

Clinical study

Correlations between P300 components and regional cerebral blood flows

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Summary To evaluate the diagnostic importance of event-related potential P300, the correlation between P300 and regional cerebral blood flow (rCBF) was investigated in various brain regions in patients with multiple cerebral infarction (16 cases), chronic alcoholism (11 cases) and Alzheimer's disease (5 cases) and in seven healthy people. Cognitive function was also evaluated by mini-mental state examination. P300 latency and rCBF was measured by recording of evoked potentials using an oddball paradigm and stable xenon computed tomographic scanning, respectively. A significant ($P < 0.05$) negative correlation between P300 and rCBF was observed in the thalamus in patients with multiple cerebral infarction and chronic alcoholism. In addition, a significant ($P < 0.01$) negative correlation between P300 latency and the mini-mental state examination score and positive correlation between rCBF in the thalamus and the mini-mental state examination score were observed. These findings suggest that P300 latency is associated with rCBF in the thalamus and cognitive function. © 2001 Harcourt Publishers Ltd

Keywords: cerebral infarction, chronic alcoholism, Alzheimer's disease, xenon CT

INTRODUCTION

The P300 latency has been used to evaluate the cognitive function but its source of generation has not yet been elucidated.¹ Although a significant negative correlation between the P300 latency and the cerebral blood flow (CBF) has been reported using single photon emission computed tomography (SPECT) or positron emission tomography (PET),^{2–5} the correlation between the P300 latency and the regional cerebral blood flow has not been fully investigated. The xenon computed tomography (CT) method has an advantage over SPECT and PET in that regional CBF can be measured by placing the region of interest (ROI) on the CT image.^{6,7} We investigated the correlation between the P300 latency and the regional cerebral blood flow in various neurological diseases.

MATERIALS AND METHODS

The 39 cases (16 cases of multiple cerebral infarction, 11 cases of chronic alcoholism, five cases of Alzheimer's disease and seven healthy controls) were studied with their informed consents. The ages (mean) of the four groups were 54–69 (62.0), 50–68 (57.0), 61–76 (69.4) and 51–65 (59.3), respectively. The number of cases with mini-mental state examination (MMSE)⁸ score < 20 points in the four groups were 4, 2, 4 and 0, respectively. The patients with multiple cerebral infarction had small infarcts in the territory of the perforating arteries or deep white matter and/or periventricular high intensity on magnetic resonance imaging and were studied more than one month after the onset of cerebral infarction. The severity of dementia was examined using MMSE. The P300 was measured according to the guideline of the Japanese Society of Clinical Neurophysiology⁹ with a Synax 1100 evoked potential

recorder (NEC Medical Systems, Tokyo, Japan). The cerebral potentials were recorded from electrodes at Fz, Cz and Pz referenced to linked earlobes. The electro-oculogram was recorded and trials with a large electro-oculogram potential were autorejected. The filter bandpass was set at 0.5–100 Hz and the analysis window was set from 160 msec prestimulus till 640 msec poststimulus. An oddball stimulus paradigm was employed in which subjects kept a running mental count of rare target tone pips ($P = 0.2$, 2,000 Hz) interspersed against a background of more frequent nontarget tone pops ($P = 0.8$, 1,000 Hz). Signals were amplified 50 000 times and averaged separately according to rare and frequent tones. Thirty responses to rare tones were averaged and two averages were obtained to ensure reproducibility. The P300 latency and amplitude were measured at Pz.

The cerebral blood flow was measured using the stable xenon computed tomography (CT) method.¹⁰ The two slices of the brain were selected as the region of interest in the head. The subjects inhaled room air followed by a mixture of 30% xenon and 50% oxygen for 3 min. Serial scanning was performed three times in the wash-in process, five times in the wash-out process of 5 min and once before xenon inhalation. The program of serial scanning consisted of a total of 18 scans consisting of nine serial scans on each slice. The xenon concentration in the end-tidal expired gas was continuously recorded by the thermoconductivity method. The xenon delivery system used was the AZ-7000 model (Anzai Sogyo, Tokyo, Japan) and the CT equipment was the PreSage (Yokogawa Medical Systems, Tokyo, Japan). The ROI was placed on the frontal, temporal, parietal and occipital cortex, the frontal, temporal and occipital white matter, the caudate nucleus, the putamen and the thalamus in head CT (Fig. 1) and the average between the bilateral regional cerebral blood flows¹¹ was calculated.

