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Pattern Visual Evoked Cortical Potentials in Patients With Toxic Optic Neuropathy Caused by Toluene Abuse

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Purpose: Electrophysiological evaluation of the visual function of patients with toxic neuropathy caused by toluene abuse.

Methods: Fifteen patients (mean age 25.6 years, eight men and seven women) were diagnosed with bilateral optic neuropathy. Pattern visual evoked cortical potentials (PVECPs) and clinical symptoms were investigated.

Results: Visual acuities at the initial visit were less than 0.1 in 5 cases and 0.1–1.0 in 10 cases. PVECPs were followed up in the 15 cases. At the first recording, PVECPs were nonrecordable in both eyes of 11 cases, the P100 peak latency was prolonged in both eyes of 3 cases, and only 1 case showed a normal P100 peak latency. After treatment, visual acuities improved more than 2 lines in 6 cases, 3 of whom showed normal P100 peak latency in the PVECPs. Visual prognosis and PVECP changes were identical in both eyes of all patients.

Conclusions: In patients with toluene optic neuropathy, the P100 peak latency of PVECP shortened as visual acuity improved. The VECP abnormalities in these patients suggest that there is a severe effect on the optic nerve after prolonged exposure to toluene. **Jpn J Ophthalmol 1999;43:438–442**

Key Words: Optic neuropathy, toluene abuse, VECP.

Introduction

Toluene is lipophilic and therefore absorbed well and retained well by the lipid-rich central nervous system. A number of case reports have described optic neuropathy caused by toluene.[1–5] Most have appeared in Japanese journals[5] because toluene has been favored by drug abusers in this country. Previously, the authors have reported only a single case; therefore, the clinical picture of visual symptoms and ophthalmic findings has been incomplete. For this study, we recruited 15 patients with decreased vision caused by toluene inhalation. All patients underwent pattern visual evoked cortical potential (PVECP) recordings. In this study, we discuss their clinical findings and VECP changes with reference to visual prognosis.

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Materials and Methods

We examined 15 patients who were suffering from bilateral optic neuropathy caused by toluene addiction. They visited our department at Chiba University Hospital between 1986 and 1996. The eight men and seven women ranged in age from 20 to 52 years (mean age 25.6 ± 8.02 years, SD). Ten of the 15 patients had associated neurological defects such as dysarthria and ataxic gait. Studies were carried out with approval from the Committee for Human Ethics of the Chiba University School of Medicine. Informed consent was obtained from all patients.

The clinical findings in these 15 patients are shown in Table 1. A black and white checkerboard pattern displayed on a television monitor was used as a stimulus for VECP recordings. The visual field of a pattern was 7 × 11 degrees, and each check subtended 28 minutes of arc from an observing distance of 170 cm. The contrast level of the checks was 80% and mean luminance was kept at 39 cd/m^2. The pattern was reversed at a rate of three times per second.

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Table 1. Clinical Findings in Study Patients

