Antihypertensive treatment class is associated with brain structure and cognitive function:

An propensity-weighted cohort analysis of the Alzheimer's Disease Neuroimaging Initiative (ADNI)

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Background

Hypertension is an important risk factor for Alzheimer's Disease (AD)[1] and is also associated with cerebral small vessel disease (SVD)[2].

Angiotensin converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) are common treatments for hypertension [3], but prior observational data suggests ARBs may have neuroprotective effects.

No previous studies have compared ***ACEIs vs.ARBs*** on ***volumetric measures*** of neurodegeneration and SVD and ***cognitive performance***

Objective

The objective of this study was to compare MRI-derived volumetric biomarkers of neurodegeneration and SVD and cognitive performance in hypertensive adults, both with and without dementia, on current or prior treatment with ACEIs, ARBs, or other anti-hypertensive medications

Discussion

This observational cohort study demonstrated a ***significant effect of treatment*** in elderly hypertensive individuals with and without dementia, with those exposed to ARBs showing less global and hippocampal atrophy and better cognitive performance than those treated with ACEIs alone

These findings support the potential protective effect of ARBs on cognition in elderly hypertensive adults with and at risk for dementia and provide ***new evidence*** for potential protective effects on brain structure

These findings are consistent with prior data suggesting that inhibiting ACE could lead to increased levels and deposition of Aβ, potentially contributing to ***amyloid-related pathogenesis in AD*** [6]

This study may have ***important practice implications*** for the treatment of hypertension in individuals at high risk for the incidence or progression of dementia

Results

Demographics: Significant differences in diagnostic class, age, history of diabetes, stroke/TIA, and ApoE status, across treatment groups (***p* < .01**)

Propensity Score: Multinomial regression was significant (χ=224.49, ***p* =.05**)

MRI Volumetric Outcomes: Individuals exposed to **ARBs** showed significantly **higher total corrected hippocampal volume and BPF** than those on ACEIs, but no association with WMH burden (Table 1)

Stratified Analyses: showed **treatment effect** for markers of SVD **(WMH) in AD** patients only and treatment effect for neurodegenerative markers **(BPF, hippocampal volume) in NC and MCI** only

Cognitive Outcomes: Those on **ARBs** showed **better performance** on the Rey Delayed Recall, Boston Naming, Trails A and B, Digit Symbol, and Logical Memory tests (***p*<.05**), adjusted for propensity scores, age, vascular risk, baseline diagnosis, ApoE status, and baseline MMSE

Table 1. Associations between treatment class and MRI volumetric measures, propensity weighted multivariate linear regression†

Outcome	Treatment Class	Mean (SD)	β	*Adjusted R-Square*	*p*-value
Total Hippocampal Volume (mm^3)	ACEIs	4354.5 (777)			
	ARBs	4381.8 (749)			
	Both	4842.0 (877)			
	Other	4339.7 (794)	0.06	0.83	**0.05**
Brain Parenchymal Fraction	ACEIs	0.81 (0.03)			
	ARBs	0.81 (0.02)			
	Both	0.83 (0.03)			
	Other	0.81 (0.03)	0.07	0.83	**0.01**
White matter hyperintensity burden (cc)ǂ	ACEIs	0.25 (0.61)			
	ARBs	0.31 (0.64)			
	Both	0.16 (0.49)			
	Other	0.37 (0.86)	0.97	0.82	0.54

†adjusted for propensity score, age, baseline diagnostic classification, prior stroke/TIA, diabetes, and ApoE status

Methods

1. Study Design and Cohort

- Cross-sectional cohort study using prospectively-collected data from ADNI: Phase 1 [4]
- Elderly hypertensive individuals (N=886; mean age=75.0, SD=6.8), with a baseline clinical status of normal control (NC; N=237), mild cognitive impairment (MCI; N=489), or AD (N=160)

2. Propensity Score Methodology

- To address selection bias for non-random treatment allocation and confounding by indication [5]
- CHEP Hypertension Clinical Guidelines:
  - ***ethnicity*** (African American vs. not)
  - **history of coronary artery or kidney disease**
  - ***prior myocardial infarction***
  - ***geographic area*** (indexed by ADNI site ID)
- Multinomial regression used to derive propensity scores for each treatment group

3. Statistical Analyses

- Propensity-weighted multivariate linear regression used to evaluate associations between ***treatment*** (ACEI, ARBs, ACEIs+ARBs, other) and ***MR volumetric outcomes*** (hippocampal volumes, brain parenchymal fraction, WMH burden) and **cognitive function** (ADNI neuropsychological battery)

References

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