Visit-to-Visit Blood Pressure Variability and CSF Alzheimer Disease Biomarkers in Cognitively Unimpaired and Mildly Impaired Older Adults

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Study Question
Is visit-to-visit blood pressure variability related to change in CSF Alzheimer disease biomarkers, and do associations differ by APOE e4 carrier status?

What Is Known and What This Paper Adds
Blood pressure variability is an emerging risk factor for cognitive impairment and dementia, including Alzheimer disease, independently of average blood pressure levels. The results of this investigation show that elevated blood pressure variability is related to change in CSF Alzheimer disease biomarker levels in directions consistent with advancing Alzheimer disease pathophysiology and that associations with phosphorylated tau were particularly evident in APOE e4 carriers, consistent with other studies relating hemodynamic factors to tau changes.

Methods
For these longitudinal analyses, the investigators analyzed data from 466 cognitively unimpaired or mildly impaired older adults (mean age 76.7 [SD 7.1] years) enrolled in the Alzheimer’s Disease Neuroimaging Initiative database. Participants underwent 3 to 4 blood pressure measurements over a 12-month period and at least 1 lumbar puncture at follow-up (6–108 months later) for the evaluation of CSF phosphorylated tau, total tau, and β-amyloid levels. APOE e4 carriers were defined as having at least 1 e4 allele. Visit-to-visit blood pressure variability was determined over 12 months as variability independent of the mean. Only CSF samples collected after the final blood pressure measurement were analyzed. Bayesian linear growth modeling investigated the role of blood pressure variability, APOE e4, and the passage of time on CSF biomarker levels after controlling for several variables, including average blood pressure, baseline hypertension, and antihypertensive medication use.

Results and Study Limitations
Elevated blood pressure variability was associated with increased CSF phosphorylated tau (β = 0.81 [95% CI 0.74–0.97]), increased total tau (β = 0.98 [95% CI 0.71–1.31]), and decreased β-amyloid levels (β = −1.52 [95% CI −3.55 to −0.34]) at follow-up. APOE e4 carriers with elevated blood pressure variability had the fastest increase in phosphorylated tau levels (β = 9.03 [95% CI 1.67–16.36]). Blood pressure variability was not significantly related to total tau or β-amyloid levels over time on the basis of APOE e4 carrier status. A limitation of the study is the largely non-Hispanic White sample with limited cerebrovascular disease, which precluded investigation in more diverse samples and in those with varying levels of cerebrovascular disease severity. Findings are further limited by the retrospective nature of analyses.

Study Funding and Competing Interests
This study was funded by the NIH and the Alzheimer’s Association. The authors report no competing interests. Go to Neurology.org/N for full disclosures.
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