



Waad Alshammari¹, Lama Rayyis¹, Hans Frykman, Pankaj Kumar, Ali Mousavi, Veronica Hirsch-Reinshagen², Ian R. A. Mackenzie², Ging-Yuek R. Hsiung¹

¹ Division of Neurology, University of British Columbia, Vancouver, BC, Canada | ² Department of Pathology & Laboratory Medicine, University of British Columbia, Vancouver, BC, Canada

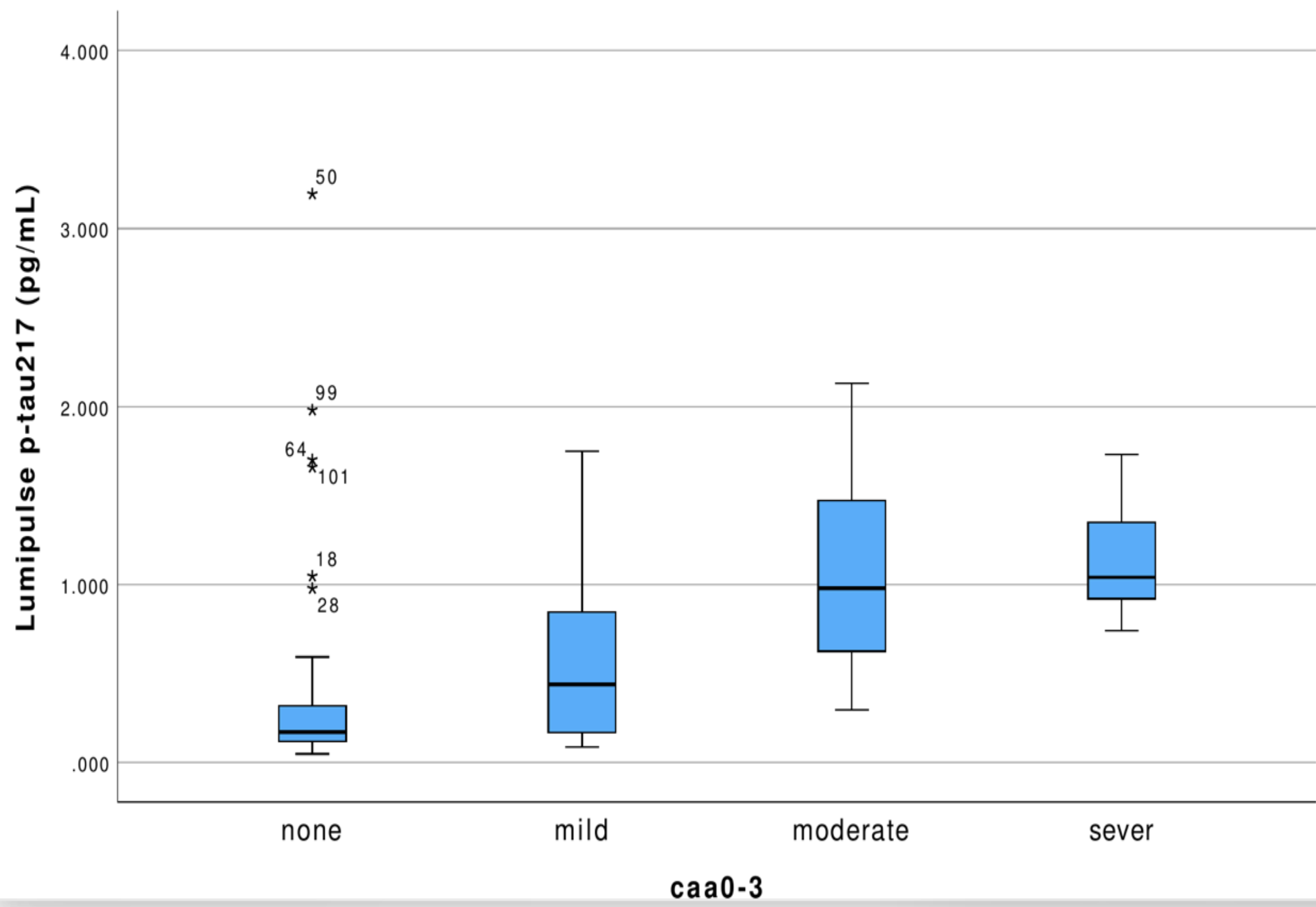
INTRODUCTION

Cerebral amyloid angiopathy (CAA) commonly co-occurs with Alzheimer’s disease (AD), but it is unclear whether CAA is associated with plasma biomarkers. Using autopsy neuropathologic staging and plasma collected during life, we examine whether plasma p-tau217 levels are affected by CAA severity versus AD neuropathological change (ADNC) using two p-tau217 assays.

