

Amyloid Burden Is Associated With Medial Temporal Atrophy: A Cross-Sectional Study

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Background

Higher amyloid PET centiloid values have recently been associated with greater clinical cognitive impairment in Alzheimer’s disease dementia. However, its association with hippocampal atrophy assessed by the medial temporal atrophy (MTA) scale, a widely used tool in routine practice, remains underexplored. Here, we aimed to investigate whether greater centiloid values are associated with clinically significant hippocampal atrophy (MTA ≥ 2).

Methods

We conducted a retrospective cross-sectional study using Alzheimer’s Disease Neuroimaging Initiative (ADNI) data from 551 individuals who underwent both MRI and amyloid PET/CT with available Centiloid measurements. Two independent neuroradiologists rated hippocampal atrophy independently using the medial temporal atrophy (MTA) scale in each hippocampus. We categorized centiloid values into quartiles and evaluated the association between amyloid burden and neurodegeneration using multivariable logistic regression adjusted for age, sex and APOE $\epsilon 4$ status, with MTA ≥ 2 as the primary outcome.

Results

Fourth quartile participants presented a 2.4-fold higher occurrence of MTA ≥ 2 (65.7%) and a higher mean MTA score (2.00 ± 0.92). Participants in Q4 were also older (73.9 ± 7.0) and had a higher prevalence of APOE $\epsilon 4$ carriers (95; 69.3%). In addition, most patients with mild cognitive impairment (MCI) (62; 45.3%) and Alzheimer’s disease dementia (42; 30.7%) were concentrated in the fourth quartile (Table 1). Centiloid distribution analysis showed that participants in the fourth quartile (99.4 ± 24.7) exhibited markedly higher amyloid burden, with Centiloid levels 3.3-fold greater than those in the third quartile (29.7 ± 14.6) (Figure 1). In multivariable logistic regression, membership in the fourth quartile was associated with a 2.38-fold higher odds of presenting pathological neurodegeneration (MTA ≥ 2) (Figure 2).

Table 1 | Demographic and Clinical Characteristics by Centiloid Quartile

	Q1 (n = 138)	Q2 (n = 138)	Q3 (n = 138)	Q4 (n = 137)	P-value
Age, mean (SD), years	69.7 (7.6)	69.6 (6.9)	71.4 (7.3)	73.9 (7.0) ^{a,b,c}	<0.001
Education, mean (SD), years	16.6 (2.4)	16.4 (2.4)	16.8 (2.1)	16.0 (2.4) ^c	0.031
Sex					0.127
Female	65 (47.1)	83 (60.1)	80 (58.0)	72 (52.6)	
Male	73 (52.9)	55 (39.9)	58 (42.0)	65 (47.4)	
APOE4 status					<0.001
Non-carrier	118 (85.5)	98 (71.0) ^a	71 (51.4) ^{a,b}	42 (30.7) ^{a,b,c}	
Carrier	20 (14.5)	40 (29.0) ^a	67 (48.6) ^{a,b}	95 (69.3) ^{a,b,c}	
Cognitive status					<0.001
CN	88 (63.8)	100 (72.5)	92 (66.7)	33 (24.1) ^{a,b,c}	
MCI	45 (32.6)	34 (24.6)	36 (26.1)	62 (45.3) ^{b,c}	
AD	5 (3.6)	4 (2.9)	10 (7.2)	42 (30.7) ^{a,b,c}	
Centiloids	-7.0 (7.1)	5.6 (3.2) ^a	29.7 (14.6) ^{a,b}	99.4 (24.7) ^{a,b,c}	<0.001
MTA global	1.45 (0.87)	1.27 (0.91)	1.44 (0.94)	2.00 (0.92) ^{a,b,c}	<0.001
MTA ≥ 2	51 (37.0)	41 (29.7)	50 (36.2)	90 (65.7) ^{a,b,c}	<0.001

Continuous variables are presented as mean (SD), and categorical variables are presented as n (%). Group comparisons across quartiles were performed using one-way analysis of variance (ANOVA) for continuous variables (age, education, centiloids, and global MTA score) and Pearson’s chi-square test for categorical variables (sex, APOE $\epsilon 4$ status, cognitive status, and MTA ≥ 2). Abbreviations: AD, Alzheimer’s disease dementia; APOE $\epsilon 4$ (APOE4), apolipoprotein E $\epsilon 4$ allele; CN, cognitively normal; MCI, mild cognitive impairment; MTA, medial temporal atrophy (Scheltens scale); MTA ≥ 2 , medial temporal atrophy cutoff ≥ 2 ; Q1–Q4, quartiles; SD, standard deviation. Superscripts indicate significant pairwise differences: ^a p<0.05 vs Q1; ^b p<0.05 vs Q2; ^c p<0.05 vs Q3.

