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OPHTHALMIC CHANGES IN ASTRONAUTS: A CURRENT UNDERSTANDING

Finn Cogswell [1]

[1] The University of Melbourne, Parkville, Victoria 3052, Australia

finncogswell_44@hotmail.com

Summary: This paper provides a brief review of the literature on ophthalmic abnormalities commonly experienced by astronauts, and introduces issues that they present for future spaceflight. Together known as the Spaceflight-Associated Neuro-Ocular Syndrome (SANS), these changes in ocular structure and visual function have been widely reported in astronauts both during and following long-duration spaceflights. With several such spaceflights planned for the near future, extensive research is taking place to further understand the aetiologies of SANS so that ophthalmic complications in astronauts may be mitigated.

Keywords: Ocular structure; visual function; astronauts; long-duration spaceflight; Spaceflight-Associated Neuro-Ocular Syndrome.

INTRODUCTION

While several significant physiological changes occur in astronauts due to microgravity, the Spaceflight-Associated Neuro-Ocular Syndrome (SANS) occurring in astronauts during long-duration (>30 days) spaceflights is one of the most significant clinical issues for humans in microgravity, and is considered by NASA to be a top risk for deep space travel. [(1)]. This syndrome encompasses several structural and functional ophthalmic abnormalities experienced by astronauts, including hyperopic shift in vision, optic disc oedema, posterior globe fattening, optic nerve sheath distension, cotton-wool spots and choroidal folds. [(2)]. Through the history of spaceflight, as mission durations have increased, so have reports of vision and ocular structure changes in astronauts. [(5)]. As nearly half of NASA astronauts during and following long-duration spaceflights have reported vision abnormalities, it is a common phenomenon among astronauts, and some even sustain permanent visual impairment upon return. [(1-3, 5)]. However, despite considerable ongoing research into their aetiologies, these ophthalmic abnormalities remain incompletely understood. [(2, 5)].

Within the next decade, NASA intends to establish a permanent human presence on the Moon, and SpaceX plans to send manned missions to Mars. These upcoming missions will require humans to spend durations in microgravity that far exceed those of any previously completed manned spaceflights. Exposure to microgravity induces many changes in the human body, and generally, the severity of these changes relates to the duration of the spaceflight. [(3)]. The current data for the impact of microgravity on human vision is limited to durations in space of approximately a year; thus, it is unknown how ophthalmic changes may progress beyond a year in space, despite the durations of upcoming missions being expected to far exceed a year. As astronauts' vision is critical to the safety and success of any mission, a thorough understanding of these ocular issues is essential to ensuring the safety and success of future long-duration spaceflights. [(1, 5)].

SPACEFLIGHT-ASSOCIATED NEURO-OCULAR SYNDROME (SANS)

Vision changes during and following spaceflight have been reported by astronauts for decades, and were initially attributed to a hyperopic shift related to the age of astronauts. [1]. As these reports of vision changes accumulated, subsequent investigations revealed a common syndrome of ocular changes in astronauts, more common among those who had spent long durations in space. [2]. The only symptom that these astronauts experienced was a degradation in visual acuity; however, underlying this were several structural ocular changes. [1, 5]. Other than the hyperopic shift in vision, these changes in SANS consist of globe flattening, choroidal folds, cotton wool spots, optic disc oedema, and optic nerve sheath distention. Currently, the precise pathophysiologic mechanisms behind SANS are not fully understood, but several possible explanations have been hypothesized.

PROBLEMS WITH THE ELEVATED ICP HYPOTHESIS

As ICP has never been measured in microgravity, there is no evidence for an increase in ICP during spaceflight. [1, 6]. While it is theorized that raised ICP due to microgravity-induced cephalad fluid shift is the primary causative factor of SANS, it is unlikely to be the sole contributor to the syndrome. [5]. The main evidence against elevated ICP being the universal cause of SANS arises from the symptoms in astronauts with SANS, which differ to those in people with a known ICP elevation. [1, 4, 5].

