EEG Signatures Associated with Resting State, Memory and Attention As Potential Reliable Biomarkers of Cognitive Decline in Alzheimer’s Disease

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INTRODUCTION

Background: EEG provides a noninvasive measure of brain activity with established utility in characterizing pathophysiologic neural processes associated with the progression of Alzheimer’s disease (AD).

Objective: To assess the validity of EEG biomarkers in disease monitoring and diagnosis of different stages of cognitive decline: Mild Cognitive Impairment (MCI) vs. AD.

METHODS

Participants: Under IRB approval, EEG was recorded from AD (n=26), MCI (n=24) and age-matched healthy controls (HC, n=26) during both resting state eyes open and eyes closed (5 min each, Table 1) and event-related potential cognitive tests (Table 2) of memory and attention.

Memory Test: During the memory test, participants were first presented with a series of 20 target images to memorize (each image was presented twice for 1.5s, 10 trials). Then, 100 images were presented (20 Target images randomly interspersed with 80 non-Target images) (stimulus duration = 4 s, ISI = 2.5 sec). The participants were asked to respond by pressing different keys on the keyboard to Targets and NonTargets stimuli.

Attention Test: The sustained attention test consisted of 37 visual stimuli (duration=0.4s) displayed in random location on the screen with variable ISI ranging from 1.5-1.0s. Participants were required to discriminate one primary and frequent Target stimulus (an up-pointing triangle, 75%) from two rare NonTarget stimuli (a down-pointing triangle and a diamond shape, 15% each).

EEG Analysis: EEG was filtered between 0.1 and 50 Hz. Artifacts were removed using independent component analysis (ICA) and the Lasso tool in EEGlab. For resting state, average power spectral density during eyes closed/opened/fixed attention bands were computed for one-second epochs and compared between groups (HC, MCI, AD). For cognitive tests, Event-related-potentials (ERPs) were calculated and compared for each stimulus type by computing average trials. Novel trials and ERPs with less than 15 trials in attention tasks and 10 trials in memory task were excluded. Components of ERPs including early components (< 200ms) and late positive potentials (>300 ms) after stimulus onset were measured.

Missing data: Most AD patients did not complete cognitive tests. However, compliance rate for individuals with MCI was higher and they were included in analysis.

RESULTS

Resting state EEG: Compared to healthy controls, AD patients showed significantly higher Theta power (t-test, p<0.05, df=103) in parietal, temporal and right frontal areas and significantly lower Alpha power (t-test, p<0.05, df=103) in frontal areas. MCI group evidenced a nonsignificant trend towards increased Theta.

Attention task: MCI group showed a significant increase in latency of ERP components (~35 ms) in frontal and central areas, a significant decrease in amplitude of LPP component (~2uv) in the right hemisphere, ~110ms delayed reaction time in response and ~10% reduction in response accuracy.

Memory task: MCI group showed a significant increase in latency of early components (~30 ms) in posterior and central areas, increase in latency of the LPP peak amplitudes in occipital area, ~60ms delayed reaction time and ~8% reduction in response accuracy.

Conclusions

Standard resting state PSD measures are reliable biomarkers for Alzheimer’s but are less sensitive to early stages of cognitive decline (MCI).

Event-related potentials (ERPs) elicited by cognitive tasks are more sensitive (than resting state EEG) to early cognitive decline (MCI). However, complex cognitive tasks might be less reliable in advanced stages of MCI and AD.

Longitudinal studies are needed to explore the validity of EEG biomarkers in diseases progression.

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