Cerebrovascular Reactivity Across the Entire Brain in Cerebral Amyloid Angiopathy

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Study Question
Is cerebrovascular reactivity (CVR) reduced across the entire brain in patients with cerebral amyloid angiopathy (CAA) and is a reduced CVR associated with the hemorrhagic, ischemic, and cognitive consequences of CAA?

What Is Known and What This Paper Adds
Patients with CAA have a reduced CVR in response to visual stimuli. However, it is unknown whether CVR is reduced across the entire brain in patients with CAA, and whether reduced gray matter (GM) and white matter (WM) CVR are associated with MRI markers of CAA and cognitive function. This study found that CVR is reduced across the entire brain in patients with CAA but has a predominantly posterior distribution, that lower WM CVR was associated with greater white matter hyperintensity (WMH) volume, and that lower GM CVR was associated with worse cognitive function, suggesting reduced CVR is a core feature of CAA.

Methods
In this cross-sectional study, patients with probable CAA (n = 26), mild cognitive impairment (MCI; n = 19), or dementia due to Alzheimer disease (AD dementia; n = 12) and healthy controls (HCs; n = 39) underwent cognitive testing and an MRI that included a 2-minute 5% carbon dioxide (CO2) challenge. CVR was quantified in GM, WM, the primary visual cortex (V1), and brain regions affected by AD (middle temporal gyrus, posterior cingulate, precuneus, and angular gyrus) as the % change in blood oxygenation level-dependent signal per mm Hg increase in end-tidal partial pressure of CO2. CVR was compared across groups using analyses of covariance (covariates: age, sex, and presence of hypertension) and the Tukey-Kramer correction for post hoc comparisons. Spatial differences in CVR were determined using permutation-based threshold-free cluster enhancement analyses adjusted for age, sex, and presence of hypertension. Associations between CVR and MRI markers of CAA and cognition were assessed using multivariable regression adjusting for age, sex, education, and the presence of hypertension.

Results and Study Limitations
Compared with HCs, GM and WM CVR averaged across the entire brain and AD regions were lower in patients with CAA and patients with AD dementia, with a predominantly posterior distribution of lower CVR in both groups (Figure). Greater WMH volume was associated with lower WM CVR ($-0.48, 95\% CI -0.90 to -0.01), while there were positive associations between GM CVR and memory (0.21, 0.07–0.36), executive function (0.20, 0.02–0.39), and processing speed (0.27, 0.10–0.45). WM CVR was also associated with better memory (0.22, 0.08–0.36) and processing speed (0.23, 0.06–0.40). Study limitations include the small number of patients with AD dementia and the use of clinical criteria to define MCI and AD dementia without amyloid and tau biomarkers.

Study Funding and Competing Interests
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