Statistical analysis was performed using Mann-Whitney's U tests for comparison of MMSE scores, using one-factor ANOVA (analysis of variance) followed by Scheffé's F post-hoc tests for comparison of P300 and regional cerebral blood flow among the four groups and using Spearman's correlation coefficients for correlation between the P300 latency and the regional cerebral blood flow.

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Table 1 The regional cerebral blood flow (mean \pm SD) and the correlation coefficient between the regional cerebral blood flow and the P300 latency

Region	Multiple cerebral infarction	Chronic alcoholism	Alzheimer's disease	Healthy controls	Total subjects
Frontal cortex	42.9 \pm 9.1 ^b $r = -0.568^d$	41.9 \pm 8.4 ^b $r = 0.141$	40.6 \pm 6.9 ^b $r = -0.560$	68.8 \pm 10.7 $r = -0.094$	47.4 \pm 13.7 $r = -0.374^c$
Temporal cortex	43.1 \pm 7.7 ^b $r = -0.080$	38.1 \pm 9.7 ^b $r = 0.260$	41.5 \pm 10.4 ^a $r = -0.998$	69.8 \pm 13.0 $r = -0.390$	46.6 \pm 14.7 $r = -0.141$
Parietal cortex	45.1 \pm 9.5 ^a $r = -0.495$	38.3 \pm 3.8 ^b $r = -0.431$	38.5 \pm 16.9 ^a $r = -0.910$	67.2 \pm 12.6 $r = -0.753$	47.6 \pm 15.3 $r = -0.410$
Occipital cortex	40.9 \pm 8.8 $r = 0.198$	38.6 \pm 8.7 $r = -0.568$	37.8 \pm 2.0 $r = -0.513$	40.4 \pm 8.9 $r = -0.185$	39.7 \pm 8.0 $r = 0.003$
Frontal white matter	18.8 \pm 3.9 ^b $r = -0.071$	16.8 \pm 4.9 ^b $r = 0.357$	16.6 \pm 3.9 ^b $r = -0.206$	41.5 \pm 7.6 $r = -0.412$	22.4 \pm 10.7 $r = -0.158$
Temporal white matter	19.6 \pm 4.9 ^b $r = -0.415$	17.6 \pm 6.6 ^b $r = 0.164$	16.3 \pm 6.6 ^b $r = -0.999$	36.4 \pm 6.4 $r = -0.404$	22.0 \pm 9.3 $r = -0.252$
Occipital white matter	18.1 \pm 5.0 $r = -0.129$	14.6 \pm 3.8 ^a $r = -0.421$	18.0 \pm 2.4 $r = 0.439$	22.6 \pm 4.7 $r = -0.443$	18.2 \pm 5.0 $r = -0.299$
Caudate nucleus	48.0 \pm 14.1 ^a $r = -0.296$	49.6 \pm 13.1 $r = -0.262$	55.8 \pm 17.3 $r = 0.100$	66.2 \pm 8.4 $r = 0.233$	53.1 \pm 16.6 $r = -0.202$
Putamen	53.7 \pm 13.9 $r = -0.318$	54.1 \pm 14.8 $r = 0.437$	53.9 \pm 9.9 $r = 0.001$	63.9 \pm 9.8 $r = 0.085$	55.7 \pm 13.2 $r = -0.105$
Thalamus	52.5 \pm 20.4 $r = -0.476^c$	54.9 \pm 15.7 $r = -0.614^c$	43.0 \pm 19.2 $r = 0.100$	64.7 \pm 10.3 $r = 0.099$	54.5 \pm 17.8 $r = -0.524^d$

a: $P < 0.05$ compared with healthy control group;b: $P < 0.01$ compared with healthy control group;c: $P < 0.05$ correlation with P300 latency;d: $P < 0.01$ correlation with P300 latency.**Fig. 1** The placement of region of interest (ROI). The round ROI with a diameter of 6 mm was used.

