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Wavelength Dependence of Photoparoxysmal Responses in Photosensitive Patients with Epilepsy

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Summary: *Purpose:* We tried to specify the relation between the photoparoxysmal response (PPR) and the wavelength spectra of flashing light in various photosensitive epileptic syndromes in the physiologic state.

Methods: Intermittent photic stimulation (IPS) by a Grass PS22 photic stimulator was performed with wavelength-specific optical filters in photosensitive patients with epilepsy (idiopathic generalized epilepsy, IGE; hereditary dentatorubral–pallidoluysian atrophy, DRPLA) and photosensitive subjects without epilepsy.

Results: Five of 19 normal trichromat patients with IGE and an IGE patient with deuteranomaly showed wavelength-dependent PPRs. The wavelength-dependent PPRs were elicited only by IPS containing wavelength spectra ~700 nm in the normal trichromat patients. Two of four patients with DRPLA showed wavelength-dependent PPRs, and two other DRPLA patients showed quantity-of-light–dependent PPRs. Quantity-of-light–dependent PPRs are elicited by IPS containing more than a certain quantity of light, independent of the wavelength composition of the flashing light. Two of five subjects without epilepsy showed wavelength-dependent PPRs.

Conclusions: There are wavelength-dependent and quantity-of-light–dependent pathophysiologic mechanisms for eliciting PPRs by low-luminance IPS. Consideration of the quantity and wavelength composition of light from electronic screens will lead to the prevention of photosensitive seizures induced by electronic screen games. **Key Words:** Photoparoxysmal response—Idiopathic generalized epilepsy—Dentatorubral–pallidoluysian atrophy—Wavelength dependence—Deuteranomaly.

Many investigators have studied the relation between the photoparoxysmal response (PPR) and the wavelength composition of flashing light in intermittent photic stimulation (IPS). Carterette and Symmes (1) reported that red flicker was more effective in provoking PPR than were other colors. Takahashi et al. (2–4) also noted a much greater incidence of PPR to red flicker than to other colors or white flicker. On the other hand, Rao and Prichard (5) reported that red flicker was less effective than other wavelengths in provoking PPR. Harding et al. (6) found no difference in the epileptogenic effect of red and other colors. Recently Leijten et al. (7) reported that the photosensitivity range of flash frequency was reduced by red filters. Earlier, Binnie et al. (8), by using an ingenious technique of silent substitution, found that the light stimulating only one class of retinal cones could elicit the PPR.

In our study, we tried to specify the exact wavelength range that could elicit PPRs with wavelength-specific optical filters in the physiologic state.

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PATIENTS AND METHODS

Patients and subjects

We studied the wavelength dependence of PPRs in photosensitive patients with epilepsy and subjects without epilepsy who had classic PPRs elicited at least once by conventional IPS. Classic PPR was the reliable PPR defined by Klass and Fischer-Williams (9) and Binnie et al. (10). The patient group consisted of 20 patients with idiopathic generalized epilepsy (IGE), and four with hereditary dentatorubral–pallidoluysian atrophy (DRPLA), a type of progressive myoclonus epilepsy common in Japan, and there were five nonepileptic subjects. All were described in previous reports (11–13). Some patients were taking antiepileptic drugs (AEDs), as described elsewhere for the IGE and DRPLA patients (11,13). One of the IGE patients had deuteranomaly, and all other patients and subjects were normal trichromats.

Methods

Conventional IPS, with a Grass PS22 photic stimulator, was performed under the following conditions: flash intensity 8, flash rate 6–33 Hz, and the flash lamp placed 300 mm from the nasion (11–14).

Examinations to determine the wavelength depen-

dence of PPRs were performed in a darkened, shielded room (illuminance, 0 lux at the nasion) with narrow bandpass filters (NBFs), sharp-cut filters, and an infrared transmitting filter (11–13). The optical filters were purchased from Hoya (Tokyo, Japan). Testing was carried out at the flash frequency that had elicited the most prominent PPR under conventional IPS, with the eyes open. The distance from the flash lamp to the nasion was usually 300 mm, but was sometimes 100 mm if PPRs did not appear at the longer distance. The NBFs used were NBF600, NBF610, at intervals of 10 nm, to NBF700 (8–10). 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 strobe light. Transmission spectra of the optical filters are shown in Fig. 1. Testing with the reactive dye MGL (Tanakanao Dye, Kyoto, Japan) and a color-compensating filter C500 (Hoya, Tokyo, Japan) was performed in a shielded room under high illuminance (1,000 lux at the nasion) at the frequency that elicited the most prominent PPR with conventional IPS (8–11).

The quantity of light was measured by a strobe meter (Minolta Strobe Meter II; Tokyo, Japan) at the first volley of IPS (18 Hz) with and without optical filters (Table 1). The quantity of light is defined as the time-integrated illuminance. The duration of a volley by Grass PS22 is 10 μs.

