Psychiatry and Clinical Neurosciences 2014; **68**: 558–567 doi:10.1111/pcn.12162

Regular Article

Evaluation of P300 components for emotion-loaded visual event-related potential in elderly subjects, including those with dementia

Yasue Asaumi,[1,3] Kiichiro Morita, MD, PhD,[1,2]* Youko Nakashima, PhD,[1] Akemi Muraoka,[1] and Naohisa Uchimura, MD, PhD[1,2]

[1]*Cognitive and Molecular Research Institute of Brain Diseases, Kurume University,* [2]*Department of Neuropsychiatry, Kurume University School of Medicine, Fukuoka and* [3]*Kyushu University of Nursing and Social Welfare, Kumamoto, Japan*

Aim: In the present study, the P300 component of the emotion-loaded visual event-related potential in response to photographs of babies crying or smiling was measured to evaluate cognitive function in elderly subjects, including those with dementia.

Methods: The subjects were 48 elderly people who consulted a memory disorder clinic. The visual event-related potential was measured using oddball tasks. Brain waves were recorded from four sites. We analyzed the P300 amplitude and latency. Subjects were divided into three groups (the dementia with Alzheimer's disease group [ADG]; the intermediate group [MG], and the healthy group [HG]) based on the Revised Hasegawa Dementia Scale, Mini-mental State Examination scores and the Clinical Dementia Rating.

Results: For all subjects, there was a significant positive correlation between P300 latency and Z-score of voxel-based specific regional analysis for Alzheimer's disease for crying or smiling faces. There was a negative correlation between P300 amplitude and Z-score for the crying face. MG subjects were divided into two groups (high risk: HRMG, low risk: LRMG) based on Z-scores (HRMG ≥ 2.0). The P300 amplitude of ADG was significantly smaller than that of HG, and the P300 latency of ADG was significantly longer than those of other groups for crying or smiling faces. The P300 latency of HRMG was significantly longer than that of LRMG for the smiling face. Furthermore, the P300 latency for the crying face was significantly shorter than that for the smiling face in HG and ADG.

Conclusion: These findings suggest that analysis of P300 components of the emotion-loaded visual event-related potential may be a useful neuropsychological index for the diagnosis of Alzheimer's disease and high-risk subjects.

Key words: Alzheimer's disease, emotion, P300 components, visual event-related potential, voxel-based specific regional analysis for Alzheimer's disease.

A LARGE NUMBER OF studies have been conducted to examine the relation between attention and cognitive function of the P300 component. Many studies support the assertion that the P300 component is an endogenous potential that is generated to address psychological uncertainty about a subject when information is provided and changes according to the type of informational stimulus.[1] However, there are different opinions regarding what kind of brain activity influences the P300 component.

The P300 component is considered to be generated from more than one source, including the hippocampus, the border between temporal and vertex areas,

Correspondence: Kiichiro Morita, MD, PhD, Cognitive and Molecular Research Institute of Brain Diseases, Kurume University, 67, Asahi-Machi, Kurume-city, Fukuoka 830-0011, Japan. Email: kiichiro@med.kurume-u.ac.jp

Received 2 September 2013; revised 22 December 2013; accepted 15 January 2014.

and the lateral prefrontal area.[2,3] Polich[1,4] suggested that the amplitude of P300 indicates the amount of attention resource allocation, and P300 latency represents the speed of allocating attention resources. This researcher also reported that the P300 component not only reflected the re-allocation of resources for information processing, but that it also changed depending on the psychological state (attitude, emotion, etc.) of a subject influenced by tasks and stimulatory conditions.[5,6]

It is known that P300 latency becomes longer with increasing age[4,6] and in Alzheimer's disease (AD) patients.[7,8] However there have been no studies supporting a significant decrease in the amplitude. Recently, we reported that P300 latency becomes longer and P300 amplitude becomes smaller in AD patients.[9] This means that the amount of allocated attention resources is smaller in AD patients, in addition to them showing a decrease in the speed of allocating attention resources and an increase in the time required for the assessment of stimulation.

In this study, subjects were divided into three groups (dementia with AD group [ADG], intermediate group [MG], and healthy group [HG]) using the Revised Hasegawa Dementia Scale (HDS-R),[10] the Mini-mental State Examination (MMSE)[11] and the Clinical Dementia Rating (CDR)[12] as scales for assessment of the symptoms of dementia. Furthermore, MG subjects were divided into two groups (high-risk [HRMG] and low-risk [LRMG]) based on Z-score[13] of voxel-based specific regional analysis for AD (VSRAD).[14] We conducted an analysis of the P300 component: its amplitude and latency. The aim was to determine whether or not P300 components are a useful neurological index for the diagnosis of AD and high-risk subjects who might develop dementia.

