Hiroshima J. Med. Sci.
Vol. 49, No.1, 37~42, March, 2000
HIJM 49–5

Visual Event-related Potentials in Progressive Supranuclear Palsy

Yoko NAKANO, Yumiko KASEDA, Shigenobu NAKAMURA and Ryuji NESHIGE*

The 3rd Department of Internal Medicine, Hiroshima University School of Medicine
**Neshige Neurological Clinic*

ABSTRACT

The purpose of this study is to assess the cognitive function in early stages of progressive supranuclear palsy (PSP). Visual event-related potentials (visual ERPs) were examined in five non-demented patients with PSP and seven control subjects. ERPs were recorded using Figure (non-verbal) and Kanji (verbal) oddball paradigms. The latencies and amplitudes of N100 and P300 components were not significantly different between the PSP and control groups. However, the score of Hasegawa's dementia scale-revised (HDSR) was correlated with P300 amplitudes in the Figure task only in the PSP group. Since the P300 amplitude is related to attentional resources, changes in visual ERP induced by non-verbal stimuli might be associated with the attentional impairment even in early stages of PSP. In the Kanji task but not in the Figure task, the reaction time was prolonged in the PSP group, and positively correlated with the P300 latency in both groups. Visual verbal stimuli might be a good tool to evaluate the information processing in the early stages of PSP.

Recording of visual ERP using both non-verbal and verbal stimuli could be helpful to assess a mild cognitive dysfunction in PSP.

Key words: *Event-related potential, Progressive supranuclear palsy, Subcortical dementia, Visual stimuli*

Progressive supranuclear palsy (PSP) is a degenerative disorder characterized by the progressive development of supranuclear gaze palsy, pseudobulbar paresis, axial rigidity, gait disturbance, and dementia[31]. It has been reported that PSP is accompanied by subcortical dementia[4]. Event-related potentials (ERP) are widely accepted as electrophysiological parameters related to cognitive function[9], especially in demented patients. Previous studies on auditory ERPs in demented patients revealed delayed latencies of the early and late components in subcortical dementia such as Huntington's disease and Parkinson's disease, and delayed latencies of the late but not early components in cortical dementia such as Alzheimer's disease[7].

Recording of ERP using different types of paradigms such as visual/auditory, or verbal/non-verbal could provide a tool to evaluate various types of cognitive dysfunctions in patients with Alzheimer's disease[28], Parkinson's disease[11], aphasia[12], corticobasal degeneration[15,16], or motor neuron disease[23].

The purpose of this study is to assess cognitive function in PSP by recording visual ERP, using non-verbal and verbal stimuli, and to compare ERP parameters with the conventional intelligence score obtained from Hasegawa's dementia scale-revised (HDSR).

PATIENTS AND METHODS

1. Subjects

Five patients with PSP (male/female=2/3, mean age ±SD 64.2±13.6 years, ranging 51–71 years) and seven age-matched control subjects (male/female=3/4, age 65.1±8.57 years, ranging 56–75 years) were examined. The diagnosis of PSP was based on the presence of the following feature: (1) age of onset, 50 years or older, (2) parkinsonian signs including bradykinesia, postural or gait disorder, and axial rigidity, without resting tremor, (3) pseudobulbar signs including dysarthria and dysphagia, (4) extraocular movement abnormalities characterized by supranuclear vertical palsy with or without horizontal palsy, (5) progressive course, and (6) no radiologic abnormalities other than subcortical or midbrain atrophy[4]. Duration of illness was 22.2±13.3 (mean ±SD) months in the PSP patients. Informed consent was obtained from all subjects concerning the present study.

2. ERP recording

The visual oddball paradigm was used to elicit ERP. We used Figure and Kanji (symbolic characters used in China and Japan) as visual oddball stimuli (Table 1). ERP was recorded around 10:00 a.m. in order to avoid the influence of a circadian variation in P300. In each trial, 100 stimuli (target, 20%; non-target, 80%) were randomly presented on a 14 inch electronic tachistoscope screen

Table 1. Oddball paradigm

		target 20%	non-target 80%
non-verbal			
	Figure	○	×, ☆, □, △
verbal			
	Kanji	川	山, 火, 田, 森

Kanji: symbolic characters used in China and Japan
川: river
山: mountain, 火: fire, 田: field, 森: forest

viewed from a distance of 1 m. The stimuli were flashed for 500 msec. The interstimulus interval was 2.0 sec. The subjects were instructed to make a push-button response and to count the target stimuli.

