This item is the archived peer-reviewed author-version of:

The two faces of the translaminar pressure difference : the biomechanical one and the biochemical one

Reference:

Wostyn Peter, De Groot Veva, Van Dam Debby, Audenaert Kurt, Killer Hanspeter Esriel, De Deyn Peter Paul.- The two faces of the translaminar pressure difference : the biomechanical one and the biochemical one
Clinical and experimental optometry - ISSN 0816-4622 - Hoboken, Wiley-blackwell, 100:1(2017), p. 102-103
Full text (Publisher's DOI): <https://doi.org/doi:10.1111/CXO.12494>
To cite this reference: <http://hdl.handle.net/10067/1389440151162165141>

Title page

Title of the article:

The two faces of the translaminar pressure difference: the biomechanical one and the biochemical one.

Running title:

The two faces of the TLCPD

Full names:

Peter Wostyn, MD^{1,*}, Veva De Groot, MD, PhD², Debby Van Dam, PhD^{3,4}, Kurt Audenaert, MD, PhD⁵, Hanspeter Esriel Killer, MD⁶, Peter Paul De Deyn, MD, PhD^{3,4,7}

Affiliations:

¹Department of Psychiatry, PC Sint-Amandus, Beernem, Belgium

²Department of Ophthalmology, Antwerp University Hospital, Antwerp, Belgium

³Laboratory of Neurochemistry and Behavior, Institute Born-Bunge, University of Antwerp, Department of Biomedical Sciences, Antwerp, Belgium

⁴Department of Neurology and Alzheimer Research Center, University of Groningen and University Medical Center Groningen, Groningen, The Netherlands

⁵Department of Psychiatry, Ghent University Hospital, Ghent, Belgium

⁶Department of Ophthalmology, Kantonsspital Aarau, Aarau, Switzerland

⁷Department of Neurology and Memory Clinic, Middelheim General Hospital (ZNA), Antwerp, Belgium

***Corresponding author:**

Peter Wostyn

Department of Psychiatry, PC Sint-Amandus, Reigerlostraat 10, 8730 Beernem, Belgium

Phone: 32-472713719

Fax: 32-50-819720

E-mail address: wostyn.peter@skynet.be

Financial Support:

None

Conflict of Interest:

None

June 5, 2016

Dear Editor,

We read with great interest the paper recently published in *Clinical and Experimental Optometry* by McMonnies.¹ We are grateful to the author for sharing his valuable review article with the scientific community, and we would appreciate the opportunity to provide an additional viewpoint about the trans-lamina cribrosa pressure difference (TLCPD), that is, the difference of intraocular pressure (IOP) minus intracranial pressure (ICP). As discussed by the author, the TLCPD may be important in pressure-related pathology of the optic nerve (ON) head region. We believe that the TLCPD may also be an index for neurotoxic burden in the anterior part of the ON.

Growing evidence in the literature provides strong support for the concept that cerebrospinal fluid (CSF) pressure and composition in the subarachnoid space surrounding the ON may have fundamental significance in the pathogenesis of glaucoma.^{2,3} Berdahl and colleagues² and others suggested that a lower ICP reported in glaucoma patients could play a role in the pathogenesis of the disease through a higher pressure difference across the lamina cribrosa influencing the physiology and pathophysiology of the ON head. However, Killer and Pircher⁴ challenged the concept of the TLCPD. One of their criticisms was that the retrolaminar pressure is measured during lumbar puncture at a site more than 100 cm away from the lamina cribrosa.⁴ Indeed, given that it is not possible to measure the retrolaminar pressure clinically, the clinical retrospective and prospective studies of CSF pressure in patients with glaucoma took the lumbar CSF pressure measurement as surrogate for pressure in the orbital CSF space.² This assumption, however, is only true if CSF pressure is

homogenous in all CSF spaces. By applying computed tomography cisternography in patients with normal-tension glaucoma (NTG), Killer and colleagues³ demonstrated that CSF does not communicate freely between intracranial subarachnoid space and the subarachnoid space of the ON, and questioned whether the CSF pressure is the same in these two CSF spaces. The authors suggested that the subarachnoid space surrounding the ON may become an isolated CSF compartment under specific pathological conditions, and that NTG may be due to sequestration of CSF within the terminus of the ON subarachnoid space, creating a stagnant region accumulating substances toxic to the adjacent ON head.³