METHODS

Subjects

The subjects were 48 elderly people who consulted a memory disorder clinic (mean age ± SD: 72.29 ± 7.01 years). They were divided into the dementia with AD group (ADG: HDS-R ≤ 20 or MMSE ≤ 23, CDR ≥ 1) using the Alzheimer's criteria of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association;[15] the intermediate group (MG: not ADG, not HG), and the healthy group (HG: HDS-R and MMSE ≥ 28, CDR = 0) based on HDS-R, MMSE scores and CDR. Furthermore, MG subjects were divided into a high-risk group (HRMG) and a low-risk group (LRMG) based on Z-scores of VSRAD plus those obtained from magnetic resonance imaging (MRI). The HRMG reflected a Z-score of more than 2.0 points, while the LRMG reflected one of less than 2.0 points, in accordance with previous research that suggests that AD is possible in patients with Z-scores of more than 2.0 points.[13] Each group included 12 subjects. The HG included three men and nine women aged 71.0 ± 5.9 years; the LRMG included six men and six women aged 71.6 ± 8.2 years; the HRMG included three men and nine women aged 74.3 ± 6.1 years; and the ADG included seven men and five women aged 74.1 ± 7.2 years. There were no significant differences in age among the four groups (see Table 1). Subjects with AD had no history of cerebral infarction or hemorrhage, and showed no impairment of motor, linguistic, or auditory functions.

Electroencephalogram recording

Event-related potential (ERP) was recorded from Ag/AgCl electrodes at Fz, Cz, Pz and Oz positions, as

Table 1. Profile of subject

	Age	HDS-R	MMSE	Z-score
HG	71.0 ± 5.9	28.5 ± 0.7	28.8 ± 0.9	1.14 ± 0.40
LRMG	71.6 ± 8.2	23.3 ± 5.5	26.3 ± 1.5	0.97 ± 0.56
HRMG	74.3 ± 6.1	25.2 ± 2.9	26.3 ± 1.7	2.58 ± 0.59
ADG	74.1 ± 7.2	17.9 ± 3.2	20.7 ± 3.1	3.48 ± 1.27

ADG, Alzheimer's disease group; HDS-R, Revised Hasegawa Dementia Scale; HG, healthy group; HRMG, high-risk intermediate group; LRMG, low-risk intermediate group; MMSE, Mini-mental State Examination.

designated by the International 10–20 System, with reference electrodes connected at the mastoids. A forehead electrode served as the ground. Electrodes were affixed above and lateral to the left eye to monitor horizontal and vertical eye movements. All impedance was kept below 5 KΩ and the band pass filter was 0.5–50 Hz. The P300 latency was estimated from the latency of the largest positive peak within the time range of 300–600 ms. The P300 amplitude was calculated from the baseline to the peak of the positive waveform within a time window of 300–600 ms (pick-up method, Polich).[4]

Protocol for recording ERP and evaluating facial expression

The visual event-related potential was measured using an oddball task (target stimulation: a crying or a smiling face; non-target stimulation: a neutral face with no facial expression). The probability of the presentation of target stimuli was 20% and that of non-target stimuli was 80%. Stimulus duration was 200 ms. Photographs were presented in a random sequence at a mean interval of 2000 ms. Emotions depicted included pleasure (smiling) and sadness (crying), with each type of photograph being presented in an equal probability for target stimuli. Each subject sat in a sound-attenuated, electrically shielded room and was asked to relax with their eyes open. All subjects were asked to gaze at the baby's face on a TV monitor positioned 1.0 m away. They were asked to push a button with their dominant hand in response to target stimuli. Subjects were requested to refrain from blinking during the test. An averaged waveform was obtained from 20 artifact-free individual target stimuli for each type of picture for each block. One block consisted of non-task and task for each type of picture. Trials that exceeded ± 50 μV were automatically rejected from the averaging process. Two blocks (smiling and neutrality, crying and neutrality) presented to each subject constituted one session. The smiling and the crying photographs were counterbalanced.[16] Sessions included the presentation of two photographs (smiling and crying) during task performance to sustain attention and arousal levels (pressing a button upon seeing the target photographs). After completing a session, subjects were asked to look closely at each of three photographs (smiling, crying and neutral) to evaluate the affective facial expression. All patients responded correctly for the three photographs: smiling face caused pleasure, crying face caused sadness, and neutral face did not cause any emotion. In the present study, we chose the subjects who correctly answered more than 80% with a reaction time of less than 650 ms.

Statistical analysis

ERP data were examined using two-way ANOVA (group × emotion) for each recording site. Next, whether interaction was obtained or not, one-way ANOVA (groups) was evaluated for each emotion or recording site, and one-way ANOVA (emotion) was evaluated for each group or recording site. Furthermore, one-way ANOVA (order) was evaluated to check the order effect. Tukey's test-determined post-hoc was used to test for significant differences between the groups. The correlation between P300 measures and symptom scores, Z-score of VSRAD, was expressed as Pearson's product-moment correlation coefficient (r). A probability lower than 5% was considered to indicate statistical significance. Values are presented as the mean ± SD in the text.

