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Long-term Blood Pressure Variability is Associated with White Matter Integrity and Cognitive Decline in Cerebral Amyloid Angiopathy

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SUMMARY: Long-term blood pressure variability was associated with loss of white matter microstructural integrity in part driven by cerebral amyloid angiopathy (CAA)

BACKGROUND

Emerging evidence suggests that blood pressure variability (BPV) may contribute to small vessel disease (SVD) progression and cognitive impairment beyond the deleterious effects of elevated blood pressure.[1,2]

AIMS

This study investigates if BPV is associated with white matter (WM) microstructural integrity and the slope of cognitive decline in elderly individuals with cerebral amyloid angiopathy (CAA).

METHODS

STUDY POPULATION: 131 non-demented individuals (73±7y, 33/101 female/male, MMSE 28±2) with and without probable CAA from a longitudinal memory clinic cohort from the Massachusetts General Hospital (MGH).

NEUROIMAGING: We measured peak width of skeletonized mean diffusivity (PSMD; Fig 1)[3,4] and rated neuroimaging markers of CAA, including lacunes and cortical cerebral microinfarcts.

NEUROPSYCHOLOGICAL MEASURES: Composite scores were calculated based for 1) Memory, 2) Language, 3) Executive Function, and 4) Processing speed/attention.

STATISTICAL ANALYSIS: We used linear regression models to evaluate the association between 1) BPV and PSMD, adjusted for age, sex, hypertension, medication, diabetes, smoking, and BMI; and 2) association between BPV and cognitive domain score change/year, adjusted for baseline function, and age.

Fig 1.

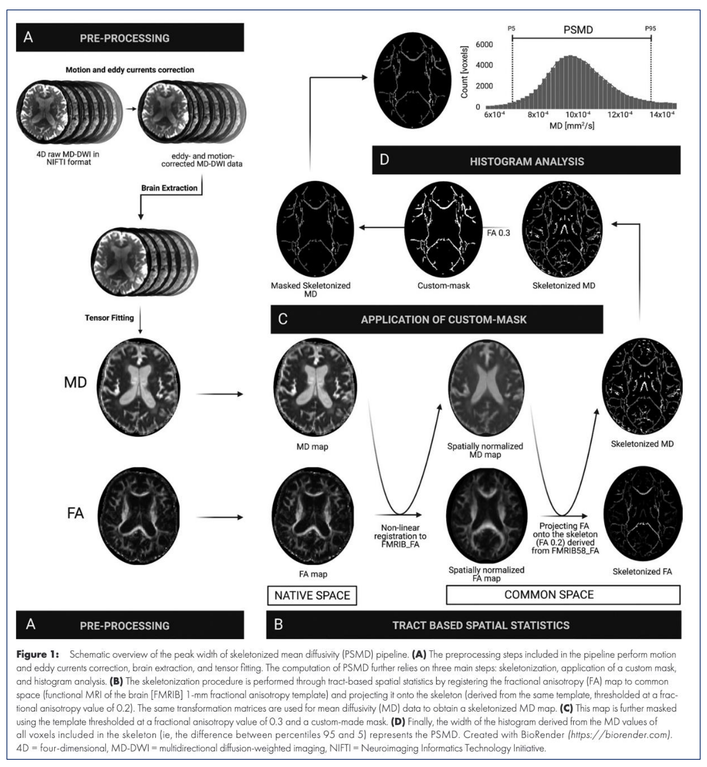
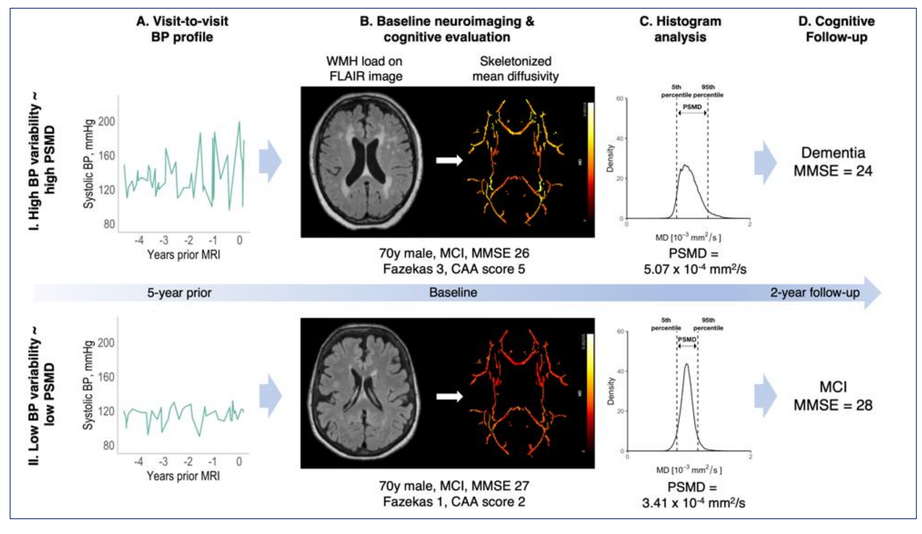