ERPs were recorded from Fz, Cz, and Pz electrodes (international 10–20 system), referred to linked earlobe electrodes (A1A2). The impedance of the electrodes was below 10kΩ. The bandpass filter was 0.05–100 Hz. EOG artifacts over±50μV from the prestimulus baseline were rejected. The analysis time was 1 sec including the 160 msec prestimulus period.

3. Psychological test

We assessed the mental function of all subjects, using HDSR. HDSR is a Japanese screening test for mental function, including orientation, immediate memory, calculation, and verbal function. The HDSR scores range from 0 to 30[17].

4. Data analysis

The N100 and P300 components were identified by two observers. The N100 component was defined as the largest negative peak within the latency window between 70 and 200 msec. The P300 component was defined as the maximum positive peak following the N100-P200-N200 components within the latency window between 275 and 500 msec[5]. The latencies of ERP components were measured from the stimulus onset to the

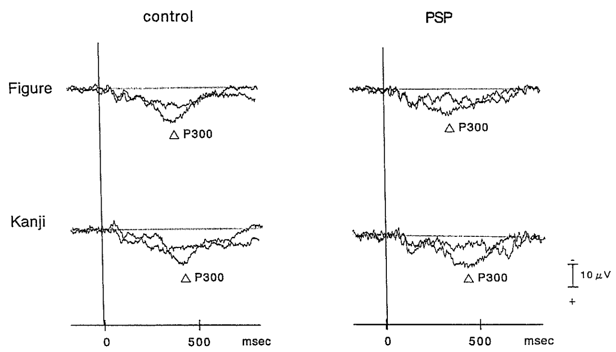

Fig. 1. Grand average waveform.
Grand average waveforms of ERPs recorded from Pz are presented. The latencies and amplitudes of N100 and P300 are not significantly different between the two groups.

Table 2. Correct rate and RT obtained from Figure and Kanji stimuli

	Figure		Kanji	
	correct rate (%)	RT (msec)	correct rate (%)	RT (msec)
PSP	98.7±0.8	487±141	96.0*±1.8	560*±126
control	98.4±0.9	467±116	98.7 ±0.8	446 ± 55

(*p<0.05 vs. control)

Table 3. ERP components

				control	PSP
				AVE SD	AVE SD
Figure	N100 latency	(msec)		148 ± 28	152 ± 31
	N100 amplitude	(μV)	Fz	3.05 ± 1.76	4.55 ± 2.31
			Cz	2.46 ± 2.14	3.84 ± 2.73
			Pz	2.24 ± 1.17	3.25 ± 1.89
	P300 latency	(msec)		428 ± 54	399 ± 51
	P300 amplitude	(μV)	Fz	7.02 ± 5.62	10.97 ± 8.60
			Cz	7.50 ± 5.88	11.88 ± 6.07
			Pz	12.03 ± 2.10	12.21 ± 5.69
Kanji	N100 latency	(msec)		185 ± 36	167 ± 30
	N100 amplitude	(μV)	Fz	4.83 ± 2.41	4.25 ± 2.97
			Cz	4.76 ± 3.30	5.26 ± 2.18
			Pz	2.02 ± 1.01	3.66 ± 2.51
	P300 latency	(msec)		438 ± 42	430 ± 50
	P300 amplitude	(μV)	Fz	7.08 ± 5.29	9.32 ± 5.36
			Cz	7.33 ± 5.18	11.87 ± 4.58
			Pz	11.77 ± 3.34	13.67 ± 3.70

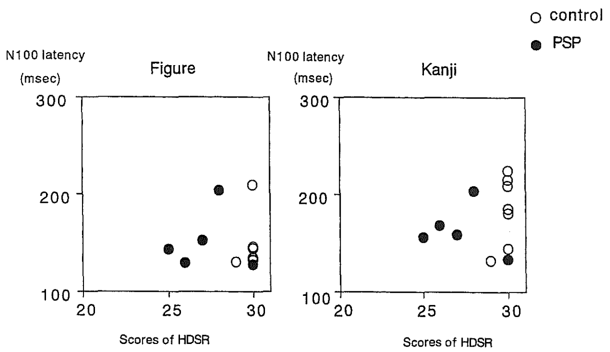

Fig. 2-a. Relationship between HDSR and N100 latencies.
N100 latencies were not significantly correlated with the HDSR scores.