RESULTS

P300 amplitude

By two-way ANOVA (group [ADG, HRMG, LRMG, HG] × emotion [crying, smiling]), a significant interaction was not obtained. A significant difference was observed between the groups (Fz: $F[3,88] = 4.91$, $P < 0.01$; Cz: $F[3,88] = 8.47$, $P < 0.001$; Pz: $F[3,88] = 7.92$, $P < 0.001$; Oz: $F[3,88] = 8.26$, $P < 0.001$), but no significant difference was observed for emotion. In one-way ANOVA (groups) for each emotion and recording site, when viewing a crying face, a significant difference was observed ($F[3,44] = 2.81$, $P < 0.05$). The amplitude in the ADG was significantly smaller than that in the LRMG ($P < 0.05$) and HG ($P < 0.05$) in Fz. The amplitude in the ADG was significantly smaller than that in the HG ($P < 0.001$) and the amplitude in the HRMG was significantly smaller than that in the HG ($P < 0.05$) in Cz. The amplitude in the ADG was significantly smaller than that in the HG ($P < 0.01$) in Pz and Oz. When viewing a smiling face, a significant difference was observed ($F[3,44] = 2.81$, $P < 0.05$). The amplitude in the ADG was significantly smaller than that in the HG ($P < 0.05$) in Cz. The amplitude in the ADG was significantly smaller than that in the HRMG ($P < 0.05$)

and HG ($P < 0.05$) in Pz. The amplitude in the ADG was significantly smaller than that in the HG ($P < 0.05$) in Oz (see Figs 1,2).

P300 latency

By two-way ANOVA (group [ADG, HRMG, LRMG, HG] × emotion [crying, smiling]), a significant interaction was not obtained. A significant difference was observed between the groups (Fz: $F[3,88] = 27.73$, $P < 0.001$; Cz: $F[3,88] = 25.04$, $P < 0.001$; Pz: $F[3,88] = 28.15$, $P < 0.001$; Oz: $F[3,88] = 22.43$, $P < 0.001$), and for emotion (Fz: $F[1,88] = 4.88$, $P < 0.05$; Cz: $F[1,88] = 10.76$, $P < 0.01$; Pz: $F[1,88] = 10.81$, $P < 0.01$; Oz: $F[1,88] = 8.16$, $P < 0.01$). When viewing a crying face, a significant difference was observed ($F[3,44] = 2.81$, $P < 0.001$). The latency in the ADG was significantly longer than that in the: HRMG ($P < 0.05$): LRMG ($P < 0.001$); and HG ($P < 0.01$) in Fz. The latency in the ADG was significantly longer than that in the: HRMG ($P < 0.05$); LRMG ($P < 0.001$); and HG ($P < 0.001$) in Cz. The latency in the ADG was significantly longer than that in the: HRMG ($P < 0.01$); LRMG ($P < 0.001$); and HG ($P < 0.001$) in Pz. The latency in the ADG was significantly longer than that in the: HRMG ($P < 0.01$); LRMG ($P < 0.001$): and HG ($P < 0.001$). The latency in the HRMG was significantly longer than that in the HG ($P < 0.05$) in Oz.

When viewing a smiling face, a significant difference was observed ($F[3,44] = 2.81$, $P < 0.001$). The latency in the ADG was significantly longer than that in the: HRMG ($P < 0.01$); LRMG ($P < 0.001$); and HG ($P < 0.001$). The latency in the HRMG was significantly longer than that in the LRMG ($P < 0.01$) in Fz.

The latency in the ADG was significantly longer than that in the: HRMG ($P < 0.05$); LRMG ($P < 0.001$); and HG ($P < 0.001$). The latency in the HRMG was significantly longer than that in the LRMG ($P < 0.05$) in Cz.

The latency in the ADG was significantly longer than that in the: HRMG ($P < 0.05$); LRMG ($P < 0.001$); and HG ($P < 0.001$). The latency in the HRMG was significantly longer than that in the LRMG (<0.05) in Pz.

The latency in the ADG was significantly longer than that in the: LRMG ($P < 0.01$); and HG ($P < 0.001$) in Oz (see Figs 1,3).

In one-way ANOVA (emotion) for each group and recording site, a significant difference was observed between the ADG and HG. In the ADG, the latency when viewing a smiling face was significantly longer than that of a crying face in Fz ($P < 0.05$), Cz ($P < 0.05$), and Pz ($P < 0.05$). In the HG, the latency when viewing a smiling face was significantly longer than that of a crying face in Cz ($P < 0.05$) and Pz ($P < 0.05$) (see Fig. 4).

Reaction time

When viewing a crying face, the reaction time in the ADG was 561.5 ± 23.3 ms; in the HRMG it was 506.8 ± 41.5 ms; in the LRMG it was 481.5 ± 46.2 ms; and in the HG it was 477.1 ± 37.6 ms. When viewing a smiling face, the reaction time in the ADG was 590.5 ± 35.6 ms; in the HRMG it was 543.3 ± 33.8 ms; in the LRMG it was 484.3 ± 52.5 ms; and in the HG it was 506.8 ± 25.9 ms.

