

Minoru Oishi
Yoko Mochizuki
Toshiaki Takasu

Difference in P300 latency in two types of leukoaraiosis

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M. Oishi · Y. Mochizuki · T. Takasu
Department of Neurology,
Nihon University School of Medicine,
30-1 Oyaguchi-kamimachi,
Itabashi-ku, Tokyo 173, Japan

Minoru Oishi (✉)
Department of Neurology,
Nihon University Nerima Hikarigaoka
Hospital, 2-11-1 Hikarigaoka,
Nerima-ku, Tokyo 179, Japan
Tel.: 81-3-3979-3611,
Fax: 81-3-3979-3868

Abstract P300 examination was performed in patients with periventricular leukoaraiosis and in patients with leukoaraiosis in the centrum semiovale. Ten patients with periventricular leukoaraiosis, ten patients with leukoaraiosis in centrum semiovale and ten age-matched controls without leukoaraiosis were studied. The P300 was measured with an evoked potential recorder using an oddball paradigm. The mini-mental state examination score was significantly lower and the P300 latency was significantly longer in the

leukoaraiosis in the centrum semiovale group than in the periventricular leukoaraiosis group and the control group. Leukoaraiosis in centrum semiovale may be related to dementia and the prolongation of P300 latency.

Key words Leukoaraiosis · Periventricular hyperintensity · Centrum semiovale · P300 · Dementia

Introduction

Leukoaraiosis [5] is a radiological finding and its pathophysiology is not uniform [19]. Leukoaraiosis can be divided into two types: periventricular leukoaraiosis and leukoaraiosis in the centrum semiovale [1, 13, 14, 19]. The two types may differ in whether they cause dementia. In order to determine the difference, we investigated the results of mini-mental state examination and P300 examination in the two types of leukoaraiosis.

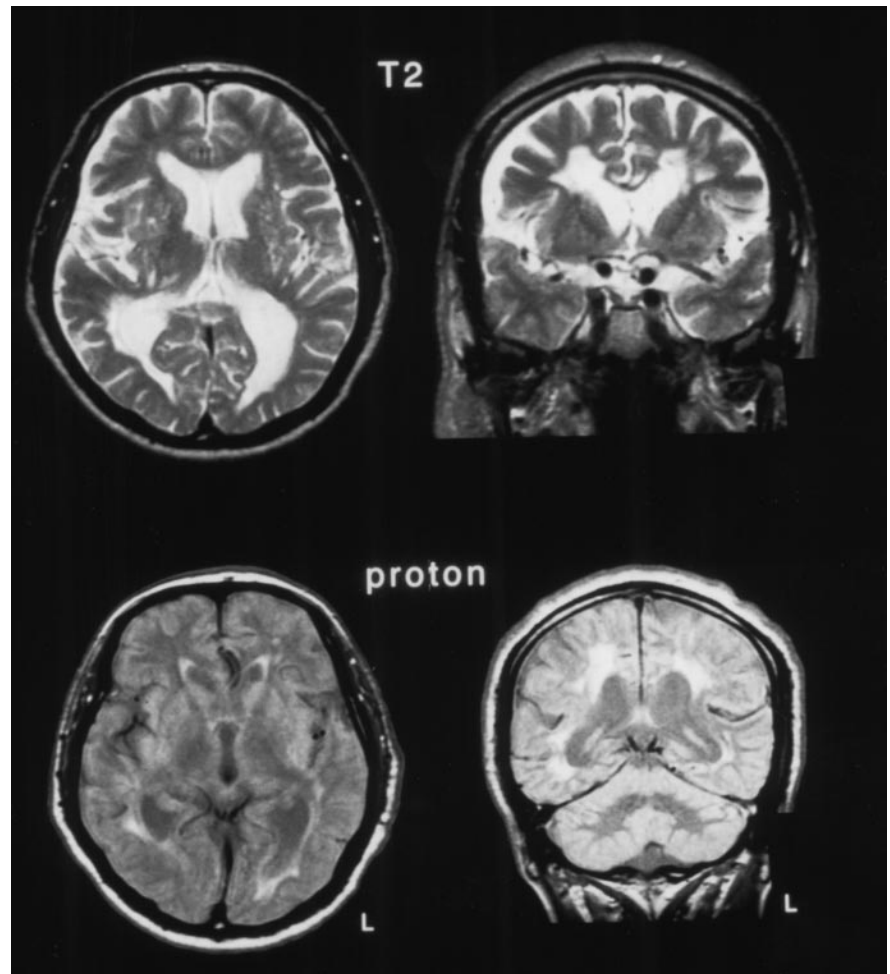
Patients and methods

Ten patients with periventricular leukoaraiosis, ten with leukoaraiosis in the centrum semiovale, and ten age-matched subjects without leukoaraiosis (control group) were studied with their informed consent. The patients came to our hospital because of lacunar infarction, gait disturbance, or dementia and were admitted for evaluation. Hasegawa dementia scale (revised) [9, 17], mini-mental state examination [4], computed tomography (CT) of the head, magnetic resonance imaging (MRI) of the head, and echocardiography were performed in the patients. Periventricular leukoaraiosis