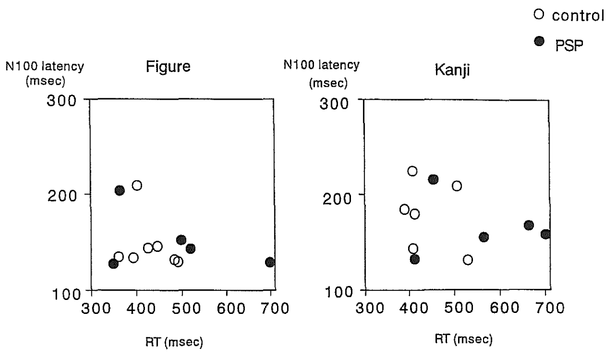

Fig. 2-b. Relationship between reaction time (RT) and N100 latencies.
N100 latencies were not significantly correlated with RT.

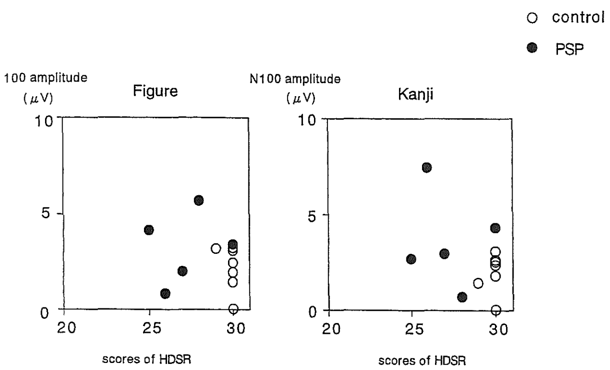

Fig. 2-c. Relationship between HDSR and N100 amplitudes.
N100 amplitudes were not significantly correlated with the HDSR scores.

peak, and the amplitudes of ERP components were measured relative to the prestimulus baseline.

One way analysis of variance (one way ANOVA) was applied to the HDSR scores, the accuracy of performance (correct rate), and the reaction time

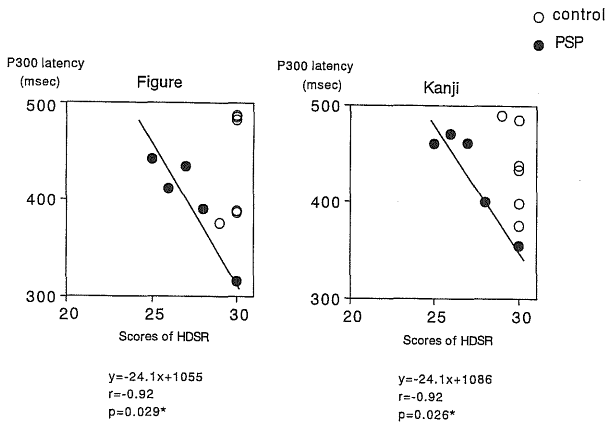

Fig. 3-a. Relationship between HDSR and P300 latencies.
P300 latencies were negatively correlated with the HDSR scores in Figure and Kanji tasks only in the PSP group (*p<0.05).

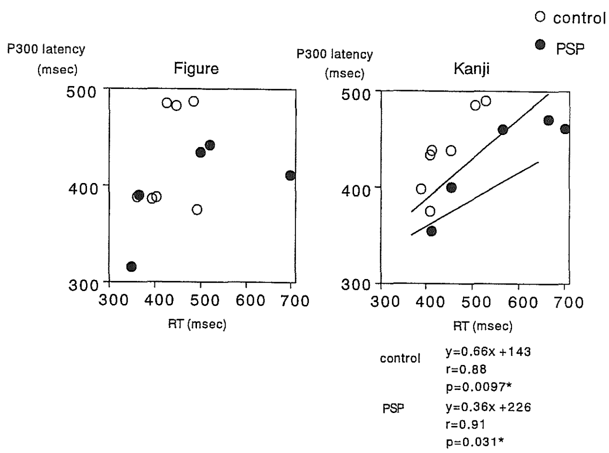

Fig. 3-b. Relationship between reaction time (RT) and P300 latencies.
In both groups, significant positive correlations between RT and P300 latency were observed in the Kanji task (*p<0.05) but not in the Figure task.

