

Cortical Excitability (TMS-EEG) as a Marker of Cognitive Impairment and Alzheimer's Pathology

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BACKGROUND

Objective neurophysiological biomarkers capable of discriminating Alzheimer's disease (AD) pathology and clinically relevant cognitive impairment across heterogeneous clinical populations are critically needed.

Early TMS–EEG components, such as the **P30**, are thought to reflect cortical excitability and effective connectivity, yet their diagnostic relevance in mixed cohorts remains underexplored.

METHODS

105
Memory-clinic patients & volunteers

17
MoCA ≤ 23 (cognitively impaired)

22
AD biomarker positive



Delphi-MD (TMS-EEG) assessment

Stimulation sites: M1L, M1R, LDLPFC, RDLPFC

Measure: P30 amplitude at contralateral central electrodes
Outcomes: (i) AD biomarker positivity (ii) MoCA ≤ 23
Analysis: Logistic regression (M1L alone; multiregional model) + 5,000 bootstrap resamples

KEY FIGURES

Figure 1. M1L Contra-electrode TEP amplitude by group

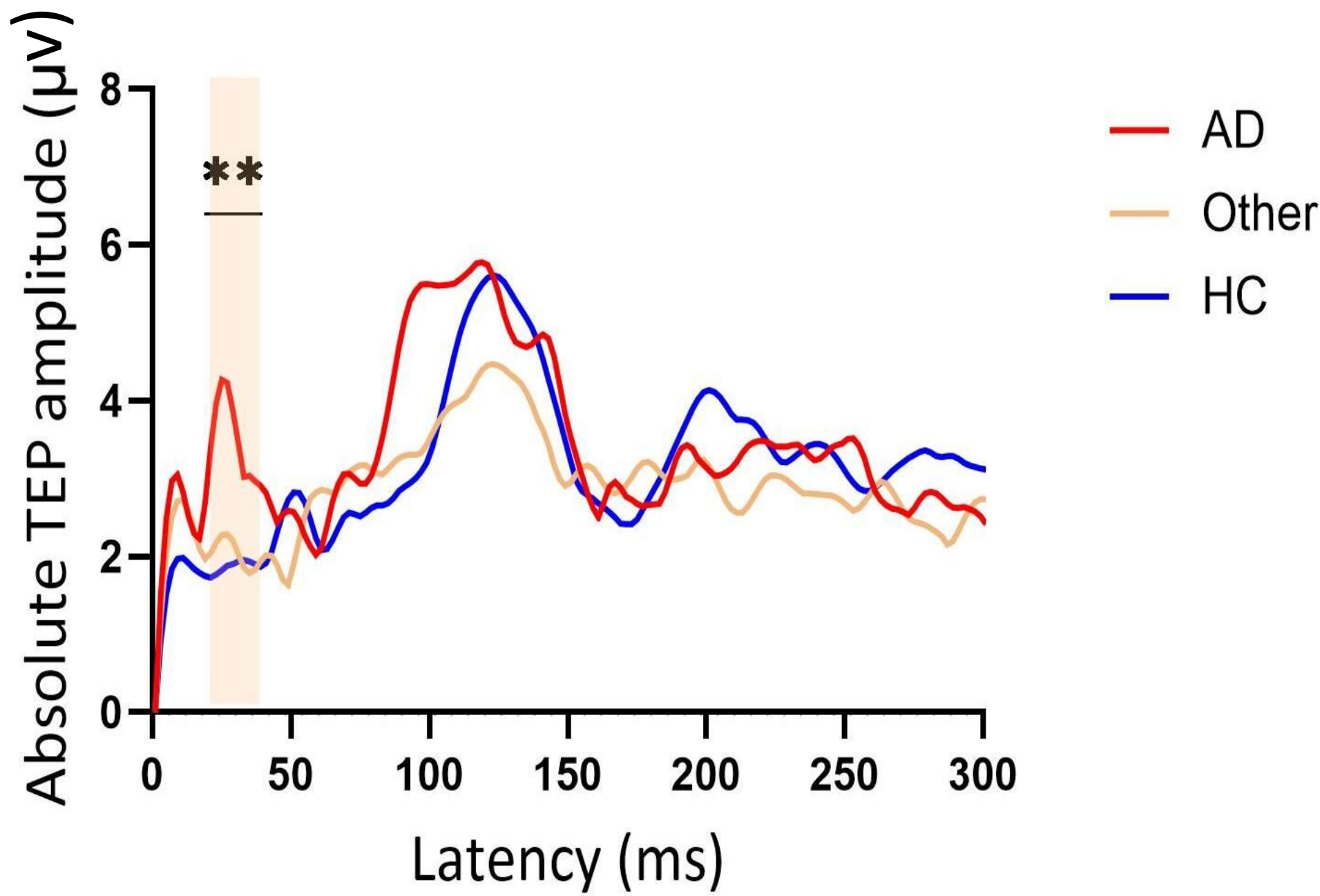
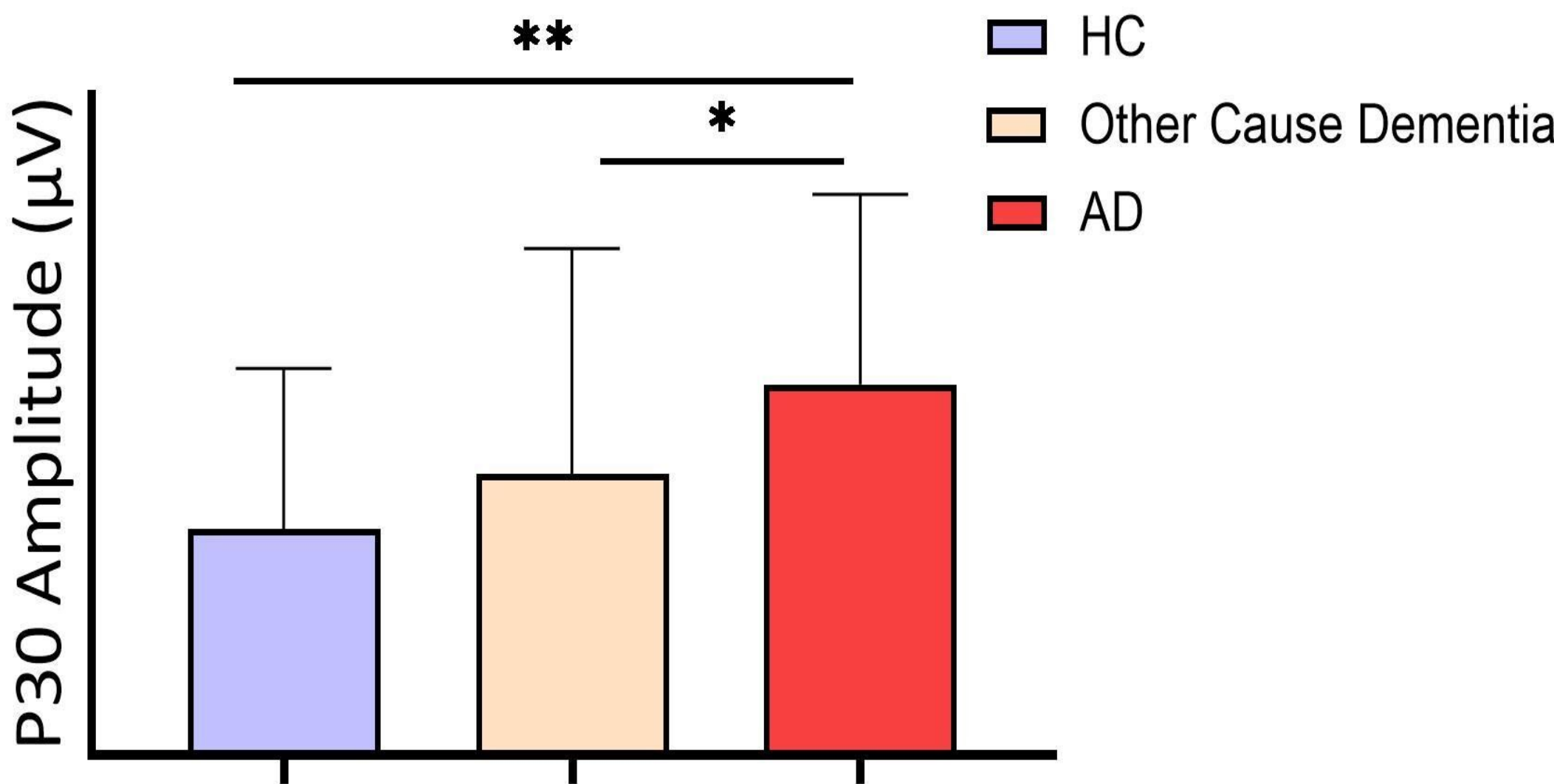
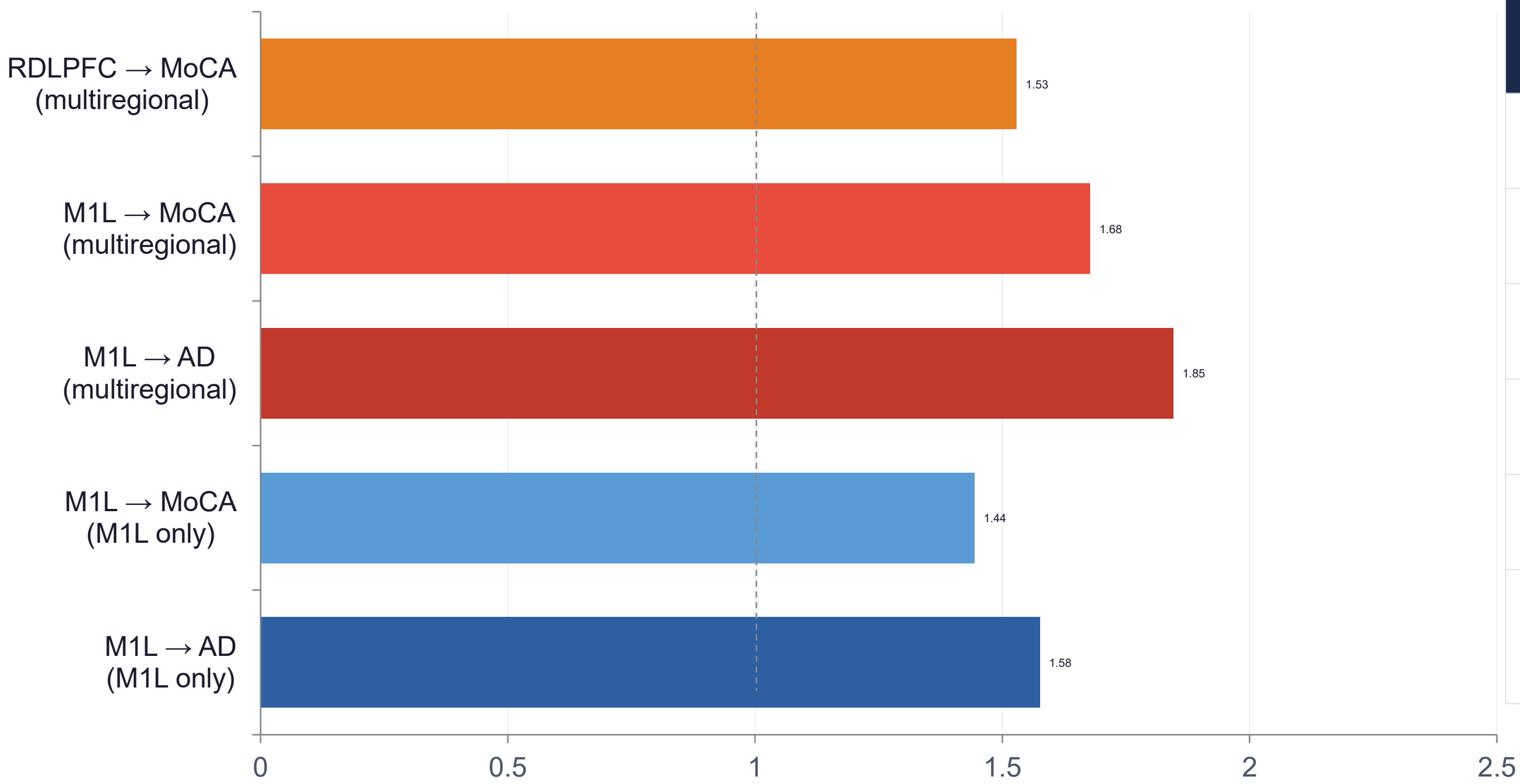


