

Symptoms and Countermeasures for Spaceflight-Associated Neuro-Ocular Syndrome (SANS)

By Samarth Kumar

Abstract

Spaceflight Associated Neuro-Ocular Syndrome (SANS) is currently a big topic of research for scientists. The effect of SANS can cause optical disturbances and be risky for astronauts in space for a long period of time. There are many potential causes of SANS, with popular theories involving Intracranial pressure (ICP). This paper gives an overview of SANS, provides potential countermeasures for prolonged space travel, and delves into further areas of research that still need to be done.

Introduction

SANS is a problem that can occur for astronauts after a prolonged time spent in space. It has a wide range of effects, and its symptoms can occur to different degrees for individuals (Stenger et al. 2017). Currently, about 96% of ISS crew members experience some level of SANS (NASA) Long Term Surveillance of Astronaut Health n.d). Symptoms can start in space and continue even after coming back to Earth, symptoms may start within 3 weeks of microgravity exposure (Mader et al.). Most International Space Station (ISS) crew members go into six-month missions with only a handful going into missions lasting around a year (Lee et al.).

Symptoms of SANS

Symptoms of SANS tend to impair one's vision. A common occurrence is choroidal folds occurring in the eye (Shen et al.). This means an astronaut can have retinal folds in his posterior pole or peripheral retina of the eye (Shen et al.). These folds can also potentially lead to other orbital or ocular diseases including scleritis, tumors, and hypotony. While in space with limited medical resources, it should be important to minimize the risk of disease for astronauts. SANS may also lead to cotton wool spots in the eye which can lead to vision loss and make an astronaut more susceptible to diabetes, mellitus, systemic hypertension, and a handful of other diseases that could potentially compromise a mission (Ioannides et al.). SANS can be split into four thresholds depending on symptom severity ranging from mild to advanced, currently about 72% of ISS crew members are at the first threshold (mild) which has mild but reversible effects. Symptoms such as vision loss and headaches fade away within a couple of months of arriving on Earth (Lee et al.). It is important that some changes in the eye caused by SANS can be prevalent years after returning to Earth, these include choroidal folds and globe flattening. 18% of crew members reach the 2nd threshold (moderate) where the symptoms are a bit more clinically concerning but shouldn't have a big impact on the astronaut's long-term health or the mission. 6% reach the 3rd threshold (severe) which can mean acute impact on the astronaut's health and ability to function in space. For now, no cases have had an impact on long-term vision health (advanced). However, it is important to note that an extended time in microgravity may lead to a more severe level of SANS, something that is a growing concern for physicians and scientists. (NASA Long Term Surveillance of Astronaut Health).

Why does SANS occur?

To understand why SANS occurs there are some important terms you need to know. Intracranial pressure (ICP) is a measurement of pressure in your skull. Intraocular pressure (IOP) is the measurement of the fluid pressure in one's eye. These two can interact with each other and their difference (IOP-ICP) is called the translaminar pressure difference (TLPD) (Shen et al.).

So how does ICP interact with IOP? A healthy eye needs balance with a stable IOP and ICP level but space travel can lead to changes in pressure in the skull. The exact mechanisms of IOP and ICP's effects on SANS are unknown but experiments conducted on mice can show us certain effects caused by pressure changes in the head. Specifically, results from a recent study in 2020 by Shen *et al.* demonstrated that when both IOP and ICP were increased the mice did not show signs of scotopic vision (object visibility) loss that we see in SANS, instead, there was a loss of photopic contrast sensitivity (vision that helps see color). A prevalent symptom of SANS is loss of scotopic vision. This shows that increasing IOP and ICP at the same time may cause problems but likely won't cause SANS, instead, it is the imbalance between the two that leads to vision loss. This can be seen by the higher likelihood of a loss of scotopic contrast sensitivity loss when TLPD is increased as well as a more significant loss of contrast sensitivity (Shen et al.).

