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Introduction

- Nearly half of adults have hypertension¹, but blood pressure (BP) declines in late-life roughly 10 years before death² and is associated with greater dementia risk³ and mortality⁴
- Higher BP predicts brain atrophy⁵, declines in cortical thickness⁶, more severe arteriosclerosis at death⁷, and faster white matter hyperintensity (WMH) progression⁸
- We have previously reported that faster BP decline is related to faster simultaneous decline in cognitive function⁹ as well as greater postmortem vessel pathology¹⁰

Problem:

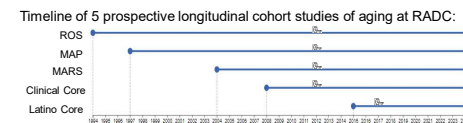
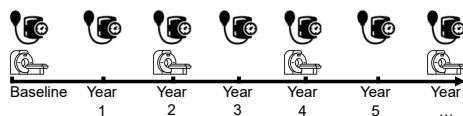
- Prior research relies on baseline BP to predict future brain outcomes, but how changes in BP change with brain structure and cerebrovascular pathology is unknown

Objective

Examine the relationship of simultaneous change in BP and changes in brain structure and cerebrovascular markers in older adults using MRI

Methods

- 671 older adults (aged 60+) from one of five longitudinal, prospective, community-based cohort studies at the Rush Alzheimer's Disease Center (RADC)
 - No missing data at baseline and 2+ measures of annually collected BP and MRI on the same scanner



- BP measured annually using an automated sphygmomanometer
- Brain structure and cerebrovascular markers measures biannually with 3T Phillips Achieva scanner (n=240, 36%) or Siemens Trio scanner (n=431, 64%) with a 32-channel coil
 - 3D T1-weighted MPRAGE sequence to collect anatomical data
 - 2D T2-weighted FLAIR acquired with a 2D fast spin-echo
 - DTI acquired with 2D spin-echo echo-planar imaging sequence
- Brain Structure**
 - Grey/white matter (% of total ICV)
 - Segmented using Statistical Parametric Mapping (SPM)
 - Cortical thickness (mean thickness (mm) of both hemispheres)
 - Segmented using FreeSurfer according to the Desikan-Killiany Atlas
- Brain Vascular Pathology**
 - ARTS in vivo marker of likelihood of arteriosclerosis
 - Assessed by fully automated publicly available program (<https://www.nitrc.org/projects/arts>) using T1 MPRAGE, T2 FLAIR, DTI, and demographic (age & sex) information
 - White matter hyperintensity volume (Log10 % of total ICV)
 - MPRAGE data registered to FLAIR using rigid body registration
 - Lesions appearing hyperintense automatically segmented based on masked FLAIR data using sysu
- Simultaneous modeling of longitudinal BP and neuroimaging markers using a bivariate mixed effects model adjusted for age, sex, education, antihypertensive medication, and scanner

Results

Table 1 Baseline Demographics	Total (n = 671)
Age (years)	78.04 ± 7.15
Sex (n, % women)	544, 81.07%
Race/Ethnicity (n, %)	
White, non-Latino	409, 60.95%
Black, non-Latino	229, 34.13%
Latino	28, 4.17%
Other	5, 0.75%
Education (years)	15.91 ± 3.26
Annual follow up visits (years)	5.55 ± 2.51
Systolic BP (mmHg)	131.94 ± 19.30
Diastolic BP (mmHg)	78.07 ± 10.72
History of hypertension (n, %)	411, 61.25%
Antihypertensive use (n, %)	471, 70.19%

Values are mean ± SD unless otherwise noted

Table 2 Change in BP and Brain Outcomes	Total (n = 671)
Outcomes	Estimate (SD)
Systolic BP	0.018 ± 0.014
Diastolic BP	-0.016 ± 0.015
Gray matter volume (%)	-0.365 ± 0.021†
White matter volume (%)	-0.156 ± 0.015†
Cortical Thickness	-0.127 ± 0.009†
Frontal thickness	-0.065 ± 0.008†
Occipital thickness	-0.074 ± 0.008†
Parietal thickness	-0.084 ± 0.007†
Temporal thickness	-0.178 ± 0.010†
ARTS	0.021 ± 0.001†
WMHV (log10%)	0.034 ± 0.002†

Linear mixed-effects models adjusted for age, education, antihypertensive medication use, sex, and years of education. † = p < 0.01