When viewing a crying face, a significant difference was observed ($F[3,44] = 12.37$, $P < 0.001$). The reaction time in the ADG was significantly longer than that in the: HRMG ($P < 0.01$); LRMG ($P < 0.001$); and HG ($P < 0.001$). When viewing a smiling face, a significant difference was observed ($F[3,44] = 17.62$, $P < 0.001$). The reaction time in the ADG was significantly longer than that in the: HRMG ($P < 0.05$); LRMG ($P < 0.001$); and HG ($P < 0.001$). The reaction time in the HRMG was significantly longer than that in the LRMG ($P < 0.01$).

The reaction time when viewing a smiling face was significantly longer than that of a crying face ($P < 0.05$).

MRI (VSRAD)

Z-scores in the ADG and HRMG were significantly higher than those in the LRMG and HG. There were significant differences between the Z-scores in the ADG and in the: HRMG ($P < 0.05$); LRMG ($P < 0.001$); and HG ($P < 0.001$); and between the Z-scores in the: HRMG and LRMG ($P < 0.001$); and HG ($P < 0.001$). However, there was no significant difference between the Z-scores in the LRMG and HG.

There was a significant positive correlation between P300 latency and Z-score when viewing crying faces (Fz: $r = 0.484$, $P < 0.01$, Cz: $r = 0.589$, $P < 0.01$, Pz: $r = 0.604$, $P < 0.01$, Oz: $r = 0.540$, $P < 0.01$) and smiling faces (Fz: $r = 0.679$, $P < 0.01$, Cz: $r = 0.653$, $P < 0.01$, Pz: $r = 0.623$, $P < 0.01$, Oz: $r = 0.552$, $P < 0.01$). There was a negative correlation between P300 amplitude and Z-score when viewing a crying face (Fz: $r = -0.477$, $P < 0.01$, Cz: $r = -0.495$,

