Prognostic Value of Event Related Potentials for Rate of Cognitive Decline in Patients with Mild Alzheimer's Disease

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Introduction

We investigated whether Event Related Potentials (ERP) can help predict rate of cognitive decline in patients with mild Alzheimer's disease (AD).

ERP methods are well suited to detect and quantify the cognitive deficits associated with AD, and their potential as a sensitive and reliable cognitive biomarker that can help AD diagnosis has been well characterized. However, the usefulness of ERP as a prognostic measure for AD has not been thoroughly investigated and is less clear.

Materials and Methods

Study Participants

Fifty-two study subjects with probable mild AD were enrolled in the study.

Subjects had an MMSE score of 21 to 26 inclusive, a clinical dementia rating (CDR) score of 0.5, 1, or 2, and an education adjusted score requirement on the delayed recall of the Wechsler logical memory II subscale.

Baseline Visit

Subjects that met inclusion criteria were administered a three-stimulus oddball paradigm using the COGNISION® System. Trials averaging, extraction of ERP features and analysis of the behavioral response from the tests were automatically performed by the COGNISION ® System software.

Follow-up Visits

Study subjects visited the clinical study sites a minimum of two additional times in the three years following the baseline visits. Visits were separated by at least 30 days, and included MMSE testing.

Data and Statistical Analysis

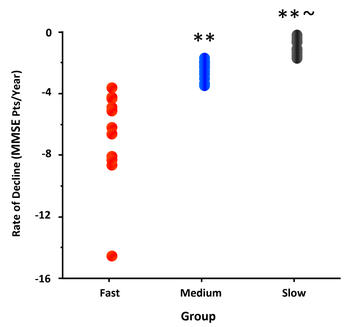
Out of the 52 subjects, 11 were lost to follow up, 4 had medication changes that could affect the MMSE score, and 4 failed to show cognitive decline over time.

The remaining 33 subjects were divided in fast, medium and slow decliners (N=11 per group) based on the rate of decline over time as measured by MMSE.

Finally, ERP measures collected at baseline were compared across fast, medium and slow decliners to investigate whether they could be predictive of future rate of cognitive decline.

Results

Rate of cognitive decline in fast, medium and slow decliners



Average yearly changes in MMSE score were -6.59±0.94 SEM for fast decliners (N=11), -2.30±0.18 SEM for medium decliners (N=11), and -0.78±0.14 for slow decliners (N=11).

Statistical analysis was performed using ANOVA followed by Neuman-Keuls *post-hoc* test. ***P <0.01* compared to fast decliners; ~=*P <0.1* compared to medium decliners.

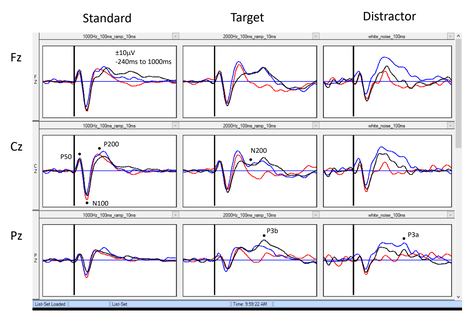
Demographics and psychometric data did not differ across groups

Test	FD (N=11)	MD (N=11)	SD (N=11)	P-Value
Age (y)	77.82±2.06	76.64±2.75	76.54±2.31	>1
Male (%)	36	64	64	>1
Education (y)	16.27±0.87	13.45±0.61	15.00±1.17	0.326

	FD (N=11)	MD (N=11)	SD (N=11)	P-Value
CDR-SB	0.95±0.12	0.91±0.06	0.82±0.08	> 1
MMSE	22.54±0.56	23.91±0.46	23.82±0.67	0.74
LM-IR	2.82±0.88	6.54±1.27	6.64±1.06	0.11
LM-DR	1.36±0.66	1.91±0.80	2.18±0.81	> 1

Data is shown as Mean ± SEM. Comparisons were analyzed using χ^2 test and ANOVA for categorical and quantitative variables, respectively. *P*-values are shown after Bonferroni correction for multiple comparisons.