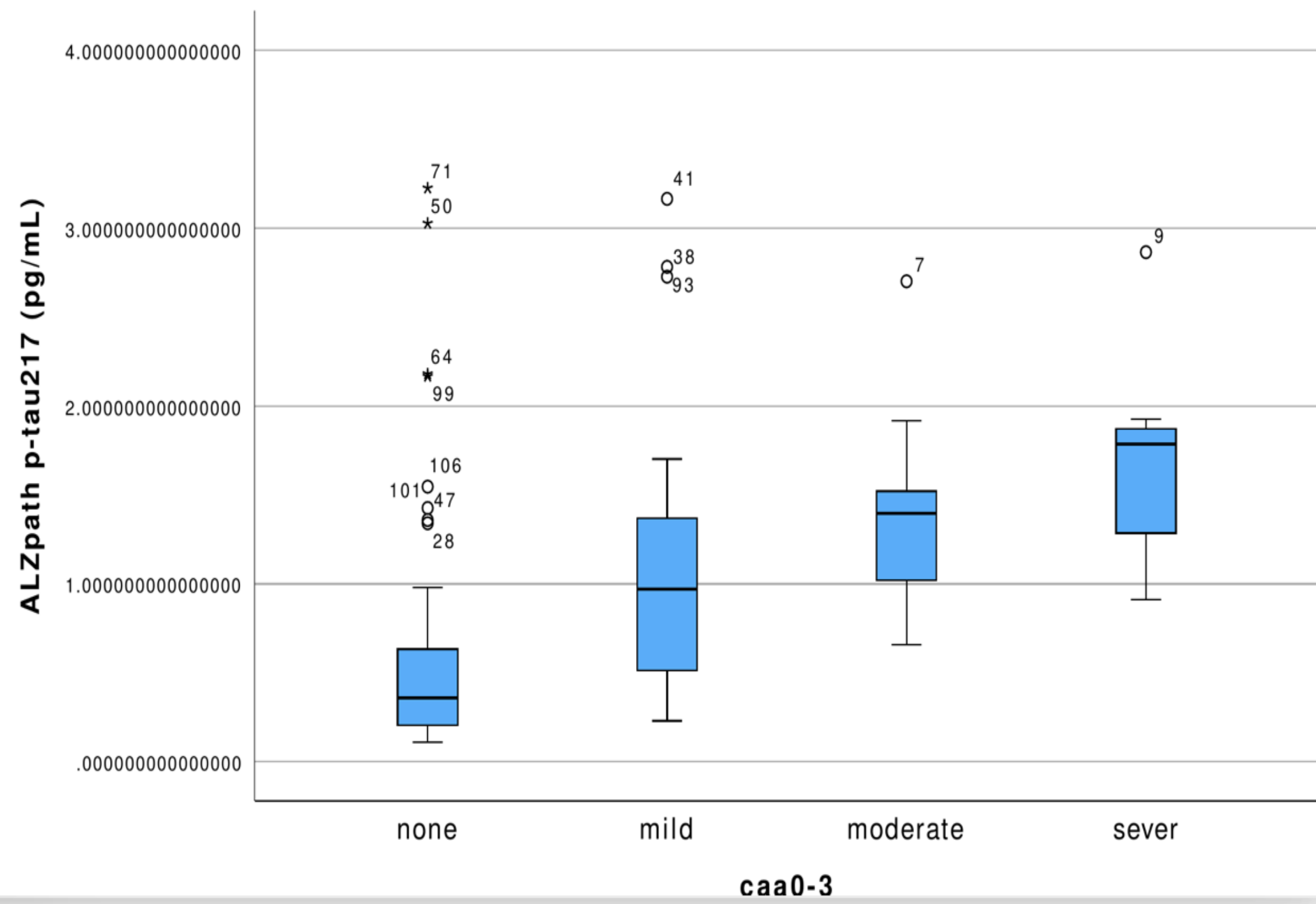
METHODS

We analyzed plasma p-tau217 levels using two assays (ALZpath and Lumipulse) in patients from the UBC Hospital Clinic for Alzheimer and Related Disorders (UBCH CARD) who had final autopsy confirmation of their diagnosis (n = 115). CAA severity was semi-quantitatively staged as 0 none, 1 mild, 2 moderate, and 3 severe. ADNC was scored as none, low, intermediate, and high. Linear regression models with logarithmic transformation of plasma levels were used to normalize the distribution. ADNC, CAA, and their interaction terms were compared using stepwise linear regression models.

A Lumipulse p-tau217 by CAA severity



B ALZpath p-tau217 by CAA severity



RESULTS

Cohort: 53.0% male; mean age at death 72.5 ± 12.0 years; mean interval from blood draw to autopsy 1.40 ± 2.51 years. No significant sex difference was observed (p = 0.327).

CAA severity: Plasma p-tau217 in both assays correlated with stepwise increase in CAA severity (Pearson R = 0.477, p < 0.001). Lumipulse rose from 0.172 pg/mL (none; n = 58) to 0.439 (mild; n = 24), 0.980 (moderate; n = 12), and 1.042 (severe; n = 8). ALZpath showed a similar rise: 0.358 pg/mL (none; n = 61), 0.971 (mild; n = 29), 1.397 (moderate; n = 15), and 1.786 (severe; n = 10).

Model comparison: When ADNC severity was examined together with CAA, ADNC showed a stronger correlation with p-tau217 levels. The ADNC × CAA interaction term was excluded.

CONCLUSIONS

Although p-tau217 levels in both assays increase with CAA severity, p-tau217 is more strongly correlated with ADNC pathology and ADNC better explains the observed association. To assess the independent contribution of CAA pathology to plasma p-tau217, future studies may need cohorts with mainly CAA pathology, such as genetic forms of CAA, with less ADNC contribution.