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REVIEW ARTICLE

Space flight-associated neuro-ocular syndrome (SANS)

Andrew G Lee[1,2,3,4,5,6] · Thomas H Mader[7] · C Robert Gibson[8] · Tyson J Brunstetter[9] · William J Tarver[10]

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Abstract

Interesting novel and somewhat perplexing physiologic and pathologic neuro-ocular findings have been documented in astronauts during and after long duration space flight (LDSF). These findings collectively have been termed the "space flight-associated neuro-ocular syndrome" (SANS). The National Aeronautics and Space Administration (NASA) in the United States has meticulously and prospectively documented the clinical, ultrasound, optical coherence tomography imaging, and radiographic findings of SANS including unilateral and bilateral optic disc edema, globe flattening, choroidal and retinal folds, hyperopic refractive error shifts, and nerve fiber layer infarcts (i.e., cotton wool spots). NASA and collaborating researchers continue to study SANS in preparation for future manned missions to space, including continued trips to the ISS, a return to the moon, or perhaps new voyages to the asteroid belt, or the planet, Mars.

Introduction

Specific neuro-ocular findings have been documented over the past decade in astronauts during and after long duration space flight (LDSF). This spectrum of novel and unusual neuro-ocular findings has been termed the "space flight-associated neuro-ocular syndrome" (SANS). The National Aeronautics and Space Administration (NASA) has meticulously and prospectively documented the findings of SANS in astronauts. The clinical findings of SANS include unilateral or bilateral optic disc edema of variable Frisen grades, globe flattening (GF), choroidal and retinal folds, hyperopic refractive error shifts, and nerve fiber layer infarcts (i.e., cotton wool spots). These clinical findings of SANS correlate with interesting structural changes on both ocular and orbital imaging studies. Although magnetic resonance imaging (MRI) is not available on the International Space Station (ISS), terrestrial orbital and cranial MRI and in flight (on ISS) and terrestrial ultrasound studies, as well as ocular optical coherence tomography (OCT), are used routinely [1–3].

In 2011, Mader et al. first described the key clinical and imaging findings in astronauts after long duration space flight on the ISS. Seven astronauts had complete eye examinations before and after their ISS missions, including cycloplegic and/or manifest refractions and fundus photography. Six astronauts had post-mission OCT and orbital/cranial MRI, and four astronauts had lumbar punctures (LP). Optic disc edema was noted in five, globe flattening in five, choroidal folds in five, nerve fiber layer infarcts in three, nerve fiber layer thickening in six, and decreased near vision (hyperopic shift) in six. Five of these six-affected astronauts experienced a hyperopic shift varying between +0.50 D to +1.75 D. These five affected cases showed globe flattening (axial shortening) on orbital MRI and orbital ultrasound. Lumbar punctures were performed in four individuals (total $n = 5$, as one individual received two LPs). These LPs documented elevated opening pressures (OP) of 22 cm of water at return +66 days (R + 66), 21 at

✉ Andrew G Lee
aglee@houstonmethodist.org

1 Department of Ophthalmology, Houston Methodist Hospital, Houston, TX, USA
2 Baylor College of Medicine, Houston, TX, USA
3 Departments of Ophthalmology, Neurology, and Neurosurgery, Weill Cornell Medical College, New York, NY, USA
4 Department of Ophthalmology, The University of Texas Medical Branch, Galveston, TX, USA
5 Department of Ophthalmology, The University of Iowa Hospitals and Clinics, Iowa City, IA, USA
6 UT MD Anderson Cancer Center Houston, TX, USA
7 US Army, Cooper Landing, Alaska, USA
8 Coastal Eye Associates, Webster, TX, USA
9 US Navy, NASA Johnson Space Center, Houston, TX, USA
10 Clinical Services, NASA Johnson Space Center, Houston, TX, USA

Table 1 Differences between terrestrial idiopathic intracranial hypertension (IIH) and space flight associated neuro-ocular syndrome (SANS)

	IIH	SANS
Typical and classic symptoms of increased intracranial pressure (e.g., chronic headache, pulse synchronous tinnitus, or diplopia) [1]	Commonly present	Absent (although mild headache is common and believed to be space-adaptation related)
Risk factors	Typically obese, young females. May have had exposure to medications that can produce elevated ICP (e.g., tetracyclines, vitamin A analogs, corticosteroids, lithium, etc.)	Non-obese, middle-aged males (female astronaut sample size is too small to make a firm conclusion on risk based upon gender). No exposure to medications that cause elevated ICP
Signs of increased intracranial pressure (e.g., bilateral papilledema, non-localizing sixth nerve palsy; sometimes-choroidal folds and hyperopic shifts)	Bilateral papilledema common and non-localizing sixth nerve palsy relatively common. Choroidal folds less common, often running circumferentially around optic nerve head. Retinal folds typically occur prior to choroidal folds	Often asymmetric disc swelling (OD >OS). No sixth nerve palsy cases. Choroidal folds common, often presenting in a linear pattern. Retinal folds occurring only in presence of significant choroidal folds
Retinal cotton wool spots (CWS)	Retinal CWS are not typically seen in terrestrial IIH (although they can be seen on or around the optic discs in papilledema)	Retinal CWS are relatively prominent features
Orbital ultrasonography, OCT, MRI and CT scan findings of posterior GF and CSF enlargement of the subarachnoid space (SAS) [3–5, 8, 10, 42]	Relatively common	Very common

