

Chronic Microinfarcts Are Associated with Differences in APOE ε4–Braak Tau Stage Relationships in Autopsied Brains

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KEY TAKEAWAY

Chronic microinfarcts were associated with differences in the relationship between APOE ε4 genotype and Braak tangle stage. The strongest estimated association was observed among ε44 carriers with microinfarcts, although this estimate was imprecise and should be interpreted cautiously.

INTRODUCTION

APOE ε4 is strongly associated with Alzheimer’s disease neuropathology. Older brains often show mixed vascular and neurodegenerative lesions. Chronic microinfarcts may alter vulnerability to tau pathology.
Objective: To test whether chronic microinfarcts modify the association between APOE ε4 genotype and Braak tangle stage.

METHOD



NACC autopsy-confirmed sample (N = 7,153)



APOE groups: ε4-noncarriers (ε33, ε22, ε23 Referent), ε4-heterozygotes (ε24, ε34) , and ε4-homozygotes (ε44).



Microinfarcts: absent vs present



Outcome: Braak tangle stage



Ordinal logistic regression

Statistical significance was set at FDR corrected p<0.05

Adjusted for age, age², sex, self-reported ancestry and education

RESULT

Table 1. Participant Characteristics

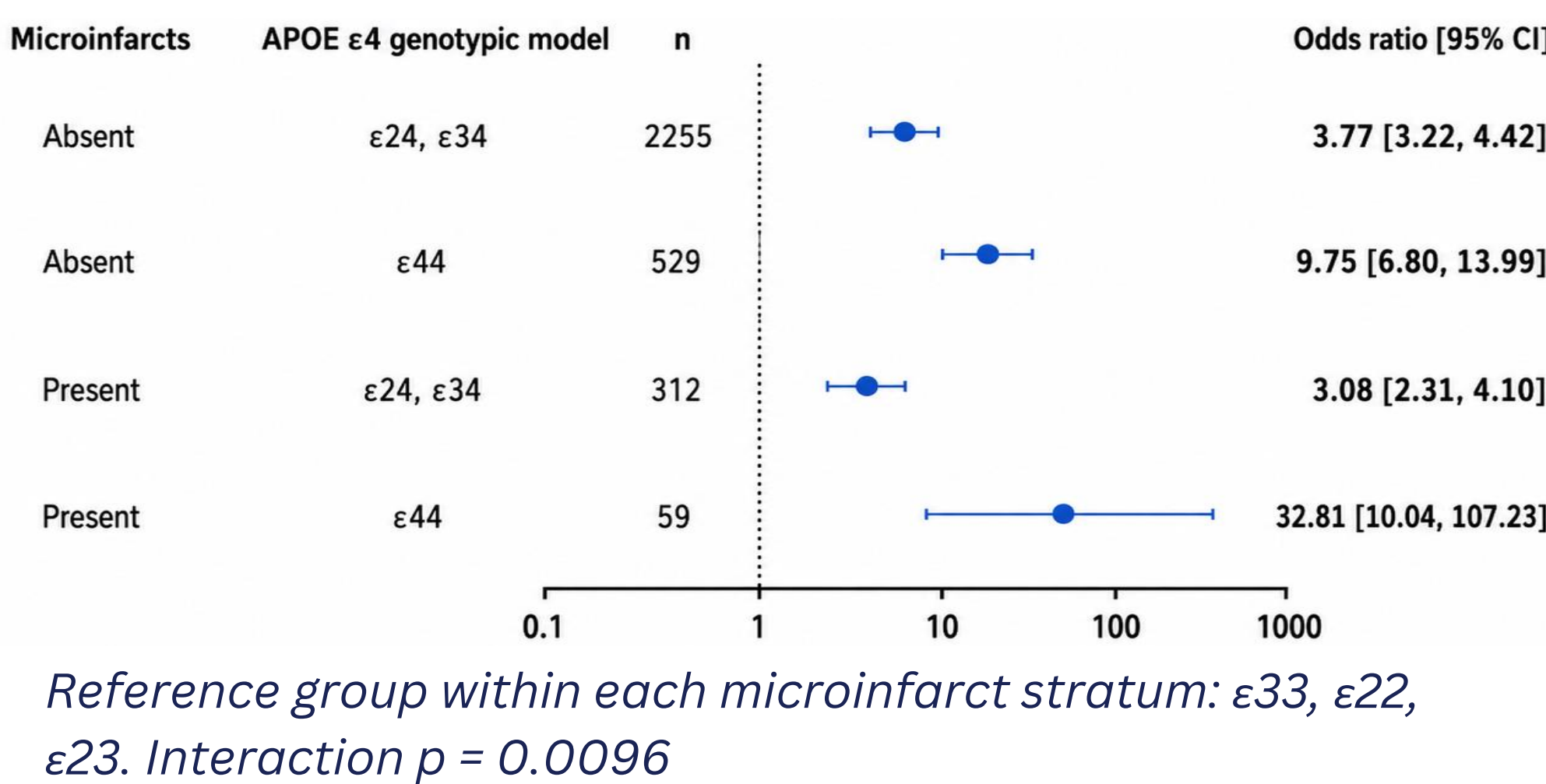
Characteristic	Overall (N=7,153)	ε33, ε22, ε23 (N=3,998)	ε24, ε34 (N=2,567)	ε44 (N=588)
Age, mean (SD), years	79 (12)	80 (12)	78 (11)	75 (9)
Female, n (%)	3,405 (48)	1,924 (48)	1,218 (47)	263 (45)
Bachelor’s degree or higher, n (%)	4,226 (59)	2,347 (59)	1,533 (60)	346 (59)
White ancestry, n (%)	6,758 (95)	3,800 (95)	2,414 (94)	544 (93)
Black/African American ancestry, n (%)	303 (4)	134 (3)	130 (5)	39 (7)
Braak stage V–VI, n (%)	3,606 (51)	1,431 (37)	1,675 (66)	500 (86)
Microinfarcts present, n (%)	917 (12.8)	546 (13.7)	312 (12.2)	59 (10.0)

CONCLUSION

- 1.Chronic microinfarcts were associated with differences in APOE ε4–Braak tangle stage relationships.
- 2.The strongest estimated association was observed among ε44 carriers with microinfarcts, but the wide confidence interval indicates limited precision.
- 3.These findings support further investigation of vascular–tau interactions in autopsy-confirmed cohorts.

MAIN FINDINGS

Figure 1. Association Between APOE ε4 Genotype and Higher Braak Tangle Stage by Microinfarct Status



LIMITATIONS

Limitations include the observational autopsy design, grouping of ε24, ε34 heterozygotes, and reduced precision for ε44 carriers with microinfarcts due to the wide confidence interval.

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REFERENCES

- 1.Nichols JB, et al. Journal of Neuropathology & Experimental Neurology 2021;80:240–246.
- 2.Besser LM, et al. Alzheimers Dementia. 2018;14:1213–1224.
- 3.Snyder HM, et al. Alzheimers Dementia. 2015;11:710–717.