

University of Groningen

## Intrathecal cerebrospinal fluid infusion as a potential therapeutic strategy for Alzheimer's disease

Wostyn, Peter; Van Dam, Debby; De Deyn, Peter Paul

*Published in:*  
Medical Hypotheses

*DOI:*  
[10.1016/j.mehy.2018.10.020](https://doi.org/10.1016/j.mehy.2018.10.020)

**IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.**

*Document Version*  
Publisher's PDF, also known as Version of record

*Publication date:*  
2019

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*

Wostyn, P., Van Dam, D., & De Deyn, P. P. (2019). Intrathecal cerebrospinal fluid infusion as a potential therapeutic strategy for Alzheimer's disease. *Medical Hypotheses*, 122, 57. <https://doi.org/10.1016/j.mehy.2018.10.020>

### Copyright

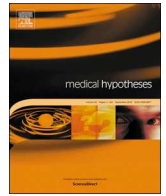
Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

### Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.



## Intrathecal cerebrospinal fluid infusion as a potential therapeutic strategy for Alzheimer's disease



Dear Editor,

We read with great interest the paper by Yin et al. [1]. The authors discuss evidence indicating that aerobic exercise may prevent or delay the occurrence and development of Alzheimer's disease (AD), but note that there are no obvious therapeutic effects in patients in the middle and late stages of AD. They hypothesize that under normal physiological conditions, or in the early stage of AD, aerobic exercise may improve glymphatic clearance by increasing cerebral arterial pulsation, a key driving force for glymphatic flow, and facilitated by aquaporin 4 (AQP4) water channels which are expressed in a highly polarized manner in astrocytic endfeet ensheathing the cerebral vasculature, but that in the mid- or late-stages of AD, loss of AQP4 polarization may destroy these neuroprotective effects. As discussed below, we believe that this hypothesis may also be relevant to another driver of glymphatic transport, intracranial pressure (ICP).

Cerebrospinal fluid (CSF) production has been reported to be decreased in AD patients [2]. In addition, several groups reported a reduction of CSF pressure in AD patients as we reviewed [3,4]. It was shown that these lower CSF pressures in AD patients correspond to lower CSF amyloid- $\beta$ 42 (A $\beta$ 42) concentrations [3]. We hypothesize that one possible explanation for the observed association between CSF pressures and CSF A $\beta$ 42 levels in AD patients could be reduced glymphatic clearance of toxins, such as A $\beta$ , from the interstitial fluid into CSF due to decreased ICP-driven glymphatic transport. We further speculate that infusing artificial CSF into the intrathecal space surrounding the spinal cord or eventually into the cerebral ventricles could represent a new approach for AD treatment through facilitating glymphatic transport via manipulation of ICP. Such CSF pump system should be implanted as early as possible, given that in the mid- or late-stages of AD, loss of AQP4 polarization could destroy the neuroprotective effects of this therapy, as hypothesized to occur with aerobic exercise [1].

### Financial support

No funding to declare.

### Conflict of interest statement

Dr. Peter Wostyn is the inventor of a pending patent application pertaining to Alzheimer's disease treatment using an intrathecal cerebrospinal fluid pump system, filed by P&X Medical NV. The other authors declare no conflicts of interest.

### Authors' contributions

Dr. Peter Wostyn developed the theoretical part of the hypothesis and drafted and wrote the manuscript. Dr. Debby Van Dam and Prof. Dr. Peter Paul De Deyn commented and revised the intellectual content of the manuscript. All authors have read and approved the final version of the manuscript.

### References

- [1] Yin M, Pu T, Wang L, Marshall C, Wu T, Xiao M. Astroglial water channel aquaporin 4-mediated glymphatic clearance function: a determined factor for time-sensitive treatment of aerobic exercise in patients with Alzheimer's disease. *Med Hypotheses* 2018;119:18–21.
- [2] Silverberg GD, Heit G, Huhn S, et al. The cerebrospinal fluid production rate is reduced in dementia of the Alzheimer's type. *Neurology* 2001;57:1763–6.
- [3] Schirinzi T, Di Lazzaro G, Sancesario GM, et al. Levels of amyloid-beta-42 and CSF pressure are directly related in patients with Alzheimer's disease. *J Neural Transm (Vienna)* 2017;124:1621–5.
- [4] Wostyn P, Audenaert K, De Deyn PP. More advanced Alzheimer's disease may be associated with a decrease in cerebrospinal fluid pressure. *Cerebrospinal Fluid Res* 2009;6(14).

Peter Wostyn\*

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

E-mail address: [wostyn.peter@skynet.be](mailto:wostyn.peter@skynet.be)

Debby Van Dam

Department of Biomedical Sciences, Laboratory of Neurochemistry and Behavior, Institute Born-Bunge, University of Antwerp, Universiteitsplein 1, 2610 Antwerp, Belgium

Department of Neurology and Alzheimer Research Center, University of Groningen and University Medical Center Groningen, Hanzplein 1, 9700 RB Groningen, The Netherlands

Peter Paul De Deyn

Department of Biomedical Sciences, Laboratory of Neurochemistry and Behavior, Institute Born-Bunge, University of Antwerp, Universiteitsplein 1, 2610 Antwerp, Belgium

Department of Neurology and Alzheimer Research Center, University of Groningen and University Medical Center Groningen, Hanzplein 1, 9700 RB Groningen, The Netherlands

Department of Neurology and Memory Clinic, Middelheim General Hospital (ZNA), Lindendreef 1, 2020 Antwerp, Belgium

\* Corresponding author.