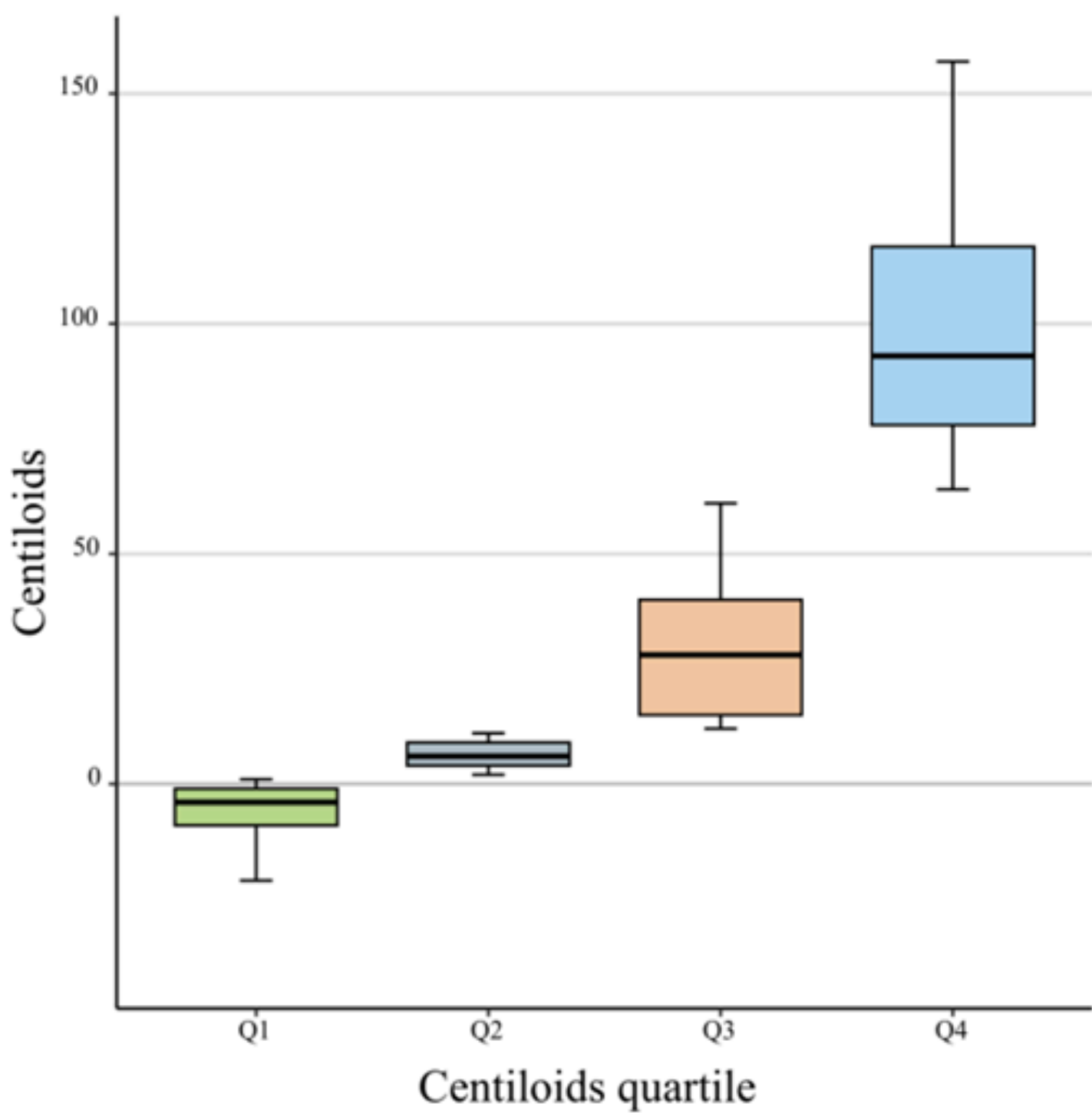


Figure 1. Centiloids quartile distribution. Boxplot illustrates the distribution of centroid values across quartiles. Adjusted for age, sex and APOE $\epsilon 4$. The horizontal line within each box represents the median, the box denotes the interquartile range (IQR), and the vertical whiskers indicate the minimum and maximum non-outlier values within each quartile.

