

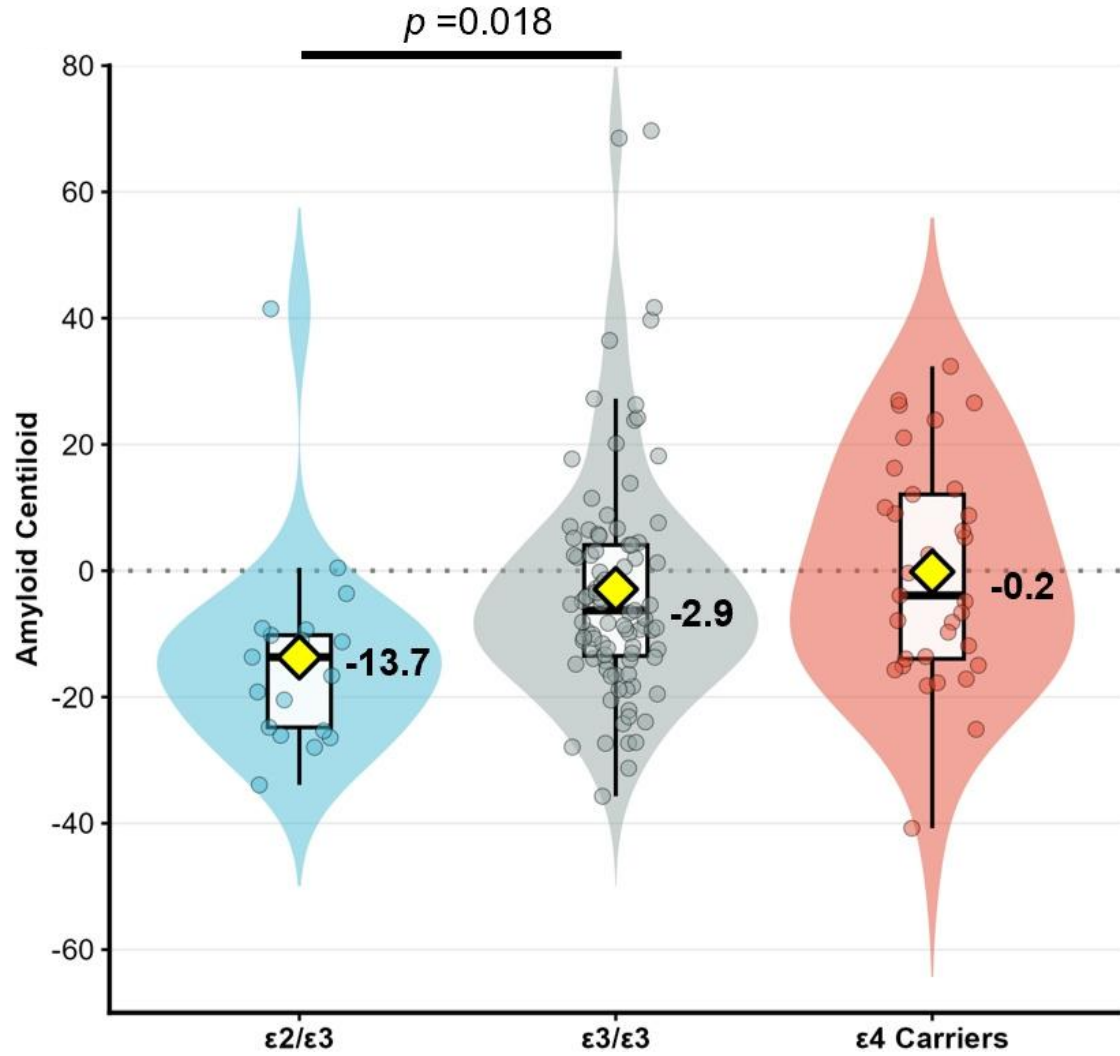
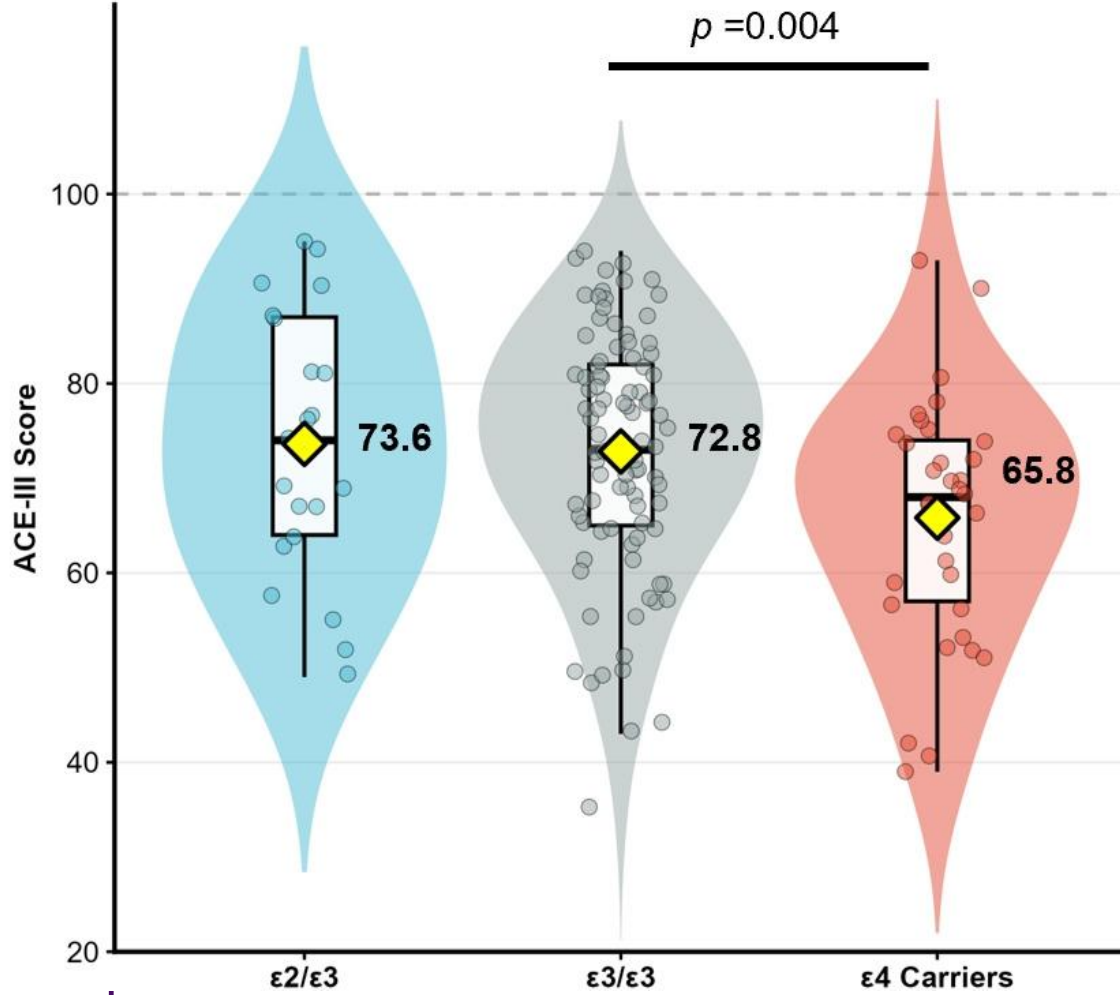
APOE Genotype Unmasks Silent Amyloidosis and Resolves the Plasma p-tau217 Gray Zone

