

# Space Flight–Associated Neuro-ocular Syndrome

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New and unique physiologic and pathologic systemic and neuro-ocular responses have been documented in astronauts during and after long-duration space flight. Although the precise cause remains unknown, *space flight–associated neuro-ocular syndrome* (SANS) has been adopted as an appropriate descriptive term. The Space Medicine Operations Division of the US National Aeronautics and Space Administration (NASA) has documented the variable occurrence of SANS in astronauts returning from long-duration space flight on the International Space Station. These clinical findings have included unilateral and bilateral optic disc edema, globe flattening, choroidal and retinal folds, hyperopic refractive error shifts, and nerve fiber layer infarcts. The clinical findings of SANS have been correlated with structural changes on intraorbital and intracranial magnetic resonance imaging and in-flight and terrestrial ultrasonographic studies and ocular optical coherence tomography. Further study of SANS is ongoing for consideration of future manned missions to space, including a return trip to the moon or Mars.

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**N**ovel and unique physiologic and pathologic systemic and neuro-ocular responses have been documented in astronauts during and after long-duration space flight. Although the precise cause of these unusual neuro-ocular findings is unknown, the term *space flight–associated neuro-ocular syndrome* (SANS) may be an appropriate designation. The Space Medicine Operations Division of the US National Aeronautics and Space Administration (NASA) has documented the variable occurrence of SANS in astronauts returning from long-duration space flight on the International Space Station. The clinical findings include unilateral and bilateral optic disc edema, globe flattening, choroidal and retinal folds, hyperopic refractive error shifts, and nerve fiber layer infarcts. These clinical findings of SANS have been correlated with structural changes on terrestrial intraorbital and intracranial magnetic resonance imaging and in-flight and terrestrial ultrasonographic studies and ocular optical coherence tomography (OCT).<sup>1-3</sup>

In 2011, Mader et al<sup>1</sup> described the historical, clinical, and imaging findings in the initial affected astronaut cohort (n = 7). All 7 astronauts underwent complete eye examinations before and after their International Space Station mission, including cycloplegic and/or manifest refractions and fundus photography. Six astronauts underwent postmission OCT and orbital and cranial magnetic resonance imaging, and 4 underwent lumbar puncture (LP). After 6 months of long-duration space flight, the 7 astronauts had the following ophthalmic findings: optic disc edema (n = 5), globe flattening (n = 5), choroidal folds (n = 5), nerve fiber layer infarcts (n = 3), thickening within the nerve fiber layer on OCT (n = 6), and decreased near vision (n = 6). Five of the 6 astronauts with decreased near vision had a hyperopic shift of +0.50 diopters (D) or greater spherical equivalent refraction in 1 or both eyes (range, +0.50 to +1.75 D) from premission to postmission evaluations. These 5 affected astronauts also showed a structural correlate of globe flattening (axial hyperopic shortening) on orbital magnetic resonance

imaging and ultrasonographic imaging. Lumbar puncture (4 individuals) documented postmission opening pressures of 22 cm H<sub>2</sub>O at 66 days, 21 cm H<sub>2</sub>O at 19 days, 28 cm H<sub>2</sub>O at 12 days, and 28.5 cm H<sub>2</sub>O at 57 days. A postflight survey of nearly 300 astronauts revealed that subjective vision changes were commonly observed during space flight. Approximately 7% of short-duration shuttle crewmembers reported on-orbit decreased distant visual acuity and 23% reported decreased near visual acuity, whereas 12% of long-duration International Space Station crewmembers reported on-orbit decreased distant visual acuity and 48% reported decreased near visual acuity. Although all visual changes have been correctable to 20/20, some residual refractive error changes have persisted as long as several years after long-duration space flight.<sup>1-4</sup>

