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Event-related Evoked Potentials in Alzheimer's Disease by a Tool-Using Gesture Paradigm

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Abstract—**The Alzheimer's disease (AD) has a wide spectrum of symptoms, ranging from cognition dysfunction to behavior disturbances and functional impairment. The evoked cerebral potentials by specific paradigms are useful for disclosing neuropsychological activities. The evolution of AD is accompanied by progressive cognitive impairment which may result in a difficulty to recognize or comprehend gestures. In the present study, a visual tool-using gesture paradigm was employed to assess the cognitive functions of 16 probable AD patients, 17 subjects mild cognitive impairment (MCI), and 17 age-matched control subjects. Each subject was conducted by visual stimuli by a series of pictures, each displaying randomly a gesture with correctly or incorrectly using a tool. The P300 amplitude was further used as a parameter to build classifiers based on support vector machine.**

I. Introduction

Alzheimer's disease (AD) is known as a degenerative brain disease. The AD is featured by deterioration in cognition and memory and progressive impairment in ability to carry out daily activities. Early diagnosis of AD becomes increasingly essential. Mild cognitive impairment (MCI) is a transitional stage between normal aging and AD. The criteria for screening MCI and AD require patient history and object neuropsychological evaluation.

Event-related potentials (ERP) provide a tool to disclose cerebral cognitive activity elicited by specific stimulus. The positive wave appearing around 300 ms after stimulus, named as P300 component, is the most frequently recorded cognitive potentials. Using auditory odd-ball paradigm based on identifying odd high-pitched from low-pitched sounds, decreased P300 amplitude and longer P300 latency were reported in AD patients against control subjects [1–3].

In addition to auditory oddball paradigm, visual cognitive tasks including the number-letter paradigm to discriminate the numerical order of two numbers or the alphabetic order of two letters [4], semantic judgment of congruent or incongruent words [5], etc. were also applied for assessing cognitive functions of AD and MCI patients. Persons with dementia have been concerned with the difficulty to discriminate, recognize, or comprehend gestures [6–11]. The ERPs related to recognize hand gestures with using tools may be potential for detecting syndromes in AD or MCI. Nevertheless, the related studies for AD or MCI are seldom reported. In the present study, a visual tool-using gesture paradigm was conducted for investigating cognitive brain activity in probable AD and MCI patients.

II. Methods

A. Subjects and Data Collection

Sixteen probable AD, seventeen MCI patients and seventeen control subjects were prospectively evaluated within the Dementia Center of Chang Gung Memorial Hospital. All patients were submitted to neuropsychological evaluations including the Mini-Metal Status Examination (MMSE), the Clinical Dementia Rating (CDR), Cognitive Assessment Screening Instrument (CASI) and the cognitive ERP assessment. The protocol of this study was approved by the local Research Ethics Committee. The participants gave their informed consent.

The electroencephalogram (EEG) data were acquired from the SCAN NuAmps Express recording system (Compumedics Limited, Victoria, Australia). The scalp electrodes placed according to the international 10/20 system: F3, C3, P3, O1, F4, C4, P4, O2, F7, T3, T5, F8, T4, T6, FZ, CZ, PZ, OZ and vertical electrooculogram (VEOG) were referred to as the average mastoids with impedances less than 5 KΩ. The EEG activities were amplified with a gain of 1000 and digitized at a sampling rate of 1000 Hz. The digital EEG signals were filtered with a bandpass of 0.5 Hz to 80 Hz.

B. ERP Paradigm and Procedure

Each subject was conducted with visual stimuli by displaying a series of pictures including hand gestures with using tool in usual way, improper tool-using gestures, and human faces. As shown in Fig. 1, six kinds of frequently used objects including a toothbrush, a pen, scissors, a spoon, chopsticks, and a hammer were selected. The tool-using in usual way makes sense and is the congruent condition whereas the improper tool-using does not match the function of that tool is the incongruent condition.