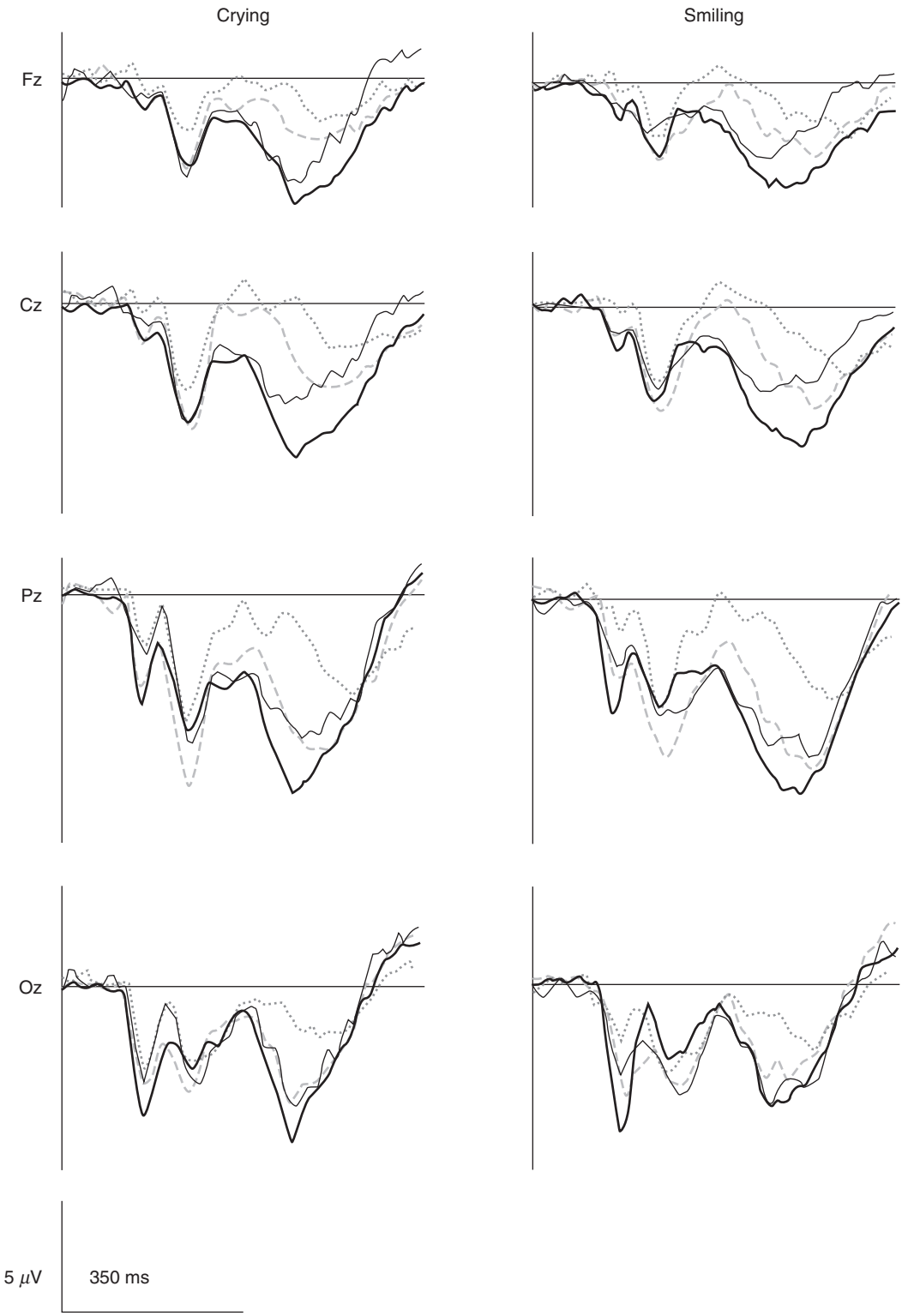

Figure 1. Grand-averaged waveforms in the Alzheimer's disease group (dotted lines), the high-risk intermediate group (broken lines), the low-risk intermediate group (unbroken lines) and the healthy group (solid lines) when viewing a crying or a smiling baby's face.

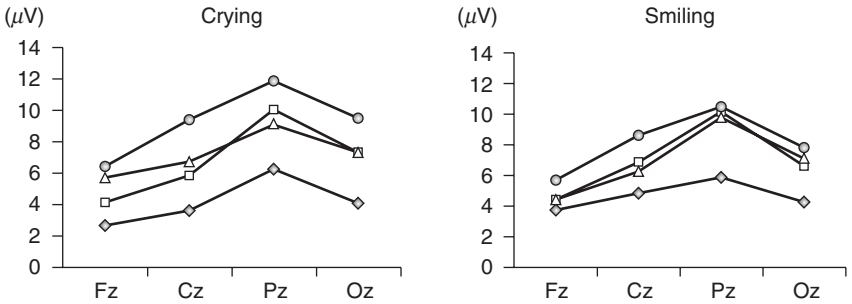

Figure 2. Peak amplitudes of P300 in the Alzheimer's disease group (ADG) (◆), the high-risk intermediate group (□), the low-risk intermediate group (△) and the healthy group (HG) (●) were plotted against recording sites (abscissa) when viewing a crying or a smiling baby's face. The P300 amplitude in ADG was significantly smaller than that in the HG when viewing crying or smiling faces.

$P < 0.01$, Pz: $r = -0.409$, $P < 0.01$, Oz: $r = -0.446$, $P < 0.01$) (see Table 2).

There was a significant negative correlation between the Z-score of VSRAD and HDS-R ($r = -0.471$, $P < 0.01$) and MMSE ($r = -0.504$, $P < 0.01$) scores for all subjects. However there was not a significant negative correlation in the ADG. There was a significant negative correlation between MMSE scores and the severity of whole-brain atrophy ($r = -0.589$, < 0.01) in the ADG.

DISCUSSION

In terms of the P300 amplitude, a significant difference was observed between the groups. When viewing a crying face, the amplitude in the ADG was significantly smaller than that in the HG (Fz: $P < 0.05$, Cz: $P < 0.001$, Pz: $P < 0.01$, Oz: $P < 0.01$). When viewing a smiling face, the amplitude in the ADG was significantly smaller than that in the HG (Cz: $P < 0.05$, Pz: $P < 0.05$, Oz: $P < 0.05$). In terms of the P300 latency, a significant difference was observed between the groups. The latency in the ADG was significantly longer than that in the HG (all recording sites: $P < 0.001$, for both emotions). In addition, the P300 latency in the HRMG was significantly longer than that in the LRMG when viewing a smiling face (Fz: $P < 0.01$, Cz: $P < 0.05$, Pz: $P < 0.05$).

We reported that P300 latency becomes longer and P300 amplitude becomes smaller in AD patients.[9] In this study, P300 amplitude in the ADG was significantly smaller than that in the HG and P300 latency was significantly longer than that in the HG. This means that the amount of allocated attention resources is smaller in AD patients, in addition to

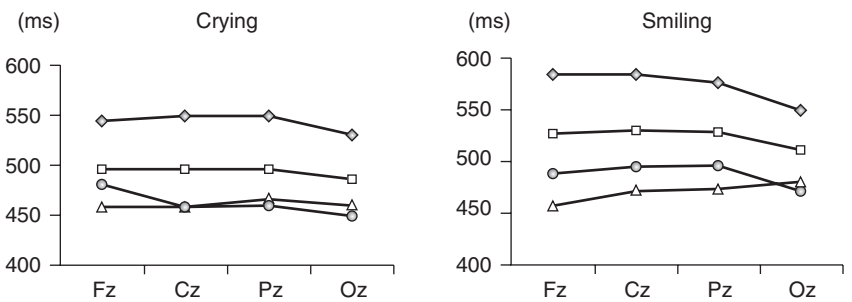

Figure 3. Mean latencies of P300 in the Alzheimer's disease group (ADG) (◆), the high-risk intermediate group (HRMG) (□), the low-risk intermediate group (LRMG) (△) and the healthy group (●) were plotted against recording sites (abscissa) when viewing a crying or a smiling baby's face. The P300 latency in the ADG was significantly longer than those of other groups when viewing crying or smiling faces. The P300 latency in the HRMG was significantly longer than that in the LRMG when viewing smiling faces.