The best terrestrial analog of SANS is Idiopathic Intracranial Hypertension (IIH), which is an elevated ICP without any known cause, and IIH patients present with ophthalmic changes similar to those in SANS. [2]. The ocular changes seen in SANS, including optic nerve sheath distention, optic disc oedema, choroidal folds and globe flattening, are all similarly seen in IIH. [2]. However, IIH also presents with chronic headaches, nausea, vomiting, transient vision loss and diplopia, all of which are absent in SANS. [1]. Additionally, the cotton wool spots featured in SANS are not commonly associated with raised ICP. [1]. The striking differences between IIH and SANS suggest a multifactorial pathophysiology, as opposed to SANS being due to elevated ICP alone. [4].

ELEVATED INTRACRANIAL PRESSURE HYPOTHESIS FOR SANS PATHOGENESIS

In the literature, it is agreed that a suspected raised intracranial pressure (ICP), caused by fluid redistribution towards the head when humans are exposed to microgravity, is most likely a large contributor to the syndrome. [1, 2, 4, 5]. According to this hypothesis, when fluid redistributes in this manner, known as a cephalad fluid shift, it causes venous congestion in the cerebral and eye circulation, with a subsequent rise in venous pressure. Previous research has illustrated that the jugular vein distends in microgravity due to this fluid shift, suggesting that cerebral venous congestion may occur in microgravity. [1]. As cerebrospinal fluid (CSF) efflux relies on the pressure difference between itself and the venous circulation, this rise in venous pressure reduces the pressure gradient, acting to reduce CSF efflux. The resulting CSF accumulation in the head, as well as the venous congestion in the cerebral and eye vasculature, combine to increase ICP. [2]. The ocular changes in SANS are all potential signs of elevated ICP.

The subarachnoid space continues along the optic nerve within the optic nerve sheath, which then extends into the posterior globe of the eye, seen as the optic disc on the retinal surface. Thus, when CSF accumulates in the intracranial subarachnoid space as proposed in the mechanism previously mentioned, it will also accumulate in the perioptic subarachnoid space, thereby increasing Intraocular subarachnoid pressure. This causes the optic nerve sheath to distend. [1, 2]. It is thought that the distention of the optic nerve sheath compresses the optic nerve fibers, impeding their venous drainage and axoplasmic flow, resulting in oedema of the optic disc. The elevated pressure in the sheath is thought to exert a force onto the posterior globe of the eye, causing indentation and thus, flattening of the eye globe. [1, 2].

Due to cephalad fluid shift in microgravity, the venous pressure of the head's vasculature increases. This is theorized to cause a rise in pressure of the vortex veins, which are responsible for draining the choroid layer of the eye, a layer of blood vessels which lack the ability to autoregulate. [1]. Subsequently, blood accumulates in the choroid due to poor venous outflow, causing it to expand. [1, 2]. The engorgement of these vessels in the choroid induces choroidal folds. [1].

The combination of globe flattening, optic disc oedema and choroidal expansion are thought to shorten the distance between the retina and the lens, thus causing the degradation in visual acuity, which is the sole symptom of SANS. [1].

Cotton Wool Spots, the final feature of SANS, are thought to be accumulations of neural cytoplasmic debris, caused by obstructions to axoplasmic flow along the optic nerve. [2]. It is theorized that these form due to the distention of the optic nerve sheath, which causes ischaemia to the nerves. The resulting ischaemia reduces axonal transport, causes axons to swell, and damages the nerve fibers. However, it should be noted that cotton wool spots are not a common feature of raised ICP. [2].

