



Comparative Analysis of Heterophile Antibody Interference in the Fujirebio Lumipulse and Roche Elecsys p-tau217 Assays

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BACKGROUND

- Heterophile antibodies (HAb) are endogenous, non-specific antibodies found in some individuals that may interfere with measurement of plasma phosphorylated tau at threonine 217 (p-tau217).
- HAb may cause immunoassay-specific positive interference (falsely elevated concentrations) or negative interference (suppressed/falsely low concentrations), potentially affecting clinical interpretation.(1)
- Comparing analyte measurements obtained after sample pretreatment with HAb blockers versus untreated (neat) measurements can help assess for the presence of HAb interference. This study evaluates HAb interference in the Fujirebio Lumipulse and Roche Elecsys p-tau217 assays.

OBJECTIVES

- Comparatively evaluate heterophile antibody (HAb) interference in the Fujirebio Lumipulse and Roche Elecsys p-tau217 assays in the same samples.
- Assess whether alternative-platform testing can detect HAb interference in cases of suspected clinical discordance.

METHODS

SAMPLES

Sequential residual patient plasma samples (n=101) sent to Mayo Clinic Laboratories for Fujirebio Lumipulse p-tau217 analysis, exhibiting intermediate (0.186–0.324 pg/mL) or positive (≥ 0.325 pg/mL) concentrations, were evaluated in December 2025. Four negative samples (≤ 0.185 pg/mL) served as controls.

TESTING

Plasma p-tau217 concentrations were measured using either the Fujirebio Lumipulse® G pTau217 (research use only) RUO assay, a chemiluminescent enzyme immunoassay (CLEIA) performed on the LUMIPULSE G1200 platform, or the Roche Elecsys® pTau217 ROU assay, an electrochemiluminescence immunoassay (ECLIA) performed on a cobas e analyzer Samples were tested in December 2025.

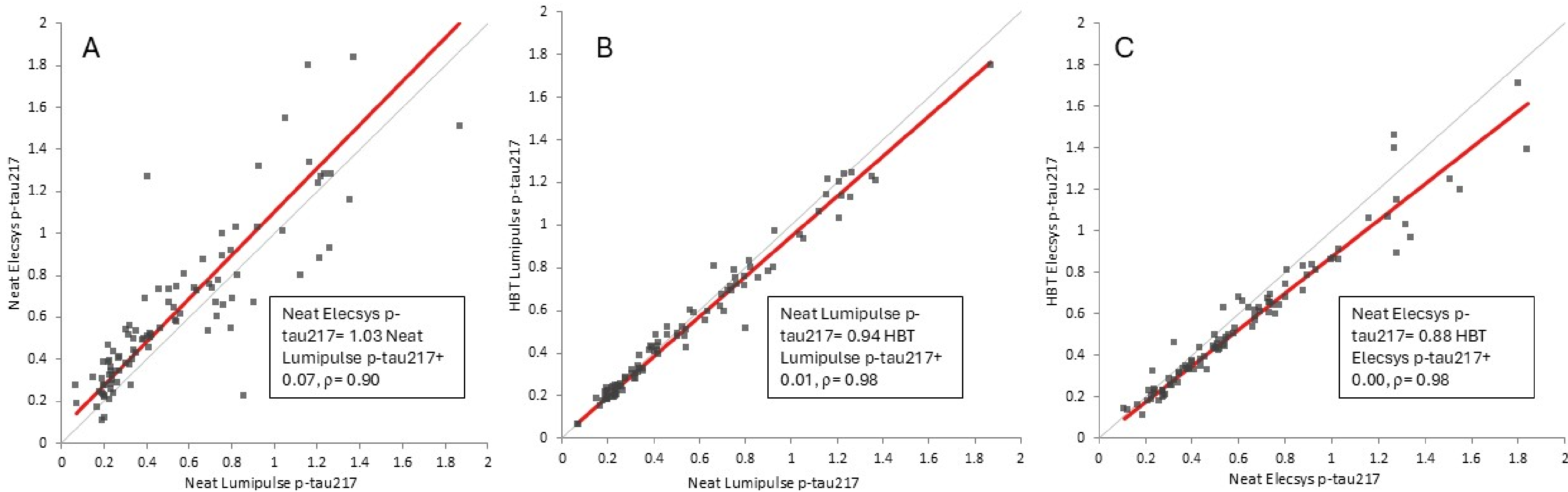
Heterophilic Blocking Tubes (HBT; Scantibodies Laboratory, Santee, CA; catalog no. 3IX762). HBT contains a unique blocking reagent composed of specific binders that inactivate heterophilic antibodies. Samples were split into neat and HBT-treated aliquots, refrigerated, and tested again within a week of each other on both the Lumipulse (Mayo Clinic) and Elecsys (Cleveland Clinic) p-tau217 immunoassays.