The participants were not asked to respond to any tool-using picture. However, the risk of doing nothing but looking is distraction. Therefore, two human face pictures were used as a control condition. 96 tool-using pictures (48 for each condition) as well as 48 face pictures were random presented. Following a 300 ms fixation at the center of screen, each picture was displayed with duration of 1700 ms. The participants were instructed to press a mouse key when a face picture appeared.

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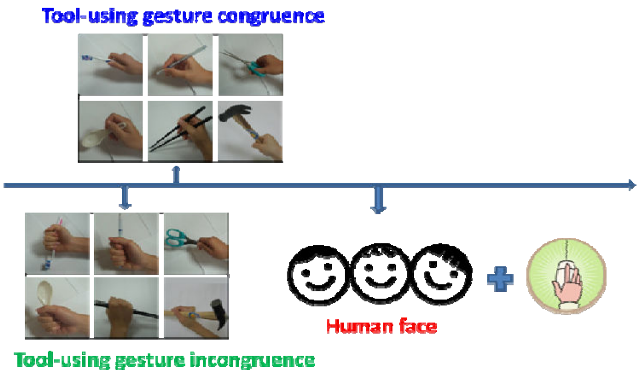

Fig 1. ERP paradigm for tool-using gesture visual stimuli. The participants were asked to press mouse button when seeing a human face.

C. ERP Characteristics

P300 was identified from the averaged ERP of each channel. P300 wave was the most positive peak between 280 and 450 ms. The crude locations of these waves were firstly determined from the global ERP defined as the mean ERP over all channels except VEOG. The corresponding wave in each channel was given by the neighbour extreme peak. Latency and amplitude were taken from the peak. The one-way ANOVA analysis was used to test the differences of the extracted parameters among probable AD, MCI, and control subjects using the nonparametric test. $p<0.05$ was considered significant. The post-hoc Scheffe test was used if the parameter was significant different among groups.

D. Classification Using Support Vector Machine

The support vector machine (SVM) is chosen to build classifiers based on ERP characteristics. One advantage of using SVM is that the classification errors of training and unknown data can be minimized. When the number of training data is small, good generalization can still be obtained [12]. The classifiers for probable AD vs. Control, AD vs. MCI, and MCI vs. Control were respectively built. 50 cross-validations was used. In each validation, half of subjects were random selected as the training set, and the others were used as the test set. The accuracies of classifications in the test set were averaged over validations.

III. Results

Table 1 lists the demographic data of probable AD patients, MCI, and control subjects.

Table 1. Demographic data of subjects

	Control	MCI	AD	p value
Gender, M/F	7/10	9/8	8/8	0.785
Age, yrs	67.88±6.67	70.68±7.87	71.85±9.68	0.328
MMSE	28.33±1.61†	23.21±5.11‡	15.6±6.34*	0.00
CDR	0.08±0.19†	0.47±0.20‡	0.95±0.60*	0.00
CASI	91.88±3.56†	76.37±18.17‡	54.8±19.28*	0.00

†p<0.05 Control vs. AD，‡p<0.05 MCI vs. Control，*p<0.05 AD vs. MCI

Figure 2 shows the average ERPs in response to tool-using gesture visual stimuli. Distinct negative waves appeared around 0.2 and 0.4 s, particularly in control subjects. The former is P200 component which is linked with cortical sensory activity. Although the latter component occurred at 0.4 s after stimulus, it can be termed as the P300 component that is commonly linked to cerebral cognitive process.

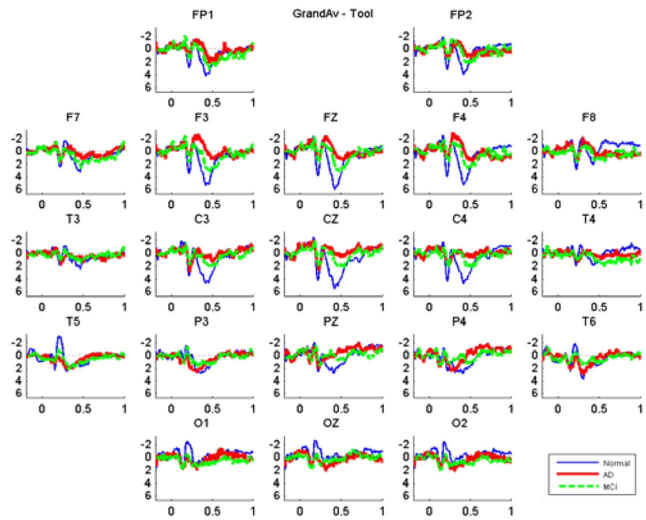

Fig 2. Group average of ERPs in response to tool-using gesture visual stimuli in probable AD, MCI, and normal subjects.

