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Wavelength Dependency of Photoparoxysmal Responses in Photosensitive Nonepileptic Subjects

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Takahashi, Y., Fujiwara T., Yagi, K. and Seino, M. *Wavelength Dependency of Photoparoxysmal Responses in Photosensitive Nonepileptic Subjects.* Tohoku J. Exp. Med., 1997, **181** (2), 311-319 —— Using specially made optical filters, we analyzed the wavelength dependency of photoparoxysmal responses (PPRs) in five photosensitive nonepileptic subjects. The wavelength spectrum around 700 nm (680-700 nm) was estimated as the only visible spectrum essential for eliciting PPRs in two normal trichromat nonepileptic subjects, although the effect of some wavelength spectra (360-400 nm and 520-580 nm) was uncertain. The wavelength dependency of PPRs in two photosensitive nonepileptic subjects was the same as that found in some patients with photosensitive idiopathic generalized epilepsy. ———— photoparoxysmal response; wavelength dependency; predisposition; idiopathic generalized epilepsy

Photosensitivity in nonepileptic subjects has been studied by many investigators from about four decades ago, and various findings have been reported. The prevalence of photosensitive nonepileptic subjects is 0.5-7.6% (Mundy-Castle 1953; Buchthal and Lennox 1953; Kooi et al. 1960; Eeg-Olofsson et al. 1971; Doose and Waltz 1993; Gregory et al. 1993; Takahashi 1996). Binnie and Jeavons (1992) described that reports of a high prevalence of photosensitivity in normal subjects were largely based on a broader definition of the photoparoxysmal response (PPR) on EEGs, and that 95% of persons with a prolonged photoconvulsive response had epilepsy. On the other hand, Doose and Waltz (1993) reported that only 3% of children with PPR of wider definition will manifest epilepsy up to the age of 20 years. Although the definition of photosensitivity alters the prevalence of photosensitive nonepileptic subjects and the incidence of epilepsy in photosensitive subjects, photosensitive nonepileptic subjects more or less exist, and a part of photosensitive nonepileptic subjects develops photosensitive epilepsy evolutionally.

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Concerning about the characteristics of photosensitivity, the effect of wavelength composition of flash light on PPRs has been studied. Red-flicker evoked more significant activating effects in provoking PPRs (Takahashi and Tsukahara 1976; Takahashi et al. 1980, 1981; Takahashi 1984). Binnie et al. (1984) reported that monocone stimulating flash light could elicit PPRs. We also investigated the relationships between wavelength of flash light and appearance of classic PPR (Klass and Fischer-Williams 1976; Binnie et al. 1986; Kasteleijn-Nolst Trenité 1989) using special optic filters in patients with idiopathic generalized epilepsy (IGE), because the prevalence of photosensitive patients in IGE was relatively high among the epilepsy (21.2%: Binnie 1992; 51%: Takahashi 1994). We found that wavelength spectrum around 700 nm (660–720 nm) is the only visible spectrum essential for eliciting PPRs in some normal trichromat IGE patients (Takahashi et al. 1995b). After the confirmation of wavelength-dependent photosensitivity in some photosensitive IGE patients, we found the wavelength-dependent and the wavelength-independent photosensitivity (dependent on the quantity of flash light) in patients with dentatorubral-pallidoluysian atrophy (DRPLA) (Takahashi et al. 1995a, 1997). Following the discovery of two different pathophysiological mechanisms for eliciting PPRs, we studied the characteristics of photosensitivity in nonepileptic subjects with classic PPR (Klass and Fischer-Williams 1976; Kasteleijn-Nolst Trenité 1989; Binnie et al. 1986), using special optical filters.