TABLE 1. *Quantity of light*

Optic filters	Distance (mm)	
	300	100
Without filter	218.2 ± 1.8	2119.7 ± 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*	*0.486 ± 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	1457 ± 10

NBF, narrow bandpass filter; R70 and R72, sharp-cut filter; IR76, infrared transmitting filter; MGL, reactive dye filter; C500, color compensating filter. Significant figures vary according to the range of each measurement. Distance is defined as the distance between the flash lamp and the nasion. The values are the mean of three separate measurements (mean ± SD, lux × second).

RESULTS

IGE

We analyzed the wavelength dependence of PPRs in 20 photosensitive patients with IGE (11). The wave-

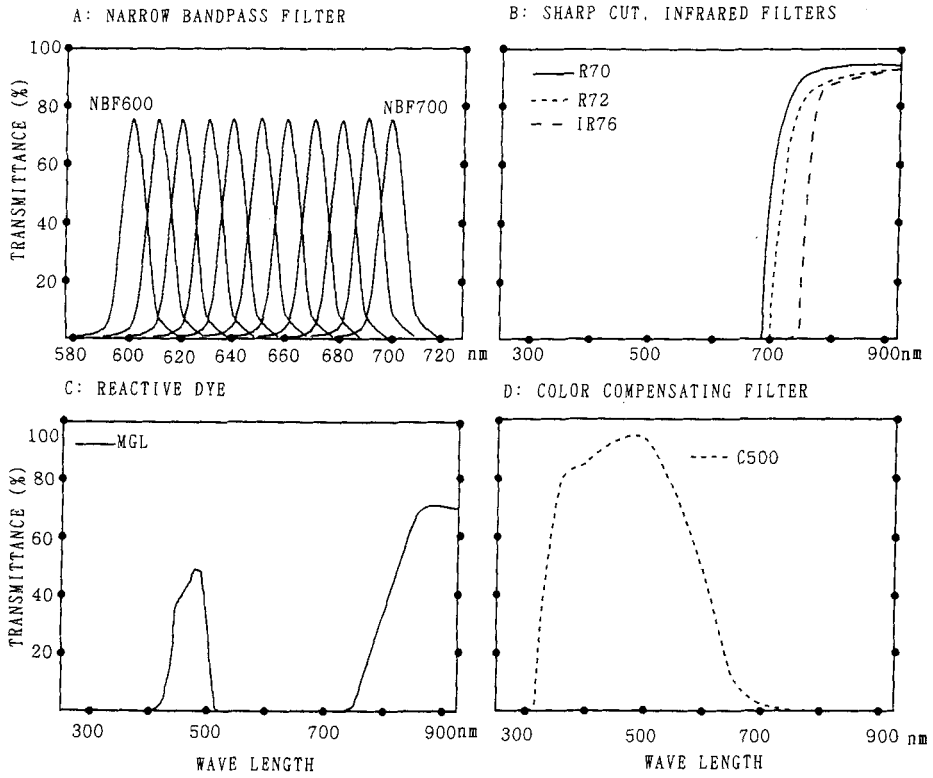

FIG. 1. Transmission spectra of the various optic filters used. **A:** Transmission spectra of NBF600 to NBF700 consecutively. NBF600 transmits the spectrum from 580 to 620 nm, and the peak of transmission is 600 nm. **B:** R70 transmits the spectrum >680 nm, and the position of 50% transmission is 700 nm. R72 transmits the spectrum >700 nm, and the position of 50% transmission is 720 nm. IR76 transmits the spectrum >720 nm, and the position of 50% transmission is 760 nm. **C:** MGL is Procion Turquoise Blue MGL, a type of reactive dye, transmitting blue and yellow. **D:** The color-compensating filter C500 transmits the wavelength spectrum ranging from 300 to ~700 nm.

length spectrum ~700 nm (660–720 nm) was estimated as the only visible spectrum essential for eliciting PPRs in five normal trichromat patients, and any flashing lights containing this essential wavelength spectrum elicited PPRs, independent of the number of stimulated retinal cones. Absorption of the wavelength spectrum ~700 nm by optical filters eliminated PPRs in normal trichromat patients. In the IGE patient with deuteranomaly, intermittent flashing lights containing a part of the wavelength spectrum from 580 to 700 nm elicited PPRs. These data were interpreted as indicating the wavelength dependence of PPRs: flashing lights containing the wavelength spectrum that does not produce antagonistic cone interactions at the level of the retinal ganglion cells can elicit PPRs in some photosensitive IGE patients.

