The “Ocular Glymphatic System”: An Important Missing Piece in the Puzzle of Optic Disc Edema in Astronauts?

We read with great interest the article by Mathieu et al. entitled “Evidence for Cerebrospinal Fluid Entry Into the Optic Nerve via a Glymphatic Pathway,” recently published in Investigative Ophthalmology & Visual Science. The authors provided the first evidence of cerebrospinal fluid (CSF) entry via paravascular spaces into the orbital optic nerve in mice and concluded that this pathway may be highly relevant to optic nerve diseases, including glaucoma. We fully agree with this notion, and we believe that the “ocular glymphatic system” may also play a key role in the development of optic disc edema in astronauts.

Ophthalmic abnormalities including optic disc edema, globe flattening, choroidal and retinal folds, hyperopic refractive error shifts, and nerve fiber layer infarcts have been reported in astronauts returning from long-duration space flight on the International Space Station. Understanding factors contributing to this space flight-associated neuro-ocular syndrome (SANS) is one of the top priorities for the National Aeronautics and Space Administration (NASA), especially in view of future long-duration interplanetary space flight missions, including trips to Mars. Currently, the exact mechanisms causing SANS are unknown. These ophthalmic findings after long-duration space flight were initially referred to as the visual impairment and intracranial pressure (VIIP) syndrome, and a leading hypothesis is that VIIP is caused by elevated intracranial pressure (ICP) resulting from microgravity-induced cephalad fluid shifts leading to venous stasis in the head and neck. This stasis could cause impairment of CSF drainage into the venous system and cerebral venous congestion, both of which could lead to a rise in ICP. The resulting elevated ICP could lead to optic nerve sheath distention, globe flattening, and stasis of axoplasmic flow with optic disc swelling. We believe that the existence of an oculary glymphatic system offers an attractive additional explanation for how microgravity may cause optic disc edema in astronauts.

Evidence from the recent study by Mathieu et al. is supportive of the hypothesis that a paravascular transport system exists within the optic nerve, analogous and likely continuous with the recently discovered glymphatic system in the brain. The authors reported the entry of CSF into the optic nerve via spaces surrounding blood vessels, bordered by astrocytic endfeet. Intriguingly, new research also indicates that the ocular glymphatic system may provide an anatomical basis for posterior fluid outflow from the eye. Indeed, in a PhD thesis defense, Xiaowei Wang demonstrated the existence of the ocular glymphatic system to IIH. Evidence to support this view was recently presented by Denniston et al. who reported the potential relevance of the ocular glymphatic system to IIH.

Peter Wostyn
Peter Paul De Deyn

1Department of Psychiatry, PC Sint-Amandus, Beernem, Belgium; 2Laboratory of Neurochemistry and Behavior, Institute Born-Bunge, University of Antwerp, Department of Biomedical Sciences, Antwerp, Belgium; 3Department of Neurology and Alzheimer Research Center, University of Groningen and University Medical Center Groningen, Groningen, The Netherlands; and the 4Department of Neurology and Memory Clinic, Middelheim General Hospital (ZNA), Antwerp, Belgium.

E-mail: wostyn.peter@skynet.be

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