Subjects and Methods

We examined five nonepileptic subjects who had definitive classic PPRs (Klass and Fischer-Williams 1976; Kasteleijn-Nolst Trenité 1989; Binnie et al. 1986) at least once under conventional intermittent photic stimulation (IPS) (Table 1). These subjects were examined consecutively in the outpatient clinic of the National Epilepsy Center between April 1993 and March 1994. All subjects were intellectually normal and had neither neurological abnormalities nor epileptic seizures at the time of examination. Subject 1 had febrile convulsions, and his mother had IGE. He had conventional EEG examinations from 2 to 11 years old, and PPRs were elicited from 7 to 11 years old. Subject 2 also had febrile convulsions. She had conventional EEG examinations from 4 to 10 years old, and PPRs were elicited at 10 years old. Subject 3 had occasional seizures when she suffered from dehydration. Conventional EEG examinations were done from 12 to 17 years old, and PPRs were elicited at 17 years old. Subject 4 had a slight head injury without unconsciousness at 7 years old. She had conventional EEG examinations from 7 to 14 years old, with PPRs elicited at the same ages. Because of nonepileptic behaviors (nightmare and headache), subject 5 had conventional EEG examinations at 7 years old, with elicitation of PPRs. All EEG recordings of five subjects did not show any abnormalities other than PPRs. We judged five subjects as nonepileptic at the time of examination from the electro-

TABLE 1. *Photoparoxysmal responses to conventional intermittent photic stimulation under three conditions (closing of eyes, eyes closed, and eyes opened)*

Suject	Age (years)	Sex	AED	Flash rates (Hz)							
				6	8	10	12	16	18	20	33
1	10	M	VPA	− − −	− − −	− − −	− − −	+ + −	+ − −	+ − −	− − −
2	10	F	—	− − −	− − −	− − −	− + −	+ − −	+ − −	+ − +	− − −
3	17	F	—	− − −	− − −	+ − +	+ + −	+ + +	+ + +	+ + +	− − −
4	14	F	—	− − −	− − −	+ − −	+ + −	− + −	+ + +	+ + +	− − −
5	7	F	—	− − −	− − −	− − −	− − −	− − −	+ − +	+ − +	− − −

AED, antiepileptic durg; VPA, valproate; M, male; F, female: Symbols indicate the presence (+) or absence (−) of photoparoxysmal responses (PPRs) under the following eye conditions: closing of eyes, eyes closed, and eyes opened. For example, + − + indicate presence of PPRs upon closing of the eyes, absence of PPRs with the eyes closed, and presence of PPRs with the eyes opened. PPRs are defined as bilateral diffuse spike-and-wave complexes elicited by intermittent photic stimulation (IPS).

clinical findings mentioned above. All subjects seemed to be normal trichromat, as indicated by results of the Ishihara test given at school.

Conventional IPS, with a Grass PS22 photic stimulator, was performed under the following conditions: flash intensity 8 (11 lumen sec/ft^2), flash rate 6 to 33 Hz, and a flash lamp placed 300 mm from the nasion. Patients lay on a bed in a shielded room with high illuminance (1,000 lux at the nasion). IPS was executed under three different conditions: upon closure of the eyes, eyes closed, and eyes opened (Kasteleijn-Nolst Trenité 1989). IPS was stopped as soon as bilateral diffuse spike-and-wave complexes were elicited. As the effect of IPS is dependent on flash frequency: 15–18 Hz is most epileptogenic (Binnie and Jeavons 1992), following the method of previous paper (Kasteleijn-Nolst Trenité 1989), IPS was started at 18 Hz, and if PPRs appeared under any of the three conditions at 18 Hz, IPS at other frequencies was subsequently performed.

Testing to determine the wavelength dependency of PPRs was performed in the darkened, shielded room (illuminance = 0 lux at the nasion) using narrow bandpass filters (NBFs), sharp cut filters, and an infrared transmitting filter. The optical filters were purchased from Hoya (Tokyo). The examinations were executed at the frequency that elicited the most prominent PPRs under conventional IPS, usually at 18 Hz, with the eyes opened. The distance from flash lamp to the nasion was usually 300 mm, but was sometimes 100 mm if PPRs did not appear at a distance of 300 mm. NBFs used were NBF600 and NBF610 to NBF700 (at intervals of 10 nm). NBFs were 50 mm in diameter and 5.02 mm thick. The sharp cut filters used were R70 and R72 (150 × 150 × 2.5 mm). The infrared transmitting filter used was IR76 (150 × 150 × 2.5 mm). These filters were fixed in front of the flash lamp, completely covering the original flash light.