DRPLA

We studied the characteristics of PPRs in patients with DRPLA who had expansion of the CAG repeat in the DRPLA gene (13). In two patients, the wavelength spectrum ~700 nm (670–720 nm) was apparently the only visible range essential for eliciting PPRs, and flashing lights containing the essential wavelength elicited PPRs (Fig. 2). In two other DRPLA patients, PPRs were elicited by flashing lights above a certain quantity of light and independent of the wavelength composition of the lights (Fig. 3). These data suggest that two different pathophysiologic conditions contribute to PPRs in DRPLA patients; one condition depends on the essential wavelength spectrum ~700 nm, and the other not on the wavelength, but only on the quantity of light. The pathophysiologic mechanism contributing to PPRs was not determined directly by the level of the CAG repeat expansion in the DRPLA gene.

Photosensitive nonepileptic subjects

We analyzed the wavelength dependence of PPRs in five photosensitive nonepileptic subjects (12). The wavelength spectrum ~700 nm (680–700 nm) was estimated as the only visible spectrum essential for eliciting PPRs in two normal trichromat nonepileptic subjects. The wavelength dependency of PPRs in two photosensitive nonepileptic subjects was the same as that found in some photosensitive patients with IGE.

DISCUSSION

We confirmed wavelength-dependent and quantity-of-light–dependent PPRs in photosensitive patients with epilepsy and nonepileptic subjects (11–13). Wavelength-dependent PPRs are elicited only by IPS containing wavelength spectra ~700 nm in normal trichromats. Quantity-of-light–dependent PPRs are elicited by IPS containing more than a certain quantity of light, independent of the wavelength composition of the flashing light. Heterogeneity of the pathophysiologic mechanisms in eliciting PPRs in photosensitive epilepsy can explain the controversy on the relation between wavelength and photosensitivity (1–6). A causal relation between photosensitivity and wavelength was thought to be supported by studies showing a pathophysiologic mechanism of photosensitivity depending on wavelength, but not by studies finding a pathophysiologic mechanism depending only on the quantity of light.

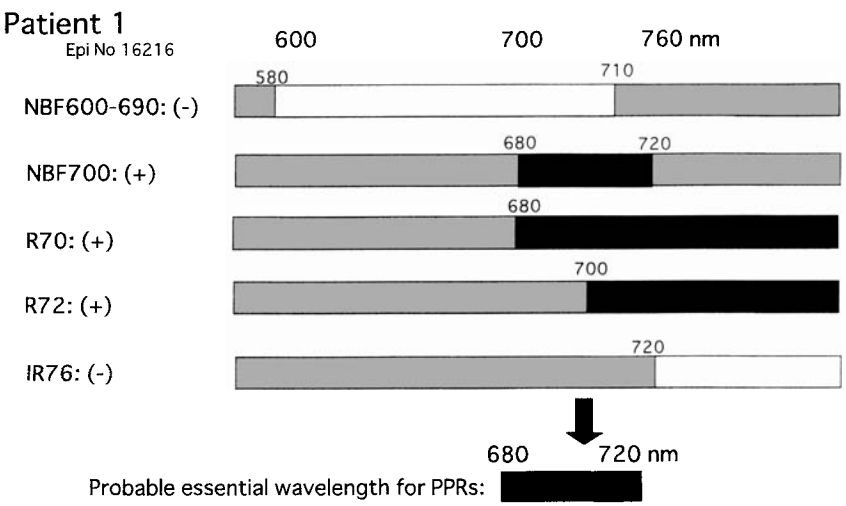

FIG. 2. Essential wavelength for eliciting photoparoxysmal responses (PPRs) in patient 1 with hereditary dentorubral–pallidoluysian atrophy (DRPLA). The solid bar indicates wavelength spectra including spectrum that can elicit PPRs, and the stippled bar those that cannot elicit PPRs. Intermittent photic stimulation (IPS) with NBF700, R70, and R72 elicited PPRs, but NBF600 to NBF690 and IR76 eliminated PPRs. These data show that IPS containing wavelengths ranging from 680 to 720 nm (NBF700) and >680 (R70) and 700 (R72) nm can elicit PPRs, and that wavelengths >720 nm or ranging from 560 to 680 nm cannot elicit PPRs. Therefore it is estimated that wavelengths ranging from 680 to 720 nm are essential for eliciting PPRs. When the essential wavelength is included, IPS with the strobe light can elicit PPRs, as with conventional white IPS. Because the quantity of flashing light transmitted through NBF690 or NBF700 is less than that transmitted through NBF600 to NBF680 (see Table 1), we conclude that PPRs in patient 1 depend not on the quantity of light, but on the essential wavelength (680–720 nm) included in the flashing light.

