Generalized Paroxysmal Discharges Induced by Visual Stimuli and Eye Movements

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Takahashi, T. and Tsukahara, Y. Generalized Paroxysmal Discharges Induced by Visual Stimuli and Eye Movements. Tohoku J. exp. Med., 1975, 115 (1), 1-10 — The generalized paroxysmal discharges (GPDs) induced by the visuo-sensory and oculomotor activations in a total of 30 patients were investigated. The patients consisted of 27 epileptics and 3 with sequelae of head trauma; all of them showed photoconvulsive response. The visuo-sensory activation with red-flicker of 15 cycles/sec or with visual stimuli containing patterns, "pattern," was carried out under the constant condition of 20 cd/m². In 22 cases (73%), G-type (simultaneous occurrence of GPD over all the areas) was induced by red-flicker, while in 28 cases (93%) P-type (GPD was preceded by posterior spikes) was induced by "pattern." With the oculomotor activation, paroxysmal discharges were induced in 11 cases of photogenic epilepsy; 10 cases (91%) were of A-type (GPD was preceded by anterior spikes), and one case (9%) showed focal spikes over the right frontal area. In 21 cases (70%), the type of GPD changed from G-type to P-type as the red-flicker activation was replaced by the "pattern" activation. Further, in seven (33%) out of the 21 cases it changed from P-type to A-type as the activation with "pattern" was replaced by the oculomotor activation. It was suggested that the non-specific thalamo-cortical system, the visual cortex, and the frontal eye field are chiefly concerned with the occurrences of G-type, P-type, and A-type, respectively, when such stimuli as described above are given independently. ——— photosensitive epilepsy; photoconvulsive response; visual stimulus; eye movement

It is a well-known fact that paroxysmal discharges are induced by various sensory stimuli (Gastaut and Tassinari 1966; Bickford and Klass 1969), and among them intermittent photic stimulation (IPS) is apparently the most effective one (Bickford and Klass 1969).

Since Walter et al. (1946), Gastaut et al. (1948), Walter and Walter (1949), and Gastaut and Hunter (1950) reported that IPS by means of a stroboscope provoked paroxysmal discharges, this has become one of the common methods for EEG activation. Carterette and Symmes (1952), Marshall et al. (1953), Brausch and Ferguson (1965), Takahashi (1973b), and Takahashi and Tsukahara (1973) reported that red-flicker evoked significant activating effects in producing paroxysmal discharges in comparison with other colored flicker stimuli. It has also been reported that paroxysmal discharges are induced by viewing some geometric patterns (Bickford and Klass 1962; Chatrian et al. 1970; Takahashi and

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Sasaki 1971). On the other hand, it has been reported that clinical seizures and/or paroxysmal discharges are induced by closing the eyes (Robinson 1939; Green 1968; Lewis 1972; Tieber 1972; Takahashi 1973a) and eye deviation (Shanzer et al. 1965; Takahashi 1974b; Takahashi and Tsukahara 1974b) as well.

Takahashi and Tsukahara (1974b) elucidated that paroxysmal discharges are often induced by eye closing and eye deviation in patients with photosensitive epilepsy associated with photoconvulsive response (Bickford et al. 1952). Based on such experiences, they proposed a new conception named ophthalmic epilepsy in which paroxysmal discharges and/or clinical seizures are induced by either visual stimuli or eye movements, or by both in epileptics.

Concerning the ophthalmic stimuli as described above, the factors inducing paroxysmal discharges are not always constant in each of the patients. Namely, red-flicker is the most effective in a large number of the patients (Takahashi and Tsukahara 1974a), and flickering-pattern is the next effective stimulus (Takahashi and Tsukahara 1974b). In addition, there are some patients in whom ocular movement is the most effective stimulus (Takahashi and Tsukahara 1974b).