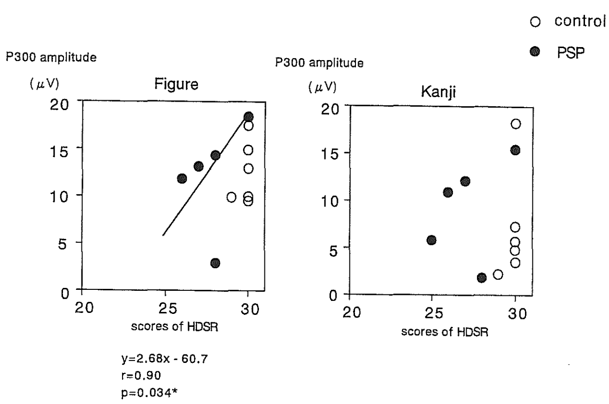

Fig. 3-c. Relationship between HDSR and P300 amplitudes.
P300 amplitudes recorded from Pz were positively correlated with the HDSR scores in the Figure task (*p<0.05) but not in the Kanji task in the PSP group.

(RTs) for comparison of the two groups. Two-way ANOVA (group × stimulus type) was applied to the latencies of each ERP component measured at Pz. Three-way ANOVA (group × stimulus type × electrode) was performed on amplitudes of each ERP component.

Correlation analysis was performed on the latencies or amplitudes of ERP components in relation to the HDSR scores. One-way ANOVA was performed to compare RT in the two groups. Correlation analysis was performed between RT and latencies of ERP components.

RESULT

1. the HDSR scores

the HDSR scores (mean ±SD) were 27.2±1.92 in the PSP and 29.9±0.38 in the control group. There was no significant difference between the two groups.

2. ERP components

The grand average waveforms are presented in Fig. 1.

Correct rates were decreased and RTs were prolonged in the PSP group compared with the control group in the Kanji task ($p<0.05$) but not in the Figure task (Table 2). Mean values and standard deviation (SD) of ERP measurements are shown in Table 3.

N100 component

Two way ANOVA of the N100 latencies (group × stimulus type) or three way ANOVA of the N100 amplitude (group × stimulus type × electrode) revealed no significant factor effect (Table 3). N100 latencies were not significantly correlated with the HDSR scores (Fig. 2-a) or RT (Fig. 2-b). N100 amplitudes were not significantly correlated with the HDSR scores (Fig. 2-c).

P300 component

Two way ANOVA of the P300 latencies revealed no significant factor effect (Table 3). P300 latencies were negatively correlated with the HDSR scores in the Figure and Kanji tasks only in the PSP group (Fig. 3-a). A significant correlation between the P300 latencies and RT was observed only in the Kanji task in both groups (Fig. 3-b).

Three way ANOVA of the P300 amplitudes revealed no significant factor effect. Fig. 3-c shows the correlations between the HDSR scores and P300 amplitudes. P300 amplitudes recorded from Pz were positively correlated with the HDSR scores in the Figure task but not in the Kanji task in the PSP group (Fig. 3-c).

DISCUSSION

1. Mental function and ERP in PSP

The slowness of mental activities associated with psychomotor retardation is an important feature in subcortical dementia[1]. It has been reported that the findings of auditory ERP are different between cortical and subcortical dementia. Patients with Alzheimer's disease showed prolonged latencies of N2 and P3 with normal latencies of N1 and P2. In contrast, latencies of N1, P2, N2, and P3 were prolonged in patients with subcortical dementia such as Parkinson's disease and Huntington's disease[7]. N1, N2, P2, and P3 described above correspond to N100, N200, P200 and P300, respectively, in our study.