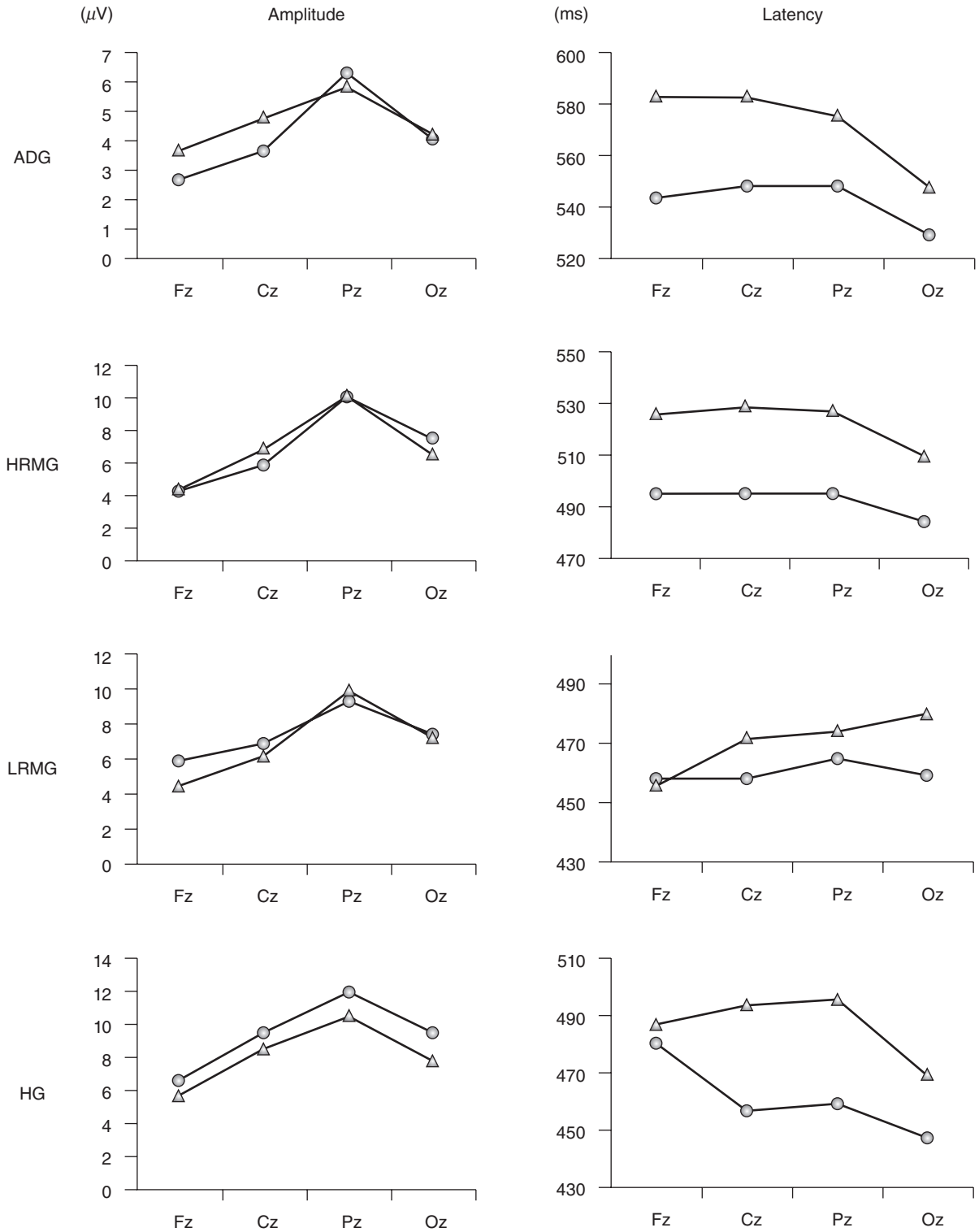

Figure 4. An influence of P300 component by emotion (crying: ●, smiling: △). The P300 latency when viewing a crying face was significantly shorter than that when viewing a smiling face in the healthy group (HG) and the Alzheimer's disease group (ADG). HRMG, high-risk intermediate group; LRMG, low-risk intermediate group.