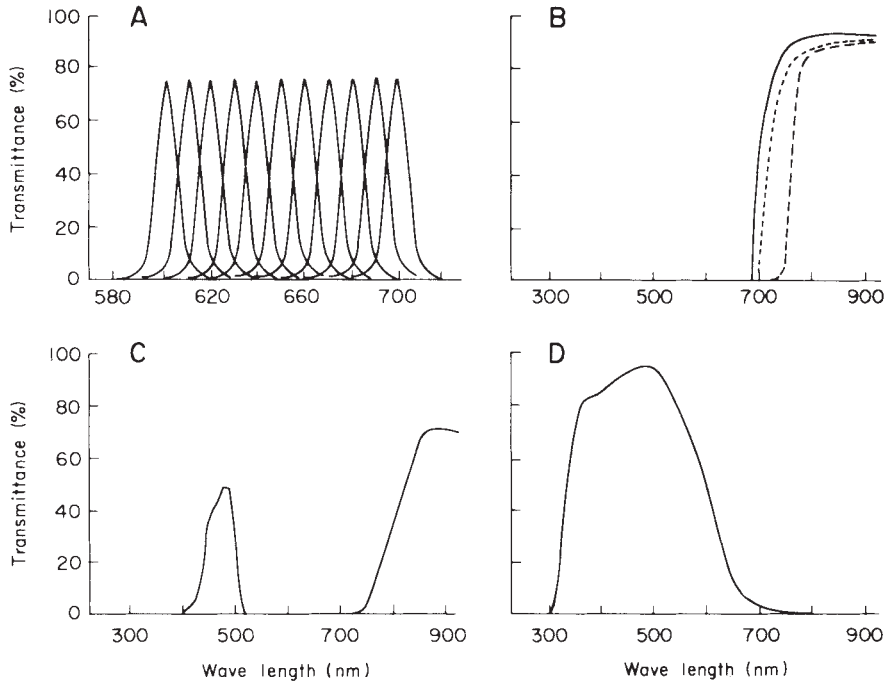

Fig. 1. Transmission spectra of the various optical filters used. A. Transmission spectra of narrow bandpass filters (NBF600 to NBF700, consecutively). For example NBF600 transmits the spectrum from 580 to 620 nm, and the peak of transmission is 600 nm. B. Sharp cut, infrared filters R70 (——) transmits the spectrum longer than 680 nm, and the position of 50% transmission is 700 nm. R72 (……) transmits the spectrum longer than 700 nm, and the position of 50% transmission is 720 nm. IR76 (- - -) transmits the spectrum longer than 720 nm, and the position of 50% transmission is 760 nm. C. MGL is Procion Turquise Blue MGL, which is a type of reactive dye, transmitting blue and yellow. D. The color compensating filter C500 transmits the wavelength spectrum ranging from 300 to approximately 700 nm.

The transmission spectra of the optical filters are shown in Fig. 1. Optical filters (NBF, Sharp cut filter, infrared transmitting filter) transmit intentional wavelength range almost completely (~80-90%) and absorb other ranges of wavelength completely. It is therefore, possible to examine the effect of only intentional wavelength range on eliciting PPRs, at the condition that preserves the quantity of light in the fraction of the intentional wavelength range almost as same level as that in conventional IPS without optical filters.

