

Cognitive Impairment and Cardiovascular Disease in Older Adults: An Evaluation Using Pooled Observational Data.

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Introduction

- The Precision Aging Network (PAN) is an NIA-funded study that seeks to develop novel models for understanding, preventing, and treating age-related cognitive impairment (ARCI) based on concepts borrowed from precision medicine¹.
- Elevated blood pressure is linked to future dementia in long-term studies, but cross-sectional research shows mixed or no associations with cognitive decline².
- This analysis seeks to evaluate the impact of hypertension management on the transition from normal cognition to mild cognitive impairment (MCI) as a benchmark while PAN data matures. The data sources for this study were National Alzheimer's Coordinating Center (NACC) and the Alzheimer's Disease Neuroimaging Initiative (ADNI).
- Primary first-line therapeutics for hypertension management included in the analysis include calcium channel blockers and thiazide-like diuretics.

Methods

- Data from the NACC and the ADNI were harmonized and combined to create a single dataset.
- The outcome variable was constructed by using a difference of mean time to event accounting for reverse progression), and a binary variable was created using the difference of mean time in each of the two states.
- The “mean months of unimpaired diagnosis” and “mean months of MCI diagnosis” was calculated for each participant. The between these two estimates is an indicator for how long it took to go from unimpaired to MCI (or vice-versa). Large differences are indicative of a longer time in the MCI state and small (or negative for those that never transition to MCI) are indicative of a longer time unimpaired. A binary variable was using a cut-off of > 0 (indicating high time in MCI state) and zero and ≤ 0 indicating greater time in unimpaired state (or never transition).
- Logistic regression modeling was used to compare those who were predominately in the MCI state to those in an unimpaired state and hypertensive medication use.

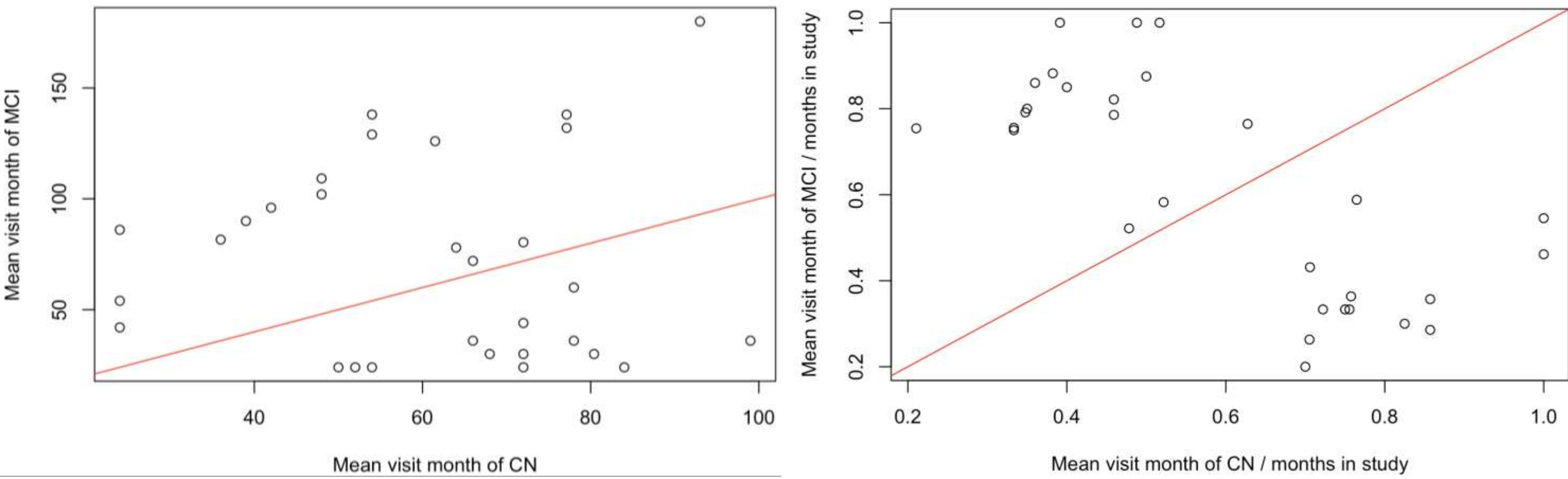


Figure 1: Scatterplot of the two mean month variables for Unimpaired (CN) and MCI showing clear separation of participants based on this measure/metric of MCI transition time.

