사상관련전위 P300 요소를 이용한 알츠하이머형 치매의 탐지와 분석

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Alzheimer Disease detection and analysis using P300 componenet of ERP in Alzheimer type Dementia

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Abstract

This study is to develop the Alzheimers disease (AD) detection and analysis system using event related potential (ERP) of AD patients. We recorded ERP in an auditory oddball paradigm in mild AD (n 25), severe AD (n 12), age matched normal aged controls (n 17), and young controls (n 7). The amplitude and latency of target P300 components were compared among 4 groups. The relationship between P300 measures and neuro psychological test (K DRS) scores were evaluated by correlations. The latency of P300 was prolonged in AD and the effects were correlated with the severity of dementia. The P300 amplitude was not affected significantly in AD. Theres no difference between normal aged group and young group. These results suggest that the P300 component is specifically affected by Alzheimer type dementia.

Key Word;

event related potential, P300, Alzheimer disease

I. INTRODUCTION

The event related potential (ERP) has been used for objective monitoring to assess age related change in cognitive brain function. Goodin & collaborator(1978) demonstrated the slowing of event related potential P300 with aging, many

researchers have studies the effects of dementia on ERP components but to be still a matter of debate and the diagnostics

roles of ERP remain to be confirmed [1]. In particular, the P300 component of ERP has been widely applied in the study of attention and memory processes [2].

P300 amplitude is thought to index brain activity that is "required in maintenance of working memory" when the model of the stimulus context is updated [3].

P300 latency is considered to be measure of stimulus classification speed[4] and is generally unrelated to response selection processes(McCarthy and Donchin 1981)[5]. Since P300 latency is processing time index before response generation, it is a sensitive temporal measure of the neural activity underlying the processes of attention allocation and immediate memory[6].

The aim of this study was to evaluate whether P300 component of ERP may be used to stage of severity of AD as well as to identify patients from normal matched controls.

II. METHOD

1) *Subject*:

Twenty five subjects just meeting the criteria of probable AD according to the definition of the K DRS and MRI scan compose the mild AD group (average age: 69.3). Twelve patients suffering with AD for more 2 years are in the severe AD group (average age: 69.6). Seventeen volunteer age matched control group (average age: 68.0) were recruited. They were carefully screened to eliminate individuals with medical or neuropsychiatric disorders. And seven normal young group (average age: 27.2) were participated in this study.

2) *Procedure*

The experiments were conducted with the subject comfortably seated in a sound attenuated room. Before EEG recording, all elderly subjects were taken the K DRS (Korean dementia rating scale) neuropsychological test.

For the auditory oddball paradigm, the stimuli consisted of a series of computer generated tone with 85dB, 300msec duration. Tones of 1kHz(standard tone) and 1.5kHz(target tone) were presented in a random sequence occurring in 75% and 25% of the 100 trials, respectively. Subjects were asked to count the number of the target tone and to report it after the session.

The EEG was recorded from Ag/Ag Cl electrodes place at 5 scalp locations (F3, F4, Cz, P3, P4) based on the 10 20 system and below the left eye, all referenced to both earlobes. The impedance of electrodes was kept below 5 kΩ. The EEG was amplified, filtered (bandpass 1 35 Hz), digitized (250Hz/ channel), and stored in a personal computer for off line analysis. Individual trials with excessive muscle activity or eye blinking were excluded.

3) *Data analysis*

We measured P300 components in ERP to standard and target stimuli. The P300 component was defined as the largest positive peak in the interval 284 500msec post stimulus. The peak amplitude of P300 component was measured relative to prestimulus baseline.

III. RESULTS

1) *Behavior*

The correct response rates to target tones showed a significant difference among groups. While normal aged group (88 %) and young group (100%) showed high accuracy, mild AD group (20%) and severe AD group (0%) had problems to count target stimuli.

2) *Neuropsychological test*

The K DRS consists of 5 categories of sub test, i.e. attention, initiation & preservations, construction, conceptualization, and memory test. The total score of K DRS of old groups are presented in Fig. 1. There are significant difference among groups ($F(2,47)$ 11.92, $p<.000$).

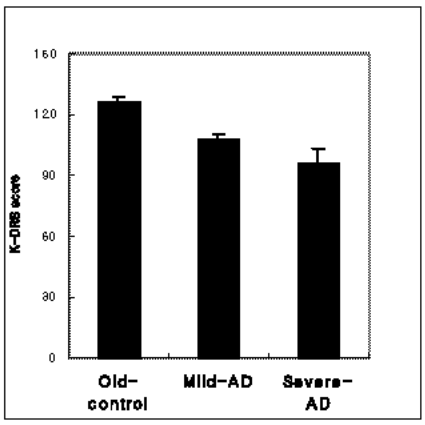

Fig1. K-DRS Score

3) *Electrophysiology*

Prominent P300 components characterized ERP elicited by target tones (Fig. 2). There was a significant group effect for the latency of P300 target tone ($F(3,52)$ 8.18, $p<.000$; $F(3,50)$ 18.42, $p<.000$). Post hoc analyses revealed that latency in severe AD group is longer than those of mild AD group and normal groups (Fig. 3).

Latency of P300 component was delayed in AD patients and delay in latency was increased as AD had been developed (Fig3).

P300 latency correlated significantly with the score of K DRS (Pearson correlation **r = -.54****, p <.01) (Fig. 4).

