

Introduction

- Ultra-sensitive immunoassays now quantify low-abundance plasma proteins relevant to Alzheimer's disease and related disorders (ADRD).
- Blood biomarkers correlate well with amyloid/tau PET, but fewer studies compare them directly with autopsy-verified AD neuropathologic change (ADNC).
 - **Goal:** Evaluate how plasma proteins measured via NULISA 120-plex CNS panel relate to ADNC at autopsy.

Methods:

- **Participants:** 212 UCI ADRC participants with plasma NULISA data and autopsy evaluation (**Table-1**).
- **Assay:** NULISA Protein Quantification (NPQ)
- **Markers:** 22 amyloid- and tau-related proteins.
- **Outcome:** ADNC approximated using B (Braak) and C (CERAD) scores.
- **Models:** Bayesian regressions:
 - Ordinal logistic regression (ADNC levels)
 - Binary logistic regression (ADNC presence)
 - Adjusted for age, sex, education, and blood-to-death interval.
- **Performance metrics:** ROC AUC and PSIS-LOO cross-validation.

	None (N=31)	Low (N=10)	Intermediate (N=48)	High (N=123)	Overall (N=212)
Age at plasma (years)					
Mean (SD)	80.8 (9.53)	83.4 (16.1)	82.6 (9.41)	78.3 (11.2)	79.9 (11.0)
Median [Min, Max]	82.0 [55.0, 102]	87.5 [51.0, 111]	83.0 [50.0, 100]	81.0 [45.0, 97.0]	81.0 [45.0, 111]
Age at death (years)					
Mean (SD)	82.8 (9.23)	85.1 (16.1)	84.5 (9.42)	81.1 (10.8)	82.3 (10.6)
Median [Min, Max]	83.0 [61.0, 104]	89.0 [52.0, 112]	86.0 [52.0, 100]	83.0 [46.0, 98.0]	84.0 [46.0, 112]
Years plasma to death					
Mean (SD)	2.00 (1.63)	1.70 (1.34)	1.88 (1.68)	2.80 (2.51)	2.42 (2.22)
Median [Min, Max]	1.00 [0, 6.00]	1.50 [0, 4.00]	1.00 [0, 8.00]	2.00 [0, 15.0]	2.00 [0, 15.0]
Sex					
Male	17 (54.8%)	6 (60.0%)	25 (52.1%)	66 (53.7%)	114 (53.8%)
Female	14 (45.2%)	4 (40.0%)	23 (47.9%)	57 (46.3%)	98 (46.2%)
Years of education					
Mean (SD)	14.9 (2.78)	16.4 (1.84)	16.0 (2.87)	15.7 (3.15)	15.7 (2.99)
Median [Min, Max]	15.0 [8.00, 20.0]	16.0 [14.0, 20.0]	16.0 [8.00, 24.0]	16.0 [3.00, 24.0]	16.0 [3.00, 24.0]
pTau-217 NPQ					
Mean (SD)	11.2 (0.986)	11.3 (0.540)	11.7 (0.788)	12.5 (0.716)	12.1 (0.928)
Median [Min, Max]	11.0 [9.91, 15.3]	11.2 [10.4, 12.3]	11.7 [10.2, 13.4]	12.5 [10.1, 14.9]	12.2 [9.91, 15.3]

Table-1: Participant characteristics by ADNC level

Results

- **Visualization:** Strong separation of NPQ distributions across ADNC.
 - Mostly for pTau markers (**Figure-1**)
- **BD outperformance:** Brain-derived (BD) pTau consistently better than standard pTau for predicting ADNC.
- **Classification performances:** AUCs for ADNC presence:
 - pTau-181: Standard 0.80 → BD 0.88
 - pTau-217: Standard 0.86 → BD 0.89
 - pTau-231: Standard 0.82 → BD 0.87
- **Cross-validation:** BD markers showed better model fit by PSIS-LOO.
 - All elpd mean differences < -4; |mean/sd| > 2