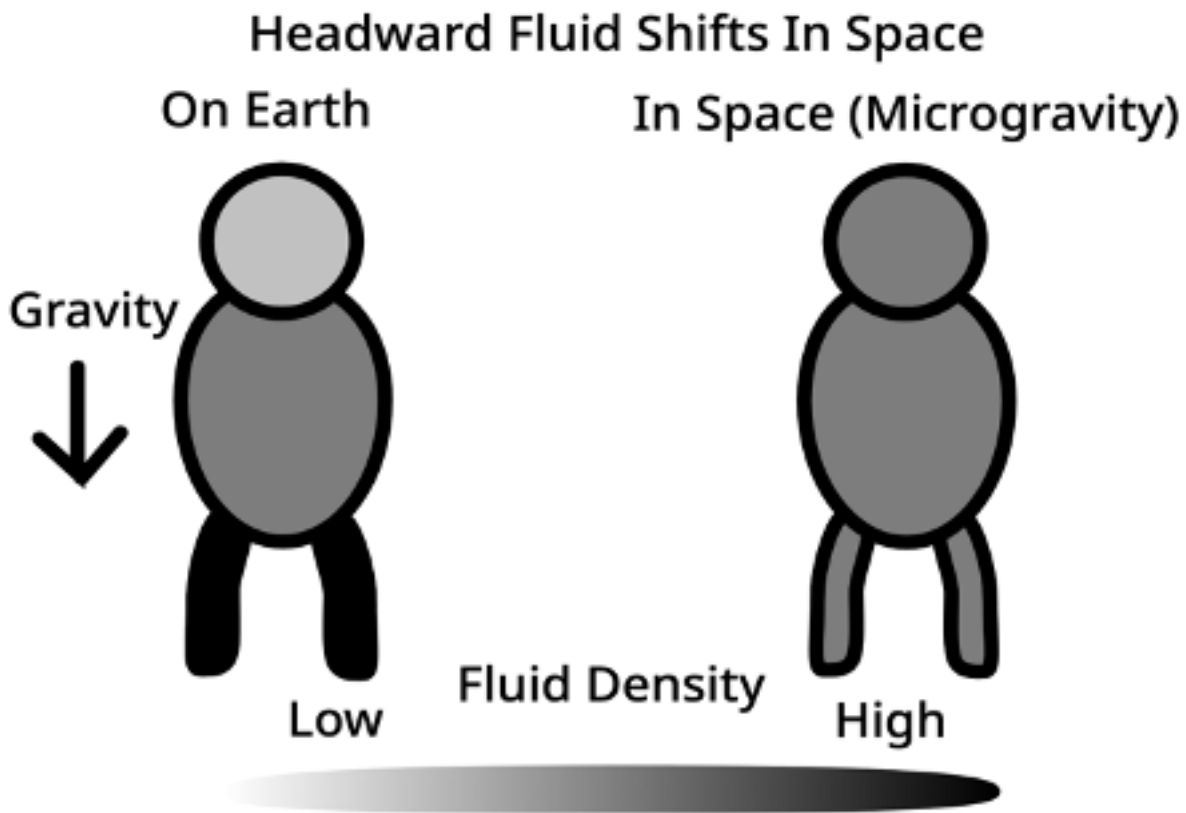


Figure 1: Showing distribution of bodily fluids after an extended period of time in space.

Why does going into space lead to changes in TLPD? This is a topic that's up for debate and one that's still being researched today. A common theory for why this occurs is headward fluid shifts (Figure 1) (Marshall-Goebel et al.). Scientists assume that a long period spent in microgravity can lead to blood and other bodily fluids rising into the skull (Marshall-Goebel et al.). A lack of gravity to pull these fluids down could potentially lead to a buildup in the head which could mean increased intracranial pressure at a rate that is faster than the rate of increase for intraocular pressure. Since TLPD is the difference between these two, a disproportionate increase could lead to a change in TLPD contributing to the development of SANS. The increase of fluid in the head could put stress on the eyeball leading to globe flattening as the eye is pushed outward away from the skull, something that can cause changes in vision (Figure 2) (Mader et al.).