Case	Age/Sex	Eye	Initial VA	P100 Latency (ms)	Best VA	P100 Latency (ms)	Associated Symptom	Toluene Abuse Period (Years)	GVF	Optic Disc	Follow-Up (Months)	Color Vision	Treatment	Light Reflex
1	20/F	R	0.5	170	0.6	145	Dysarthria	8		Normal		Unknown	Unknown	Prompt
		L	0.5	170	0.6	160	Ataxic gait			Normal				
2	22/F	R	0.3	105	0.5			3		Normal	1	Unknown	Vit B_{12}	RAPD (+)
		L	0.4	110	0.5					Normal				
3	52/M	R	0.9	150	1.0	100		Unknown	Central scotoma	Normal		RG	Vitamin	Prompt
		L	0.7	140	0.8	110			Central scotoma	Normal				
4	23/M	R	0.1	Nonrecordable	0.1	Nonrecordable	Tremor	7	Blind spot enlargement	Normal	2	Unknown	Unknown	Unknown
		L	0.1	Nonrecordable	0.1	Nonrecordable	Nystagmus		Blind spot enlargement	Normal				
5	29/M	R	0.3	Nonrecordable	0.8	Nonrecordable	Nystagmus	Unknown	Central depression	Normal	22	Unknown	Vitamin	Prompt
		L	0.2	Nonrecordable	0.9	Nonrecordable			Central depression	Normal				
6	24/M	R	0.6	Nonrecordable	1.5	144	Dysarthria	1	Blind spot enlargement	Pale	11	RG	Vitamin	Prompt
		L	0.15	Nonrecordable	1.0	177	Ataxic gait		Blind spot enlargement	Pale				
7	29/M	R	0.9	Nonrecordable		116	Cerebellar	10		Normal		RG	Unknown	Prompt
		L	0.8	Nonrecordable		119	Ataxia			Normal				
8	27/M	R	0.05	Nonrecordable	1.0	114	Ataxic gait	1		Normal	7	RG	Unknown	Prompt
		L	0.05	Nonrecordable	0.8	120				Normal				
9	22/F	R	1.0	Nonrecordable	0.9	107		8		Normal	6	Normal	Vitamin	Prompt
		L	0.8	Nonrecordable	1.2	105				Normal				
10	24/F	R	0.4	Nonrecordable	0.9	126	Cerebellar	Unknown	Central scotoma	Normal	4	Unknown	Unknown	Sluggish
		L	0.5	Nonrecordable	0.9	119	Ataxia		Central scotoma	Normal				
11	22/F	R	1.2	161	1.5	123	Cerebellar	6	Central scotoma	Normal	28	Unknown	Unknown	Prompt
		L	1.0	164	1.5	122	Ataxia			Normal				
12	21/F	R	0.5	Nonrecordable	0.5	Nonrecordable		4	Central scotoma	Normal	3	RG	Vitamin	Prompt
		L	0.1	Nonrecordable	0.15	Nonrecordable			Central scotoma	Normal				
13	29/M	R	0.06	Nonrecordable	0.8	144	Cerebellar	14	Blind spot enlargement	Pale	45	Unknown	Unknown	Prompt
		L	0.06	Nonrecordable	1.2	126	Ataxia		Blind spot enlargement	Pale				
14	20/F	R	0.1	Nonrecordable	0.1	Nonrecordable	Ataxic gait	5	Central scotoma	Pale		RG	Unknown	Sluggish
		L	0.06	Nonrecordable	0.1	Nonrecordable	Tremor		Central scotoma	Pale				
15	20/M	R	0.1	Nonrecordable	1.2	134		4		Pale	9	Normal	Vitamin	Sluggish
		L	0.1	Nonrecordable	1.2	129				Pale				

VA: visual acuity. GVF: Goldmann visual field. RG: red-green blindness. Vit B_{12}: vitamin B_{12}. RAPD: relative afferent pupillary defect.

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Pupils were dilated with 0.5% tropicamide and 0.5% phenylephrine hydrochloride, and the subjects were asked to fixate on the center of the pattern under full refractive correction from a 170-cm distance through an artificial pupil 3 mm in diameter. The VECP responses were recorded with one electrode placed at Oz referred to another at the earlobe. The responses were amplified by a pre-amplifier (VC-9; Nihon Koden, Tokyo), with an electric filter set between 1.5 and 100 Hz. One hundred responses were averaged (ATAC 350; Nihon Koden) and printed out with an X-Y recorder (Riken Kagaku, Tokyo). The amplitude and peak latency of the first scalp positive component (P100) were evaluated. Visual fields were examined using a Goldmann perimeter (Takagi, Nagano), and color vision was evaluated with the Panel D-15 test (Luneau Ophtalmologie, Paris, France).

