results [11]. It is possible to develop SANS without significant elevation of ICP. Furthermore, Wåhlin et al. [34] demonstrated that the average length of the optic nerve increased by 0.80 mm ($P< 0.001$) in astronauts. This is primarily due to the displacement of the optic nerve head and is significantly associated with mission length, pre-flight body mass, and severity of SANS symptoms. Currently, there is no gold standard for diagnosis, and each method has its own advantages and limitations. It is important to note that diagnostic methods on the ISS are constrained compared to Earth conditions due to limited storage space on the station and the maximum allowable weight for individual shipments to the ISS. Currently available diagnostic methods for SANS on the ISS include: OCT, Amsler grid, refraction testing, and subjective visual quality surveys [11,35].

OCT is very effective in detecting optic disc swelling, thickening of the optic nerve fibers, and choroidal and retinal folds. However, it is not effective in detecting refractive changes. Until recently, it was not available on the ISS. It is now one of the primary diagnostic tools for SANS [11].

Fundus photography is moderately effective in detecting choroidal and retinal folds and is very effective and specific in detecting retinal ischemia and visible cotton wool spots or hard exudates [11]. Vyas et al. [33] developed the "Subclinical Vascular Pathology Index," a biomarker that assesses potential subclinical microvascular damage and risk of SANS based on changes in retinal vascular patterns following prolonged exposure to microgravity. The higher the index, the greater the likelihood of microvascular damage and SANS occurrence [33]. Despite this, fundus photography is less effective in diagnosing optic disc swelling and does not detect other SANS symptoms [11].

Among the remaining methods, MRI is highly sensitive to eyeball flattening. Although MRI has high sensitivity to eyeball flattening, it has very low sensitivity for detecting optic disc swelling [11]. Ultrasonography (USG) has high sensitivity for assessing the length of the eyeball and thus for evaluating refractive errors [11]. However, USG is not effective in diagnosing other SANS symptoms. Visual field testing may indirectly indicate the presence of optic disc swelling but does not provide direct diagnostic information [11].

Waisberg et al. [35] suggest expanding diagnostic methods to include Dynamic Visual Acuity (DVA) and Contrast Sensitivity (CS). DVA is the ability to see moving objects, which is crucial in the spaceflight environment. It has been shown that 24 hours after returning from a prolonged space mission, astronauts had significantly reduced DVA [35]. Current research focuses on assessing DVA using head-mounted devices to evaluate astronauts' visual quality [35]. It has also been shown that disturbances in CS in the peripheral visual field without affecting the central part of the visual field are significantly more common in patients with IIH and may be helpful in differentiating SANS [35].

Effective prevention requires an understanding of the pathomechanism. For SANS, based on available knowledge, pharmacological prophylaxis is suggested to modulate the one-carbon pathway [18,19,24,29,31], mechanical prophylaxis using suits that create negative pressure in the lower part of the body [20,26,36], and swim goggles to improve the translaminar pressure gradient (the difference between ICP and IOP) [11]. Preliminary findings from NASA's simulation studies indicate that the use of pressure cuffs on the thighs of participants during sleep in the -6° head-down position does not effectively prevent SANS [28]. Additionally, passive head elevation in astronauts' "beds" is likely an effective method for preventing SANS, though further research is needed [30].

Other Ocular Disorders Induced by Spaceflight

Dry Eye Syndrome (DES) is observed in 30% of the ISS crew [3]. The previously mentioned shift of body fluids toward the head and the resulting increased intraocular pressure (IOP) and intracranial pressure (ICP) affect the shape and volume of the

tear film, blinking frequency, tear drainage, and the condition of the eye surface. The atmosphere inside the ISS also increases the risk of tear film evaporation and surface eye inflammation. This increased risk is due to the strong airflow from continuous ventilation, relatively low air humidity at 60%, and elevated CO2 levels in the air [3]. Additionally, astronauts work extensively in front of screens and are exposed to artificial lighting throughout the day. Diagnosing tear film disorders in space is challenging due to the complexity, invisibility, and small volume of the tear film. Limited diagnostic and therapeutic tools are available on the ISS. Potential treatment options in space include neurostimulation, blinking exercises, heating, Meibomian gland massage, and cleaning around the eyes. Moisturizing drops are not suitable for treating dry eye syndrome in space for several reasons. They are difficult to use in microgravity because they cannot be "dropped" into the eye but must be "sucked" in using surface tension forces. This can potentially contaminate the bottle with microorganisms from the eye surface and surrounding tissues. They also occupy considerable space and have a limited shelf life, which is impractical for long-duration space missions [3].

Cortical Cataract is another spaceflight-induced ocular disorder [4]. Cosmic radiation, which astronauts are exposed to during long-duration space missions, is considered one of the main causes of cataract formation in space. Cucinotta et al. [4] reported that cataract occurs in 13.6% of crew members who participated in a study with a 30-year observation period called "Lifetime Surveillance of Astronaut Health" (LSAH). The authors estimated an average induction period of 5–10 years post-spaceflight and identified a cumulative effect of repeated space missions. In a 5-year NASA study on cataract in astronauts (NASCA), it was found that the incidence of cortical cataract was significantly higher among exposed astronauts [4]. The authors identified a dose-dependent relationship between exposure to galactic cosmic rays and posterior subcapsular opacities, but no correlation was found between cosmic radiation and nuclear cataract. The risk of cataract development is higher with exposure to high doses of radiation (over 8 mSv), and the incidence increases among astronauts who participated in lunar missions [4].

CONCLUSION

SANS is undoubtedly the most severe and prevalent ocular condition associated with spaceflight. Adequate prevention and treatment will be essential for long-term human presence in space and on the Moon. Further research and technological solutions to this medical issue are an integral part of the future of space exploration. Other conditions, such as cataracts or dry eye syndrome, do not pose as significant a challenge due to established treatment or prevention methods. However, more effective solutions are undoubtedly needed for both symptomatic and causal treatment of dry eye syndrome in space.

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