

## A New Look at Glaucoma

Peter Wostyn<sup>1</sup>, MD; Veva De Groot<sup>2</sup>, MD, PhD; Kurt Audenaert<sup>3</sup>, MD, PhD; Peter Paul De Deyn<sup>4,5,6</sup>, MD, PhD

<sup>1</sup>Department of Psychiatry, PC Sint-Amandus, Reigerlostraat 10, 8730 Beernem, Belgium

<sup>2</sup>Department of Ophthalmology, Antwerp University Hospital, Wilrijkstraat 10, 2650 Antwerp, Belgium

<sup>3</sup>Department of Psychiatry, Ghent University Hospital, De Pintelaan 185, 9000 Ghent, Belgium

<sup>4</sup>Department of Biomedical Sciences, Laboratory of Neurochemistry and Behavior, Institute Born-Bunge, University of Antwerp, Universiteitsplein 1, 2610 Antwerp, Belgium

<sup>5</sup>Department of Neurology and Memory Clinic, Middelheim General Hospital (ZNA), Lindendreef 1, 2020 Antwerp, Belgium

<sup>6</sup>Department of Neurology and Alzheimer Research Center, University of Groningen and University Medical Center Groningen, Hanzeplein 1, 9700 RB Groningen, The Netherlands

*J Ophthalmic Vis Res* 2015; 10 (4): 502-503.

Dear Editor,

We read with great interest the paper by Jain and Aref<sup>[1]</sup> entitled "Senile Dementia and Glaucoma: Evidence for a Common Link" published recently in *Journal of Ophthalmic and Vision Research*. We are grateful to the authors for sharing their valuable review article with the scientific community, and we would appreciate the opportunity to provide an additional viewpoint about a possible common clearance pathway linking Alzheimer's disease (AD) and glaucoma.

Although the potential link between glaucoma and AD is intriguing, the basis for this association remains elusive, despite many years of intensive research. Nevertheless, further elucidation of a common pathophysiological process linking both diseases might offer new perspectives for the development of novel diagnostic and therapeutic strategies for both disorders. As discussed by the authors,<sup>[1]</sup> our group proposed low intracranial pressure (ICP) occurring in AD as a factor leading to the increased risk of glaucoma. Indeed, the lower ICP reported in AD patients could play a role in the pathogenesis of glaucoma by exerting a higher pressure difference across the lamina cribrosa influencing the physiology and pathophysiology of the optic nerve head, and/or through its association with cerebrospinal fluid (CSF) circulatory failure ultimately resulting in reduced neurotoxin clearance along the optic nerve.<sup>[2,3]</sup> The movement of CSF along the outside of the optic nerve is well known. Furthermore, previous studies investigating the flow of fluids in the anterior part of the optic nerve at least suggest some level of exchange between the interstitial fluid (ISF) of the optic nerve and

the surrounding CSF.<sup>[4]</sup> Interestingly, recent insights into the physiology of CSF circulation may shed new light on the link between AD and glaucoma. In particular, Iliff et al<sup>[5]</sup> have recently proposed the existence of a brain-wide network of paravascular channels, which they termed the 'glymphatic' pathway, along which a large proportion of subarachnoid CSF recirculates through the brain parenchyma, facilitating the clearance of interstitial solutes, including amyloid- $\beta$  (A $\beta$ ), from the brain. One implication is that glymphatic pathway dysfunction may play an important role in the pathogenesis of AD. In light of the key role that the glymphatic pathway may play in the clearance of interstitial solutes and metabolic waste from the brain, this knowledge could be of great importance to our understanding of how solutes are cleared from the ISF in the optic nerve. The observation of such an anatomically distinct clearing system in the optic nerve could provide new insight into the pathogenesis of glaucoma, and introduce a new look at the disease. Indeed, if confirmed, one might expect that a dysfunctional glymphatic system could ultimately result in reduced neurotoxin clearance from the optic nerve and lead to glaucomatous neurodegeneration.<sup>[4]</sup> Moreover, glymphatic pathway dysfunction as a potential mechanistic link between AD and glaucoma is an attractive hypothesis since this could explain the reported comorbidity of the two disorders. Obviously, further studies are needed to determine whether failure of this clearance system may explain the clinical overlap between AD and glaucoma.

### Correspondence to:

Peter Wostyn, MD. Department of Psychiatry, PC Sint-Amandus, Reigerlostraat 10, 8730 Beernem, Belgium.  
E-mail: wostyn.peter@skynet.be

Received: 12-10-2015

Accepted: 28-12-2015

### Financial Support and Sponsorship

Nil.

### Conflicts of Interest

There are no conflicts of interest.

## REFERENCES

1. Jain S, Aref AA. Senile dementia and glaucoma: Evidence for a common link. *J Ophthalmic Vis Res* 2015;10:178-183.
2. Wostyn P, Audenaert K, De Deyn PP. Alzheimer's disease and glaucoma: Is there a causal relationship? *Br J Ophthalmol* 2009;93:1557-1559.
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;156:5-14.e2.
4. Wostyn P, Van Dam D, Audenaert K, Killer HE, De Deyn PP, De Groot V. A new glaucoma hypothesis: A role of glymphatic system dysfunction. *Fluids Barriers CNS* 2015;12:16.
5. Iliff JJ, Wang M, Liao Y, Plogg BA, Peng W, Gundersen GA, et al. A paravascular pathway facilitates CSF flow through the brain parenchyma and the clearance of interstitial solutes, including amyloid  $\beta$ . *Sci Transl Med* 2012;4:147ra111.

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

Access this article online	
<b>Quick Response Code:</b> 	<b>Website:</b> <a href="http://www.jovr.org">www.jovr.org</a>
	<b>DOI:</b> 10.4103/2008-322X.176901

**How to cite this article:** Wostyn P, De Groot V, Audenaert K, De Deyn PP. A new look at glaucoma. *J Ophthalmic Vis Res* 2015;10:502-3.