INTERPRETATION

Changes $\geq \pm 50\%$ for HBT-treated versus neat samples were considered indicative of, and $\geq \pm 45\%$ borderline for, heterophile antibody interference.

RESULTS

Figure 1: Comparison of Treated (HBT) versus untreated (neat) p-tau217 measurements in the Fujirebio Lumipulse and Roche Elecsys p-tau217 assays.



Passing-Bablok linear regression correlations for (a) Neat Elecsys vs. Neat Lumipulse p-tau217, (b) HBT vs. Neat Lumipulse p-tau217, and (c) HBT vs. Neat Elecsys p-tau217. All sequential and negative samples were included except suspected heterophile Cases 1–7 (n=98).

Table 1: Heterophile Classification of Patient samples in the Fujirebio Lumipulse and Roche Elecsys p-tau217 assays.

Case #	Heterophile Interference Type	Lumipulse Neat pg/mL	Lumipulse HBT pg/mL	Lumipulse % Change from Neat	Lumipulse Interpretation (Neat)	Elecsys Neat pg/mL	Elecsys HBT pg/mL	Elecsys % Change from Neat	Elecsys Interpretation (Neat)
Case 1	Negative Lumipulse	0.442	2.06	+366%	Positive	0.268	0.321	+20%	Intermediate
Case 2	Positive Lumipulse	0.329	0.144	-56%	Positive	0.232	0.191	-11%	Intermediate
Case 3	Positive Lumipulse	0.697	0.281	-60%	Positive	0.430	0.343	-20%	Positive
Case 4	Positive Lumipulse	0.364	0.112	-69%	Positive	0.172	0.153	-11%	Negative
Case 5	Negative Elecsys	0.687	0.719	+5%	Positive	0.150	0.645	+330%	Negative
Case 6	Negative Elecsys	0.192	0.168	-13%	Intermediate	0.056	0.510	+811%	Negative
Case 7	Borderline Positive Elecsys	0.189	0.173	-8%	Intermediate	0.421	0.222	-47%	Positive

Lumipulse (neat) classified as negative (≤ 0.185 pg/mL), intermediate (0.186–0.324 pg/mL), or positive (≥ 0.325 pg/mL). Elecsys (neat) classified as negative (< 0.220 pg/mL), intermediate (0.220–0.293 pg/mL), or positive (≥ 0.294 pg/mL). Relative percent changes indicative of potential heterophile interference are highlighted in bold. (2)

Results

Among 101 sequential intermediate/positive samples, three showed suspected positive and one suspected negative HAb interference in the Lumipulse assay In the Elecsys assay, two showed suspected negative and one borderline suspected positive interference (Table 1).

Affected samples differed between assays, yet HBT-treated concentrations in the affected assay roughly reflected the other assay's pattern except for Cases 1 and 6. Excluding suspected heterophile samples, platform correlation for neat samples was Elecsys = 1.03(Lumipulse) + 0.07 ($r = 0.90$); HBT treatment generally did not affect either assay ($\text{bias} \leq \pm 12\%$, $r \geq 0.98$) (Figure 1).

CONCLUSIONS

- Suspected positive and negative HAb interference was observed in both the Fujirebio Lumipulse and Roche Elecsys p-tau217 assays.
- HBT treatment did not appear to affect either assay performance.
- Affected samples generally did not overlap between the two assays, suggesting that alternative immunoassay testing may detect HAb interference in cases of suspected clinical discordance.
- HAb interference represents a newly recognized, and incompletely understood, confounding factor in the interpretation of p-tau217 immunoassays.

References

- Algeciras-Schimmich A, Theobald JP, Figdore DJ, Ashrafzadeh-Kian S, Bornhorst JA. False positive plasma p-tau217 results associated with heterophilic antibody interference: a potential clinical pitfall. *Alzheimers Dement*. 2025;21(12):e71045. doi:10.1002/alz.71045.
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