Association of MRI Indices of Glymphatic System With Amyloid Deposition and Cognition in Mild Cognitive Impairment and Alzheimer Disease

Koji Kamagata, MD, PhD, Christina Andica, MD, PhD, Kaito Takabayashi, MS, et al., for the Alzheimer’s Disease Neuroimaging Initiative

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Study Question
Can noninvasive MRI measures be used to show whole-brain perivascular network alterations that may play a pivotal role in amyloid β (Aβ) accumulation in patients with mild cognitive impairment (MCI) and Alzheimer disease (AD), and are these alterations associated with cognitive function and CSF biomarkers?

What Is Known and What This Paper Adds
Several noninvasive MRI measures have been proposed to assess the perivascular network related to the glymphatic system function. However, its involvement in AD pathogenesis is not fully understood. This study’s findings indicate that the noninvasive MRI measures can be used to detect changes in the whole-brain perivascular network in patients with MCI and AD and that they are associated with Aβ deposition, neuronal change, and cognitive impairment.

Methods
This retrospective case-control study included 36 patients with AD, 44 patients with MCI, and 31 healthy controls from the Alzheimer’s Disease Neuroimaging Initiative database (adni.loni.usc.edu). MRI measures, including perivascular space volume fraction (PVSVF), fractional volume of free water in white matter (FW-WM), and index of diffusivity along the perivascular space (ALPS index), were compared among groups using a general linear model. Partial correlation tests were then used to evaluate the associations of MRI measures and neuropsychologic scores, CSF biomarkers, PET standardized uptake value ratios (SUVRs), and hippocampus volume in the MCI and AD groups combined. Age, sex, years of education, scanning site, and APOE e4 gene carrier status were included as confounding factors in all statistical analyses.

Results and Study Limitations
Patients with AD had higher PVSVF (total, WM, and basal ganglia) and FW-WM and a lower ALPS index than healthy controls. Meanwhile, patients with MCI only showed significantly higher total and WM PVSVFs than healthy controls. In the combined subcohort of patients with MCI and AD, a lower ALPS index was associated with lower CSF Aβ42 (rs = 0.41), lower FDG-PET uptake (rs = 0.54), and worse multiple cognitive domain deficits. Furthermore, higher FW-WM was associated with lower CSF Aβ42 (rs = −0.47) and worse cognitive performance. The main limitation of this study was that the ALPS index does not exclusively measure the diffusivity of the perivenous space around the deep medullary vein—that is, it is also influenced by the surrounding white-matter microstructure included in the region of interest.

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