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

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Long-term blood pressure variability is associated with loss of white matter microstructural integrity and cognitive decline in part driven by cerebral amyloid angiopathy (CAA)

INTRODUCTION

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, but the mechanisms remain largely unknown.[1,2] 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), a well characterized type of SVD.

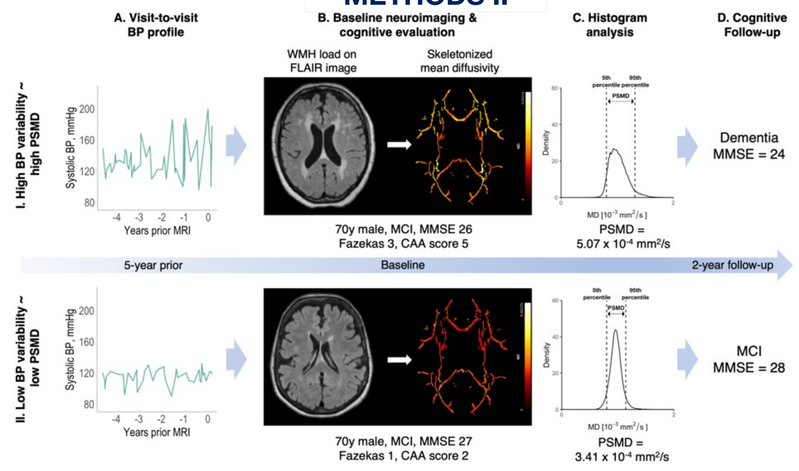
METHODS I

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

NEUROPSYCHOLOGICAL MEASURES: Composite scores were calculated based on neuropsychological test battery 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.

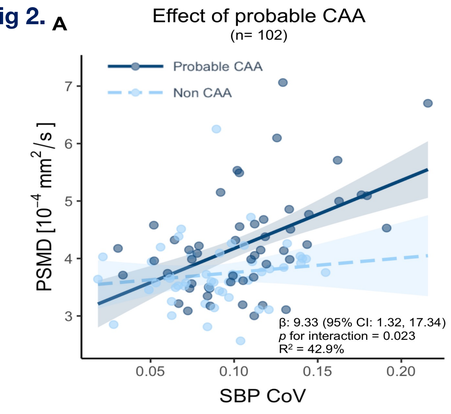
METHODS II

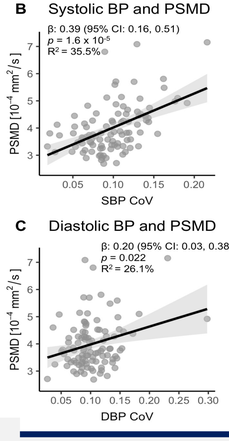


RESULTS

- We found a significant association between systolic BPV and loss of WM integrity (*β = 0.37, P < 0.001;* ***Fig 1***). We did not find an association between mean BP and WM integrity.
- The association of BPV with WM integrity was stronger when CAA was present as seen in ***Fig 2*** (*P for interaction = 0.023*).
- Higher BPV was associated with decline in global cognition (*β* = -0.24, P = 0.035) and processing speed (*β* = -0.30, P = 0.022).

Fig 2.





