

Systematic baseline shifts in plasma pTau217 require cohort-specific calibration

POSTER

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KEY TAKEAWAY

Plasma pTau217 tracks amyloid burden consistently across cohorts, but absolute cutoffs are not transferable. The cross-cohort gap is a systematic baseline shift, rather than cohort-specific biology, so fixed external cutoffs

INTRODUCTION

Plasma pTau217 is a highly accurate Alzheimer's biomarker, yet whether externally derived cutoffs transfer across cohorts is uncertain, variability may reflect **biological diversity** or **pre-analytical differences**. Using Centiloids as a standardized continuous measure of amyloid burden, we tested whether Western-derived pTau217 thresholds misclassify an East Asian cohort, and whether any gap reflects altered biological **scaling (slope)** or a systematic **baseline shift (intercept)**.

METHODS

- Cohorts: **ADNI** (North America, n = 370) and **BRMH** (Korea, n = 91).
- pTau217 by **ALZpath Simoa** assay; amyloid PET standardized to **Centiloids** (Amy+ > 25 CL). ADNI: FBP, BRMH: FBB
- Compared within- vs cross-cohort **cutoffs**.
- Interaction models centered at the diagnostic threshold mapped the pTau217–Centiloid trajectory, adjusting for age, sex, APOE ε4 and MMSE.

COHORT SUMMARY

Cohort	n	Amy +/-	Cutoff	AUC
ADNI · N. America	370	162 / 208	0.45	0.88
BRMH · Korea	91	41 / 50	0.73	0.95

Table 1. Cohort composition and within-cohort pTau217 cutoffs (pg/mL).

RESULTS

Fig 1. Within-cohort discrimination — pTau217 by amyloid status and performance.