R + 19, 28 at R + 12, and 28.5 cm H_2O at R + 57. All of these visual changes have been correctable to 20/20 vision, but residual refractive error changes have persisted in some cases for several years after LDSF [1–4].

Idiopathic intracranial hypertension (IIH) has been the closest terrestrial analog to SANS. Table 1 summarizes the differences, however, between IIH on earth and SANS in space [1–12].

Although SANS was initially termed the visual impairment and intracranial pressure (VIIP) syndrome, it remains unclear whether the optic disc edema (variable Frisen scale and often asymmetric) represents true papilledema (i.e., optic disc edema due to increased ICP). In addition, many of the ocular findings are difficult to attribute to elevated ICP (e.g., disproportionate presence of choroidal folds, marked asymmetry or unilaterality, and retinal CWS). In addition, the LP opening pressures to date (albeit performed days to weeks after return to Earth) have been borderline elevated. Compartmentalization of CSF has been proposed [13–16] in terrestrial cases of asymmetric or unilateral papilledema from increased intracranial pressure, and we (AGL) and others (personal communication from Anthony Arnold, MD) have also seen this phenomenon in compressive lesions of the optic canal or the optic nerve sheath (e.g., meningioma). Some authors hypothesize that SANS-related compartmentalization of CSF within the orbital SAS, with locally elevated sheath pressures rather than elevated ICP alone may help to explain the optic disc edema observed [1, 2, 4, 5].

Since the end of the NASA space shuttle program, astronauts currently use the Russian Soyuz spacecraft for launch to the ISS and return to Earth. The return includes a deceleration of more than +4.0 G and a hard, parachute-assisted landing in Kazakhstan in the former Union of Soviet Socialist Republics (USSR). Landing in Kazakhstan creates unique political, operational, and logistical barriers to performing an expedited and safe LP in returning astronauts. More rapid and direct transportation to Houston TX, USA currently provides a better window of opportunity for performing LPs after return from the ISS and for measuring true ICP values closer in time to the actual return.

Microgravity studies have documented that cerebral arterial diameter and blood flow velocity are autoregulated and do not change significantly during space flight [17, 18]. Microgravity fluid shifts have been documented to cause jugular vein distension [19–22] and mild thickening of the retinal nerve fiber layer of the optic nerve (via OCT). These same OCT changes have also been seen in head-down bed rest studies (the terrestrial analog for the cephalad fluid shift in microgravity). The possible role of lymphatics and the venous system in SANS however remains ill defined, but have sparked additional debate and hypotheses [13–16, 23–30].

OCT, both on ISS and on return to Earth, has demonstrated more widespread than previously believed (based on clinical exams alone) choroidal expansion that may also at least partially account for the hyperopic shift and the choroidal folds. OCT angiography (OCTA), which was not available previously, has demonstrated excellent potential for studying retinal and choroidal disease on Earth and appears promising for the examination of returning astronauts. Additional OCT capability including enhanced depth imaging (EDI) OCT and OCTA might thus be useful in further defining the structural changes seen to date with OCT. The cephalad fluid shift has been hypothesized to produce venous congestion in the neck and head that might lead to elevated vortex vein pressures [31–34] and perhaps decreased choroidal drainage and stagnation or pooling of blood in the choroid. Choroidal expansion has been documented during head-down tilt and transient microgravity studies [31–35]. We anticipate documenting these choroidal volume changes in a more detailed and quantitative manner with newer OCT technology [36–38].

In summary, strange and novel neuro-ocular findings have been documented in astronauts during and after LDSF. The space flight-associated neuro-ocular syndrome (i.e., SANS) is a topic of vigorous debate and some controversy, but remains under intensive prospective study by NASA. Although a single unifying predominant mechanism has yet to be proven [1, 2, 4, 5, 36–41] and a multifactorial pathogenesis may still be possible, the cephalad and orbital fluid shifts and the changes in ICP remain the current areas of most concentrated study. Understanding the possible mechanisms for SANS (and potentially developing preventive or counter measures before or during space flight) will be helpful as NASA in the United States and its international partners in space travel prepare for even longer duration space flight missions including return trips to the ISS or the moon, visits to the asteroid belt, or a potential manned mission to Mars.

Disclaimer

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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