pagepress

ORAL PRESENTATIONS

Probing cerebrospinal fluid mobility for human brain clearance imaging MRI: Water transport across the blood-cerebrospinal fluid barrier and mobility of cerebrospinal fluid in perivascular spaces

Matthias J.P. van Osch,[1,2] Léonie Petitclerc,[1] Lydiane Hirschler[1]

[1]C.J. Gorter MRI center, Department of Radiology, Leiden University Medical Center, Leiden, The Netherlands; [2]Leiden Institute for Brain and Cognition (LIBC), Leiden University, Leiden, The Netherlands

Background

The growing interest in the brain clearance system in the last decade has led to great insights into how waste clearance via perivascular spaces acts like a lymphatic-like system. However, most of these observations have been done in rodent studies, often with invasive techniques. When aiming to understand the human brain clearance system, the main technology has so far relied on intrathecal injections[1] and cerebrospinal fluid (CSF) flow in larger structures like the fourth ventricle[2] or the aqueduct. The availability of non-invasive imaging technology would be an important driver to probe human brain clearance in health and disease.

Methods

When looking at the current knowledge on brain clearance, it is clear that CSF and interstitial fluid (ISF) are the main solvents that propel waste out of the brain. The insight that CSF and ISF mainly consist of water makes magnetic resonance imaging (MRI) an attractive modality, since many possibilities exist to measure cerebral water dynamics, such as transitions between compartments, as well as water flow/diffusion in sub-compartments. MRI does provide excellent opportunities to image CSF/ISF, due to the long T2 of these compared to background tissue. By using long echo-time imaging, MRI sequences can be tuned towards CSF and ISF. This approach is applied both to arterial spin labeling (ASL) MRI to measure water transport across the blood-CSF barrier, as well as to high spatial resolution imaging at 7 tesla MRI to measure CSF mobility in perivascular spaces.

Results

By using ASL that magnetically labels inflowing blood, we could prove that water exchange into CSF is not only taking place in the choroid plexus, but also in the subarachnoid space.[3] We refer to the reference for a complete description of the method and results.[3] The second technique also exploits long echo times to isolate CSF-signal, but combines this with high spatial resolution readouts and motion-sensitizing gradients to allow measurement of the CSF-mobility in the perivascular spaces of penetrating arteries (Figure 1) and *e.g.* the subarachnoid space around the MCA. Retrospective triggering allows studying how the cardiac and respiratory cycle influence the CSF-mobility, *i.e.* the driving forces of propulsion and mixing processes within the perivascular spaces (PVS). Preliminary results show approximately equal contributions from the cardiac and respiratory cycles in smaller PVS.[4]

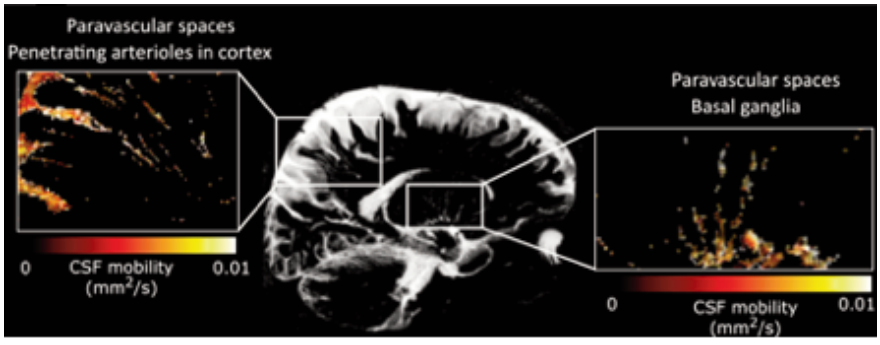

Figure 1. Cerebrospinal fluid mobility measurements in the perivascular spaces in the basal ganglia and in penetrating arteries in the white matter.

Conclusions

The exchange of water between the vascular and CSF compartments does not exclusively happen in the choroid plexus, but also in the subarachnoid arteries along the cortex. CSF mobility is influenced both by cardiac and respiratory cycles in approximately equal contributions in the PVS of penetrating arteries.

References

1. Eide PK, Vinje V, Pripp AH, et al. Sleep deprivation impairs molecular clearance from the human brain. Brain. 2021;144:863-874.
2. Fultz NE, Bonmassar G, Setsompop K, et al. Coupled electrophysiological, hemodynamic, and cerebrospinal fluid oscillations in human sleep. Science. 2019;366:628-631.
3. Petitclerc L, Hirschler L, Wells JA, et al. Ultra-long-TE arterial spin labeling reveals rapid and brain-wide blood-to-CSF water transport in humans. Neuroimage. 2021;245:118755
4. Hirschler L, Runderkamp B, Van Veluw S, et al. Effects of the cardiac and respiratory cycles on CSF-mobility in human subarachnoid and perivascular spaces. Proceedings of the annual meeting of the ISMRM. London; 2022:320.

Correspondence: Matthias J.P. van Osch, C.J. Gorter MRI Center, Department of Radiology, PO Box 9600, 2300, Leiden, The Netherlands. Tel. +31 71 526 3678. Fax: +31 71 5248256. E-mail: m.j.p.van_osch@lumc.nl

Received for publication: 26 September 2022.
Accepted for publication: 14 October 2022.

Veins and Lymphatics 2022; 11:10942
doi:10.4081/vl.2022.10942