Although PSP is accompanied by subcortical dementia[4], the ERP abnormalities are different from those in Parkinson's disease and Huntington's disease[7]. On visual stimuli, decreased amplitudes and increased latencies of P300 have been reported in PSP[14,26]. Decreased amplitudes of auditory N1 and P3 without changes in latencies have been demonstrated in PSP without dementia or with mild dementia[30]. In the present study, the latencies and amplitudes of N100 and P300 were not different between the PSP and control groups. We assume that the lack of changes in N100 and P300 in PSP may be explained by a mild cognitive dysfunction in such patients at the early stages of PSP, as examined in this study.

2. Relationship between P300 and neuropsychological test

The relationship between ERP parameters and scores of neuropsychological tests have been assessed in neuropsychological diseases, including Alzheimer's disease[32] and Parkinson's disease[2]. It has been reported that latencies of P300 induced by non-verbal visual stimuli showed a negative correlation with scores of mini-mental state examination (MMSE) in patients with psychiatric disorders (cognitively impaired, schizophrenic and depressed patients)[25] and Alzheimer's disease[32]. The latencies of auditory P300 and N200 were negatively correlated with scores in the cognitive test in non-demented Parkinson's disease[2].

In the present study, the lowest score of HDSR was 25 in PSP patients. HDSR is a Japanese screening test for mental function including orientation, immediate memory, calculation, and verbal function[17]. It has been reported that the HDSR scores correlate with mini-mental state examination in stroke patients (Hosokawa et al[12]) and regional cerebral blood flow in patients with Alzheimer's disease including the early stage of dementia (Koshi et al[18]). We assume that HDSR, when combined with other examinations such as ERPs, would be useful for evaluation of the mental function even in non-demented subjects.

We have demonstrated that the HDSR scores were significantly correlated with P300 latencies in Figure and Kanji tasks and P300 amplitudes in the Figure task in PSP. It has been suggested that the P300 latency is related to the discriminative difficulty[10,21] and that the P300 amplitude is related to attentional resources[19]. Frontal dysfunction, particularly attentional impairment, has been demonstrated in PSP[27]. In the present study, the association between the parameters of visual ERPs and the HDSR scores was observed in PSP but not in the control group. Pierrot-Deseilligny et al[26] have shown that the global score related to the frontal lobe function was significantly correlated with P300 latency and RT. It is likely that visual P300 might be a sensitive parameter for the attentional impairment in PSP. Sato et al[30] have reported that auditory P300 latencies are not correlated with scores of HDS in non-demented PSP. The discrepancy in findings reported by Sato et al[30] and the present results may be due to the difference in stimuli; auditory vs. visual, and the duration of illness. The PSP patients examined in our study were in the early stages (mean duration less than 2 years), while those studied by Sato et al[30] were patients at various stages (duration ranging 2~8 years). We have shown that the HDSR scores are correlated with the P300 amplitude in the Figure task but not in the Kanji task in PSP. The association between ERP parameters and psychological tests is detected when non-verbal stimuli are used for ERP recording as seen in previous studies[2,25,32]. ERPs induced by non-verbal visual stimuli could be useful for the evaluation of mental dysfunction, particularly attentional impairment, in the early stages of PSP.

3. Correlation between RT and P300 latency

In the Kanji task, RT was prolonged and the P300 latency was unchanged in PSP compared with the control group. RT is expected to be useful for discriminating deficits in the stimulus evaluation process from motor deficits[33], and for detecting a minimal difficulty in sensory discrimination[6]. McCarthy and Donchin[22] have reported that RT is influenced by both discriminability and stimulus-response compatibility and the P300 latency only by stimulus discriminability.

Previous reports have demonstrated a positive correlation[23,29] or dissociation between the P300 latency and RT[3]. Kutas et al[19] have reported that the correlation between RT and the P300 latency is larger in the accuracy instruction than in the speed instruction. A positive correlation between RT and P300 latency was observed only in the Kanji task in both groups. ERPs were recorded under the accuracy instruction in the present study, and the Kanji task might possibly require greater accuracy than the Figure task.

The lack of difference in RT in the Figure task between the PSP and control groups suggests that motor impairment does not directly affect RT in the PSP group. Thus, the increased RT in the Kanji task in the PSP group would be related to the stimulus evaluation process rather than motor impairment. Goodin et al[8] have shown that the interval between ERP and RT is increased when sensory discrimination becomes more difficult. The Kanji task, which is more difficult to discriminate than the Figure task, could possibly reveal a mild impairment of information processing in the early stages of PSP in the present study.