Bringing together the above mechanical and biochemical theories, our group recently proposed that decreased ICP and ON-sheath compartmentation could be seen as sequential steps in the disease process of NTG.⁵ Indeed, given that the lower ICP in NTG patients may result from decreased CSF production, we postulated that this lack of CSF production and the resulting general decline in CSF flow could ultimately result in compartmentation of the subarachnoid space of the ON.⁵ Evidence in support of this viewpoint now comes from a recent dog study by Hou and colleagues.⁶ During CSF shunting from the brain ventricle, the intraventricular ICP gradually decreased in a linear fashion together with the optic nerve subarachnoid space pressure.⁶ But when the ICP fell below a critical breakpoint, optic nerve subarachnoid space pressure remained constant despite further ICP decline.⁶ The authors interpreted this as a sign of CSF communication arrest between the intracranial and ON subarachnoid space.⁶ Indeed, when ICP drops too low, the breakpoint is reached and CSF flow stops.⁶ This means that the ICP is too low for CSF to freely flow through the optic canal.⁶

Here, we raise another point concerning the TLCPD that we believe merits further discussion. From a biomechanical perspective, it must be acknowledged that it is the optic nerve subarachnoid space pressure, and not the ICP, that determines the TLCPD since the optic

nerve subarachnoid space pressure represents the true counter-pressure against the IOP across the lamina cribrosa. Thus, the TLCPD as the difference of IOP minus optic nerve subarachnoid space pressure may reflect the mechanical load to the tissues of the ON head. However, the TLCPD as the difference of IOP minus ICP may reflect the neurotoxic burden in the anterior part of the ON. Indeed, the imbalance between IOP and ICP may reflect the imbalance between production and clearance of neurotoxins. Previous findings at least suggest that high IOP may generate neurotoxins, such as amyloid- β , that could then be cleared via the CSF.⁷ In addition, the dog study by Hou and colleagues⁶ suggests that, if the ICP is too low, CSF flow from the intracranial subarachnoid space into the ON subarachnoid space stops, creating a CSF compartment syndrome. From this point of view, the TLCPD, calculated as the difference of IOP minus ICP, may be considered as an index for neurotoxic burden in the anterior part of the ON. The TLCPD, therefore, may have two faces: a biomechanical one and a biochemical one.

Sincerely yours,

Peter Wostyn, MD

Veva De Groot, MD, PhD

Debby Van Dam, PhD

Kurt Audenaert, MD, PhD

Hanspeter Esriel Killer, MD

Peter Paul De Deyn, MD, PhD

References

1. McMonnies CW. The interaction between intracranial pressure, intraocular pressure and lamina cribrosa compression in glaucoma. Clin Exp Optom 2016
2. Berdahl JP, Allingham RR. Intracranial pressure and glaucoma. Curr Opin Ophthalmol 2010;21:106-111.
3. Killer HE, Miller NR, Flammer J, *et al.* Cerebrospinal fluid exchange in the optic nerve in normal-tension glaucoma. Br J Ophthalmol 2012;96:544-548.
4. Killer HE, Pircher A. What do we really know about translaminal pressure? J Neuroophthalmol 2016;36:112-113.
5. Wostyn P, De Groot V, Van Dam D, *et al.* Senescent changes in cerebrospinal fluid circulatory physiology and their role in the pathogenesis of normal-tension glaucoma. Am J Ophthalmol 2013;156:5-14.
6. Hou R, Zhang Z, Yang D, *et al.* Intracranial pressure (ICP) and optic nerve subarachnoid space pressure (ONSP) correlation in the optic nerve chamber: the Beijing Intracranial and Intraocular Pressure (iCOP) study. Brain Res 2016;1635:201-208.
7. Wostyn P, De Groot V, Van Dam D, *et al.* Glaucoma considered as an imbalance between production and clearance of neurotoxins. Invest Ophthalmol Vis Sci 2014;55:5351-5352.