

Reactive EEG Biomarkers for Diagnosis and Prognosis of Alzheimer's Disease

P3-06

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Reactive EEG: A novel biomarker for Alzheimer's disease and mild cognitive impairment.

INTRODUCTION

**Background:** We previously introduced reactive electroencephalography(rEEG), a novel approach for the early diagnosis and prognostic evaluation of Alzheimer's disease (AD) and mild cognitive impairment (MCI), based on the ionic resilience of neural cells in response to externally applied electrical perturbations. rEEG measures brain voltage responses to controlled electrical perturbations, revealing distinct electrochemical response patterns in healthy and pathological neural tissues.

**Objective:** To validate our previous findings, we assessed the diagnostic performance of rEEG in an independent cohort.

METHODS

**Participants:** 105 elderly participants were enrolled (45 AD, 30 MCI, 30 NC; mean age 76.57 ± 6.63 years).

METHODS

**Clinical Assessment:** Diagnoses were established at Seoul National University Bundang Hospital using MMSE, CERAD-K, CDR, K-IADL, SGDS, and MRI.

**rEEG Acquisition:** rEEG was measured using the Diastim20 system (Megnosis Co., Ltd., Korea) with 20 electrodes positioned according to the international 10–20 system. Scalp voltages were measured while applying a controlled current (<20 kHz, <100 μA). All electrodeskin contact impedances below 10 kΩ to ensure signal quality.

**Analysis:** Responses were analyzed in low-frequency (<100 Hz) and high-frequency (1–20 kHz) bands. Under current-controlled conditions, rEEG voltages reflect brain impedance, denoted as Z-LFB and Z-HFB.

**Statistics:** Group differences were evaluated using two-way ANOVA.

RESULTS

rEEG demonstrated high diagnostic performance, achieving accuracies of 95% for AD vs. NC, 93% for AD vs. MCI, and 95% for MCI vs. NC, with an overall multiclass accuracy of 90% (Table 1). Z-HFB differentiated AD and MCI from NC, whereas Z-LFB further discriminated AD from MCI (Fig. 1). Notably, the MCI group exhibited concurrent alterations in both Z-HFB and Z-LFB. Representative Z-HFB and Z-LFB patterns for AD, MCI, and NC are presented in Fig. 2.

Table 1. Classification performance of rEEG biomarkers for AD, MCI, and NC.

| Classification | rEEG             |    |                   |    |                   |    |
|----------------|------------------|----|-------------------|----|-------------------|----|
|                | AD-NC separation |    | AD-MCI separation |    | MCI-NC separation |    |
|                | T                | F  | T                 | F  | T                 | F  |
| Positive       | 42               | 1  | 42                | 2  | 27                | 0  |
| Negative       | 3                | 29 | 3                 | 28 | 3                 | 30 |
| Accuracy       | 95%              |    | 93%               |    | 95%               |    |