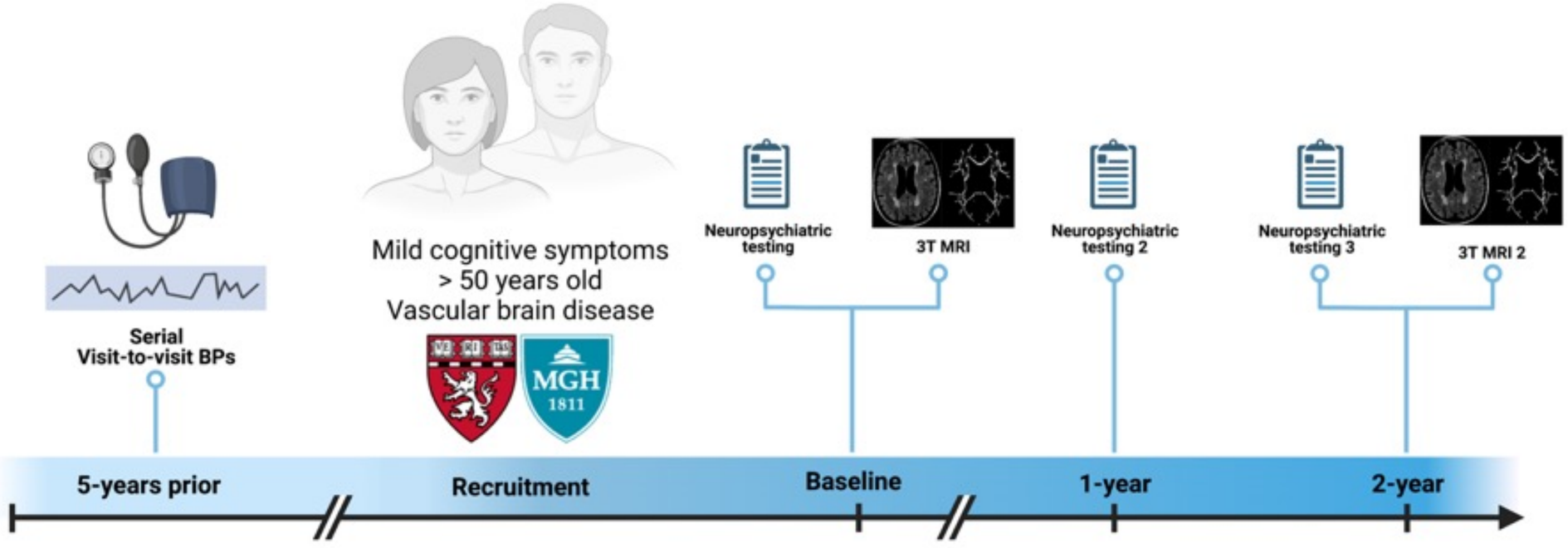
CONCLUSIONS

Our findings show that long-term BP variability is associated with loss of WM microstructural integrity and domain-specific cognitive decline. The association between BP variability and WM integrity might be partly driven by CAA pathology. Better control of BP variability could be a novel therapeutic target to slow cognitive decline over time. Further studies are warranted to disentangle the relationship between BP fluctuations, microvascular injury, and cognitive impairment.

References:

