Event-related Potentials in Alzheimer’s Disease and Alcohol Associated Dementia

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We investigated event-related potentials (P300) in two types of demented patients. Twelve patients with Alzheimer's disease (AD), 11 with alcohol associated dementia (AAD) and 28 normal controls participated in this study. We measured the latencies of N100 and P300 at Pz and Cz after odd-ball paradigm. N100 peaks at Pz and Cz were within the normal range in all patients. However, P300 peaks at Pz and Cz were significantly delayed in all demented patients. There were no statistical differences in the latencies of P300 in each demented group. P300 latencies at Cz and Pz were found to be negatively correlated with Hasegawa's dementia scale. These results suggest that demented illness has the same influence on the P300 latency regardless of the cause of dementia and P300 may be a useful means to assess the degree of dementia.

Introduction

The P300 component of event-related brain potential (ERP) is generated when subjects discriminate between stimuli which differ from one another on some dimension. This component is thought to be an objective parameter of cognitive disturbance (16).

Prolongation of the P300 component in demented illness has been reported (4, 7, 12, 13). However, comparative studies in various types of dementia are relatively scarce (4, 6, 13). Furthermore, there are no reports which compare the ERP findings of Alzheimer’s disease (AD) and alcohol associated dementia (AAD). And the relationship between dementia rating scale and P300 component is still a controversial issue.

In this study we investigated the comparison of the latency of P300 component in AD and AAD. We also examined the relationship between the Hasegawa’s dementia scale and P300 latencies.
Materials and Methods

Twelve patients with AD, 11 with AAD and 28 normal controls participated in this study. The first two groups had matched dementia ratings and age. All demented group were out patients of Department of Neuropsychiatry in Osaka Medical College Hospital. The diagnosis of AD and AAD was made according to DSM-III-R's diagnostic criteria and selected mild to moderate mental deterioration with scores between 10 to 25 on 32.5 points in Hasegawa's dementia scale (8). All were conducted brain CT scan. The mean ages and SD of each group were 55.5±3.2, 56.7±4.8 and 54.3±18.7, respectively. The mean Hasegawa's score and SD of each group was 19.8±3.8, 19.5±4.1 and 31.8±1.4, respectively.

ERP was elicited by presenting a series of tone bursts (1000 and 2000 Hz) at 70 dB sound pressure level with 10 msec rise/fall and 100 msec plateau times. The tones were presented at a rate of one trial every one second in a random sequence with the high (target) tone occupying 20% and the low (nontarget) tone 80% of the total number. All subjects were instructed to press a button with the thumb whenever the target tone burst was heard. They were instructed to keep their eyes open at rest, to gaze at the indicator and to pay attention to the stimuli. Electroencephalogram (EEG) for both the target and nontarget stimuli was averaged separately. Stimuli were presented until 3 artifact-free target trials were recorded (Fig. 1). Each subject was tested twice.

![ERP Procedure](image1)

![ERP](image2)

Fig. 1 The schema of the experiment.  Fig. 2 The ERP findings of normals, AD and AAD.
The ERP was recorded using Ag/AgCl electrodes placed at Cz and Pz (international 10-20 system), referred to linked earlobes with a forehead ground and an impedance of 5 kΩ or less. The filter bandpass was 0.1-50 Hz. ERP was digitized for 1000 msec with a 100 msec prestimulus baseline. The electric baseline was taken as the mean voltage level over the 100 msec baseline period prior to stimulus onset. Wave forms were averaged by a computer which also controlled the stimulus presentation and artifact rejection. Trials in which EEG exceeded 100 μV were automatically rejected. The latencies of components N100 and P300 were measured to find the target averages at Cz and Pz. In this study amplitude of each wave was not examined. Examples of ERP were presented in Fig. 2.

Statistical comparison among each demented group was done using one-way analysis of variance techniques (ANOVA) and Bonferroni’s test. Correlations of P300 component with age and Hasegawa’s dementia scale were analysed using Pearson’s correlation matrix.

Results

1) Aging and P300 latencies: There were tendencies that P300 latencies were prolonged in normal agings. N100 latencies had no relations with agings at Pz ($r = -0.058$) and Cz ($r = 0.046$). P300 latencies at Pz ($r = 0.73, p < 0.05$) and Cz ($r = -0.636, p < 0.01$).
0.73, P < 0.05) had correlated with agings (Fig. 3). Thus, we compared each demented group with age matched groups.

2) Comparison of N100 and P 300 peaks in AD and AAD: Table 1 shows the mean latencies and SD of N100 and P300. As preliminary analysis, a one way analysis of variance (ANOVA) of within subject variables was performed. At Cz there was no statistical difference of N100 peaks (F = 0.208). However, the main effect for P300 peaks at Cz was significant (F = 4.699, p < 0.05). Ad hoc analysis used Bonferroni’s test presented that statistical difference was found between AD and normals (t = 3.02, p < 0.05). At Pz there was no statistical difference of N100 peaks (F = 1.857). However, the main effect for P 300 peaks at Pz was significant (F = 28.05, p < 0.01). Subordinate test by Bonferroni’s test revealed that statistical difference was found between the latencies of P300 in demented group and normal controls; AD and normals (t = 7.436, p < 0.01), AAD and normals (t = 2.92, p < 0.05). Yet, there was no statistical difference in the latencies of P300 among the demented groups.