(A) Pairwise classification results for AD vs. NC, AD vs. MCI, and MCI vs. NC

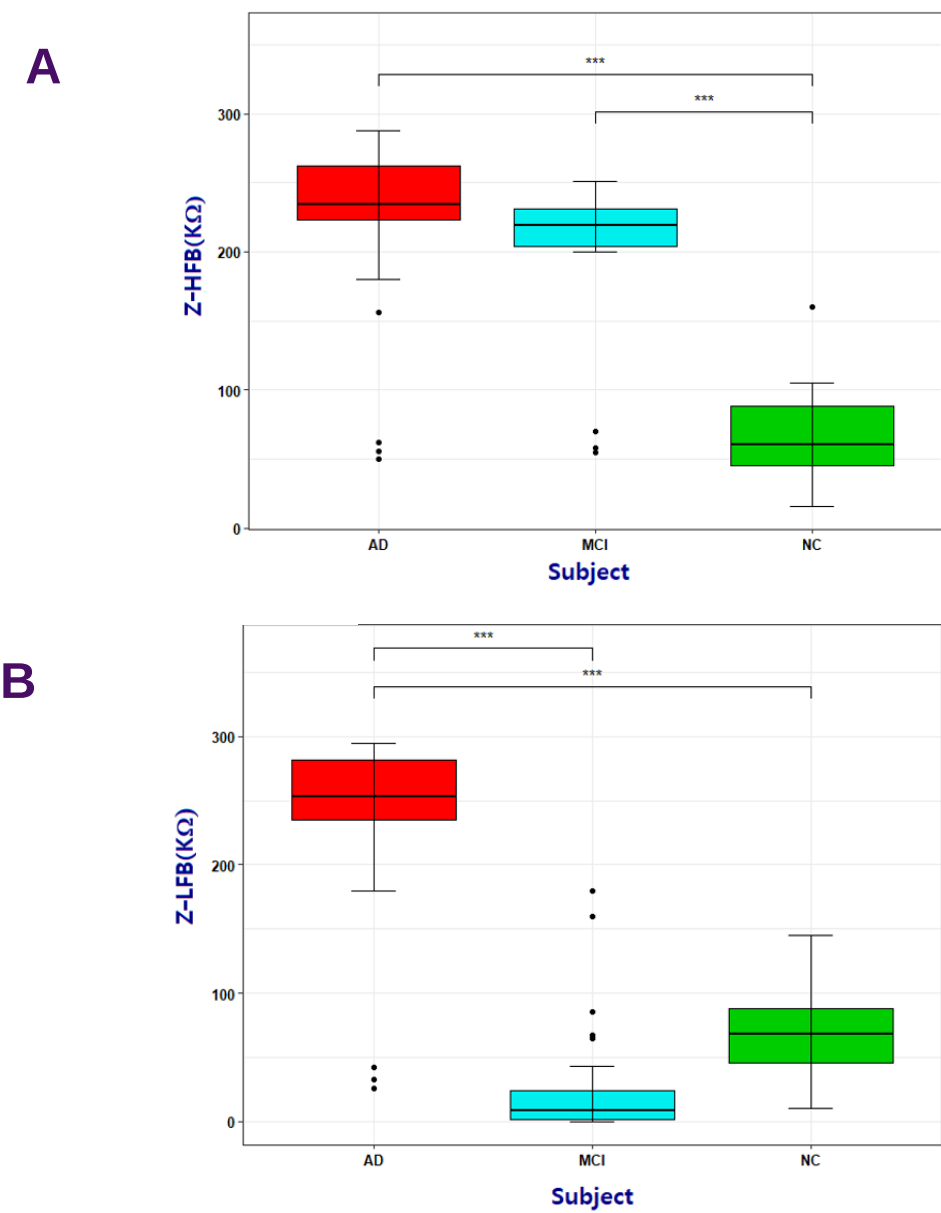


Fig. 1. Comparison of rEEG-derived brain impedance values (Z-HFB and Z-LFB) among AD, MCI, and NC groups. HI-AD and LI-AD denote AD subgroups with high and low brain impedance, respectively. \*\*\*p < 0.001.

| Classification | rEEG |     |    |
|----------------|------|-----|----|
|                | AD   | MCI | NC |
| AD(measured)   | 40   | 2   | 0  |
| MCI(measured)  | 2    | 25  | 0  |
| NC(measured)   | 3    | 3   | 30 |
| Accuracy       | 90%  |     |    |

(B) Multiclass confusion matrix for simultaneous classification of AD, MCI, and NC.