When we observed carefully the generalized paroxysmal discharges (GPDs) induced by such ophthalmic stimuli, we found that their types of occurrence differ according to the kind of ophthalmic stimuli, even in the same patients (Takahashi 1974b). As a result, we came to the conclusion that when the GPDs are induced by ophthalmic stimuli, probably different regions of the brain are concerned with their occurrence according to the difference of the kind of ophthalmic stimuli.

**SUBJECTS AND METHODS**

Subjects were 27 epileptics, consisting of 17 photogenic epilepsy patients and 10 with photosensitivity in terms of EEG response, and 3 patients with sequelae of head trauma; all of them showed photoconvulsive response. Ages ranged from 5 to 39 years, and the mean age was 17.8 years. Of these 30 patients, 21 (70%) were female and 9 (30%) were male. In all 30 cases GPDs (sharp and wave complex, spike and wave complex, high voltage slow burst) were induced by both red-flicker and stimuli containing patterns in the visuo-sensory activation described below.

Our specially designed EEG activation method by the ophthalmic stimulation consisted of the following two: (1) visuo-sensory activation, and (2) oculomotor activation (Takahashi 1974b; Takahashi and Tsukahara 1974b).

For the visuo-sensory activation (Takahashi and Tsukahara 1974a) the "visual stimulator" (Tsukahara and Takahashi 1973) was used. We used 15 cycles/sec, red-light, and patterns of A and B as shown in Fig. 1 for flicker, color and pattern, respectively, and kept the brightness of all visuo-sensory stimuli on the screen (in the cases of pattern, it means the brightness of the ground) at 20 cd/m². As visuo-sensory stimuli, the following 11 kinds of visual stimulation were given: (1) flicker of white light, (2) continuous red-light, (3) A-pattern, (4) B-pattern, (5) red-flicker, (6) red-A-pattern (the ground of A-pattern was red), (7) red-B-pattern (the ground of B-pattern was red), (8) flickering-A-pattern, (9) flickering-B-pattern, (10) red-flickering-A-pattern, and (11) red-flickering-B-pattern. First of all, we gave (1) for 10 sec. After keeping the subject quiet under the same condition of eyes opened for 30 sec, we carried out the activation by (2). Then we continued to carry out the activation by the visual stimuli in the order from (3) to (11), and if paroxysmal discharges were induced by any stimulation, we immediately stopped giving the stimula-
After the paroxysmal discharges disappeared, we recorded the EEG under the condition of eyes opened for 30 sec, and the successive activation continued.

Next we carried out the oculomotor activation (Takahashi 1974b). This activation was, like the visuo-sensory activation, carried out with the subject sitting in a dark room. First, the subjects were asked to close their eyes firmly. After we made them keep their eyes closed for 5 sec, we told them to open their eyes. After 5 sec we made them repeat closing and opening their eyes in the same way 5 times. Next, after keeping the subjects gazing forward, we made them move their eyeballs upward and keep this position for 5 sec and then look forward for 5 sec. Following this, we made the subjects move their eyes downward, forward, rightward, forward, leftward, and forward in this order in the same way, and we made them repeat these serial eye movements 5 times. When paroxysmal discharges were induced during such oculomotor activation, we waited till they disappeared. From the EEG findings we judged whether the subjects were cooperative to the examination, and gave advice if necessary.

Grass' electrodes for EEG recording were attached with paste on the scalp and placed according to the 10–20 International System. The EEG was recorded by means of a 13-channel (Sanei-sokki) electroencephalograph from the left and right frontal-pole, frontal, central, parietal, occipital, and posterior-temporal regions; monopolar lead with ipsilateral ear lobe reference was used. If the patient took anticonvulsants, tranquilizers and so forth at the time of EEG recording, the recording was made under this condition in principle, but, when necessary, the recording was made again after he ceased taking them for 12 to 24 hr.

