Influence of Regional Cerebral Blood Flow on Event-related Potential (P300)

Toshikazu KUWATA, Kazuyoshi FUNAHASHI, Shinichiro MAESHIMA,
Mitsuhiro OGURA, Genhachi HYOTANI, Tomoaki TERADA,
Toru ITAKURA, Seiji HAYASHI and Norihiko KOMAI

Department of Neurological Surgery, Wakayama Medical College, Wakayama

Abstract

The relationships between event-related potential (P300), higher brain functions, and regional cerebral blood flow (rCBF) were examined in 31 neurosurgical patients. The P300 latency, evaluated by an acoustic "odd-ball" paradigm, was normal in 14 and prolonged in 17 patients. Fourteen of 17 prolonged P300 patients had reduced rCBF in the right cerebral hemisphere, especially the frontal lobe and/or thalamus. There was a significant inverse relationship between P300 latency and laterality index (rt rCBF/lt rCBF) in the frontal lobe. Prolonged P300 patients revealed significant abnormalities in psychological tests compared to normal P300 patients. There were significant inverse relationships between the P300 latency and "orientation" and "memory" test scores. Decreased rCBF in the right cerebral hemisphere, especially the frontal lobe and/or thalamus, is associated with prolonged P300 latency, suggesting that the right cerebral hemisphere is important in human cognitive processes.

Key words: P300, cerebral blood flow, brain function

Introduction

Cognitive or emotional impairments may occur in patients disturbing their capacity for work and social reintegration. The P300 is an event-related potential that reflects human cognitive processes and has been used to examine higher brain functions in neurological^{1,7)} and neuropsychological disorders.^{6,12)}

The origin of the P300 potential is controversial, but may be various neural structures including the parietal¹⁴⁾ or frontal association cortex,¹⁰⁾ hippocampus,¹¹⁾ or thalamus.¹⁷⁾ Little is known about the influence of cerebral blood flow on the P300 in humans.¹⁶⁾

In this study, we examined the P300 potential and higher brain functions in neurosurgical patients and investigated the relationship between the regional cerebral blood flow (rCBF) and the human P300 potential.

Materials and Methods

Thirty-one right-handed patients (15 females and 16 males) underwent pre- or postoperative analysis of P300 potential and rCBF. Twenty-four patients had cerebrovascular diseases (13 hypertensive intracerebral hemorrhage, 6 arteriovenous malformation, 4 cerebral infarction, and 1 cerebral aneurysm), six had brain tumors (3 glioma and 3 meningioma), and one had hydrocephalus. Ages ranged from 25 to 81 years (mean, 55.1 yrs). Patients with impaired hearing or communication due to aphasia or severe dementia were excluded. All patients had unilateral lesions (17 right and 14 left hemispheres) on computed tomography (CT) (Fig. 1). The P300 potential and rCBF were also measured in 27 and eight normal subjects, respectively, to determine the normal range (mean $\pm$ 2 SD).

P300 potentials were recorded from the central (Cz) and parietal (Pz) locations (International 10-20 System), referenced to linked-earlobes using an "odd-ball" paradigm. The subjects were asked to count silently the rare tones (2000 Hz; probability = 0.2) occurring at random among non-target events

Fig. 1 Size and location of the lesions defined by CT at various levels. *upper*: left hemispheric lesions, *lower*: right hemispheric lesions.

(1000 Hz; probability = 0.8). All subjects could hear the tones clearly and distinguish the two pitches. Counting errors never exceeded two for normal subjects and five for patients. Thirty potentials were averaged separately following target and non-target stimuli (bandpass, 0.1–1000 Hz; analysis time, –100–900 msec). The response to rare tones was defined as a large positive peak with a peak latency of 300 msec or more.

rCBF was measured by the cold xenon CT method. The mean interval between the P300 and rCBF measurements was 5 days. Following one control scan, five serial scans were made after inhalation of 35% cold xenon gas. Seven more scans were made after stopping xenon inhalation. Regions of interest (ROIs) were selected symmetrically in the frontal, temporal, and occipital lobes, thalamus, and basal ganglia. rCBF was evaluated with a laterality index (LI), defined as:

$$LI = \text{right rCBF} / \text{left rCBF}$$

Reduction in rCBF was defined as deviation from the mean $LI \pm 2$ SD in the eight normal subjects.

Four psychological tests were performed on the same day as the P300 measurement, including the Rating Scale for Psychological Function by Sano *et al.*,¹³ Mini-mental State,² Hasegawa's Dementia Scale,⁸ and the Kanahiroi test. These tests all assess a specific aspect of psychological function. For example, the Rating Scale for Psychological Function mainly evaluates the spontaneity and activity of the patients, whereas the Mini-mental State emphasizes

verbal function. The Kanahiroi test is designed for Japanese patients, who have to locate five vowels within 2 minutes in a story written in Japanese characters.

Results

There was a significant relationship between the P300 latency and age in 27 normal subjects ($p < 0.005$) (Fig. 2). The P300 latencies of the patients were divided into two groups: normal (14 cases with a mean latency of 353.1 ± 22.2 msec) and prolong-

Fig. 2 P300 latency and age in 27 normal subjects. There was a significant relationship ($Y = 0.972X + 303.9$, $r = 0.7501$, $p < 0.005$). Solid and interrupted lines indicate mean and ± 2 SD, respectively (SD = 14.4 msec).

Fig. 3 P300 latency and age in 31 patients. The P300 latencies were normal in 14 cases and prolonged in 17. Shaded area represents the normal range (mean $\pm$ 2 SD in normal subjects).

ed (17 cases with a mean latency of 444.1 ± 72.5 msec) (Fig. 3).