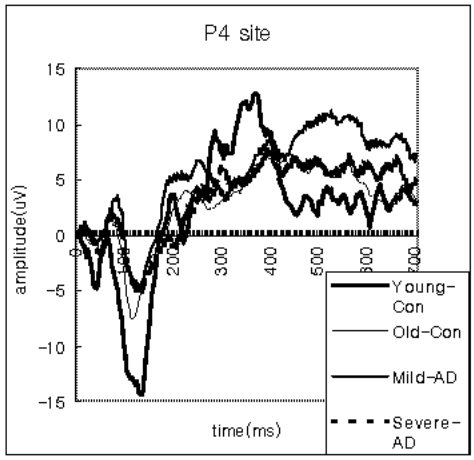

Fig2. Grand average ERP waveform

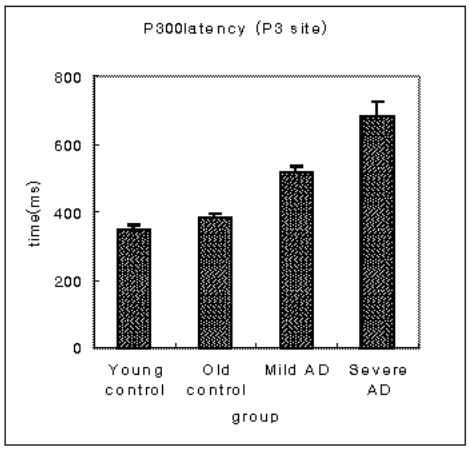

Fig3. P300 latency

Latency is negatively correlated K-DRS total score.

IV. DISCUSSION

The major finding of this study was the latency of P300 component in AD patients, whereas the amplitude of P300 was not different with normal controls. The prolonged effects of P300 latency were correlated with the severity of dementia.

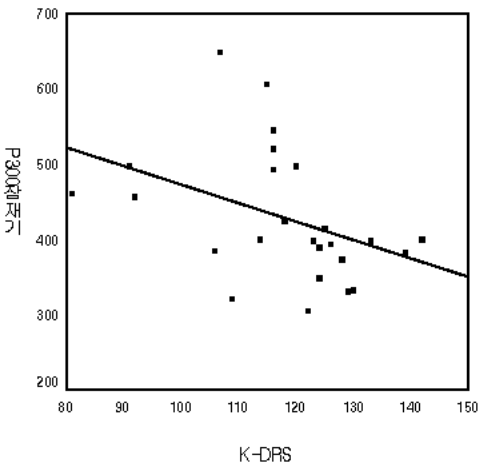

Fig4. K-DRS and P300 latency Correlation

P300 latency is considered as an index of the processing time required before response generation. It reflects the neural activity underlying the process of attention allocation and information processing. In our study, P300 latency was correlated with the scores of neuropsychological test(K DRS).

These results suggest that the P300 components of ERP could be useful indices in detection of AD the representation of the neural plasticity. These indices could be used not only to score the severity of AD but also predict and diagnose the disease.

REFERENCES

[1] Goodin DS,Squire KC,Henderson B,Starr A.Age related brain potentials to auditory stimuli in normal human subjects. *Electroenceph clin Neurophysiol* 1978;44:447 458

[2] Breslau J, Starr A, Sicotte N, Higa J, Buchsbaum MS. Topographic EEG changes with normal aging and SCAT. *Electroenceph clin Neurophysiol* 1982;72:281 289.

[3] Donchin, E. & Coles, M.G.H.(1988). Is the P300 component a manifestation of context updating?. *Behavioral and Brain Science, 11*, 357 374.

[4] Polich, J., Ehlers, C. L., Otis, S., Mandell, A. J., & Bloom, F. E.(1986). P300 latency reflects the degree of cognitive decline in dementing illness. *Electroencephalogr. Clin. Neurophysiol., 63,* 138 144.

[5] McCarthy, G., & Donchin, E. (1981). A metric for thought: a comparison of P300 latency and reaction time. *Science* 211, 77 80.

[6] Polich, J., Herbst, K.L. (2000). P300 as a clinical assay: rationale, evaluation, and findings. *International Journal of Psychophysiology*, 38, 3 19.

[7] Casteneda, M., Ostrosky Solis,F., Perez,M., Bobes,M.A., & Rangel,L.E. (1997). ERP assessment of semantic memory in Alzheimer disease. *International Journal of Psychophysiology, 27,* 201 214.

[8] Rodriguez G, Nobili F, Arrigo A, Priano F, De Carli F, Fancione S, Gambaro M, Rosadini G. Prognostic significance of quantitative

electroencephalography in Alzheimer patients: preliminary obsevations. *Electroenceph clin Neurophysiol* 1996;99:123 128.
[9] Duffy FH, Albert MS, McAnulty GB. Brain electrical activity in patients with presenile and senile dementia of Alzheimer's type. *Ann Neurol* 1984;16:439 448.
[10] Ford, J.M., Woodward,S.H., Sullivan, E.V., Isaacks, B.G., Tinklenberg, J.R., Yesavage, J.A., Roth, W.T.(1996) N400 evidence of abnormal responses to speech in Alzheimer's disease. *Electroencephalography and Clinical Neurophysiology.* 99:3 235 46
[11] Hamberger, M.J., Friedman, D., Ritter, W., & Rosen. J.(1995)Event related potential and behavioral correlates of semantic processing in Alzheimer's patients and normal controls. *Brain and Language* 48:1 33 68
[12] Holt, L.E., Raine, A., Pa, G., Schneider, L.S., Henderson, V.W., & Pollock, V.E. (1995). P300 topography in Alzheimer disease. *Psychophysiology, 32,* 257 265.
[13] Iragui, V., Kutas, M., & Salmon, D.P.(1996). Event related brain potentials during semantic categorization in normal aging and senile dementia of the Alzheimer's type. *Electroencephalography and Clinical Neurophysiology.* 100:5, 392 406.