Table 2 lists the P300 amplitudes, in response to tool-using gesture, of the electrodes that exhibited significant difference. P300 amplitudes at F3, F4, C3, P3, PZ, T5, and T6 in normal control were significant higher than probable AD. The P300 amplitudes in MCI were also lower than normal control but significant channels were reduced to F4, P3, PZ, T5, and T6.

Table 2. Statistical significance of P300 amplitudes among probable AD, MCI and control subjects

	Control	MCI	AD	*p* value
F3	6.47±3.7†	5.00±3.81	1.94±3.66	0.013
F4	6.53±4.43†	3.61±4.23‡	3.20±3.88	0.05
C3	5.63±4.01†	3.69±3.12	2.40±2.86	0.028
P3	7.45±4.88†	3.80±3.30‡	3.52±3.09	0.008
PZ	7.74±5.76†	4.33±3.72‡	3.08±4.14	0.016
T5	5.53±3.83†	3.24±3.50‡	2.30±2.22	0.002
T6	5.56±4.19†	3.15±3.97‡	2.54±2.46	0.005

†p<0.05 Control vs. AD，‡p <0.05 MCI vs. Control

Table 3 shows the accuracies of classifications based on P300 amplitudes using SVM. Using the P300 amplitude of F3 and T3 had an accuracy of about 76% for discriminating probable AD from normal control. P300 amplitude at CZ had an accuracy of 70% to discriminate MCI from normal control. The accuracy of distinguishing MCI and probable AD was reduced to 68% using P300 amplitude at P4.

Table 3. Accuracy of classification based on P300 amplitude using support vector machine

	Control vs. AD	Control vs. MCI	MCI vs. AD
FP1	66.25%	61.38%	55.31%
FP2	69.58%	62.25%	58.68%
F7	74.48%	65.5%	60%
F3	76.25%	69.38%	61.67%
FZ	72.33%	66.33%	61.04%
F4	65.63%	69.06%	65.31%
F8	75.17%	68.33%	67.81%
T3	76.56%	69.38%	64.28%
C3	69.67%	66.25%	62.5%
CZ	72.42%	70.18%	67.81%
C4	71.88%	67.5%	62.5%
T4	65.63%	53.13%	60.94%
T5	70%	66.13%	61.25%
P3	66.06%	62.5%	56.25%
PZ	69.25%	63.75%	67.19%
P4	60%	65.31%	68.58%
T6	67.92%	66.88%	65.5%
O1	56.88%	50.62%	56.88%
OZ	50%	56.25%	58.58%
O2	50%	55.63%	50%

IV. Discussion

Difficulty to discriminate, recognize, or comprehend gestures in AD patients were demonstrated in literatures. The ERP characteristics in respect congruent and incongruent conditions did not show significant within-group differences. This may be due to that subjects paid more attention on the discrimination of tool-using gestures and human faces and less on distinguishing congruent and incongruent tool-using gestures. Nevertheless, directional decrease of P300 amplitude in response to tool-using gesture stimulus from normal aging to MCI to probable AD was presented. The P300 potential is generally liked with cerebral coordination for cognitive processing. This directional reduction implied the decline of recognizing hand gestures.

The P300 latency did not show significant differences among AD, MCI, and controls. This insignificance is different from the findings from auditory oddball paradigm. The discrimination of tool-using gesture and human face may involve a more complicated cognitive process than discriminating high-pitched from low-pitched sounds, thereby giving longer time to deal with this processing work.

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