is defined as areas of hyperintensity on MRI images of the head which are contiguous to the ventricles (Fig. 1) and leukoaraiosis in the centrum semiovale is defined as areas of hyperintensity on MRI images which are located at a distance from the ventricles (Fig. 2). Patients who have both periventricular leukoaraiosis and leukoaraiosis in the centrum semiovale, patients with hydrocephalus, and patients with leukodystrophy were excluded from this study. The location and extent of leukoaraiosis were assessed according to the method of Bowen et al. [1]. The total volume of leukoaraiosis on MRI was determined according to the method of Waldemar et al. [20]. Ten cases in each group were selected by the order of admission date. Table 1 compares subject characteristics in the three groups. Hypertension was defined as systolic pressure ≥ 160 mmHg and/or diastolic pressure ≥ 95 mmHg.

P300 was measured according to the guideline of the Japanese Society of Electroencephalography and Electromyography [3] with a Synax 1100 evoked potential recorder (NEC San-ei, 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 automatically rejected. The filter bandpass was set at 0.5–100 Hz and the analysis window was set from 160 ms pre-stimulus to 640 ms poststimulus. An oddball stimulus paradigm was employed in which subjects kept a running mental count of rare target tone pips ($P = 0.2$, 2000 Hz) interspersed against a background of more frequent nontarget tone pops ($P = 0.8$, 1000 Hz). Signals were amplified 50 000 times and averaged separately ac-

Fig. 1 Axial and coronal sections of T2-weighted (*above*) and proton-density (*below*) magnetic resonance imaging of the head in a patient with periventricular leukoaraiosis. Hyperintensity areas are contiguous to the ventricles



ording to rare and frequent tones. Thirty responses to rare tones were averaged and two averages were obtained to ensure reproducibility. The N100 and N200 latencies and amplitudes were measured at Fz, the P200 latency and amplitude were measured at Cz, and the P300 latency and amplitude were measured at Pz.

Statistical analysis was performed using Mann-Whitney's U tests for comparison of the P300 latency and using Fisher's exact probability tests for comparison of underlying diseases among the three groups.

Results

Hasegawa dementia scale (revised) and mini-mental state examination scores were significantly lower in the leukoaraiosis in the centrum semiovale group than in the periventricular leukoaraiosis and the control groups (Table 1).

Figure 3 shows an actual record of P300 examination in a patient with periventricular leukoaraiosis, a patient with leukoaraiosis in the centrum semiovale, and a control. The P300 latency was significantly longer in the leukoaraiosis in the centrum semiovale group than in the periventricular leukoaraiosis and the control groups (Table 1).

The P300 amplitude did not show any significant difference among the leukoaraiosis in the centrum semiovale group, the periventricular leukoaraiosis group and the control group.