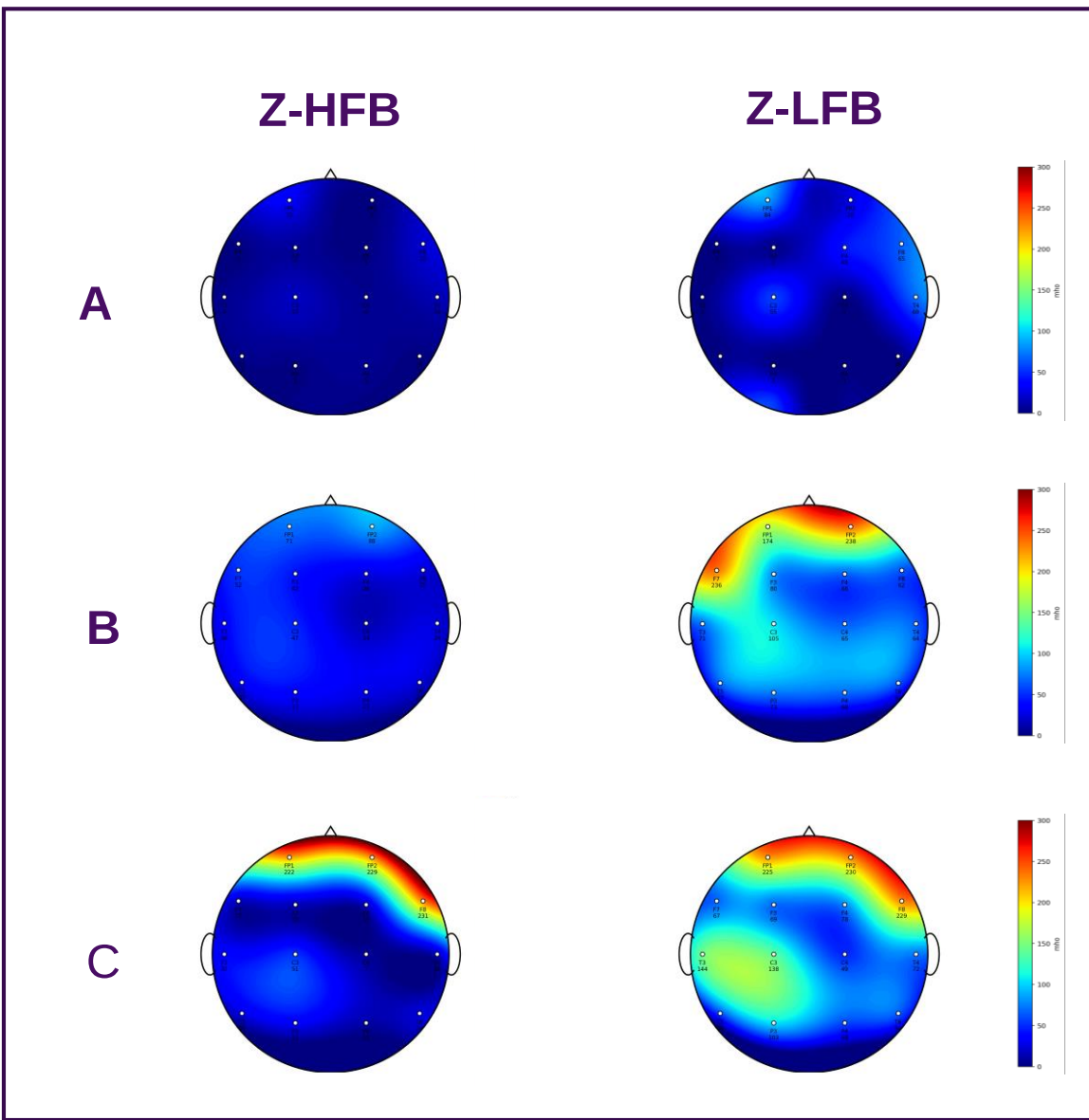


Fig. 2. Typical rEEG patterns in (A) AD, (B) MCI, and (C) NC based on Z-HFB and Z-LFB.

CONCLUSIONS

rEEG demonstrated high diagnostic accuracy for distinguishing AD and MCI, supporting its potential as a clinically applicable tool for early screening and a biomarker for neurodegenerative diseases.

Disease stage-dependent variations in rEEG patterns further suggest its value for prognostic evaluation.

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