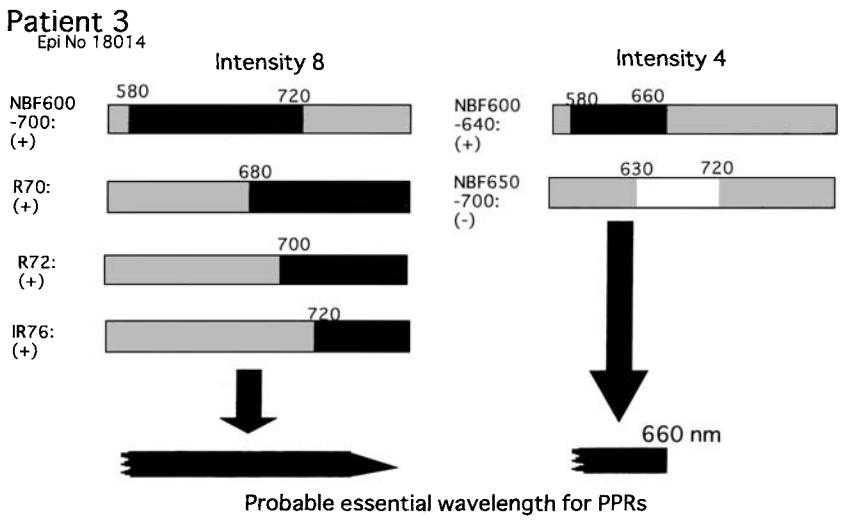

FIG. 3. Photoparoxysmal responses (PPRs) in patient 3 with hereditary dentorubral–pallidoluysian atrophy (DRPLA). The solid bar indicates wavelength spectra including spectrum that can elicit PPRs, and the stippled bar indicates those that cannot elicit PPRs. Intermittent photic stimulation (IPS) at the conventional flash intensity of eight elicited PPRs with NBF600 to NBF700, R70, R72, and IR76. Therefore it is estimated that the wavelength spectrum between 580 and 720 nm can elicit PPRs, and that wavelengths >720 nm also seem to elicit PPRs. IPS at a flash intensity of 4 elicited PPRs with NBF600–NBF640, but not with NBF650–NBF700. Thus wavelengths between 580 and 660 nm elicited PPRs at the intensity of 4 and 8, but wavelengths between 660 and 720 nm elicited PPRs only at the higher intensity of 8. As the quantity of flashing light transmitted through optical filters NBF600–NBF640 is more than that transmitted through NBF650–NBF700 (see Table 1), it is conceivable that IPS containing more than a certain quantity of light can elicit PPRs, independent of the wavelength composition of the flashing lights.

We found wavelength-dependent PPRs in six of 20 patients with IGE, but we could not confirm wavelength-dependent PPRs or quantity-of-light–dependent PPRs in the remaining 14 patients. Patients with wavelength-dependent PPRs had a relatively broad range of flash frequency of photic stimulation, and one had generalized tonic–clonic seizures inadvertently induced by IPS (11). The 14 patients without a confirmed pathophysiologic mechanism had a relatively narrow range of flash frequency (11), which suggests that the absence of wavelength-specific PPRs was related to their relatively low photosensitivity.

The characteristics of the photosensitivity, as shown in Table 2, might suggest a relation between the pathophysiologic mechanisms of PPRs and the classification of photosensitive epileptic syndromes. Photosensitive patients with IGE and photosensitive nonepileptic subjects had wavelength-dependent PPRs only. It is estimated that wavelength-dependent pathophysiologic mechanisms usually play a role in persons with predispositional photosensitivity, and that quantity of light-dependent pathophysiologic mechanisms play a role in persons with nonpredispositional photosensitivity. Patients with DRPLA had photogenic seizures, whereas patients with IGE or nonepileptic subjects did not have photogenic seizures. The difference in pathophysiologic mechanisms of PPRs may regulate the level of photosensitivity, which might determine the occurrence of photogenic seizures.

TABLE 2. *Characteristics of the photosensitivity in photosensitive epileptic syndromes*

Epileptic syndrome	n	Wavelength dependent	Quantity of light dependent
IGE	20	6	—
DRPLA	4	2	2
Nonepileptic	5	2	—

IGE, idiopathic generalized epilepsy; DRPLA, hereditary dentatorubral–palliodoluysian atrophy; N, number of patients or subjects.

Evolution of the pathophysiologic mechanisms of PPRs is a possibility, because patients with DRPLA showed two types of mechanisms. However, a definitive conclusion must await further investigations, such as longitudinal studies of qualitative change in pathophysiologic mechanisms of PPRs, and molecular biologic studies of transmitters and receptors in many photosensitive patients.

Although epileptic seizures induced by electronic screen games (15) may have several pathophysiologic origins, photosensitivity is an important mechanism for induction. Our finding of two types of pathophysiologic mechanisms of photosensitivity suggest that consideration of the quantity and wavelength composition (~700 nm) of light from electronic screens will lead to the prevention of epileptic seizures induced by electronic screen games.

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