Globe Flattening in Space Due to Headward Fluid Shifts

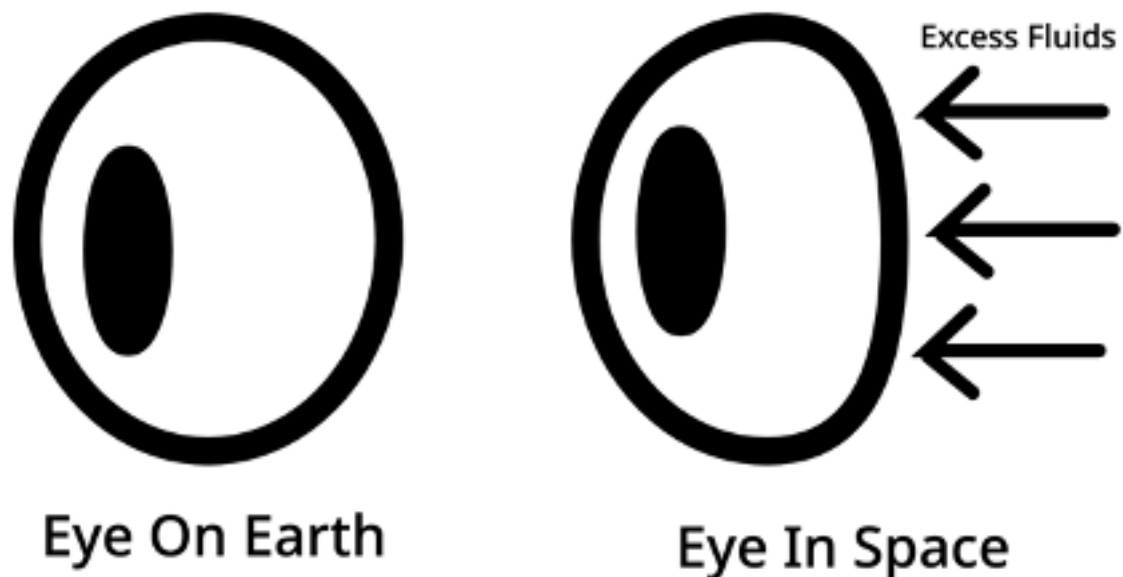


Figure 2: Diagram of changes in eye shape due to headward fluid shifts (globe flattening).

Other potential causes of SANS include cytotoxic oedema which hypothesizes that an inflammatory stress pathway mechanism might lead to SANS. The choroidal expansion that occurs in an eye upon reaching a microgravity environment may be another reason. Similar to the headward fluid shift theory, fluid shifts would increase IOP and this increased pressure on the eye could lead to globe flattening (Galdamez et al.).

While SANS may be less problematic for short duration missions, scientists are not sure how it will affect astronauts on long duration missions away from Earth. In addition, Martian gravity is 38% of Earth's gravity while lunar gravity is about 17% of Earth's gravity (Broome). A big

question is if Martian and lunar gravity will help alleviate the symptoms caused by SANS. It's important to find a solution to this problem before planning Mars or other distant missions. Symptoms like visual impairment or ocular disease in space can hinder crew members and could potentially compromise a mission, making it a high-priority risk for NASA's proposed Mars missions (Human Research Roadmap). For example, if a crew member specializing in medical assistance has visual impairment it could make it difficult for the crew to respond to a medical emergency. Additionally, if the pilot suffers from visual impairment, it could make it difficult to take manual control of the spaceship and land it on Mars, causing the mission to be potentially unsuccessful.

Potential Countermeasures for SANS Development

Currently, there aren't any working countermeasures to SANS that scientists are confident in. Many ideas have been proposed for potential countermeasures but there isn't comprehensive data to back their efficiency. There's still a lot of testing and research to be done when it comes to SANS countermeasures to make a proper decision on what works best. This section overviews potential countermeasures that can be used to mitigate the effects of SANS.

Lower body negative pressure (LBNP) is a technique that redistributes blood in one's body, specifically by bringing more blood down to the legs and lower body area (Crystal and Salem). Since a likely reason SANS occurs is fluid shifts in the body, LBNP can be a way to simulate gravity on Earth while an astronaut is in space. On Earth, most fluids in the body are pulled down towards the legs due to gravity but in a microgravity environment, these fluids will become more evenly spread out in the body and therefore accumulate in the head, something that can cause globe flattening. While LBNP may not completely simulate gravity, its effects can play a role in reducing the change in TLPD, something commonly associated with SANS. Ways of making LBNP easily accessible in space are currently being researched, one popular idea is integrating a LBNP device into wearable trousers (Bird; Ashari and Hargens).

Another potential countermeasure would be swimming or equinox balance goggles. Equinox balance goggles work by making a vacuum around the eye which can help normalize pressure (Berdahl). Lowering this pressure can help bring TLPD levels back to normal. This can help prevent potential optical diseases from occurring while in space. The effectiveness of the solution can be debatable though, there still needs to be research done on how much of an effect these goggles have on IOP and ICP (both important when calculating TLPD) (Shen et al.). There have been promising studies though such as one run by Scott et. al, which showed that swimming goggles when combined with exercise can increase IOP (Scott et al.). If goggles do turn out to be an effective countermeasure, they can be cost-effective and easy to implement.