Results

Clinical information and VECP results for the 15 patients are summarized in Table 1. Optic disc appearance at the initial visit was normal in both eyes of 11 patients (73.3%) and pale in both eyes of 4 patients (26.7%). Goldmann visual field findings at the initial visit were abnormal in 17 eyes (56.7%). Thirteen eyes appeared normal (43.3%). Only one case showed improvement of the visual field in both eyes later. Pupillary light reflex was sluggish in 6 of the 30 eyes, and was prompt in the other 24 eyes. Relative afferent pupillary defect was found in one patient.

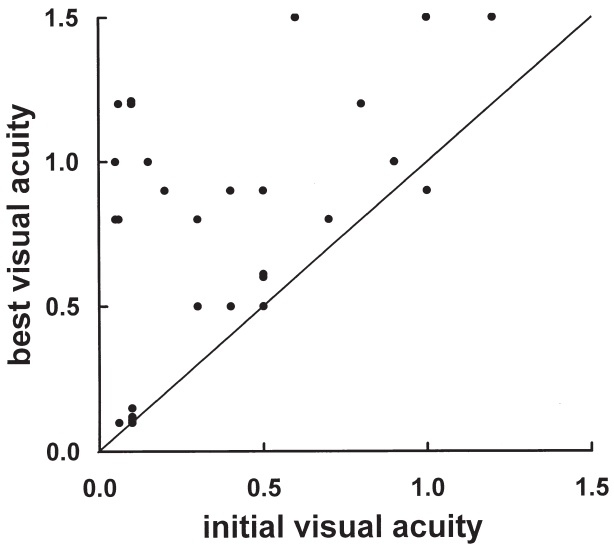

Figure 1. Initial visual acuity versus final visual acuity in 15 toxic neuropathy patients.

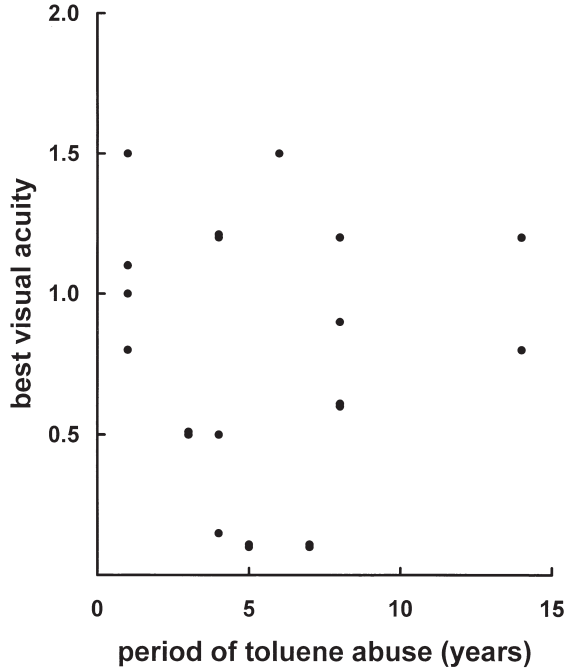

Figure 2. Relationship between visual acuity and periods of toluene inhalation (years).

The visual acuity at the initial visit was reduced in most cases, and it varied from mild to severe loss. Visual acuity improved in 23 (76.7%) of the 30 eyes (Figure 1). No relationship was found between visual acuity and period of toluene inhalation (Figure 2).

Figure 3 shows actual VECP recordings in a representative patient whose VECPs were recordable and could be followed up. She (case 11) was a 22-year-old woman who complained of blurred vision. This patient had a visual field defect in the left eye and cerebeller ataxia. Her visual acuity was 1.2 in the right eye and 1.0 in the left eye. She had been addicted to toluene for 6 months. The P100 component of VECP was prolonged in both eyes at the initial visit on October 20, 1995. Thereafter, the latency became shortened as subjective visual acuity improved. However, it remained still longer than what we consider normal range (between 90.5 ms and 119 ms, mean $\pm$ 2 SD).

VECPs at the initial visit were nonrecordable in 22 (73%) of the 30 eyes. The high rate of nonrecordable VECPs demonstrated no relationship to the grade of visual acuity loss (Table 2). The rate of nonrecordable VECPs decreased to 26.7% during the recovery stage of visual disturbance.