In conclusion, we suggest that the evaluation of ERP and RT using various types of stimuli, such as verbal and non-verbal visual stimuli, might serve to detect a mild mental dysfunction in early stages of PSP.

ACKNOWLEDGEMENTS

This work was supported by grants-in-aid from the Ministry of Education, Science and Culture and from the Ministry of Health and Welfare of Japan.

(Received November 30, 1999)
(Accepted January 25, 2000)

REFERENCES

1. **Benson, D.F.** 1984. Clinical differences among type of dementia. Ann. Neurol. **15:** 403–404.
2. **Bodis-Wollner, I., Borod, J.C., Cicero, B., Haywood, C.S., Raskin, S., Mylin, L., Sliwinski, M., Falk, A. and Yahr, M.D.** 1995. Modality dependent changes in event-related potentials correlate with specific cognitive functions in nondemented patients with Parkinson's disease. J. Neural. Transm. Park. Dis. Dement. Sect. **9:** 197–209.
3. **Cohen, L. and Polich, J.** 1997. On the number of trials needed for P300. Int. J. Psychophysiol. **25:** 249–255.
4. **Dobois, B., Pillon, B., Legault, F., Agrid, Y. and Lhermitte, F.** 1988. Slowing of cognitive processing in progressive supranuclear palsy. Arch. Neurol. **45:** 1194–1199.
5. **Fruhstorfer, H.** 1971. Habituation and dishabituation of the human vertex response. Electroencephalogr. Clin. Neurophysiol. **30:** 306–312.
6. **Geisler, M.W. and Polich, J.** 1994. P300 habituation from visual stimuli? Physiol. Behav. **56:** 511–516.
7. **Goodin, D.S. and Aminoff, M.J.** 1986. Electrophysiological differences between subtypes of dementia. Brain **109:** 1103–1113.
8. **Goodin, D.S., Aminoff, M.J. and Mantle, M.M.** 1987. Sensory discrimination and its relationship to the cerebral processing of infrequent stimuli. Can. J. Neurol. Sci. **14:** 642–648.
9. **Goodin, D.S., Squires, K.C. and Starr, A.** 1978. Long latency event-related components of the auditory evoked potential in dementia. Brain **101:** 635–648.
10. **Gratton, G., Bosco, C.M., Kramer, A.F., Coles, M.G.H., Wickens, C.D. and Donchin, E.** 1990. Event-related brain potentials as indices of information extraction and response priming. Electroencephalogr. Clin. Neurophysiol. **75:** 419–432.
11. **Hansch, E.C., Syndulko, K., Cohen, S.N., Goldberg, Z.I., Potvin, A.R. and Tourtellotte, W.W.** 1982. Cognition in Parkinson disease: an event-related potential perspective. Ann. Neurol. **11:** 599–607.