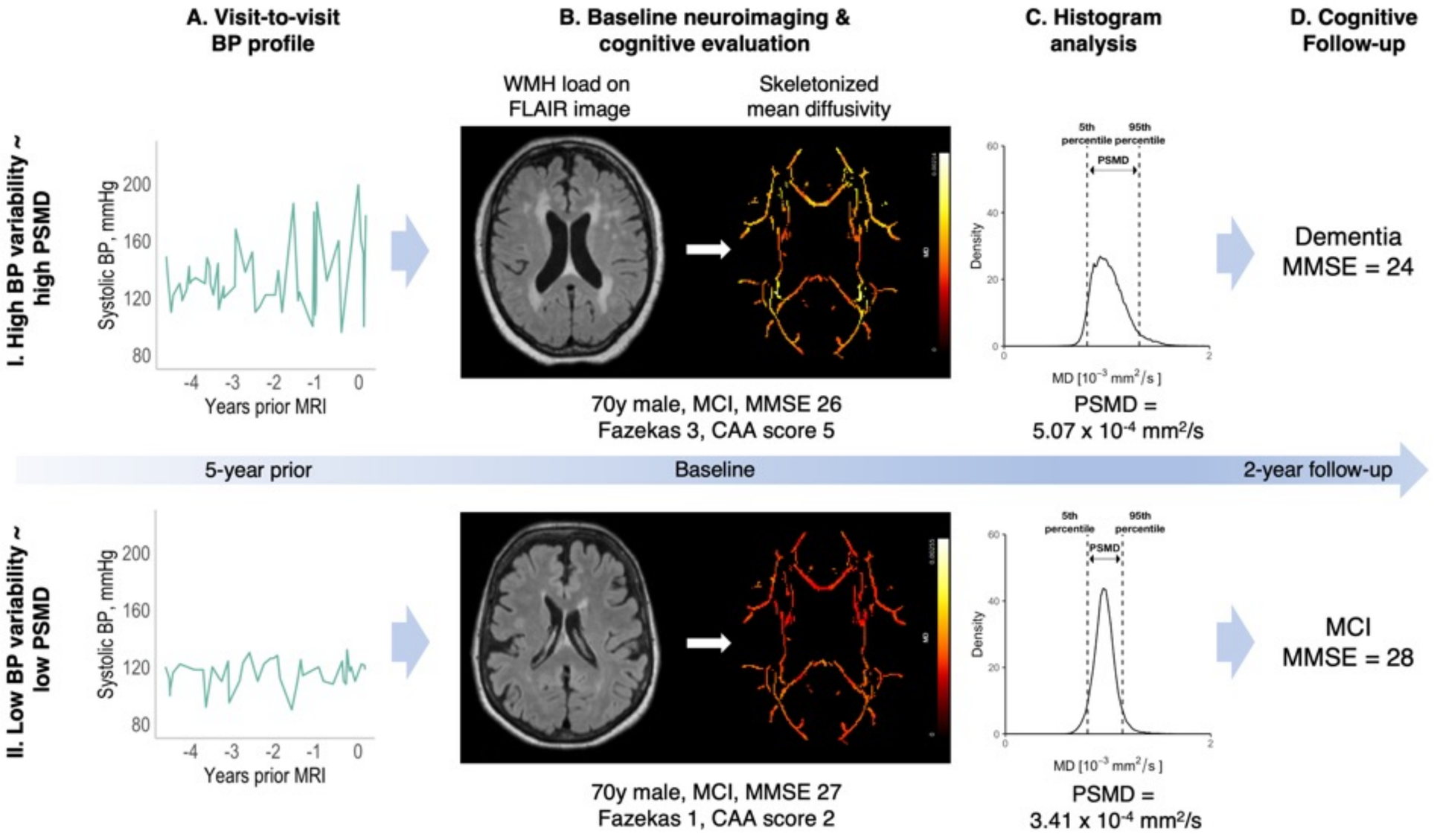
1. P. M. Rothwell, *Lancet*. **375**, 938–48 (2010).
2. Y. Ma *et al.*, *J Am Coll Cardiol*. **75**, 2387–2399 (2020).
3. E. Baykara *et al.*, *Ann Neurol*. **80**, 581–592 (2016).

