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Commentary

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# Exploring the role of intraocular pressure fluctuation in the development of spaceflight associated neuro-ocular syndrome

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## Abstract

Spaceflight associated neuro-ocular syndrome (SANS) is a mission-critical limitation of long-duration spaceflight. The syndrome is comprised of globe flattening, hyperopic shifts, chorioretinal folds, optic disc edema, and cotton-wool spots; however, not every astronaut develops this pathology. Here, we present a hypothesis regarding one potential mechanism, intraocular pressure fluctuations, for the pathophysiology of the development of SANS. Further, we suggest ways in which this mechanism can be tested terrestrially.

## Commentary

One of the critical roadblocks to a successful deep space mission is the phenomenon of spaceflight associated neuro-ocular syndrome, or SANS [1]. Some of the main features of the syndrome, explored in the landmark paper by Mader et. al. in 2011, include flattening of the posterior globe, symmetric and asymmetric optic disc edema, choroidal folds and changes in vision resulting in worsening farsightedness [2]. Their foundational work proposed three possible explanations for these findings: elevated intracranial pressure, local factors at the intraorbital optic nerve, and ocular hypotony. To date, there are essentially two prevailing theories to explain the underlying physiology of SANS: elevated intracranial pressure or compartmentalization of cerebrospinal fluid within the optic nerve sheath [3]. There are strengths and weaknesses to both of these theories. In addition to these two major hypotheses, we argue that one of the original hypotheses, ocular hypotony, warrants revisiting and further consideration as a plausible mechanism contributing to the development of SANS.

As enumerated in the article from Lee et. al., features of spaceflight-associated neuro-ocular syndrome include bilateral optic disc edema, globe flattening, choroidal and retinal folds, hyperopic refractive error shifts, and cotton wool spots [3]. Nearly all of these findings can be attributed to the well-described terrestrial disease of ocular hypotony [4]. This might be a more obvious culprit for SANS if the underlying mechanisms were more intuitive. As it stands, however, the connection between intraocular pressure, intracranial pressure, and central venous pressure in microgravity remain to be elucidated. Furthermore, measurements of intraocular pressure (IOP) during spaceflight have actually shown an *increase* of anywhere from 5-13 mmHg within the first day in space, after which there is a return to baseline after 4 days [5]. Therefore, if hypotony is the underlying, or even a contributing, cause of the features of SANS, there is perhaps a *relative* hypotony rather than the conventional definition of hypotony.

Another finding in the spaceflight literature also supports the relative hypotony theory. It has been shown that there is a paradoxical decreased central venous pressure during spaceflight [6-9]. Assuming no disruption to the normal venous drainage pathways of the globe, we would expect that a decrease in central venous pressure (CVP) would also reflect decreased pressure in the episcleral veins and therefore increased outflow of aqueous humor. However, this assumption is countered by theories that the cephalic fluid shift induced by microgravity would elevate episcleral venous pressure [5]. As with most of the pathophysiology of SANS, this relationship warrants further explanation and clarification. The technology that allows frequent and highly precise measurements of intraocular pressure before, during, and after spaceflight would be monumental in clarifying the relationship between the IOP and clinical manifestations of SANS. Indeed, matching precise and accurate eye pressures during spaceflight with more frequent retinal and optic nerve imaging may provide valuable insight to the development and progression of this phenomenon.

It seems to us that during zero gravity, the transmission of changes between the central venous pressure and the episcleral pressure, with the expected significant fluctuation in the intraocular pressure, plays a major role in explaining this syndrome. The relationship between the central venous pressure, episcleral venous pressure, intraocular pressure, and intracranial pressure is complex and difficult, if not impossible, to study in a real-time, zero gravity situation over a lengthy period of time. The most practical way to study this hypothesis may be to observe either the development or mitigation of SANS when the transmission of fluctuations between the central venous pressure and the episcleral venous pressure are minimized or even abolished. We suggest that one way to accomplish this would be the placement of a 360-degree encircling scleral buckle post-equatorially to cause

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pressure on the vortex veins as they exit the sclera. Because the anatomy of the ocular venous drainage system is well-characterized, placing the buckle in the correct position could be done with relative ease. However, current technology does not allow for real-time adjustment of the circumference of the buckle. Furthermore, there is no indication for scleral buckle placement on healthy human subjects. As such, experimentation in animal models may be warranted to determine if this procedure can minimize the interplay between central venous pressure, episcleral venous pressure, and (by extension) intraocular pressure for the purpose of investigational studies. Another potential experimental design to test the IOP fluctuation hypothesis might include simulated space conditions (i.e. head down tilt) in terrestrial volunteers who have already undergone scleral buckling for other conditions such as retinal detachment.

While generally safe, scleral buckling has been associated with intraoperative complications, postoperative diplopia, and pain [10]. Choroidal blood flow following these procedures can be reduced and take several months to return to baseline [11]. Visual outcomes can be complicated by myopia secondary to axial length increases. However, this procedure is relatively simple and safe, making it a candidate for research in those having already undergone the procedure or in animal experimentation.

Other researchers have endeavored to show that deliberately elevating intraocular pressure might be a useful preventive measure for counteracting the effects of spaceflight-associated neuro-ocular syndrome [12,13]. However, elevation of IOP can have devastating effects, including the development of glaucoma [14]. In contrast, our proposed method of scleral buckling has a different endpoint: namely, the reduction of pressure fluctuations between IOP, CVP, and episcleral venous pressure when exposed to microgravity. While subjecting healthy astronauts to a prophylactic scleral buckle procedure is not warranted, we propose this as an investigational means to help clarify the etiology of SANS. We reiterate that the role of hypotony, if even a relative hypotony, in SANS pathophysiology warrants further exploration. Finding practical ways to mitigate the effects of spaceflight-associated neuro-ocular syndrome is critical for future missions to deep space, including Mars.

## Competing interests

The Authors declare no Competing Financial or Non-Financial Interests

## Author contributions

MAH: Alternative hypothesis to prevailing theories, concept for future experimental countermeasures

MBW: Background information and research, technical writing

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