Fig 2. Faster BP Decline Related to Faster Decline in Cortical Thickness

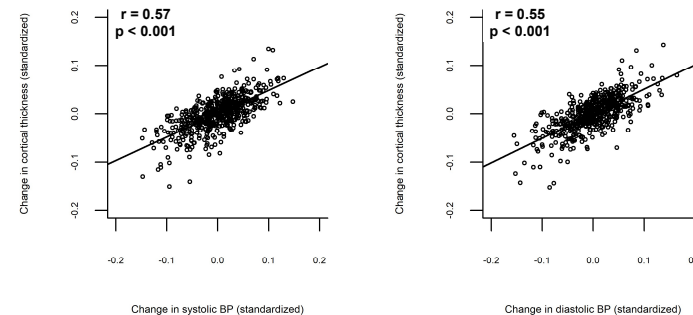


Fig 4. Faster Increase in BP Increase Related to Faster Increase in Cerebrovascular Pathology

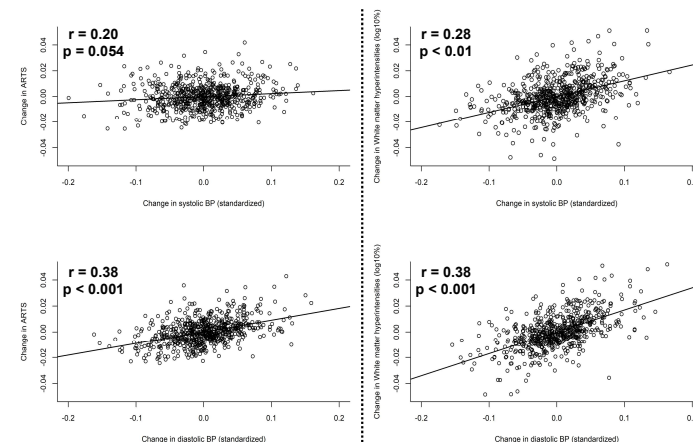


Fig 1 Forest plot. Correlation of Change in BP with Change in Brain Outcomes

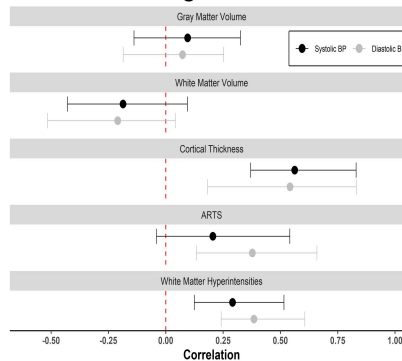
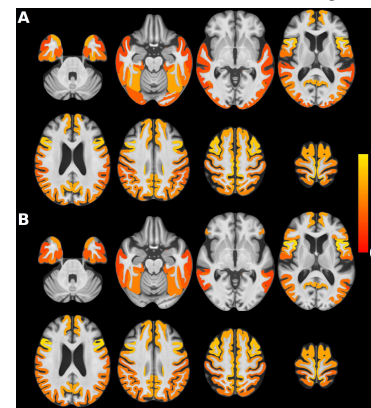


Fig 3. Faster BP Decline Related to Faster Decline in Cortical Thickness across Regions



Bivariate Outcomes		Change, r value	Change, p-value
Systolic BP	Frontal Lobe Thickness	0.48	<0.01
	Occipital Lobe Thickness	0.24	0.19
	Parietal Lobe Thickness	0.60	<0.001
	Temporal Lobe Thickness	0.66	<0.001

CLINICAL TAKE AWAY:

- Longitudinal changes in BP trajectory are differently related to concurrent changes in brain structure and cerebrovascular pathology
- Monitoring BP trajectory at annual visits may provide a non-invasive measure of underlying brain and cerebrovascular pathology in old age

Conclusions

- A faster late-life **decline** in BP was related to a faster simultaneous decline in cortical thickness
 - Across frontal, parietal, and temporal but not occipital lobes
 - Strongest association with temporal lobe
- Faster late-life **increase** in BP was related to a faster simultaneous **increase** in cerebrovascular pathology
 - Including larger white matter hyperintensities and a greater likelihood of arteriosclerosis
- Longitudinal BP trajectories show different relationships with simultaneous changes in brain structure and cerebrovascular pathology
 - Changes in BP and both brain and cerebrovascular pathology occur simultaneously in old age
 - BP treatment must be personalized to individual patients, matching their goal of reducing the risk of brain atrophy or cerebrovascular pathology

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- Data sharing: <https://www.radc.rush.edu/>

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