There were often distinct topological differences in the GPDs induced by the visuo-sensory and oculomotor activations. The GPDs were thus arbitrarily classified into the
following four: (1) posterior type (P-type), (2) generalized type (G-type), (3) unclassified (UC), and (4) anterior type (A-type). P-type is the GPD preceded by apparent posterior spikes. In G-type, GPD occurs over all the regions at the same time. The GPD in which posterior spikes slightly precede GPD, not as apparent as in the P-type, is called UC. A-type is the GPD preceded by apparent anterior spikes. In addition to such GPDs, focal paroxysmal discharges induced by the EEG activation as described above are named focal type (F-type).

RESULTS

Fig. 2 is an example of the findings recorded on a case of photogenic epilepsy (9-year-old female). The left figure shows the GPD induced by A-pattern and the right figure that by red-flicker. The GPD induced by A-pattern was apparently preceded by spikes over the left occipital, posterior-temporal, and parietal regions. In striking contrast, the GPS induced by red-flicker occurred over all the regions at the same time, although minimal focal accentuation over the left occipital and posterior-temporal regions was observed. In this case GPDs were induced by all visuo-sensory stimuli except for continuous red-light. Comparing latencies of the GPDs in response to various stimuli of the visuo-sensory activation, that of red-flicker was the shortest (0.6 sec, see the right part of Fig. 2); namely red-flicker was the most effective for GPDs. When the GPDs induced by the stimuli containing patterns (abbreviated as “pattern” hereafter) and those by red-flicker were compared, such a distinct difference was noticed that the GPDs

![Fig. 2. EEGs of a 9-year-old female patient with photogenic epilepsy. Generalized paroxysmal discharges were induced by pattern (left) and red-flicker (right). For this EEG activation “visual stimulator” was used. Monopolar lead with ipsilateral ear lobe reference.](image)
Fig. 3. EEGs of a 23-year-old male patient with photogenic epilepsy. Generalized paroxysmal discharges were induced by red-flicker (RF) (left), red-flickering-pattern (RFP) (center) and eyes closing (right). The downward and upward arrows indicate the beginning and end of the stimuli.

induced by "pattern" were always preceded by spikes either over the left or right posterior regions, or over both posterior regions. The GPDs induced by "pattern" and red-flicker which were the findings as shown in the left and right parts of Fig. 2 will hereafter be called P-type and G-type, respectively.

Fig. 3 shows the GPDs induced by red-flicker (left) and red-flickering-B-pattern (center) in a case of photogenic epilepsy (23-year-old male). When GPD was induced by red-flicker, it started in all the regions at the same time (G-type). On the other hand, when GPD was induced by red-flickering-B-pattern, it was preceded by spikes over occipital, posterior-temporal and parietal regions (P-type).

Fig. 4 also shows the GPDs induced by red-flicker (left) and flickering-A-pattern (center) in a case of photogenic epilepsy (25-year-old female). Differing from those of Figs. 2 and 3, when GPD was induced by red-flicker, spikes over the occipital areas slightly preceded the GPD and then generalized. Such GPDs induced by red-flicker could be called neither G-type nor P-type, so we named it UC provisionally. In addition, there was one case in which frontal spikes preceded the GPD were induced by red-flicker. This was named A-type. When GPDs were induced by eyes closing as shown in the right parts of Figs. 3 and 4, they started from both frontal-central regions. Such GPDs were also called A-type. In the patient of Fig. 3, similar A-type GPDs were induced not only by eyes closing but also by eyes opening and all eyes movements of the oculomotor activation. In the patient of Fig. 4, eyes closing and upward deviation of the eyes of the oculomotor activation were effective to induce GPDs; they were all A-type.

In Table 1, the classification into such five types of GPDs in a total of 30 cases is shown. When GPD was induced by red-flicker, the number of cases
Fig. 4. EEGs of a 25-year-old female patient with photogenic epilepsy. Generalized paroxysmal discharges were induced by red-flicker (RF) (left), flickering-pattern (FP) (center) and eyes closing (right).