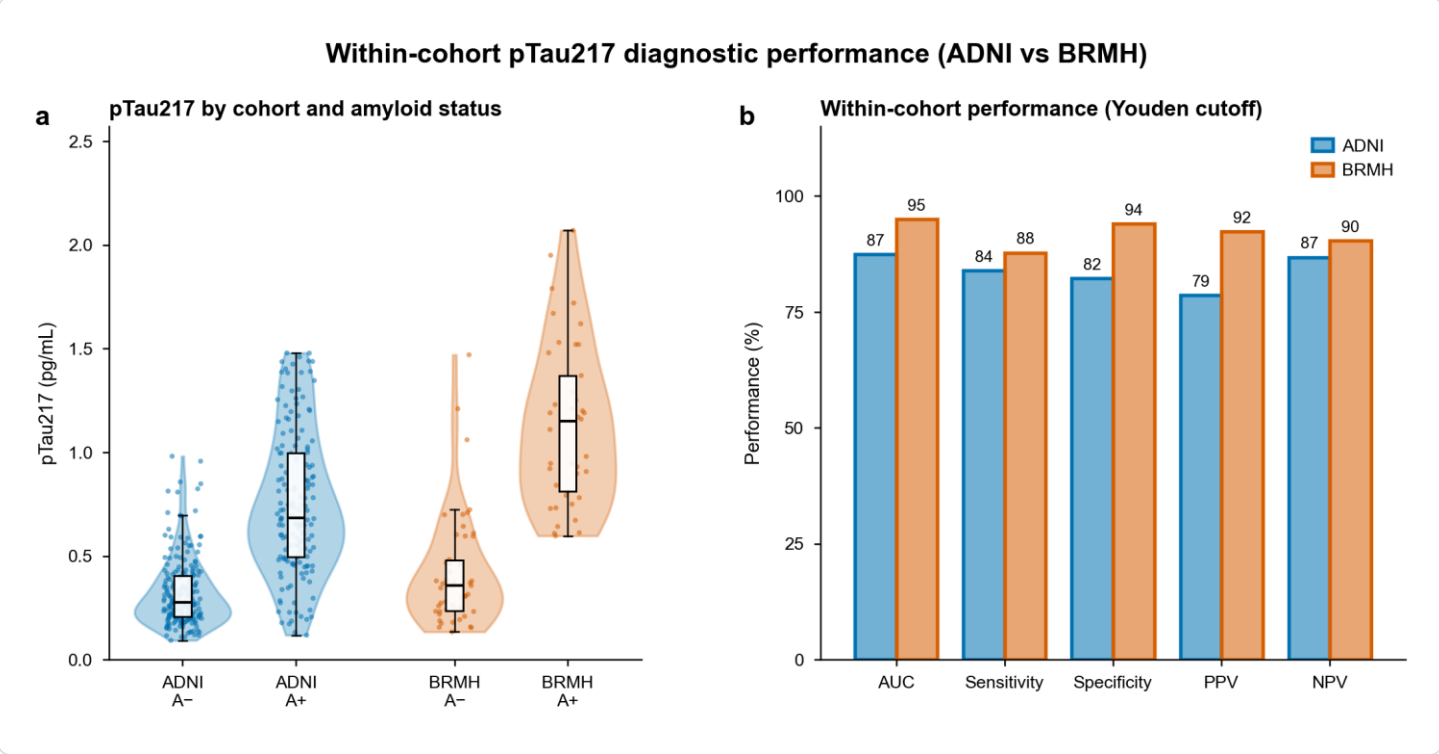


Fig 2. Cross-cohort cutoff mismatch — BRMH performance under the ADNI cutoff.