Figure 2. M1L P30 amplitude: HC vs. Other-Cause Dementia vs. AD



RESULTS

Odds Ratios — P30 Predicting AD Biomarker Status & Cognitive Impairment
OR = 1.0



Summary Table — Logistic Regression Results

Model / Predictor	Outcome	OR (95% CI)	p
M1L P30 (M1L only)	AD biomarker	1.58 (1.10–2.26)	.014*
M1L P30 (M1L only)	MoCA ≤ 23	1.44 (0.99–2.10)	.054†
M1L P30 (multi)	AD biomarker	1.85 (1.21–2.82)	.004**
M1L P30 (multi)	MoCA ≤ 23	1.68 (1.08–2.62)	.023*
RDLPFC P30 (multi)	MoCA ≤ 23	1.53 (1.05–2.24)	.028*
Model fit (multi, MoCA)		$\chi^2(4) = 14.7, p = .005; Nagelkerke R^2 = 0.23$	

CONCLUSIONS

M1L P30 amplitude independently predicts both **AD biomarker positivity** and **cognitive impairment** in a mixed memory-clinic cohort.

- 1

Higher P30 at M1L is significantly associated with AD biomarker positivity (OR 1.58, p=.014), confirmed by 5,000-bootstrap resampling.
- 2

M1L P30 shows borderline association with MoCA ≤ 23 (OR 1.44, p=.054) when tested alone.
- 3

In a multiregional model (M1L+M1R+LDLPFC+RDLPFC), overall model fit is significant ($\chi^2=14.7, p=.005; R^2=0.23$).
- 4

M1L (OR 1.68, p=.023) and RDLPFC (OR 1.53, p=.028) independently discriminate cognitive impairment within the network model.
- 5

P30-based TMS–EEG markers may serve as objective indicators of cortical dysfunction relevant to neurodegeneration and cognitive decline.
- Future directions: longitudinal validation, ROC analysis, and multi-site replication in larger cohorts.