

Harmonization Models Of Resting-state EEG Features For Multisite Studies And Cost-effective Dementia Prevention Strategies



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This study demonstrates that resting-state EEG, when properly harmonized across sites and modeled against lifespan norms, can reliably distinguish individuals at different stages of dementia risk, from preclinical to symptomatic, using spectral features that are both interpretable and clinically actionable. The proposed framework is scalable, reproducible, and cost-effective, making it particularly relevant for global dementia prevention strategies and underserved populations where accessible, affordable biomarkers are most urgently needed.

INTRODUCTION

METHODS

Multisite EEG studies face challenges such as heterogeneous acquisition systems, unbalanced sample sizes, and inter-site variability, which can limit the reliability and generalizability of neurophysiological markers in dementia research.

We propose a unified framework that combines data harmonization, statistical sample enrichment, and normative modeling to enhance early detection in at-risk individuals and assessment in symptomatic populations.

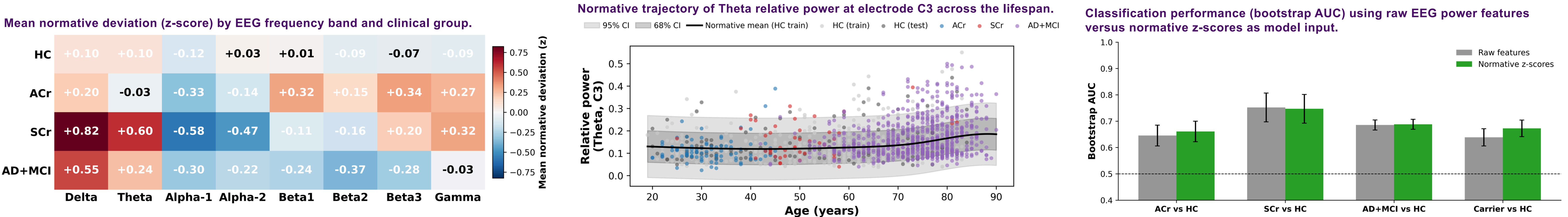
EEG data were collected from participants across multiple international clinical and research sites, including asymptomatic individuals with risk factors, symptomatic patients, and healthy controls. **Site-related variability was reduced using ComBat-based harmonization while preserving biological covariates such as age and sex.**

Propensity Score Matching (PSM) at varying ratios balanced control samples relative to at-risk participants. Computational EEG features were derived from independent components, and normative models across the lifespan were used to quantify individual deviations in spectral features (theta, alpha, beta, gamma).

Variable	HC (N=683)	ACr (N=91)	SCr (N=47)	AD+MCI (N=669)	Statistics	Post-hoc (Dunn-Bonf. / Tukey)
Age (years)	56.7 ± 17.0	31.9 ± 6.5	51.9 ± 12.2	73.5 ± 8.5	KW H=586.50, eta2p=0.393, p=<0.00001	HC vs ACr; HC vs AD+MCI; ACr vs SCr; ACr vs AD+MCI; SCr vs AD+MCI
Education (years)	10.1 ± 6.0 (n=100)	11.9 ± 3.1	8.7 ± 4.3	8.4 ± 4.1 (n=7)	KW H=17.48, eta2p=0.060, p=<0.001	ACr vs SCr
Sex (F:M)	218:169	58:33	17:11	27:16	chi2=2.15, V=0.063, p=0.542	—
MMSE	29.2 ± 1.3 (n=123)	29.2 ± 1.0	22.7 ± 5.3	18.3 ± 4.9 (n=43)	KW H=185.69, eta2p=0.609, p=<0.00001	HC vs SCr; HC vs AD+MCI; ACr vs SCr; ACr vs AD+MCI
MoCA (not assessed in AD+MCI)	25.3 ± 3.3 (n=40)	25.4 ± 3.0 (n=38)	12.3 ± 7.2 (n=13)	—	KW H=27.51, eta2p=0.290, p=<0.00001	HC vs SCr; ACr vs SCr

RESULTS

This integrated approach improved early detection of at-risk participants, achieving high classification accuracy across cohorts. Normative modeling revealed distinct neurophysiological trajectories: **theta power deviations were most associated with cognitive impairment**, while **higher-frequency (beta/gamma) alterations identified preclinical at-risk individuals**. In symptomatic populations, **slowing of delta and alpha rhythms correlated with cognitive, motor, and functional deficits**, supporting clinical relevance.



CONCLUSIONS

Combining multisite harmonization, statistical enrichment, and normative modeling provides a scalable, reproducible, and interpretable framework for rsEEG studies. This approach enables **cost-effective early detection**, monitoring across disease stages, and translation from research to clinical assessment. Harmonized EEG features offer a robust tool to guide global dementia prevention strategies and support applications across diverse populations.

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