Table 1. Mean (S.D.) of the latencies of N100 and P300 in AD and AAD at Pz and Cz.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Age</th>
<th>Number of Cases</th>
<th>N100</th>
<th>Pz</th>
<th>N100</th>
<th>P300</th>
</tr>
</thead>
<tbody>
<tr>
<td>AD</td>
<td>55.5</td>
<td>12</td>
<td>103.8</td>
<td>408.7**</td>
<td>102.8</td>
<td>408.6*</td>
</tr>
<tr>
<td></td>
<td>(3.2)</td>
<td></td>
<td>(12.0)</td>
<td>(33.6)</td>
<td>(11.9)</td>
<td>(103.9)</td>
</tr>
<tr>
<td>AAD</td>
<td>56.7</td>
<td>11</td>
<td>95.2</td>
<td>392.6*</td>
<td>95.5</td>
<td>383.6*</td>
</tr>
<tr>
<td></td>
<td>(4.8)</td>
<td></td>
<td>(11.5)</td>
<td>(40.4)</td>
<td>(10.2)</td>
<td>(44.6)</td>
</tr>
<tr>
<td>Normals</td>
<td>54.3</td>
<td>28</td>
<td>97.6</td>
<td>354.6</td>
<td>97.4</td>
<td>354.1</td>
</tr>
<tr>
<td></td>
<td>(18.7)</td>
<td></td>
<td>(10.1)</td>
<td>(35.2)</td>
<td>(9.2)</td>
<td>(25.8)</td>
</tr>
</tbody>
</table>

* * p < 0.01
* p < 0.05

3) The relationships between P300 latencies and Hasegawa’s dementia scale: The P300 latencies were found to be negatively correlated with Hasegawa’s dementia scale at Pz (r = -0.636, p < 0.01) and Cz (r = -0.556, P < 0.01) (Fig. 4). However, the N100 peaks did not correlate with Hasegawa’s dementia scale at Pz (r = -0.173) and Cz (r = -0.128).

Discussion

The P300 component of ERP, first described by Sutton et al. (16) is generated when subjects discriminate between stimuli which differ from one another. An auditory discrimination paradigm is often employed to elicit P300. The peak latency of the P300 component is thought to reflect the information processing time involving
the discrimination of stimuli, reference, determination to evaluation and is used as an objective measure of cognitive impairment. The P300 component itself seems to be associated with the processing of stimuli either through context updating, information content or uncertainty resolution.

Averages of the EEG for the target stimulus yield a robust, positive-going potential with a modal latency of approximately 300 msec in normal young adults. Variations in the peak latency of P300 have been observed. One cause, aging produces an increase in auditory P300 latencies. From this reason we compared age matched demented group and normals.

Abnormalities of P 300 have been reported in cases with schizophrenia (12, 15), depression (3), infantile autism (11), dementia (4, 6, 7, 12, 13) and various neurological disorders (1, 5). However, matched studies of age and dementia ratings in AD and AAD have never been reported. There were no statistical differences between the latencies of P 300 in each demented group. We found similar prolonged latencies in these two groups of dementia. This suggests that demented illness has the same influence on the P 300 latency regardless of the cause of dementia.

The relationship between P 300 latencies and dementia scales is a controversial issue. Polich et al. (13) also studied the relationships between the Global Deterioration Rate and P 300 latencies. They concluded that the rating of cognitive impairment significantly correlated with P300 latencies. In contrast with these authors, Pfefferbaum et al. (12) reported that P 300 latencies were within normal range in some demented patients and dementia rating scores did not necessarily correlate with P300 latencies. The relationship between P300 latencies and Hasegawa's dementia scale has never been investigated until now. We found that Hasegawa's dementia rating scale negatively correlated with P300 latencies. This result suggests that P 300 may be useful as an objective parameter of dementia.

In the present study we could not find the differences of P 300 between AD and AAD. However, the findings of cerebral blood flow in AD and AAD have revealed the different pattern (9, 10). From this standpoint topographic studies of ERP must be done in the near future.

References

7) Hansch EC, Syndulko K, Cohen SN, Goldberg ZI, Potvin AR, Tourtellotte WW.
アルツハイマー病とアルコール痴呆の事象関連電位
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アルツハイマー病およびアルコール痴呆の事象関連電位（P300）の検討を行ったところ、N100潜時は両群とも統制群と有意な差異は認められなかったが、P300潜時は延長していた。痴呆の程度がほぼ同じ場合、アルツハイマー病とアルコール痴呆の間にはP300潜時の差は認められなかった。また、P300潜時と長谷川式痴呆尺度の間には相関が認められ、P300潜時は痴呆の他覚的指標として有用と考えられた。