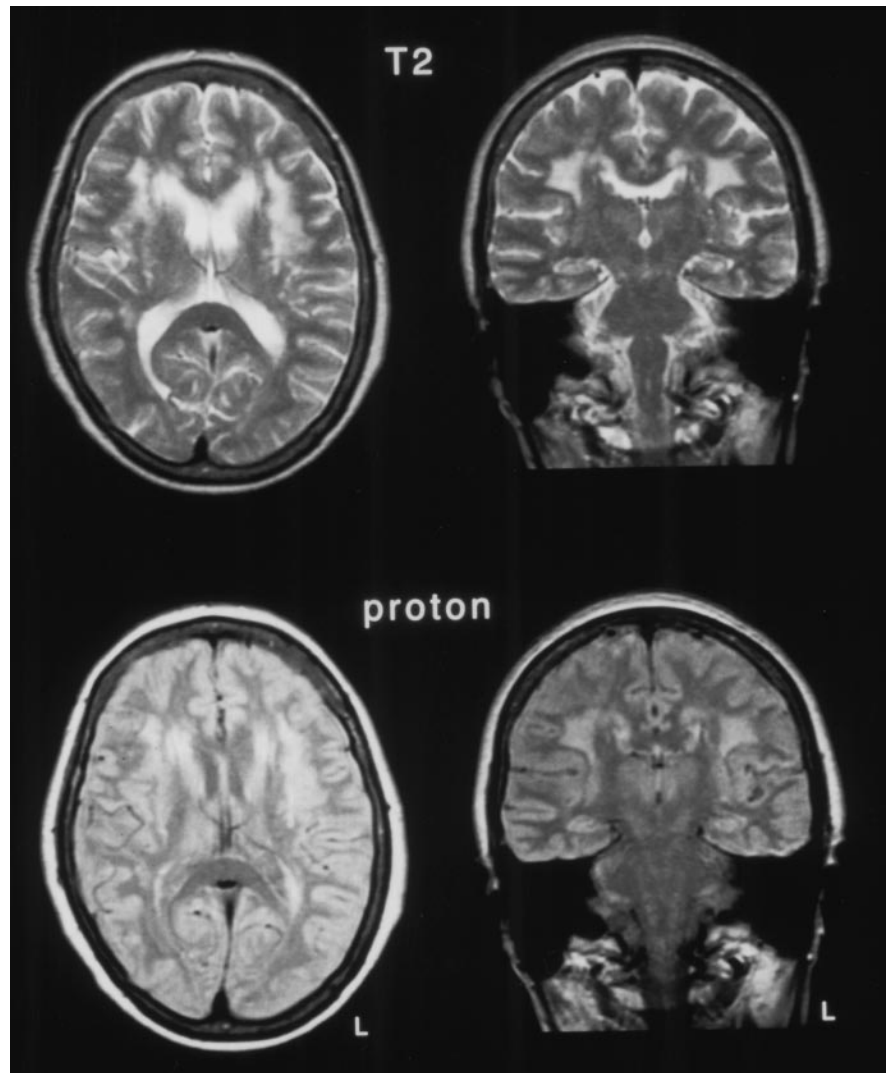
The rate of association of hypertension was significantly higher in the leukoaraiosis in the centrum semiovale group than in the other groups (Table 1). There was no significant difference in total volume of leukoaraiosis on MRI (Table 1).

The correlation coefficient between the P300 latency and the mini-mental state score was -0.52 ($P < 0.01$) and the correlation coefficient between the P300 latency and the total volume of leukoaraiosis on MRI in the leukoaraiosis in the centrum semiovale group was 0.58 ($P < 0.01$).

Discussion

Leukoaraiosis has many causes [19] but the common causes are considered to be arteriosclerosis [8, 18, 22] and normal aging [2, 10, 12]. Leukoaraiosis can be di-

Fig. 2 Axial and coronal sections of T2-weighted (*above*) and proton-density (*below*) magnetic resonance imaging of the head in a patient with leukoaraiosis in the centrum semiovale. Hyperintensity areas are located at a distance from the ventricles



vided into two types: (1) periventricular leukoaraiosis and (2) leukoaraiosis in the centrum semiovale [1, 13, 14, 19]. The mechanism of the two types is considered to be different [13, 14]. The P300 latency in leukoaraiosis has been reported to be prolonged [16] or normal [21] but there is no report on the difference in P300 latency between the two types.

The Hasegawa dementia scale is well established in Japan as a screening tool for dementia in older people [17] and the Hasegawa dementia scale (revised) score has been shown to correlate with the full scale IQs on the Wechsler Adult Intelligence Scale-Revised [9]. In the present study, the Hasegawa dementia scale (revised) score and the mini-mental state examination score were significantly lower and the P300 latency was significantly longer in the leukoaraiosis in the centrum semiovale group than in the periventricular leukoaraiosis group and the control group. Because the difference in total volume of leukoaraiosis on

MRI was not significant between the two groups, the difference in P300 latency between the two groups is not considered to be due to the amount of leukoaraiosis but rather to its location. The prolongation of P300 latency in leukoaraiosis in the centrum semiovale may be related to the white matter conduction disturbance of information necessary for cognitive function.

The P300 is considered to reflect cognitive function [7] and the P300 latency has been reported to be prolonged in dementia [6, 11, 15]. Leukoaraiosis in the centrum semiovale may be related to dementia and the prolongation of P300 latency. Because the sample size is small in the present study, we hope that large-scale investigations will be conducted.