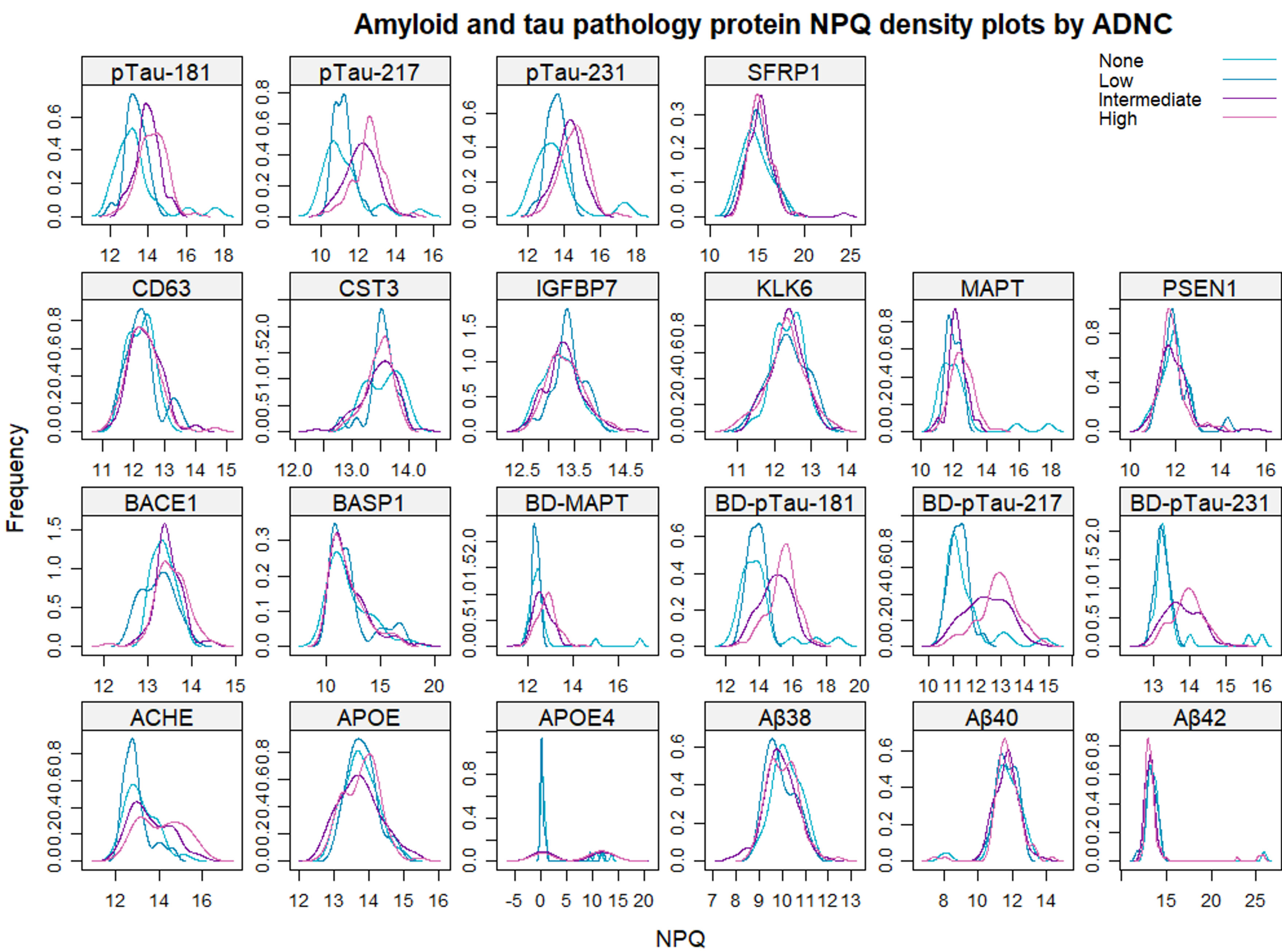


Figure-1: Lattice plot of NPQ density by ADNC level

Summary

- pTau plasma NPQ values from NULISA are strong predictors of autopsy-defined ADNC, while other measures (e.g. AB) did not appear to distinguish as well.
- The BD-pTau levels, in particular, provided better differentiation of ADNC levels and outperformed the non-BD versions
 - **Take-home:** Our findings support BD pTau as a promising, scalable blood-based biomarker for AD neuropathology.