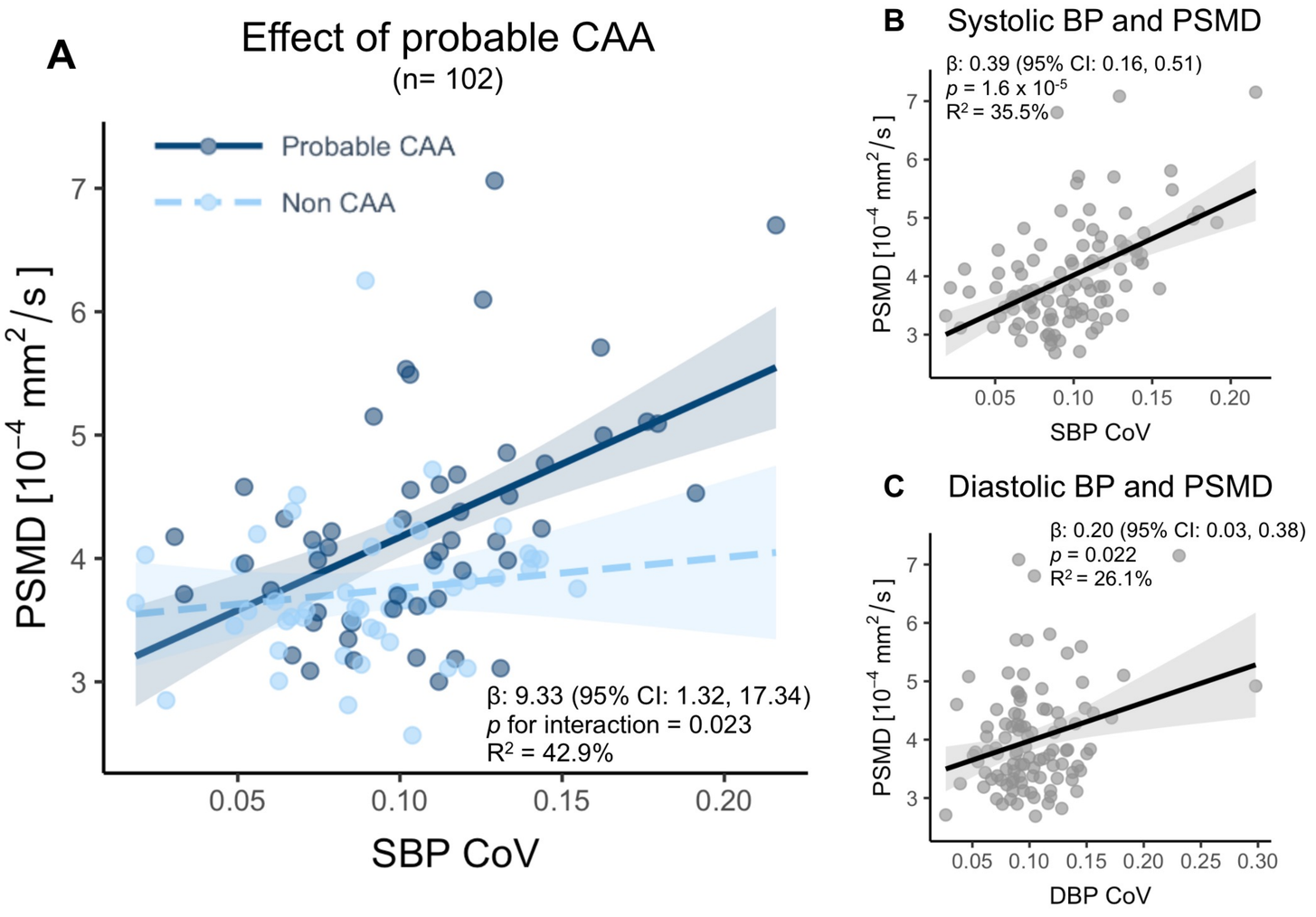
BPV in CAA
Study Timeline



BP variability:
- CoV = SD/mean

Composite z-scores of cognitive domains:
- Global cx
- Executive fx
- Processing speed


A. Visit-to-visit BP profile
B. Baseline neuroimaging & cognitive evaluation
C. Histogram analysis
D. Cognitive Follow-up
I. High BP variability ~ high PSMD
II. Low BP variability ~ low PSMD
WMH load on FLAIR image
Skeletonized mean diffusivity
Systolic BP, mmHg
200
160
120
80
-4 -3 -2 -1 0
Years prior MRI
5th percentile
95th percentile
PSMD
Density
MD [10⁻³ mm²/s]
70y male, MCI, MMSE 26
Fazekas 3, CAA score 5
PSMD = 5.07 x 10⁻⁴ mm²/s
Dementia
MMSE = 24
5-year prior
Baseline
2-year follow-up
70y male, MCI, MMSE 27
Fazekas 1, CAA score 2
PSMD = 3.41 x 10⁻⁴ mm²/s
MCI
MMSE = 28



LM: PSMD ~ BPV + BPV*Probable_CAA + Age

Sveikata et el. *In Prep.*

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Conclusions

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The association between BP variability and WM integrity might be partly driven by CAA pathology.

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Further studies are warranted to disentangle the relationship between BP fluctuations, microvascular injury, and cognitive impairment.