Eight (57.1%) of the 14 patients with a normal P300 latency and 16 (94.1%) of the 17 patients with a prolonged P300 latency had reduced rCBF in at least one or more ROIs (Table 1). All except one of the eight normal P300 patients demonstrated reduced rCBF in the left cerebral hemisphere. In contrast, 14 of the 16 prolonged P300 patients had reduced rCBF in the right cerebral hemisphere, mostly localized in the frontal lobe (53.8%) and/or thalamus (76.5%) (Fig. 4).

The LIs of the prolonged P300 patients were

Table 1 Results of rCBF and P300 studies in 31 patients

rCBF	P300 latency	
	Normal	Prolonged
Normal	6	1
Reduced	8	16
right side	1	14
left side	7	2

Fig. 5 LI in normal (○) and prolonged P300 patients (●), and in normal subjects (×). In the frontal lobe and thalamus, the LIs of the prolonged P300 patients were significantly lower than those of normal subjects (* $p < 0.05$, ** $p < 0.01$). NS: not significant.

significantly lower in the frontal lobe (0.79 ± 0.21 ; $p < 0.05$) and thalamus (0.76 ± 0.22 ; $p < 0.01$) compared to the normal subjects (frontal lobe,

Fig. 4 Side and location of reduced rCBF in normal (open column) and prolonged P300 patients (shaded column). Most prolonged P300 patients had reduced rCBF in their right cerebral hemisphere, particularly the frontal lobe and/or thalamus.

Fig. 6 P300 latency and the LI for the frontal lobe of the prolonged P300 patients. There was a significant inverse relationship ($Y = 574.74 - 183.71X$, $r = -0.6030$, $p < 0.01$).

1.01 ± 0.13 ; thalamus, 1.03 ± 0.06) (Fig. 5). Moreover, there was a significant inverse relationship between the P300 latency and the LI in the frontal lobe ($p < 0.01$) (Fig. 6).

The prolonged P300 patients revealed significant abnormalities on the Mini-mental State and Hasegawa's Dementia Scale when compared to normal P300 patients (Fig. 7). In subtests of cognitive performance, the prolonged P300 patients had significantly lower scores in "orientation" and "memory" (Fig. 8). There were significant correlations between P300 latency and patient scores in these two subtests (Fig. 9).

Discussion

The human P300 is a positive event-related potential with a latency of 300 msec or greater, typically elicited by rare target stimuli in a detection task. Since the P300 potential appears to be related to human cognitive processes, it has been used to evaluate the higher brain functions of neurological or neuropsychological patients. Ebner *et al.*¹⁾ reported that P300 abnormalities in patients with focal brain lesions correlated significantly with impairments detected by some psychological tests. Goodin *et al.*⁵⁾ reported that P300 latency correlates with the Mini-mental State score in patients with dementia. Similarly, our study showed that patients with prolonged P300 latency caused by focal brain lesions have significant abnormalities detected by the Mini-mental State and Hasegawa's Dementia Scale tests. We also found that a prolonged P300 latency correlates significantly with disturbances in orientation and memory.

Fig. 7 Scores in cognitive performance tests for normal (open column) and prolonged P300 patients (shaded column). The prolonged P300 patients had significant abnormalities detected by Mini-mental State and Hasegawa's Dementia Scale tests compared to normal P300 patients ($*p < 0.05$). A higher score indicates greater abnormality in the Rating Scale for Psychological Function.

Fig. 8 Scores in cognitive subtests for normal (open column) and prolonged P300 patients (shaded column). The prolonged P300 patients had significantly lower scores in "orientation" and "memory" than normal P300 patients ($*p < 0.05$).

Our previous study showed that patients with a right hemispheric or midline lesion were more likely to have prolonged P300 latency than those with a left hemispheric lesion.³⁾ Wada *et al.*¹⁵⁾ also reported that right hemispheric lesion correlates with prolonged P300 latency. However, little is known about the influence of changes in rCBF on human P300.¹⁶⁾

Fig. 9 P300 latency and subtest scores of the patients. There were significant inverse relationships between the P300 latency and scores for "orientation" ($Y = 543.56 - 12.02X$, $r = -0.7132$, $p < 0.01$) and "memory" ($Y = 518.14 - 16.32X$, $r = -0.6671$, $p < 0.01$).

Our present study focused on the rCBF change in patients with a prolonged P300 latency to investigate the mechanism by which the P300 becomes abnormal. We found most prolonged P300 patients to have reduced rCBF in their right cerebral hemisphere, localized primarily in the frontal lobe and/or thalamus. Moreover, there was a significant correlation between the P300 latency and the LI in the frontal lobe. Therefore, decreased right hemispheric rCBF, especially in the frontal lobe and/or thalamus, is associated with prolonged P300 latency. Gainotti⁴⁾ reported that an indifference reaction is characteristic of patients with right hemispheric lesions. Heilman and Van Den Abell⁹⁾ suggested that the right hemisphere is dominant for attention. We suggest, therefore, that the right cerebral hemisphere is important in the processes underlying human cognition, and that reduced rCBF in the right hemisphere may affect the higher brain functions.

rCBF reduction alone does not prolong P300 latency in any given area. In neurosurgical patients, prolonged P300 latency or cognitive defects may also result from metabolic disturbances directly or indi-

rectly reducing rCBF. Since there are many neural projections from the thalamus to the frontal lobe, rCBF reduction in the right frontal lobe may be a secondary event resulting from dysfunction of the thalamus. Further research is required to investigate the relationship between rCBF, cerebral metabolism, and the P300 latency throughout the brain.

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Address reprint requests to: T. Kuwata, M.D., Department of Neurological Surgery, Wakayama Medical College, 27 7-bancho, Wakayama 640, Japan.