

No Association Of Plasma P-tau217 And Apoe ε4 With Practice Effects In Subjective Cognitive Decline - Brascodes Cohort

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INTRODUCTION

Practice effects (PE), defined as performance improvements observed upon repeated cognitive testing, represent an important marker of early cognitive efficiency and neural plasticity. These short-term learning gains — thought to reflect the brain’s adaptive capacity in response to prior test exposure, have increasingly been recognized as meaningful indicators of early neurocognitive functioning. Whether plasma p-tau217 levels or APOE ε4 carrier status modulates such gains in individuals with subjective cognitive decline (SCD), however, remains unclear, a gap that is particularly notable in low- and middle-income settings.

METHODS

Baseline plasma p-tau217, *APOE* genotyping, and detailed cognitive assessments were obtained in participants of the Brazilian Subjective Cognitive Decline (BRASCODE) cohort. Cognitive testing was repeated after 12 months. Domain-specific practice effects were computed as z-standardized change scores from baseline. Linear regression models examined whether p-tau217 (log-transformed) or *APOE* ε4 status predicted 12-month practice effects across memory, executive function, and language, adjusting for baseline domain performance, age, sex, and education.

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RESULTS

We included 139 participants in the analysis. At baseline, their mean (SD) age was 70.25 (4.53) years, their mean education was 14.06 (5.55) years, and the sample was predominantly White (93.2%). Neither plasma p-tau217 nor *APOE* ε4 status was associated with global practice effects (p = 0.68 and p = 0.34, respectively). Domain-specific analyses confirmed the absence of biomarker or genetic modulation of PE across memory (p-tau217 p = 0.12; *APOE* ε4 p = 0.57), language (p-tau217 p = 0.59; *APOE* ε4 p = 0.61), and executive function (p-tau217 p = 0.27; *APOE* ε4 p = 0.25). In contrast, education consistently predicted larger PE, most prominently in executive function (estimate = 0.108, p < 0.0001), while higher baseline cognitive performance was strongly associated with reduced PE across all domains.

Table 1: Summary of associations with practice effects (PE) across cognitive domains (N = 139)

Variable	Domain	Effect on Practice Effects	Statistic	Significance
Sample characteristics				
Plasma p-tau217	Global	No association	p = 0.68	ns
APOE ε4 status	Global	No association	p = 0.34	ns
Plasma p-tau217	Memory	No association	p = 0.12	ns
APOE ε4 status	Memory	No association	p = 0.57	ns
Plasma p-tau217	Language	No association	p = 0.59	ns
APOE ε4 status	Language	No association	p = 0.61	ns
Plasma p-tau217	Executive Function	No association	p = 0.27	ns
APOE ε4 status	Executive Function	No association	p = 0.25	ns
Education	Executive Function	Larger PE (strongest effect)	estimate = 0.108	p < 0.0001
Education	All domains	Larger PE	—	Significant
Baseline cognitive performance	All domains	Reduced PE	—	Strong association

CONCLUSIONS

In the BRASCODE cohort, short-term learning gains were not shaped by early Alzheimer’s disease pathology (p-tau217) nor by genetic susceptibility (*APOE* ε4). Instead, practice effects reflected cognitive reserve proxies, particularly education and baseline ability. These findings indicate that PE in SCD predominantly captures general cognitive learning potential rather than early biomarker-related decline, reinforcing their value for characterizing individual variability in preclinical cognitive dynamics before biomarker–cognition coupling becomes detectable.