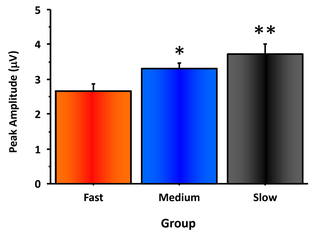
ERP measures collected at baseline showed significant differences across study groups



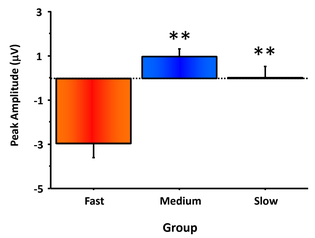
ERP grand average waves at the midline electrodes for fast decliners (in Red, N=11), medium decliners (in Blue, N=11), and slow decliners (in Black, N=11).

ERP features are shown at the electrode of maximum amplitude.

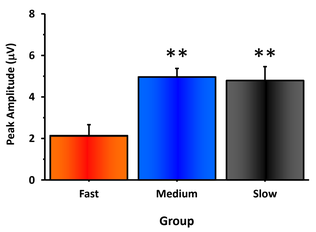
P50 Amplitude



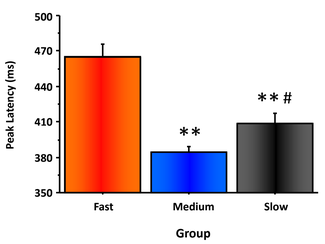
N200 Amplitude



P3b Amplitude



P3b Latency



Data is Mean ± SEM. Comparisons were analyzed using ANOVA followed by Neuman-Keuls *post-hoc* test. *P*-values were adjusted using Bonferroni correction for multiple comparisons. ***P <0.01* compared to fast decliners; **P <0.05* compared to fast decliners; #*= P <0.05* compared to medium decliners.

ERP measures with no significant differences across groups

	FD (N=11)	MD (N=11)	SD (N=11)	P-Value
P50 L (ms)	42.45±0.97	41.14±0.99	45.30±1.20	0.12
N100 A(uV)	-6.69±0.35	-6.12±0.36	-6.00±0.47	>1
N100 L (ms)	96.66±1.18	94.34±1.31	94.92±0.89	>1
P200 A (uV)	3.70±0.30	4.68±0.32	4.26±0.32	0.48
P200 L (ms)	207.77±2.19	215.61±2.50	212.07±2.25	0.31
N200 L (ms)	273.76±4.84	259.57±3.72	272.51±5.77	0.3
P200 A (uV)	3.70±0.30	4.68±0.32	4.26±0.32	0.48
P200 L (ms)	207.77±2.19	215.61±2.50	212.07±2.25	0.31
P3a A (uV)	2.7±0.43	4.73±0.55	2.05±1.04	0.11
P3a L (ms)	430.04±9.21	408.98±6.79	429.03±6.14	0.59

Data in the Behavioral Task of the ERP test did not show group differences

	FD (N=11)	MD (N=10)	SD (N=11)	P-Value
Button Press Accuracy (%)	76.1±8.4	82.7±6.1	90.6±3.4	0.81
False Alarms (%)	4.3±1.2	1.4±0.6	3.9±2.4	>1
Median Reaction Time (ms)	498.18±23.68	502.80±36.78	430.18±30.45	0.54

Data is Mean ± SEM. Comparisons were analyzed using ANOVA. *P*-values are shown after Bonferroni correction for multiple comparisons.

Conclusions

- Fast, medium and slow declining AD subjects did not differ by demographics or psychometric scores at baseline.
- Fast decliners had significantly lower P50, N200 and P3b peak amplitudes at baseline than the other groups. They also showed significantly prolonged P3b latency.

To our knowledge, this is the first study to investigate whether ERP can have prognostic value for patients with mild AD. Study results show that ERP measures might prove to be reliable predictors of cognitive decline in this patient population for the three years post-test.

References

- Cecchi M, et al. A clinical trial to validate event-related potential markers of Alzheimer's disease in outpatient settings. Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring, 1(4), 387–394.
- Bennys K, et al. Diagnostic value of event-related evoked potentials N200 and P300 subcomponents in early diagnosis of Alzheimer's disease and mild cognitive impairment. J Clin Neurophysiol 2007;24:405–12.

Acknowledgments

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