

Prognostic Value Of Early Practice Effects After Adjustment For Plasma P-tau217 And Amyloid PET In Preclinical AD (A4)

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Jiaxuan Pei, Zixuan Lin
College of Biomedical Engineering & Instrument Science, Zhejiang University, Hangzhou, China

Early practice effects provide modest incremental prognostic value beyond plasma p-tau217 and amyloid PET.				
INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES
- Practice effects (PE) from repeated testing may reflect learning capacity and cognitive resilience. - p-tau217 and amyloid PET quantify pathology, but may not fully capture resilience. - We tested whether early PE improves prediction of later cognitive decline and confirmed CDR progression in amyloid-positive, cognitively unimpaired A4 participants.	- 982 cognitively unimpaired, amyloid-positive A4 participants with early Cogstate assessments. - PE = Empirical Bayes-stabilized Cogstate learning-curve slope across Weeks 1-21; residualized for baseline Cogstate and z-scored. - Outcomes: PACC from Week 48 onward (n = 832; 4,615 observations) and confirmed CDR-GS progression from 0 to >=0.5 (n = 701). - Adjusted for age, sex, education, APOE e4, amyloid PET SUVR, plasma p-tau217, and baseline Cogstate.	- 223/701 participants (31.8%) progressed during post-Week 48 follow-up. - Progression by PE group: 23.9% High, 29.8% Moderate, 41.1% Low. - Low PE predicted faster PACC decline vs High: beta = -0.072 points/year; 95% CI -0.101 to -0.042; p = 2.3e-6. - Low PE predicted higher CDR progression risk: HR = 1.84; 95% CI 1.36-2.50; p = 9.2e-5. - Adding PE improved C-index 0.678 to 0.697; Delta = 0.0193; LR chi2 = 15.75; p = 3.8e-4; CV Delta = 0.015. - Standardized 1-year progression risk: 27.1% High PE vs 42.8% Low PE.	- Lower early PE predicted faster cognitive decline and short-term CDR progression after adjustment for p-tau217, amyloid PET, demographics, education, and baseline cognition. - PE may capture learning efficiency and cognitive reserve not fully represented by static biomarkers. - Early repeated testing could support biomarker-adjunct risk stratification for preclinical AD trials.	1. Sperling RA et al. N Engl J Med. 2023;389:1096-1107. 2. Donohue MC et al. JAMA Neurol. 2014;71:961-970. 3. Palmqvist S et al. JAMA. 2020;324:772-781. 4. Duff K et al. Am J Geriatr Psychiatry. 2011;19:932-939. CONTACT Jiaxuan Pei Zhejiang University jiaxuan_pei@zju.edu.cn Presentation format: Online ALZHEIMER'S ASSOCIATION AAIC26