

Are Generalized Reduced Cerebrospinal Fluid Dynamics and Optic Nerve Sheath Compartmentation Sequential Steps in the Pathogenesis of Normal-Tension Glaucoma? [Letter]

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Dear editor

I read with great enthusiasm the recently published article in Eye and Brain by Pircher et al¹ reporting a higher concentration of lipocalin-type prostaglandin D synthase (L-PGDS) in the perioptic subarachnoid space (SAS) compared to the concentration in the lumbar SAS in a group of normal-tension glaucoma (NTG) patients with optic nerve (ON) sheath compartmentation. I greatly appreciate the tremendous contributions Prof. Killer and his team have made to our understanding of perioptic cerebrospinal fluid (CSF) flow dynamics and their role in glaucoma pathogenesis, and I am grateful to the authors for sharing their new work with the scientific community. I would appreciate the opportunity to comment on their discussion of the L-PGDS levels in the lumbar SAS.

Pircher et al¹ found significantly higher lumbar CSF levels of L-PGDS in their cohort of NTG patients with ON sheath compartmentation when compared to other studies on L-PGDS in healthy subjects. Reference values for L-PGDS concentrations in normal human lumbar CSF are 16.6 ± 3.6 mg/L.² Remarkably, compared with these normal values, the mean L-PGDS concentration in the lumbar CSF was significantly elevated in their group of NTG patients (24 ± 8 mg/L).¹ This finding is consistent with a hypothesis previously proposed by my colleagues and me, according to which NTG, in at least some cases, may result from CSF circulatory dysfunction.³ We speculated that changes in the CSF circulation and the subsequent decrease in overall CSF turnover could ultimately result in reduced neurotoxin clearance in the SAS surrounding the ON and lead to ON sheath compartmentation.³ Indeed, it is conceivable that the reduced neurotoxin clearance along the ONs might have an influence on meningo-endothelial cells, eventually leading to increased proliferation and CSF compartmentation.³ The accumulation of biologically active molecules in this blocked ON compartment might further produce a toxic effect on the ON and lead to glaucomatous damage.⁴ According to the above hypothesis, generalized reduced CSF dynamics and ON sheath compartmentation could then be seen as sequential steps involved in the development of NTG.³ To assess whether there

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is evidence in support of this hypothesis, in our 2013 paper, we proposed that L-PGDS concentrations in lumbar CSF could be compared between NTG patients and control subjects.³ A significantly higher lumbar CSF L-PGDS concentration in NTG patients compared with controls would add support to our hypothesis of CSF circulatory failure, given the reported increase of L-PGDS concentration in lumbar CSF in case of decreasing CSF flow rate.³

Obviously, further studies are needed to elucidate whether changes in the CSF circulatory system may play a role in the pathogenesis of NTG. If confirmed, disruptions in CSF flow during aging, and neurological diseases involving impaired CSF dynamics would be expected to predispose individuals to the development of NTG. Some cases of NTG might then actually be the expression of generalized impaired CSF dynamics in natural brain aging and CNS diseases such as Alzheimer's disease (AD). In this respect, it is interesting to note that several studies demonstrated a positive association between NTG and AD.⁵

Disclosure

The author reports no conflicts of interest in this communication.

References

1. Pircher A, Neutzner A, Montali M, et al. Lipocalin-type prostaglandin D synthase concentration gradients in the cerebrospinal fluid in normal-tension glaucoma patients with optic nerve sheath compartmentation. *Eye Brain*. 2021;13:89–97. doi:10.2147/EB.S297274
2. Tumani H, Reiber H, Nau R, et al. Beta-trace protein concentration in cerebrospinal fluid is decreased in patients with bacterial meningitis. *Neurosci Lett*. 1998;242(1):5–8. doi:10.1016/S0304-3940(98)00021-4
3. Wostyn P, De Groot V, Van Dam D, Audenaert K, De Deyn PP. Senescent changes in cerebrospinal fluid circulatory physiology and their role in the pathogenesis of normal-tension glaucoma. *Am J Ophthalmol*. 2013;156(1):5–14. doi:10.1016/j.ajo.2013.03.003
4. Killer HE, Jaggi GP, Flammer J, Miller NR. Is open-angle glaucoma caused by impaired cerebrospinal fluid circulation: around the optic nerve? *Clin Exp Ophthalmol*. 2008;36(4):308–311. doi:10.1111/j.1442-9071.2008.01735.x
5. Chen YY, Lai YJ, Yen YF, et al. Association between normal tension glaucoma and the risk of Alzheimer's disease: a nationwide population-based cohort study in Taiwan. *BMJ Open*. 2018;8(11):e022987. doi:10.1136/bmjopen-2018-022987

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