RESULTS

The mean and standard deviation of P300 latencies (amplitudes) in the multiple cerebral infarction group, chronic alcoholism

group, Alzheimer's disease group, healthy control group and total subjects were 371.5 ± 41.2 (8.6 ± 4.6), 379.1 ± 39.5 (7.3 ± 3.5), 388.2 ± 10.8 (5.2 ± 5.2), 355.0 ± 6.9 (10.8 ± 6.7) and 372.8 ± 34.6 (8.2 ± 4.9), respectively. The P300 latencies and amplitudes did not show any significant difference among the four groups.

Table 1 shows the regional cerebral blood flow and the correlation coefficient between the regional cerebral blood flow and the P300 latency. The cerebral blood flow was decreased in various neurological diseases in comparison with that in healthy controls. Significant negative correlations between the P300 latency and rCBF were present in the frontal cortex ($r = -0.374$, $P < 0.05$) and the thalamus ($r = -0.524$, $P < 0.01$) in the total subjects (Fig. 2). Significant negative correlations between the P300 latency and rCBF were present in the frontal cortex ($r = -0.568$, $P < 0.01$) and the thalamus ($r = -0.476$, $P < 0.05$) in the multiple cerebral infarction group. A significant negative correlation ($r = -0.614$, $P < 0.05$) between the P300 latency and rCBF was present in the thalamus in the chronic alcoholism group. There were no significant correlations between the P300 amplitude and the regional cerebral blood flow and between the P300 latency and the age of patients. There was a significant ($r = -0.47$, $P < 0.01$) negative correlation between the P300 latency and the mini-mental state examination score (Fig. 3). There was a significant ($r = 0.49$, $P < 0.01$) positive correlation between the thalamus blood flow and the mini-mental state examination score (Fig. 4).

DISCUSSION

The P300 is considered to reflect information processing in the brain and the P300 latency has been used to evaluate cognitive function. Although the source of P300 generation has not yet been elucidated, multiple areas in bilateral cerebral hemisphere such as the medial part of the temporal lobe, hippocampus, temporo-parietal junction, prefrontal area, inferior parietal lobe, midbrain, thalamus and basal ganglia have been considered to play a role in P300 generation.¹ The significant negative correlation between the P300 latency and the cerebral blood flow has been reported^{2,3} in multiple cerebral infarction using ¹³³Xe inhalation method. Sakai

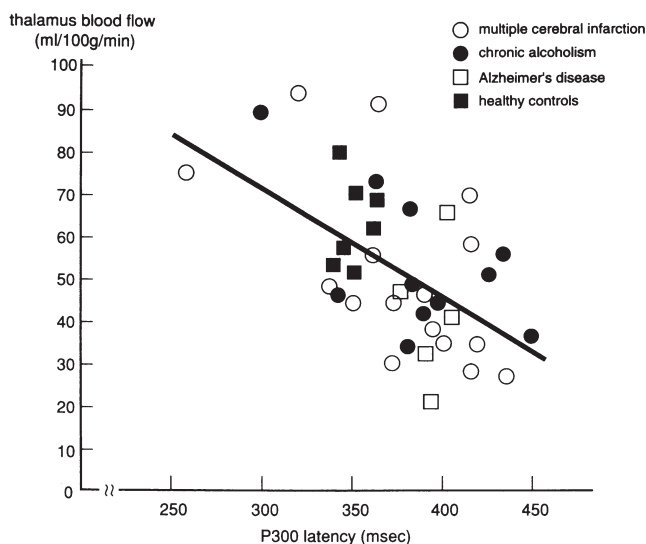


Fig. 2 The correlation between the P300 latency and the thalamus blood flow. There were significant negative correlations in the multiple cerebral infarction group ($r = -0.476$, $P < 0.05$), in the chronic alcoholism group ($r = -0.614$, $P < 0.05$) and in the total subjects ($r = -0.524$, $P < 0.01$).