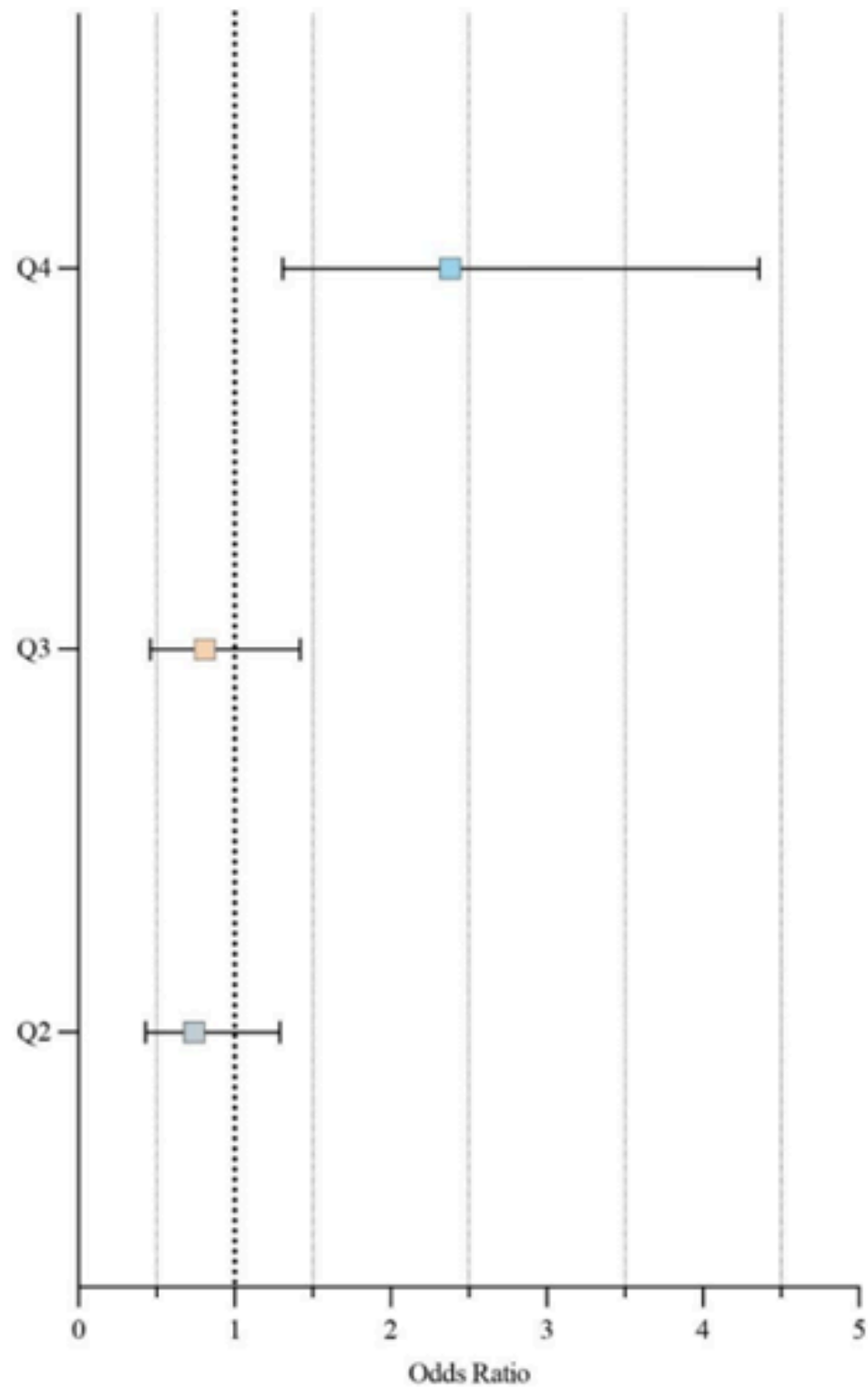


Figure 2. Centiloids quartile predicting hippocampus atrophy. Forest plot of odds ratios (ORs) and 95% confidence intervals (95% CIs) for the outcome MTA ≥ 2 , comparing quartiles Q2–Q4 with the reference quartile (Q1). Adjusted ORs by Quartile. Adjusted for age, sex and APOE $\epsilon 4$. Squares represent point estimates of ORs, and horizontal lines indicate 95% CIs. The vertical dotted line denotes OR = 1.

Conclusion

In this cohort, higher amyloid burden, particularly within the highest Centiloid quartile, was associated with hippocampal atrophy in the MTA scale. Older age, APOE $\epsilon 4$ carrier status, MCI and AD also aligned with greater hippocampal atrophy, supporting the role of elevated amyloid deposition as a key correlate of more advanced neurodegenerative change. The results reinforce the influence of the Centiloid scale on the prediction of neurodegeneration.

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