Testing using the reactive dye MGL (Tanakanao Dye, Kyoto) and the color compensating filter C500 (Hoya) were performed in the shielded room under high illuminance (1,000 lux at the nasion), at the frequency that elicited the most prominent PPRs under conventional IPS. The optical filters were placed in front of the patient's eyes, completely covering the eyes. MGL was diluted to a concentration of 2.0 g/liter, and the solution was installed in two containers of transparent acrylic resin (1 vessel: $70 \times 80 \times 2$ mm) for use as an optical filter. The C500 filter ($50 \times 150 \times 2$ mm) is made of special glass.

The quantity of light was measured by a strobe meter (Minolta Strobe Meter

TABLE 2. *Quantity of light*

Optical filter[a]	Quantity (lx×sec)	
	300 mm[b]	100 mm[b]
Without filter	218.2±1.8	2,119.7±5.2
NBF600	1.68±0.04	20.81±0.65
NBF610	1.44±0.04	17.44±0.38
NBF620	0.90±0.03	8.38±0.21
NBF630	0.62±0.03	5.94±0.15
NBF640	0.36±0.02	4.30±0.10
NBF650	0.210±0.004	2.8±0.0
NBF660	0.119±0.002	1.1±0.1
NBF670	0.049±0.001	0.710±0.018
NBF680	0.017±0.002	0.2441±0.0267
NBF690	0.011±0.000	0.1600±0.0010
NBF700	0.008±0.001	0.0582±0.0016
R70	0.271±0.004	0486±0.349
R72	0.185±0.001	0.518±0.005
IR76	0.0791±0.001	0.139±0.001
MGL	21.87±0.25	185.0±1.9
C500	179.2±0.3	1,457±10

Values are the mean ±S.D. of three separate measurements.

[a]NBF, narrow bandpass filter; R70 and R72, sharp cut filters; IR76, infrared transmitting filter; MGL, reactive dye filter; C500, color compensating filter. Significant figures vary according to the range of each measurement.

[b]Distance between the flash lamp and the nasion.

II, Tokyo) at the first volley of IPS (18 Hz) with and without optical filters (Table 2). The quantity is defined as the time-integrated illuminance. The duration of a volley by PS22 is 10 μsec.

RESULTS

Conventional IPS elicited PPRs mainly at frequencies of 16 to 20 Hz, and did not elicit PPRs at frequencies of 6, 8, or 33 Hz (Table 1).

The PPRs to IPS using special optical filters are shown in Table 3. Two subjects (subjects 1, and 5) had wavelength-dependent PPRs with NBFs or sharp cut filters. In subject 1, IPS using optical filters NBF700 and R70 elicited PPRs, but IR76 and R72 eliminated PPRs to conventional white IPS. Results obtained with NBF700 indicated that PPRs were elicited by IPS consisting of the wavelength spectrum ranging from 680 to 720 nm. Results obtained with R70 indicated that PPRs were elicited by IPS consisting of the wavelength spectrum longer than 680 nm. Elimination of PPRs by R72 or IR76 indicated that PPRs were not elicited by IPS consisting of the wavelength spectrum longer than 700 nm or

TABLE 3. *Photoparoxysmal responses to intermittent photic*

Subject	NBF 600	NBF 610	NBF 620	NBF 630	NBF 640	NBF 650	NBF 660	NBF 670
1	—	—	—	—	—	—	—	—
2	—	—	—	—	—	—	—	—
3	—	—	—	—	—	—	—	—
4	—	—	—	—	—	—	—	—
5	—	—	—	—	—	—	—	—

NBF, narrow bandpass filter; R70 and R72, sharp cut filter; IR76, infrared transmitting filter; MGL, reactive dye filter; C500, color compensating filter. Symbols indicate the presence (+) or absence (—) of a photoparoxysmal response.