Although some similarities between the clinical and imaging findings in SANS and terrestrial idiopathic intracranial hypertension (IIH) were noted, interesting differences occurred.<sup>1-12</sup> First, astronauts with SANS did not report the typical and classic symptoms of terrestrial IIH (eg, chronic headache, pulse synchronous tinnitus, or diplopia).<sup>1</sup> Although some astronauts have reported mild headaches during space flight, these headaches have not been attributed to possible elevated intracranial pressure owing to differences with terrestrial descriptions of the headache of IIH. Instead these headaches have been attributed to other causes, such as space adaptation syndrome, which is beyond the scope of this article. Second, none of the astronauts had any typical risk factors for terrestrial IIH. None were obese or taking any medications that can produce elevated intracranial pressure (eg, tetracyclines, vitamin A analogues, corticosteroids, or lithium). Third, although choroidal folds and hyperopic shifts are sometimes seen in terrestrial IIH, these findings seem to occur disproportionately in SANS. Fourth, retinal cotton-wool spots are not seen in terrestrial IIH (although they can be seen on or around the optic discs) but are a relatively prominent feature in SANS. Fifth, in contrast to the unilateral or markedly asymmetric findings in SANS,

most terrestrial IHH-related papilledema is bilateral and symmetric.<sup>4</sup> Sixth, the orbital ultrasonography, OCT, magnetic resonance imaging, and computed tomographic scan findings of posterior globe flattening and cerebrospinal fluid enlargement of the subarachnoid space appear to be more prominent in SANS than in terrestrial IHH.<sup>3-5,8,10,13</sup>

Although these findings after long-duration space flight were initially referred to as the *visual impairment intracranial pressure syndrome*, whether these findings consistently represent true papilledema remains unclear. As described above, predominantly borderline elevation of LP opening pressures (albeit performed days to weeks after return to Earth) have thus far been measured. Space flight-induced compartmentalization of cerebrospinal fluid in the orbital subarachnoid space with locally elevated cerebrospinal fluid sheath pressures has been proposed as an additional alternate hypothesis that may account for these findings.<sup>1,2,4,5</sup>

Since the end of the US space shuttle program, NASA astronauts have had to make the launch from and return to Earth from the International Space Station via the Russian Soyuz spacecraft with a hard landing in Kazakhstan. In the past, the return from Kazakhstan created political and operational logistical delays for measuring intracranial pressure in US astronauts. More direct transportation and more rapid (24-48 hours) return to Houston, Texas, however, provides a better window of opportunity in the future for measuring intracranial pressure.

Head-down and microgravity studies have documented that cerebral arterial diameter and blood flow velocity are autoregulated and do not change significantly during space flight,<sup>14,15</sup> but micro-

gravity fluid shifts have been documented to cause jugular vein distension and mild OCT thickening of the retinal nerve fiber layer of the optic nerve.<sup>16-19</sup> The possible role of lymphatics and the venous system in SANS, however, remains ill defined.<sup>20-31</sup>

Newer and more detailed analysis of the choroid with OCT on-board the International Space Station has detected choroidal expansion, which we believe may at least partially account for the hyperopic shift and the choroidal folds. Optical coherence tomographic angiography has not been performed to date, but future OCT modalities, including enhanced depth imaging OCT and OCT angiography, might be useful in further defining the structural changes seen with OCT. One additional hypothesis has been that cephalad fluid shift could produce venous congestion in the neck and head that might lead to elevated vortex vein pressures<sup>32-35</sup> and perhaps decreased choroidal drainage and stagnation or pooling of blood in the choroid.

## Conclusions

Unusual and novel neuro-ophthalmic findings have been documented in astronauts during and after long-duration space flight. This syndrome, SANS, remains under intensive study by NASA, and a single unifying predominant mechanism has yet to be proven.<sup>1,2,4,5,35-38</sup> Understanding and possibly treating SANS with specific preflight, in-flight, or postflight countermeasures may be necessary as the United States prepares for a return to even longer-duration space flight missions, including return trips to the International Space Station, the moon, or the asteroid belt or a future human mission to Mars.

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