Table 2. Correlation between P300 measures and symptom

			HDS-R	MMSE	Z-score
Amp	Fz	Cry	0.312*	0.359*	−0.477**
		Smile	0.083	0.187	−0.041
	Cz	Cry	0.477**	0.340*	−0.495**
		Smile	0.404**	0.264	−0.251
	Pz	Cry	0.482**	0.262	−0.409**
		Smile	0.438**	0.278	−0.317*
	Oz	Cry	0.489**	0.385**	−0.446**
		Smile	0.355*	0.270	−0.268
Lat	Fz	Cry	−0.401**	−0.427**	0.484**
		Smile	−0.450**	−0.476**	0.679**
	Cz	Cry	−0.558**	−0.521**	0.589**
		Smile	−0.285*	−0.354*	0.653**
	Pz	Cry	−0.570**	−0.566**	0.604**
		Smile	−0.353*	−0.429**	0.623**
	Oz	Cry	−0.603**	−0.574**	0.540**
		Smile	−0.356*	−0.387**	0.552**

*$P < 0.05$, **$P < 0.01$.
HDS-R, Revised Hasegawa Dementia Scale; MMSE, Mini-mental State Examination.

them showing a decrease in the speed of allocating attention resources and an increase in the time required for the assessment of stimulation.[1,4]

The amplitude of the P300 is controlled multiplicatively by the subjective probability and the task relevance of the eliciting events, whereas its latency depends on the duration of stimulus evaluation. The P300 is a manifestation of activity occurring whenever the context-updating model of the environment must be revised.[17]

The P300 latency in response to crying was significantly shorter than that when reacting to smiling in the Cz and Pz sites in both the ADG and the HG, but not the MG, especially the LRMG. A possible reason for this is the difference in the influences of the two facial expressions as targeted stimulation, smiling and crying, on emotion; emotions are more vividly evoked by crying (unpleasant stimulus) than smiling (pleasant stimulus). According to the results of previous studies, the P300 component is affected by emotions.[1,18] The stimulus of watching crying is assumed to draw more attention from subjects, and to enhance the allocation function.[16,18]

As the feelings of joy and sorrow evoked by pleasant and unpleasant stimuli and emotional responses caused by these feelings are important functions in interpersonal relationships, it is interesting that these emotional responses were noted in the ADG as well as in the HG.

More women than men have AD; thus the sex difference is important in both P300 factors and the influence of the emotion. Further study is needed to evaluate the sex gap in the emotional process of AD.

Reinholdt-Dunne *et al.*[19] reported that the combination of high anxiety and poor attention control was associated with greater cognitive interference by emotional faces.

In this study, the facial cognitive and emotional effects in the MG were similar to responses in the HG. Social functioning in the LRMG was better than in the ADG. Because LRMG subjects felt strong anxiety in their present conditions, they could not generate as natural a response to emotional stimulation as the HG, whereas the HRMG had atrophy of the brain and showed a response similar to the ADG.

There was a significant positive correlation between Z-score of VSRAD and P300 latency in all recording sessions when the subjects were stimulated by both crying and smiling faces. For a crying face, a negative correlation was noted between Z-scores and the P300 amplitude in all recording sessions. There was a significant negative correlation between Z-score of VSRAD and HDS-R ($r = -0.471$, $P < 0.01$) and MMSE ($r = -0.504$, $P < 0.01$) scores for all subjects. Indeed, Li *et al.*[20] reported that HDS-R tended to be negatively correlated with Z-score of VSRAD, and VSRAD was a useful indictor of early diagnosis of AD.

Oishi *et al.*[21] reported that a more severe degree of atrophy of the entorhinal cortex, higher Z-scores, and longer P300 latency were noted in their AD group compared with those in the healthy group. These results are consistent with those of this study: Z-scores of VSRAD in the ADG were significantly higher than those in the HG and the P300 latency in the ADG was markedly longer than that in the HG. The results of our study indicate a marked correlation between Z-scores of VSRAD and the P300 latency, as reported by Oishi *et al.*, although there was no significant negative correlation between Z-scores of VSRAD and MMSE scores in the ADG. This may be because the MMSE score of the AD group of Oishi *et al.*[21] was lower than that of the ADG in this study.

While a negative correlation between Z-score of VSRAD and MMSE scores may be observed in advanced dementia, it is likely that the latter remains relatively high in the majority of mild cases.

In fact, in the present study, HDS-R and MMSE scores were correlated with the severity of whole-brain atrophy more markedly than Z-score of VSRAD in the ADG. This was probably because HDS-R and MMSE scores reflected the level of atrophy of the brain as a whole as the entorhinal cortex, and tended to be influenced by aging and academic background.[9,22]

In this study, there was a significant correlation between P300 components and Z-score for all subjects. In addition, the amplitude in the ADG was significantly smaller, and the latency in the ADG was significantly longer than those in the HG. Therefore, P300 components are a useful neurological index for the diagnosis of AD.

We hope to identify a 'high-risk intermediary group'[12] during the early stages, and perform preventive evaluations, such as eye movement measurement, in consideration of the risk of developing AD among HRMG patients.

In this study, the scores of HDS-R and MMSE in the HRMG and the LRMG classified by Z-scores of VSRAD did not differ significantly.

Therefore, the scores of HDS-R and MMSE are useful as scales for assessment of the symptoms of dementia, but they are not useful as scales for distinguishing between HRMG and LRMG.

The P300 latency in the HRMG was significantly shorter than that in the ADG, and significantly longer than that in the LRMG when viewing a smiling face in particular. Therefore, P300 latency is important for the early detection of high-risk subjects. Further study is needed to evaluate the cut-off point of P300 latency when viewing a smiling face.