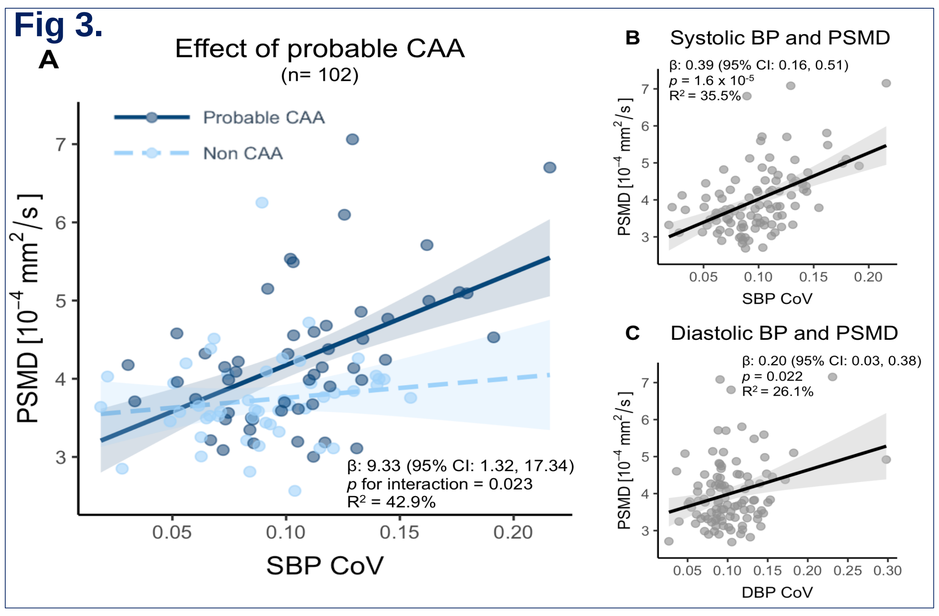
Figure 1: Schematic overview of the peak width of skeletonized mean diffusivity (PSMD) pipeline. **(A)** The preprocessing steps included in the pipeline perform motion and eddy currents correction, brain extraction, and tensor fitting. The computation of PSMD further relies on three main steps: skeletonization, application of a custom mask, and histogram analysis. **(B)** The skeletonization procedure is performed through tract-based spatial statistics by registering the fractional anisotropy (FA) map to common space (functional MRI of the brain [FMRIB] 1-mm fractional anisotropy template) and projecting it onto the skeleton (derived from the same template, thresholded at a fractional anisotropy value of 0.2). The same transformation matrices are used for mean diffusivity (MD) data to obtain a skeletonized MD map. **(C)** This map is further masked using the template thresholded at a fractional anisotropy value of 0.3 and a custom-made mask. **(D)** Finally, the width of the histogram derived from the MD values of all voxels included in the skeleton (ie, the difference between percentiles 95 and 5) represents the PSMD. Created with BioRender (*https://biorender.com*). 4D = four-dimensional, MD-DWI = multidirectional diffusion-weighted imaging, NIFTI = Neuroimaging Informatics Technology Initiative.

Fig 2.



- Systolic BPV had a dose-dependent association with PSMD (standardized β=0.22, 95% CI: 0.06, 0.39, p=0.010), adjusted for risk factors.
- The presence of probable CAA strengthened the association between BPV and PSMD (β=9.33, 95% CI: 1.32, 17.34, p interaction = 0.023).
- Higher BPV correlated with more significant ischemic injury (lobar lacunes and cortical cerebral microinfarcts) and a decline in global cognition and processing speed.

Fig 3.



CONCLUSION

Long-term BPV had a dose-dependent association with altered white matter integrity, lobar lacunes, and cortical cerebral microinfarcts and predicted cognitive decline. Controlling BPV might be a potential strategic approach to prevent cognitive decline in memory clinic patients with CAA and mild cognitive symptoms.

References:
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4. M.C. Zanon Zotin et al. *Radiology*. 306, e212780 (2023).

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