In Figure 4, the P100 latency was plotted as a function of the best visual acuity at the recovered stage

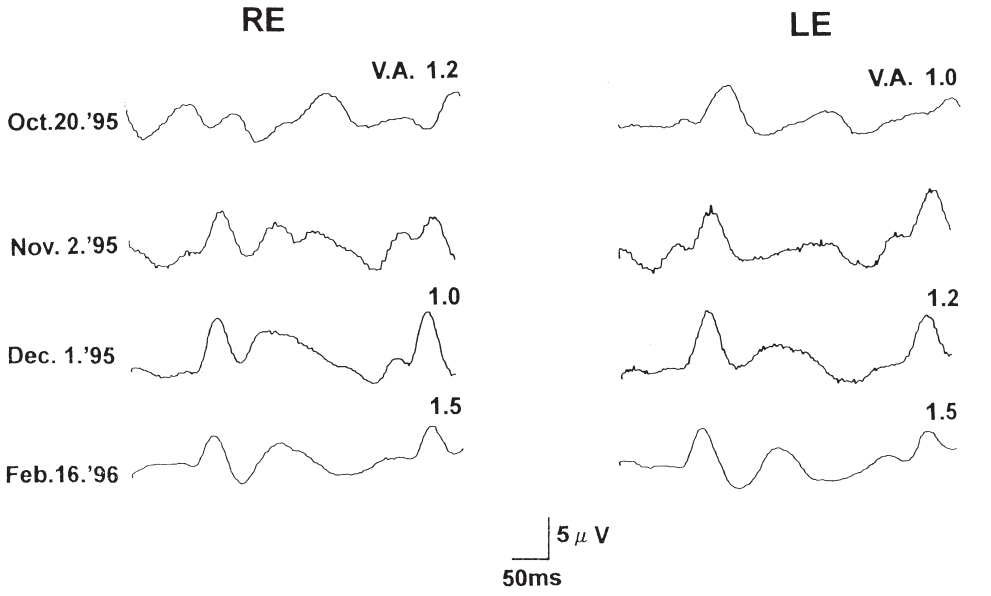

Figure 3. VECP recordings in patient with toluene optic neuropathy.

of visual disturbance. There was no significant correlation between best visual acuity and P100 latency. In fact, the recovery of latency was not found at the stage when subjective vision improved.

Discussion

Toluene is inexpensive and readily available, and its use has continued to increase. Central nervous system disorders resulting from the inhalation of toluene have been well described in the literature.[6,7] The present study reports the ophthalmological findings and the results of VECP evaluations in 15 patients whom we examined at our clinic.

In 1918, the first case of optic neuropathy caused by binitrotoluene was reported by Hamilton and Nixon.[1] Keane[3] described the case of a 20-year-old man with a 3-year history of inhaling primarily toluene. His visual acuity was 4/200 in both eyes, with normal fundi. His vision improved to 20/30 in each eye within 2 months after treatment. Pattern reversal VECPs after visual recovery were abnormal although the latency was less prolonged, whereas an electroretinogram (ERG) was normal.

Ehyai and Freemon[4] reported a 27-year-old man who developed bilateral optic atrophy over a 5-year period of extensive toluene glue sniffing. There was a total absence of VECPs in both eyes. The ERG showed no abnormalities. The optic discs had a mild pallor, and the visual acuity was 20/400 bilaterally. No improvement was described.