Thigh Cuffs, which are circular straps that go around the thigh and can be tightened, are another countermeasure that should be considered. Thigh cuffs serve a similar purpose as LBNP, they both work to stop the headward fluid shifts that occur during space travel. Thigh cuffs could be used to constrict blood vessels which can slow or even block the flow of fluids. Since fluids have a harder time circulating, they won't be able to build up in the head and cause a change in pressure. Poor blood circulation can have other potential side effects on the body though (Cleveland Clinic). Astronauts may experience muscle pain, numbness, and tingling

sensations. A 5 day study run by Robin et. all showed that most astronauts didn't feel too much discomfort after use of thigh cuffs, but long-term use may provide different results (Robin et al.). While thigh cuffs may seem like a cost-effective and easy-to-implement solution, when compared to LBNP the potential side effects that could occur just don't seem to outweigh the benefits. Thigh cuffs are something that should have further research on it because a feasible way to implement them could save a lot of time and money on long space missions.

Conclusion

Out of all the countermeasures, the best option is LBNP. For one, there has already been a lot of research around LBNP (found in head-down tilt studies) compared to the equinox balance goggles and thigh cuffs. LBNP as a countermeasure would likely produce promising results when it comes to preventing SANS on longer-term spaceflight missions. The biggest drawback to LBNP is figuring out how it should be implemented. As mentioned above, NASA is working to make compact LBNP pressure devices for astronauts and people are also looking at implementing LBNP into wearable trousers (Bird; Ashari and Hargens). Examining the effectiveness of LBNP devices as well as researching potential side effects are big areas of research that should continue to be done to mitigate the risk of SANS on long spaceflight missions. It's also important to note the side effects of LBNP which can include hypotension, decreased heart rate and dizziness (Goswami et al.).

Swimming goggles would be a cheap and easy to implement solution for SANS as a study found promising results on the effects of exercise and swimming goggles on intraocular pressure. 20 healthy men were used for the study in which some exercised with goggles while others exercised without swimming goggles. The exercise decreased IOP, and then when swimming goggles were worn it subsequently increased it (Scott et al.). If a proper exercise regimen is established with the addition of swimming goggles the difference between ICP and IOP can potentially be decreased leading to lower TLPD and countering SANS. The main problem lies in the fact that not enough research has been done on these effects. Research needs to be done on if the change in IOP is significant enough to produce noticeable results. Also, side effects of the goggles would also need to be researched.

Thigh cuffs are another cheap and easy solution. The problem with thigh cuffs lies in the amount of side effects that result from their use. A study run by Robin et al. showed promising results when it came to a solution using both LBNP and thigh cuffs (Robin et al.). For one, the tolerance for LBNP with or without thigh cuffs remained about the same. There was also a decrease in fluid shifts when thigh cuffs were used. While the subjects felt discomfort on the first day of utilizing this solution, a couple days into the study many of the symptoms were alleviated. Thigh cuffs were only applied intermittently during this study. Limiting the use of thigh cuffs to make sure discomfort doesn't get out of control and astronauts don't experience other potentially dangerous side effects is also an important part of this solution. So, while thigh cuffs may work, especially alongside the use of LBNP more research needs to be done on a way to implement this solution in a safe and effective manner.

More research is needed to better understand the underlying biological mechanisms of SANS development and its potential effects when astronauts are exposed to extended periods of microgravity. These countermeasures listed need further examination. Importantly, we aren't

quite sure why SANS occurs at different magnitudes for different people. We also need to research why symptoms of SANS don't occur at all for others. Determining factors that could make SANS more likely or more harmful could be an important step when analyzing potential countermeasures for SANS.

Acknowledgments

Thanks to my advisor Hannah Gustafson and the Polygence research program for assisting in the making of this paper.