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APOE status changes what an intermediate or discordant plasma p-tau217 result means: ϵ 4 unmasks PET-silent amyloidosis and cognitive vulnerability, while ϵ 2 marks lower amyloid burden in the gray zone.

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES
Plasma p-tau217 is a strong blood marker of amyloid pathology. Problem: intermediate gray-zone values and blood/PET discordance remain difficult to interpret. Aim: test whether APOE modifies p-tau217-amyloid coupling and resolves gray-zone ambiguity.	C-PAS cohort: 1,016 individuals with plasma p-tau217, amyloid-PET Centiloid, and ACE-III. Dual thresholds: PET-validated p-tau217 cutoffs classified negative, gray-zone, and positive groups. Analyses: blood/PET concordance, p-tau217-Centiloid coupling, and cognitive-stage interactions. Gray zone: compared ϵ2, ϵ3/ϵ3, and ϵ4 groups. Adjustment: age, sex, and education.	 Discordance: 9.94% blood/PET discordant; 15.35% fell into the p-tau217 gray zone. ϵ4 signal: enriched in Blood+/PET- and higher Centiloid than noncarriers (13.7 vs -3.6, $p < 0.001$). Early coupling: ϵ4 showed steeper p-tau217-Centiloid association, strongest in cognitively unimpaired participants. Gray-zone split: ϵ2 had lower amyloid; ϵ4 had worse cognition despite similar amyloid levels.	 APOE changes the meaning of an intermediate p-tau217 result. ϵ4 may indicate PET-silent amyloidosis and cognitive vulnerability. ϵ2 marks lower pathology; APOE-adjusted interpretation may reduce gray-zone uncertainty.	Selected references - Jack CR Jr, et al. <i>Alzheimers Dement.</i> 2024;20:5143-5169. doi:10.1002/alz.13859 - Ashton NJ, et al. <i>JAMA Neurol.</i> 2024;81:255-263. doi:10.1001/jamaneurol.2023.5319 - Brum WS, et al. <i>Nat Aging.</i> 2023;3:1079-1090. doi:10.1038/s43587-023-00471-5 - Wang Y, et al. <i>Front Aging Neurosci.</i> 2025;17:1660755. doi:10.3389/fnagi.2025.1660755 - Woo MS, et al. <i>Alzheimers Dement.</i> 2025;21:e71048. doi:10.1002/alz.71048 CONTACT Zhangyang Wang zhangyang_wang@163.com  ALZHEIMER'S ASSOCIATION AAIC 26