In addition to these papers published in English, several case reports are available in Japanese. Toyo-

Table 2. Rate of Nonrecordable VECPs at Initial Visit (22 Eyes of 30 Eyes: 73.3%)

VA	No. of Eyes	%
0.1>	5	22.7
0.1–0.5	12	54.6
0.5<	5	22.7
Total	22	100.0

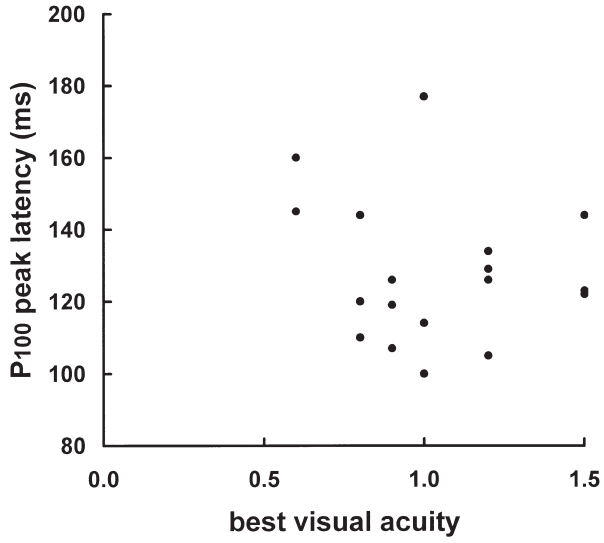

Figure 4. P100 peak latency as function of best visual acuity at recovered stage.

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naga et al[5] reported electrophysiological results such as electrooculogram, ERG, and pattern VECP in three patients with optic neuropathy resulting from toluene addiction for 1.5, 5, and 7 years. Their VECPs were prolonged in latency. Among these papers, only Keane[3] reported a follow-up case.

Our particular interest was in the VECP findings in our study as well as the clinical ophthalmological findings. On the initial visit, pattern VECPs were nonrecordable in 22 eyes of 11 patients, and recordable in 8 eyes of 4 patients in whom the P100 peak latency was prolonged. The P100 peak latency decreased concomitantly with improvement of visual acuity. This result agrees with findings in the case reported by Keane[3] on less-prolonged VECPs after recovery of visual acuity.

Pathological studies[8] of the effects of toluene inhalation based on biopsies of the sural nerve have shown swelling of the axons and an extremely thin lamella of the myelin sheath. Furthermore, Skoog and Nilsson[9] in experiments with monkeys after toluene infusion, found clear changes in the amplitude of the c-wave and the standing potential of the eye. To date, no histopathological retinal changes caused by toluene addiction have been reported. It is, however, assumed that functional retinal changes caused by toluene might occur. The VECP abnormalities in our patients suggested that the agent has a more severe effect on the optic nerve, where the axons and myelin sheath are affected by the toxin.

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References

1. Hamilton AS, Nixon CE. Optic atrophy and multiple neuritis developed in the manufacture of explosives (Binitrotoluene). JAMA 1918;70:2004–6.
2. Pratt-Johnson JA. Retrobulbar neuritis following exposure to vinyl benzene (styrene). Can Med Assoc J 1964;90:975–7.
3. Keane JR. Toluene optic neuropathy. Ann Neurol 1978;4:390.
4. Ehyai A, Freemon FR. Progressive optic neuropathy and sensorineural hearing loss due to chronic glue sniffing. J Neurol Neurosurg Psychiatry 1983;46:349–51.
5. Toyonaga N, Adachi-Usami E, Asanagi K, Takasoh M. Electrophysiological studies on visual toxicity of toluene. Nippon Ganka Gakkai Zasshi (Acta Soc Ophthalmol Jpn) 1988;92:1875–80.
6. Fornazzari L, Wilkinson DA, Kapur BM, Carlen PL. Cerebellar, cortical and functional impairment in toluene abusers. Acta Neurol Scand 1983;67:319–29.
7. Escobar A, Aruffo C. Chronic thinner intoxication: clinicopathologic report of human case. J Neurol Neurosurg Psychiatry 1980;43:986–94.
8. Altenkirch H, Mager J, Stoltenburg G, Helmbrecht J. Toxic polyneuropathies after sniffing a glue thinner. J Neurol 1977;214:137–52.
9. Skoog KO, Nilsson SEG. Changes in the c-wave of the electroretinogram and in the standing potential of the eye after small doses of toluene and styrene. Acta Ophthalmol 1981;59:71–9.