Works Cited

- Ashari, Neeki, and Alan R. Hargens. "The Mobile Lower Body Negative Pressure Gravity Suit for Long-Duration Spaceflight." *Frontiers in Physiology*, vol. 11, 2020, p. 977, <https://doi.org/10.3389/fphys.2020.00977>.
- Berdahl, John. "Equinox Balance Goggles: The Effects of Local Orbital Pressure Changes on Intraocular Pressure." *National Space Biomedical Research Institute*, [http://nsbri.org/index.html?p=21972.html#:~:text=The%20Balance%20Goggles%20function%20Oby,and%20intraocular%20pressure%20\(VIIP\)](http://nsbri.org/index.html?p=21972.html#:~:text=The%20Balance%20Goggles%20function%20Oby,and%20intraocular%20pressure%20(VIIP)). Accessed 20 July 2023.
- Bird, Elizabeth. *Compact Flexible Lower Body Negative Pressure Device for Integrated Exercise Microgravity and Fluid Shift Countermeasure*. 4 Sept. 2018, https://www.nasa.gov/directorates/spacetech/strg/nstrf_2018/Compact_Flexible_Lower_Body_Negative_Pressure_Device/.
- Broome, Kate. "What Is The Gravity On Mars Vs. Moon Vs. Earth." *Science Trends*, 12 Dec. 2017, <https://sciencetrends.com/gravity-mars-vs-moon-vs-earth/#:~:text=Kate%20Broome&text=We%20all%20know%20that%20gravity,17%20percent%20of%20Earth's%20gravity>.
- Cleveland Clinic. "Poor Circulation." *Cleveland Clinic*, <https://my.clevelandclinic.org/health/diseases/21882-poor-circulation#:~:text=How%20does%20poor%20circulation%20affect,%2C%20fingers%2C%20feet%20and%20toes>. Accessed 13 Aug. 2023.
- Crystal, George J., and M. Ramez Salem. "Lower Body Negative Pressure: Historical Perspective, Research Findings, and Clinical Applications." *Journal of Anesthesia History*, vol. 1, no. 2, Apr. 2015, pp. 49–54, <https://doi.org/10.1016/j.janh.2015.02.005>.
- Galdamez, Laura A., et al. "Origins of Cerebral Edema: Implications for Spaceflight-Associated Neuro-Ocular Syndrome." *Journal of Neuro-Ophthalmology*, vol. 40, no. 1, 2020, https://journals.lww.com/jneuro-ophthalmology/Fulltext/2020/03000/Origins_of_Cerebral_Edema__Implications_for.12.aspx.
- Goswami, Nandu, et al. "Lower Body Negative Pressure: Physiological Effects, Applications, and Implementation." *Physiological Reviews*, vol. 99, no. 1, Jan. 2019, pp. 807–51, <https://doi.org/10.1152/physrev.00006.2018>.
- Human Research Roadmap. "Risk Of Spaceflight Associated Neuro-Ocular Syndrome (SANS)." *Human Research Roadmap*, 15 Aug. 2022, <https://humanresearchroadmap.nasa.gov/risks/risk.aspx?i=105>.
- Ioannides, Antonis, et al. "Isolated Cotton-Wool Spots of Unknown Etiology: Management and Sequential Spectral Domain Optical Coherence Tomography Documentation." *Clinical Ophthalmology (Auckland, N.Z.)*, vol. 5, 2011, pp. 1431–33, <https://doi.org/10.2147/OPHTH.S16272>.

-
- Lee, Andrew G., et al. "Spaceflight Associated Neuro-Ocular Syndrome (SANS) and the Neuro-Ophthalmologic Effects of Microgravity: A Review and an Update." *Npj Microgravity*, vol. 6, no. 1, Feb. 2020, p. 7, <https://doi.org/10.1038/s41526-020-0097-9>.
- Mader, Thomas H., et al. "Optic Disc Edema, Globe Flattening, Choroidal Folds, and Hyperopic Shifts Observed in Astronauts after Long-Duration Space Flight." *Ophthalmology*, vol. 118, no. 10, Oct. 2011, pp. 2058–69, <https://doi.org/10.1016/j.ophtha.2011.06.021>.
- Marshall-Goebel, Karina, et al. "Mechanical Countermeasures to Headward Fluid Shifts." *Journal of Applied Physiology (Bethesda, Md. : 1985)*, vol. 130, no. 6, June 2021, pp. 1766–77, <https://doi.org/10.1152/jappphysiol.00863.2020>.
- Robin, Adrien, et al. "DI-5-CUFFS: Venoconstrictive Thigh Cuffs Limit Body Fluid Changes but Not Orthostatic Intolerance Induced by a 5-Day Dry Immersion." *Frontiers in Physiology*, vol. 11, 2020, p. 383, <https://doi.org/10.3389/fphys.2020.00383>.
- Scott, Jessica M., et al. "Association of Exercise and Swimming Goggles With Modulation of Cerebro-Ocular Hemodynamics and Pressures in a Model of Spaceflight-Associated Neuro-Ocular Syndrome." *JAMA Ophthalmology*, vol. 137, no. 6, June 2019, pp. 652–59, <https://doi.org/10.1001/jamaophthalmol.2019.0459>.
- Shen, Guofu, et al. "Modeling a Potential SANS Countermeasure by Experimental Manipulation of the Translaminar Pressure Difference in Mice." *NPJ Microgravity*, vol. 6, 2020, p. 19, <https://doi.org/10.1038/s41526-020-00109-5>.