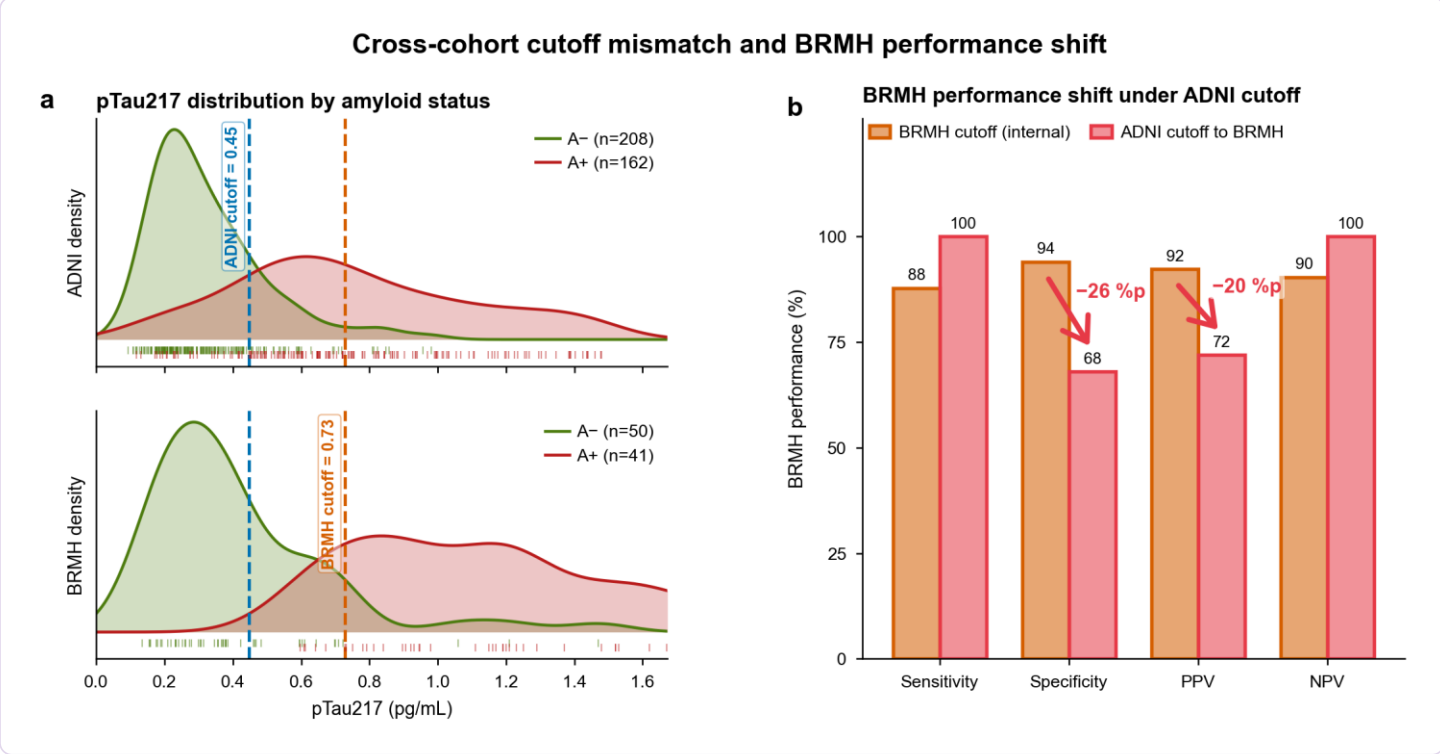
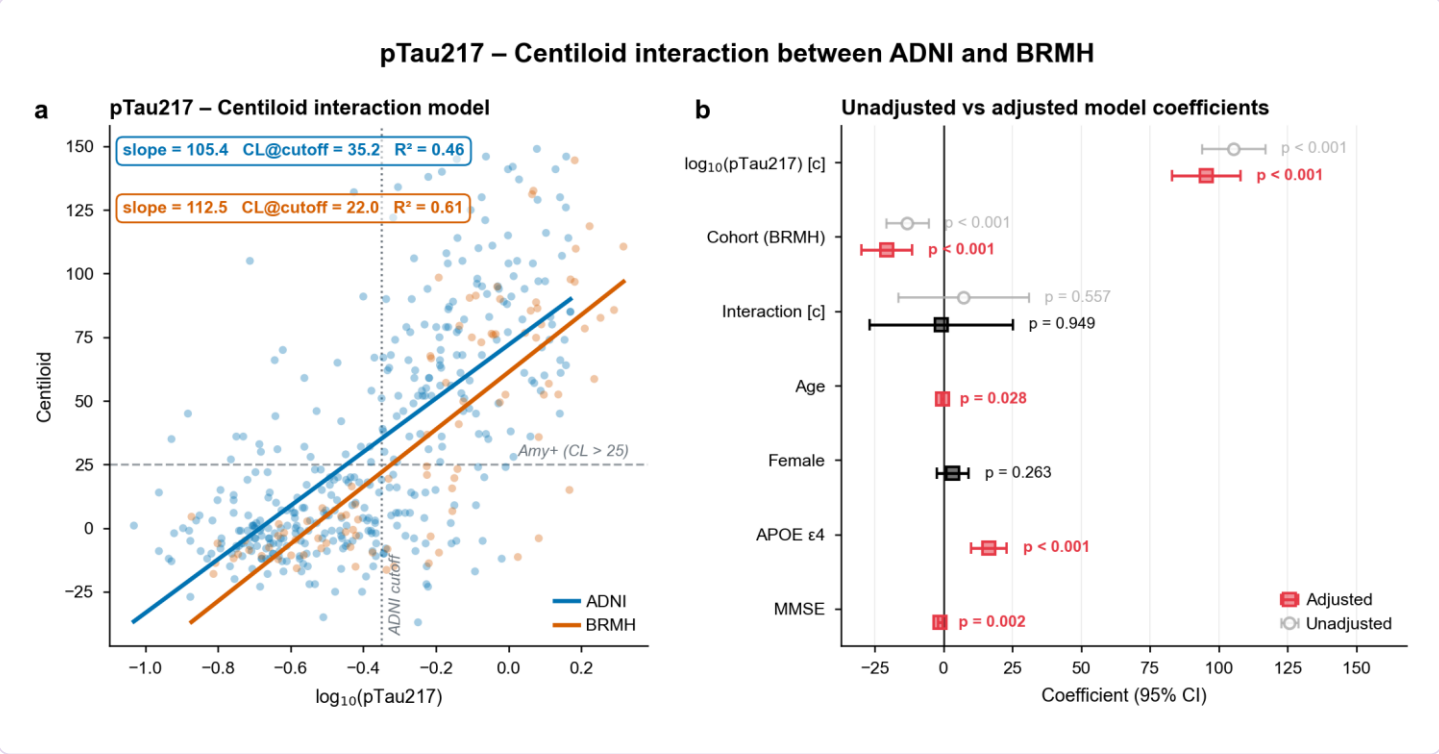


Fig 3. pTau217–Centiloid interaction — slope vs. baseline across cohorts.



Key findings.

Robust but non-portable.
AUC 0.88 / 0.95; the cutoff (pg/mL) differs between cohorts.

Mismatch inflates false positives.
ADNI's cutoff on BRMH cuts specificity (94→68) and PPV (92→72).

A baseline shift, not cohort-specific biology.
Slope preserved (interaction p = 0.949); BRMH intercept lower by 20.7 CL (p < 0.001).

CONCLUSIONS

Plasma pTau217 tracks amyloid consistently across diverse settings, but **absolute cutoffs are not transferable**. Cross-cohort discrepancies reflect systematic baseline shifts rather than cohort-specific biology. **Local validation and cohort-specific calibration are needed before clinical use.**

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