Table 1 Subject characteristics in the three groups

	Periventricular leukoaraiosis group	Leukoaraiosis in the centrum semiovale group	Age-matched controls (control group)
Number of subjects	10	10	10
Age (years) ^a	65.5 (8.6)	64.1 (8.5)	65.3 (8.7)
Male:female	6:4	5:5	5:5
Hypertension	4/10	8/10*	3/10
Diabetes mellitus	4/10	5/10	2/10
Hyperlipidemia	3/10	3/10	2/10
Smoking	3/10	3/10	2/10
Lacunar infarction	4/10	4/10	0/10
Gait disturbance	5/10	4/10	0/10
Echocardiographic abnormality	0/10	0/10	0/10
Anterior white matter lesion ^a	2.3 (1.2)	2.1 (1.1)	—
Central white matter lesion ^a	1.2 (1.5)	1.4 (2.2)	—
Posterior white matter lesion ^a	1.4 (1.8)	1.2 (2.1)	—
Total volume of leukoaraiosis on MRI (cm ³) ^a	7.0 (4.5)	6.6 (4.4)	—
Hasegawa dementia scale-revised score ^a	25 (4)	16 (5)**	30 (0)
Mini-mental state examination score ^a	26 (3)	17 (4)**	30 (0)
N100 latency (ms) ^a	88 (17)	91 (19)	92 (18)
P200 latency (ms) ^a	163 (25)	165 (27)	162 (24)
N200 latency (ms) ^a	214 (27)	246 (31)***	204 (26)
P300 latency (ms) ^a	358 (36)	403 (41)***	316 (38)

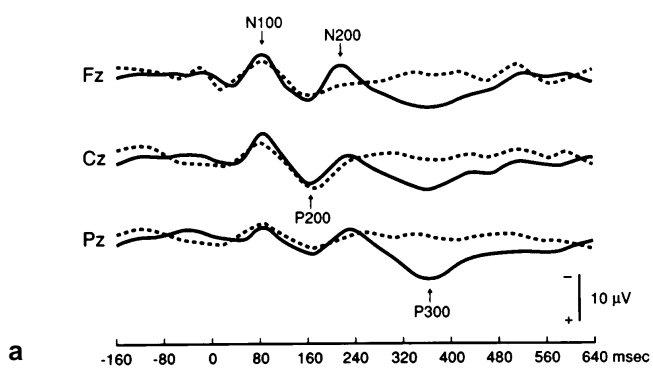
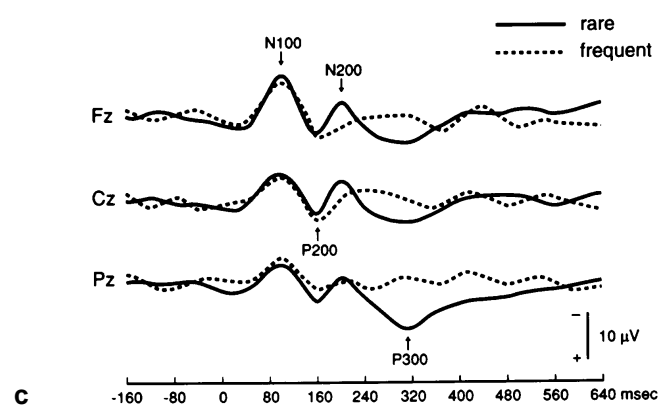
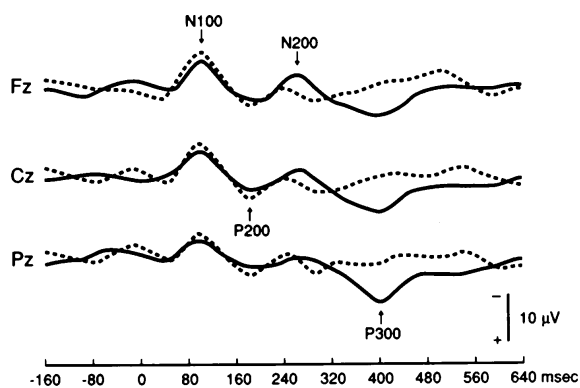
^a Mean (standard deviation)* $P < 0.05$ versus the other two groups** $P < 0.01$ versus the other two groups*** $P < 0.05$ versus the periventricular leukoaraiosis group and $P < 0.01$ versus the control group**a****b****c**

Fig. 3a–c The P300 examination in a patient with periventricular leukoaraiosis (a), a patient with leukoaraiosis in the centrum semiovale (b) and in a control (c). Cerebral potentials were averaged separately according to rare ($P = 0.2$) target tone pips and frequent ($P = 0.8$) nontarget tone pops. The P300 latency is prolonged in a patient with leukoaraiosis in the centrum semiovale

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