720 nm, respectively. Elimination of PPRs by MGL indicated that IPS consisting of the wavelengths ranging from 400 to 520 nm and longer than 720 nm could not elicit PPRs in subject 1. Therefore, the wavelength ranging from 680 to 700 nm is apparently the only one that elicits PPRs in subject 1. In visible range (360–760 nm), the range longer than 700 nm cannot elicit PPRs (data using R72), the range from 580 to 680 nm cannot elicit (data using NBFs), and the range from 400 to 520 nm cannot elicit (data using MGL), but the possibilities of eliciting PPRs by the wavelength range from 360 to 400 nm or from 520 to 580 nm on PPRs are uncertain.

In subject 5, IPS using R70 elicited PPRs. This result indicated that PPRs were elicited by IPS consisting of the wavelength spectrum longer than 680 nm. Elimination of PPRs by R72 or IR76 indicated that the wavelength spectrum longer than 700 nm could not elicit PPRs. Elimination of PPRs by MGL indicated that the PPRs were not elicited by IPS in the wavelength spectrum ranging from 400 to 520 nm or longer than 720 nm. These results suggested that the wavelengths ranging from 680 to 700 nm might be the only one that elicits PPRs, although we could not deny the possibility of eliciting PPRs in the wavelength spectrum of 360 to 400 nm or 520 to 580 nm.

DISCUSSION

Our investigation using special optical filters revealed that the visible range around 700 nm (680–700 nm) might be the only visible wavelength spectrum that was essential for eliciting PPRs in two normal trichromat nonepileptic subjects, although the effect on PPRs of the wavelength spectra of 360 to 400 nm and 520 to 580 nm was uncertain. Strobe light containing the essential wavelengths around 700 nm could elicit PPRs in these photosensitive nonepileptic subjects. These results indicate that wavelength dependent pathophysiological mechanism contributes to the PPRs in two of five photosensitive nonepileptic subjects. Pathophysiological mechanisms in the other three nonepileptic subjects could not

stimulation using special optical filters

NBF 680	NBF 690	NBF 700	R70	R72	IR76	MGL	C500
−	−	+	+	−	−	−	+
−	−	−	−	−	−	−	+
−	−	−	−	−	−	−	+
−	−	−	−	−	−	−	+
−	−	−	+	−	−	−	+

be confirmed in our study.

We reported that the pathophysiological mechanism depending on wavelength spectrum around 700 nm (660–720 nm) contributed to the PPRs in five of 19 normal trichromat IGE patients (Takahashi et al. 1995b). Subsequently we found the same pathophysiological mechanism depending on the wavelength and another type of pathophysiological mechanism for eliciting PPRs, which depends on the quantity of exposed flash light independent of the wavelength of exposed flash light in three patients with DRPLA having similar level of CAG repeat elongation in DRPLA gene (Takahashi et al. 1995a, 1997). It is suggested that the characteristic wavelength-dependency in some photosensitive nonepileptic subjects is the same as that found in some photosensitive patients with IGE and DRPLA.

In three photosensitive nonepileptic subjects and 14 photosensitive patients with IGE (Takahashi et al. 1995b), we could not find wavelength-dependent PPRs or PPRs dependent on the quantity of light. These photosensitive subjects and patients without wavelength dependency or quantity dependency of PPRs might show wavelength dependency of PPRs in examinations using stronger strobe light than PS22, or might have PPRs dependent on quantity of light in stronger condition of photic stimulation. Therefore, we cannot conclude the characteristics of PPRs in photosensitive subjects and patients without wavelength-dependency or quantity-dependency in this study.

The longitudinal study indicated that some photosensitive nonepileptic subjects manifested epilepsy evolutionally (Binnie and Jeavons 1992; Doose and Waltz 1993). Our data might suggest that the characteristics of the photosensitivity, at least wavelength-dependency, might not change evolutionally before and after the epilepsy onset. It is therefore, suggested that onset of the photosensitive epilepsy dose not necessarily need the change of the characteristics of photosensitivity. Photosensitivity might be only a predisposition of epilepsy. We must await further longitudinal study about qualitative change of

wavelength-dependency before and after the onset of epilepsy.

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