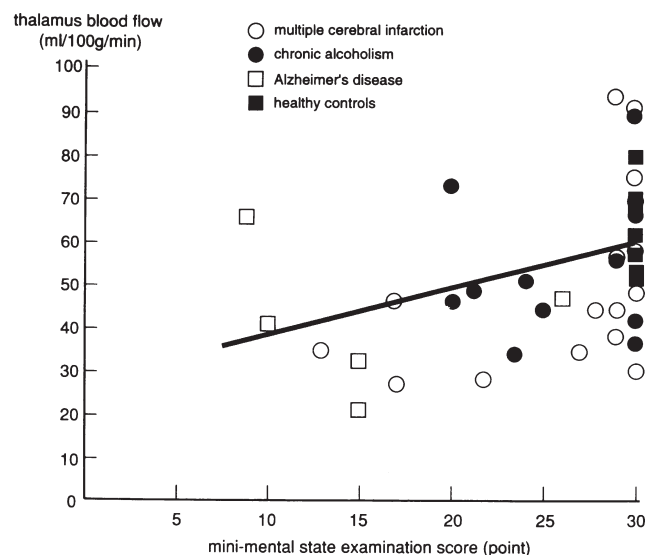


Fig. 4 The correlation between the thalamus blood flow and the mini-mental state examination score. There was a significant positive correlation in the total subjects ($r = 0.49$, $P < 0.01$).

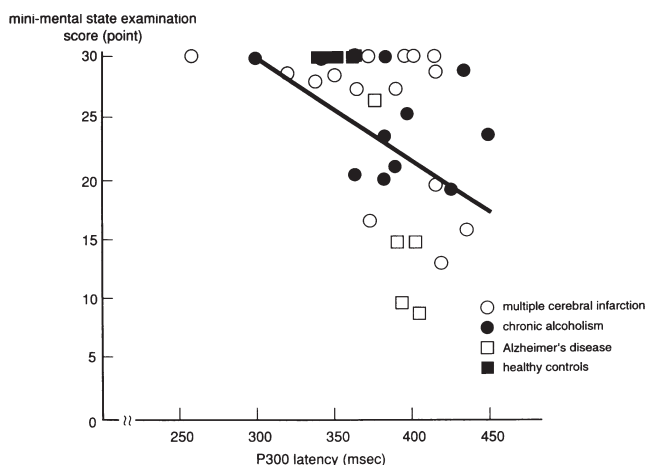


Fig. 3 The correlation between the P300 latency and the mini-mental state examination score. There was a significant negative correlation in the total subjects ($r = -0.47$, $P < 0.01$).

et al.⁴ investigated P300 and PET in various neurological diseases and suggested that the blood flow in the right parietal lobe, bilateral thalamus and bilateral temporal lobes is related to the prolongation of P300 latency. Kuwata et al.¹² investigated P300 and cold xenon CT in neurosurgical patients and suggested that the right cerebral hemisphere and the thalamus is related to the prolongation of P300 latency. Although Kasada et al.¹³ reported the negative correlation between the P300 latency and the maximum width of the third ventricle and the maximum width of the cerebral sulci in chronic alcoholism, there are no reports on the correlation between the P300 latency and the cerebral blood flow in chronic alcoholism.

Little is known about the influence of changes in regional cerebral blood flow on human P300.¹² In the present study, significant negative correlations were present between the P300 latency and the thalamus blood flow in the total subjects, between the P300 latency and the frontal cortex blood flow and the thalamus blood flow in the multiple cerebral infarction group and between the P300 latency and the thalamus blood flow in the chronic alcoholism group.

Some relationship is considered to be present between the P300 latency and the regional cerebral blood flow. Because the thalamus blood flow showed significant negative correlation with the P300 latency in the total subjects, multiple cerebral infarction group and chronic alcoholism group and significant positive correlation with the mini-mental state examination score in the present study, the thalamus is considered to be related to cognitive function. In the analysis of correlation between the P300 latency and the regional cerebral blood flow, the same significant correlations were observed when the dominant side regional cerebral blood flow and the non-dominant side regional cerebral blood flow were calculated separately.

Kawamura et al.¹¹ reported that the blood flows in the putamen and thalamus were decreased more in multiple infarction with severe dementia than in multiple infarction with mild dementia. The cognitive function disturbance in chronic alcoholism is considered to be related to the dysfunction of the frontal lobe¹⁴ or the cholinergic fibers¹⁵ from the nucleus basalis of Meynert to the cerebral cortex and hippocampus. We could not measure the hippocampal blood flow because the hippocampus is too small to be always seen on the two slices of xenon CT. The thalamus has nerve fiber connections with cerebral cortex, limbic system and basal ganglia and the decreased thalamus blood flow may be related to cognitive dysfunction.

In the present study, the P300 latency was almost constant despite the variation in MMSE scores in patients with Alzheimer's disease. As this may be due to the small sample size, we hope that large scale examinations will be performed.

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