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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-β42 (Aβ42) concentrations [3]. We hypothesize that one possible explanation for the observed association between CSF pressures and CSF Aβ42 levels in AD patients could be reduced glymphatic clearance of toxins, such as Aβ, 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].

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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.

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