We are planning to examine the utility of the P300 component to facilitate the above-mentioned early detection and prevention of dementia through a periodic medical check-up.

ACKNOWLEDGMENT

This research was supported by MEXT-Supported Program for the Strategic Foundation at Private Universities from the Ministry of Education, Culture, Sports, Science and Technology. We state no conflicts of interest.

REFERENCES

1. Polich J. Clinical application of the P300 event-related brain potential. *Phys. Med. Rehabil. Clin. N. Am.* 2004; **15**: 133–161.
2. Picton TW. The P300 wave of the human event-related potential. *J. Clin. Neurophysiol.* 1992; **9**: 456–479.
3. Soltani M, Knight RT. Neural origins of the P300. *Crit. Rev. Neurobiol.* 2000; **14**: 199–224.
4. Polich J. P300 in clinical applications: meaning, method and measurement. *Am. J. EEG Technol.* 1991; **31**: 201–231.
5. Suto T, Fukuda M, Ito M, Uehara T, Mikuni M. Multichannel near-infrared spectroscopy in depression and schizophrenia: cognitive brain activation study. *Biol. Psychiatry* 2004; **55**: 501–511.
6. Morita K. Characteristics of cognitive function in senior persons evaluated by movements, p300 and fMRI using smiling or crying affective stimuli. *Geriatr. Neurosurg.* 2007; **19**: 13–18 (in Japanese).
7. Katada E, Sato K, Ojika K, Ueda R. Cognitive event-related potentials: Useful clinical information in Alzheimer's disease. *Curr. Alzheimer Res.* 2004; **1**: 63–69.
8. Polich J, Corey-Bloom J. Alzheimer's disease and P300: Review and evaluation of task and modality. *Curr. Alzheimer Res.* 2005; **2**: 515–525.
9. Asaumi Y, Morita K, Fujiki R, Nakashima Y, Muraoka A, Shoji Y. Characteristic of P300 components in the emotional loaded visual event-related potential in elder subjects. *Jpn. J. Geriatr. Psychiatry* 2011; **22**: 194–202 (in Japanese).
10. Katoh S, Shimogaki H, Hasegawa K *et al*. Development of the revised version of Hasegawa's Dementia Scale (HDS-R). *Jpn. J. Geriatr. Psychiatry* 1991; **11**: 1339–1347 (in Japanese).
11. Folstein MF, Folstein SE, McHugh PR. 'Mini-Mental State': A practical method for grading the cognitive state for the clinician. *J. Psychiatr. Res.* 1975; **12**: 189–198.
12. Nakashima Y, Morita K, Ishii Y, Shoji Y, Uchimura N. Characteristics of exploratory eye movement in elderly people: Possibility of early diagnosis of dementia. *Psychogeriatrics* 2010; **10**: 124–130.
13. Shibuya Y, Kawakatsu S, Otani K *et al*. Comparison of entorhinal cortex atrophy between early-onset and late-onset Alzheimer's disease using the VSRAD, a specific and sensitive voxel-based morphometry. *Int. J. Geriatr. Psychiatry* 2013; **28**: 372–376.
14. Matsuda H. The role of neuroimaging in mild cognitive impairment. *Neuropathology* 2007; **27**: 570–577 (in Japanese).
15. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: Report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services task Force on Alzheimer's Disease. *Neurology* 1984; **34**: 939–944.
16. Mori K, Morita K, Shoji Y, Matsuoka Y, Fujiki R, Uchimura N. State and trait markers of emotionally charged visual event-related potentials (P300) in

drug-naïve schizophrenia. *Psychiatry Clin. Neurosci.* 2012; **66**: 261–269.
17. Donchin E, Coles MGH. Is the P300 component a manifestation of context updating? *Behav. Brain Sci.* 1988; **11**: 357–374.
18. Johnston VS, Miller DR, Burleson MH. Multiple P3s to emotional stimuli and their theoretical significance. *Psychophysiology* 1986; **23**: 684–694.
19. Reinholdt-Dunne ML, Mogg K, Bradley BP. Effects of anxiety and attention control on processing pictorial and linguistic emotional information. *Behav. Res. Ther.* 2009; **47**: 410–417.
20. Li X, Jiro J, Shimizu S, Jibiki L, Watanabe K, Kubota T. Correlations between atrophy of entorhinal cortex and cognitive function in patients with Alzheimer's disease and mild cognitive impairment. *Psychiatry Clin. Neurosci.* 2012; **66**: 587–593.
21. Oishi M, Yano K, Fujioka K. VSRAD and P300 in Alzheimer disease and Parkinson disease. *Clin. Neurophysiol.* 2008; **36**: 241–246 (in Japanese).
22. Crum RM, Anthony JC, Bassett SS, Folstein MF. Population-based norms for the Mini-Mental State Examination by age and education level. *JAMA* 1993; **269**: 2386–2391.