12. **Hosokawa, T., Yamada, Y., Isagoda, A. and Nakamura, R.** 1994. Psychometric equivalence of the Hasegawa Dementia Scale-Revised with the Mini-Mental State Examination in stroke patients. Percept. Mot. Skills **79:** 664–666.
13. **Itoh, T., Neshige, R., Murayama, N., Wada, I., Igasaki, T. and Takano, K.** 1998. Non-verbal and verbal P300 of auditory and visual stimuli in dementia, dysarthria and aphasia. Jpn. J. Rehabil. Med. **35:** 164–169.
14. **Johnson, R., Litvan, I. and Grafman, J.** 1991. Progressive supranuclear palsy: altered sensory processing leads to degraded cognition. Neurology **41:** 1257–1262.
15. **Kaseda, Y., Jiang, C., Nakano, Y., Katsuoka, H., Noda, K., Kohriyama, T., Nakamura, S. and Kamakura, N.** 1998. Event-related potentials in corticobasal degeneration. Electroencephalogr. Clin. Neurophysiol. **106:** P65.
16. **Kaseda, Y., Nakano, Y., Jiang, C., Nakamura, S. and Neshige, R.** 1998. Event-related potentials in corticobasal degeneration. Jpn. J. Electroencephalogr. **26:** 332–337.
17. **Kato, S., Shimogaki, H., Onodera, A., Oikawa, K., Ikeda, K., Kosaka, A., Imai, Y. and Hasegawa, K.** 1991. Development of the revised version of Hasegawa's dementia scale [in Japanese]. Jpn. J. Geriatr. Psychiatry **2:** 1339–1347.
18. **Koshi, Y., Kitamura, S., Komiyama, T., Sakayori, O., Komaba, Y., Ohyama, M., Tsuganesawa, T., Mishina, M., Ishiwata, A., Soya, H., Nakazawa, M. and Terashi, A.** 1996. A quantitative study of regional cerebral blood flow in patients with dementia of Alzheimer type using single photon emission computed tomography-clinical application of the IMP autoradiographic method (IMP ARG method). Jpn. J. Nucl. **33:** 991–998.
19. **Kutas, M., McCarthy, G. and Donchin, E.** 1977. Augmenting mental chronometry: the P300 as a measure of stimulus evaluation time. Science **197:** 792–795.
20. **Lammers, W.J. and Badia, P.** 1989. Habituation of P300 to target stimuli. Physiol. Behav. **45:** 595–601.
21. **Maclean, V., Ohman, A. and Lader, M.** 1975. Effects of attention, activation and stimulus regularity on short-term 'habituation' of the averaged evoked response. Biol. Psychol. **3:** 57–69.
22. **McCarthy, G. and Donchin, E.** 1981. A metric for thought: a comparison of P300 latency and reaction time. Science **211:** 77–80.
23. **Nakano, Y., Kaseda, Y., Tomohiko, O. and Nakamura, S.** 1999. Event-related potentials in patients with amytrophic lateral sclerosis (ALS). Electroencephalogr. Clin. Neurophysiol. **110** (Supple): P199.
24. **Novak, G.P., Ritter,W., Vaugham, H.G. Jr. and Wiznitzer, M.L.** 1990. Differentiation of negative event-related potentials in an auditory discrimination task. Electroencephalogr. Clin. Neurophysiol. **75:** 255–275.
25. **Pfefferbaum, A., Wenegrat, B.G., Ford, J.M., Roth, W.T. and Kopell, B.S.** 1984. Clinical application of the P3 component of event-related potentials. II. Dementia, depression and schizophrenia. Electroencephalogr. Clin. Neurophysiol. **59:** 104–124.
26. **Pierrot-Deseilligny, C., Turell, E., Penet, C., Lebrigand, D., Pillon, B., Chain, F. and Agid, Y.** 1989. Increased wave P 300 latency in progressive supranuclear palsy. J. Neurol. Neurosurg. Psychiatry **52:** 656–658.
27. **Pillon, B., Dubois, B., Lhermitte, F. and Agid, Y.** 1986. Heterogeneity of cognitive impairment in progressive supranuclear palsy, Parkinson's disease, and Alzheimer's disease. Neurology **36:** 1179–1185.
28. **Polich, J., Ladish, C. and Bloom, F.E.** 1990. P300 assessment of early Alzheimer's disease. Electroencephalogr. Clin. Neurophysiol. **77:** 179–189.
29. **Putam, L.E. and Roth, W.T.** 1990. Effects of stimulus repetition, duration, and rise time on startle blink and automatically elicited P300. Psychophysiology **27:** 275–297.
30. **Sato, K., Takeuchi, H., Kamoda, M., Touge, T., Yamada, A. and Nishioka, M.** 1993. Event-related potentials in progressive supranuclear palsy. Jpn. Clin. Neurol. **33:** 382–388.
31. **Steele, J. C., Richardson, J. C. and Olszewski, J.** 1964. Progressive supranuclear palsy. Arch. Neurol. **10:** 333–359.
32. **Tanaka, F., Kachi, T., Yamada, T. and Sobue, G.** 1998. Auditory and visual event-related potentials and flash visual evoked potentials in Alzheimer's disease: correlations with Mini-Mental State Examination and Raven's Coloured Progressive Matrices. J. Neurol. Sci. **156:** 83–88.
33. **Thompson, R. F. and Spencer, W. A.** 1966. Habituation: A model phenomenon for the study of neuronal substrates of behavior. Psychol. Rev. **73:** 16–43.