Results

Table 1. Demographics for NACC and ADNI Data

Variables	ADNI (n = 2255)	NACC (n = 44908)	Overall (n = 47163)
Diagnosis at Baseline			
CN (Unimpaired)	863 (38.3%)	17665 (39.3%)	18528 (39.3%)
Dementia	410 (18.2%)	15433 (34.4%)	15843 (33.6%)
MCI	948 (42.0%)	9817 (21.9%)	10765 (22.8%)
Impaired, not MCI	0 (0%)	1993 (4.4%)	1993 (4.2%)
Missing	34 (1.5%)	0 (0%)	34 (0.1%)
Sex			
Female	1069 (47.4%)	25647 (57.1%)	26716 (56.6%)
Male	1186 (52.6%)	19261 (42.9%)	20447 (43.4%)
Age (years)			
Mean (SD)	73.1 (7.32)	71.3 (10.3)	71.4 (10.2)
Missing	4 (0.2%)	476 (1.1%)	480 (1.0%)
Race			
Hispanic/Latino	103 (4.6%)	3614 (8.0%)	3717 (7.9%)
Non-Hispanic Black	152 (6.7%)	6109 (13.6%)	6261 (13.3%)
Non-Hispanic White	1916 (85.0%)	33355 (74.3%)	35271 (74.8%)
Undefined	84 (3.7%)	1830 (4.1%)	1914 (4.1%)
Education (years)			
Mean (SD)	16.1 (2.75)	15.1 (3.46)	15.2 (3.43)
Missing	0 (0%)	356 (0.8%)	356 (0.8%)
BMI			
Mean (SD)	26.7 (4.67)	27.1 (5.32)	27.1 (5.30)
Missing	671 (29.8%)	5025 (11.2%)	5696 (12.1%)
Systolic BP (mm Hg)			
Mean (SD)	133 (16.9)	135 (24.2)	135 (23.9)
Missing	34 (1.5%)	4212 (9.4%)	4246 (9.0%)
Diastolic BP (mm Hg)			
Mean (SD)	74.1 (9.68)	75.5 (19.9)	75.4 (19.5)
Missing	34 (1.5%)	5079 (11.3%)	5113 (10.8%)

Table 2. Association of Antihypertensives with Cognitive Transition among Individuals with High Blood Pressure

	Odds Ratio (95% CI)	
Antihypertensive Medication Use	Unadjusted Model	Adjusted Model*
No vs Yes	0.82 (0.70, 0.97)	0.94 (0.79, 1.12)

*Model adjusted for age, sex, race, and education.

Conclusions

While there is some evidence in the literature suggesting that hypertension (and other chronic diseases) can accelerate ARCI, not associated with AD or dementia, it is not known whether therapeutic interventions can be used to slow or reverse this process. This analysis suggests that the use of hypertensive medications is associated with a higher probability of ARCI, however, since the timing of therapeutic use was not included in relation to the transition state it is unclear whether the reverse state (from MCI to unimpaired) is impacted by therapy. Future work will include examining transition states through hidden Markov models and including other comorbid disease’s influence on potentially modifiable ARCI.

Limitations

Potential for selection bias and confounding as data obtained from observational studies. The analysis need to consider the time factor when analyzing antihypertensive therapy around ARCI transition.

References

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2. Cheng, Y.-w., T.-F. Chen, and M.-J. Chiu, *From mild cognitive impairment to subjective cognitive decline: conceptual and methodological evolution. Neuropsychiatric Disease and Treatment*, 2017; p. 491-498.

Funded in part by 5U19AG065169
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