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ADDITIONAL HYPOTHESES FOR SANS PATHOGENESIS

As a result of the notable differences between SANS and IIH, other potential local contributing factors to the development of SANS have been proposed. It has been hypothesized that the perioptic subarachnoid space may compartmentalize in microgravity, leading to elevated CSF pressures within the optic nerve sheath, thus causing optic nerve sheath distention and subsequent optic disc oedema, globe flattening, and hyperopic shift. [2, 6-8]. This is thought to occur due to microgravity-induced venous and lymphatic stasis, combined with anatomical variations in the connection between the perioptic and intracranial subarachnoid spaces, causing less CSF to be absorbed in the perioptic subarachnoid space, thus accumulating and increasing pressure. [7, 8]. This hypothesis, suggesting a local rise in perioptic subarachnoid space pressure independent from a rise in ICP, is supported by the fact that the ocular changes in SANS are typically asymmetrical, with one eye more affected than the other. [9].

An important metabolic pathway in the human body, 1-Carbon metabolism, has been implicated with SANS. Zwart et al. have investigated the 1-Carbon metabolic pathway's connection to SANS, as it was discovered that astronauts who experience ophthalmic abnormalities in spaceflight have alterations in this metabolic pathway compared to those who don't experience ocular abnormalities. [9, 10]. These researchers then revealed that SANS-affected astronauts had certain variations in genes coding for enzymes in this 1-Carbon pathway. Abnormalities in the 1-Carbon metabolism enzymes may cause B-Vitamin insufficiency in tissues, which could lead to depletion of antioxidants and thus, oxidative stress and endothelial dysfunction. [10]. The resulting endothelial dysfunction, amplified by cephalad fluid shift, is hypothesized to cause leakage from blood vessels resulting in oedema, which can subsequently impair CSF efflux. [10]. As a result, CSF accumulates and pressure increases in the perioptic subarachnoid space, impinging the optic nerve and pressing on the eye globe, causing globe flattening and the resulting hyperopic shift. [10]. This process can occur with or without an increase in ICP.

Other research has indicated the possible implication of microgravity-induced changes in translaminar pressure, which is the difference between intraocular pressure (IOP) and intracranial pressure. The pressure difference between IOP and ICP is important for maintaining eye shape and thus, visual function. It is known that upon prolonged exposure to microgravity, IOP decreases. [2, 3]. This decrease in IOP, coupled with a suspected increase in ICP in microgravity, may result in a decreased translaminar pressure gradient, which can lead to optic disc oedema and visual impairment. [3, 4].

DISCUSSION

There are multiple hypotheses that have been proposed to explain the pathogenesis of Spaceflight-Associated Neuro-Ocular Syndrome. While the exact mechanism is still not fully understood, SANS is likely the product of a combination of factors. It is likely that an elevation in intracranial pressure, secondary to fluid redistribution in the absence of gravity, occurs in astronauts in space, and contributes to SANS. To elucidate the exact pathophysiological mechanism driving SANS, extensive future research will likely occur both terrestrially and in microgravity. This syndrome's impacts on human vision and eye structures beyond a year in space are unknown, and with many long-duration missions anticipated in the future, ensuring the safety of astronauts' vision for these missions is essential. Elucidating the mechanism of SANS is critical to mission success, as the importance of an astronaut's vision cannot be understated.

As not all astronauts experience SANS, it is important to elucidate risk factors which predispose individuals to the visual disturbances in SANS. Once risk factors have been identified, more rigorous astronaut selection can identify those at high risk of experiencing visual impairment in microgravity. Additionally, investigations into suitable countermeasures against ophthalmic alterations should also continue. These, in turn, can increase the likelihood of mission success by mitigating the possibility of ophthalmic complications during future long-duration spaceflights.

CONCLUSION

Many hypotheses exist to explain the ophthalmic alterations experienced by some humans when in space, and further research is required to confirm the exact pathophysiological mechanism. With large, long-duration spaceflights planned within the next decade, understanding this Spaceflight-Induced Neuro-Ocular Syndrome is of the upmost importance in order to preserve the health of astronauts and mitigate mission risk.

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