Table 1. Types of generalized paroxysmal discharges (GPDs) induced by the visuo-sensory activation (red-flicker (RF) and “pattern” (PAT)) and the oculomotor activation (OMA) in the 30 patients

<table>
<thead>
<tr>
<th>Types of GPDs</th>
<th>RF</th>
<th>PAT</th>
<th>OMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>A-type</td>
<td>1(3.3%)</td>
<td>0</td>
<td>10(90.9%)</td>
</tr>
<tr>
<td>P-type</td>
<td>0</td>
<td>28(93.3%)</td>
<td>0</td>
</tr>
<tr>
<td>G-type</td>
<td>22(73.3%)</td>
<td>1(3.3%)</td>
<td>0</td>
</tr>
<tr>
<td>UC</td>
<td>7(23.3%)</td>
<td>1(3.3%)</td>
<td>0</td>
</tr>
<tr>
<td>F-type</td>
<td>0</td>
<td>0</td>
<td>1(9.0%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>30(99.9%)</strong></td>
<td><strong>30(99.9%)</strong></td>
<td><strong>11(99.9%)</strong></td>
</tr>
</tbody>
</table>

which were of A-type was 1 (3.3%), P-type 0, G-type 22 (73.3%), and UC 7 (23.3%). In contrast, when it was induced by “pattern,” the number of cases which were of A-type was 0, P-type 28 (93.3%), G-type 1 (3.3%), and UC 1 (3.3%). These results clearly indicate that red-flicker and “pattern” induced predominantly G-type and P-type of GPDs, respectively.

With the oculomotor activation, activation effect was observed in 11 cases of photogenic epilepsy; of the 11 cases, 10 (90.9%) were A-type and 1 (9%) was focal spikes over right frontal area (F-type).

Table 2 shows shifts of types of the GPDs induced by red-flicker, “pattern,” and the oculomotor activation in 30 cases. In 21 (69.9%) of the 30 cases the type of GPDs changed from G-type to P-type as the kind of activation changed from red-flicker to “pattern,” and in 7 (33.3%) of the 21 cases it changed from P-type to A-type as the kind of activation changed from “pattern” to the oculomotor activation.
Generalized Paroxysmal Discharges

TABLE 2. Shifts of types of generalized paroxysmal discharges induced by the visuo-sensory activation (red-flicker (RF) and "pattern" (PAT)) and the oculomotor activation (OMA) in the 30 patients

<table>
<thead>
<tr>
<th>RF</th>
<th>PAT</th>
<th>OMA</th>
<th>Case</th>
</tr>
</thead>
<tbody>
<tr>
<td>A-type</td>
<td>G-type</td>
<td>A-type</td>
<td>1(3.3%)</td>
</tr>
<tr>
<td>G-type</td>
<td>P-type</td>
<td>A-type</td>
<td>7(23.3%)</td>
</tr>
<tr>
<td>G-type</td>
<td>P-type</td>
<td>F-type</td>
<td>1(3.3%)</td>
</tr>
<tr>
<td>G-type</td>
<td>U-type</td>
<td>A-type</td>
<td>1(3.3%)</td>
</tr>
<tr>
<td>U-type</td>
<td>P-type</td>
<td>A-type</td>
<td>1(3.3%)</td>
</tr>
<tr>
<td>U-type</td>
<td>P-type</td>
<td></td>
<td>6(20.0%)</td>
</tr>
</tbody>
</table>

Total 30(99.8%)

DISCUSSION

Hishikawa et al. (1967) classified GPDs induced by IPS into the 1st group (the discharges appeared first in the occipital area, and subsequently spread almost simultaneously to other areas) and the 2nd group (the epileptiform discharges were induced simultaneously over all head regions or appeared earlier in the anterior than in the occiptial areas). After that, Aoki (1969) called the 1st group and the 2nd group P-type and G-type, respectively. Takahashi (1973a, b) also classified the GPDs induced by IPS into four; P-type, G-type, A-type and F-type. By applying this classification to the GPDs induced by the visuo-sensory and oculomotor activations, we have reported their clinical-EEG findings (Takahashi and Tsukahara 1973; Takahashi 1974a; Takahashi and Tsukahara 1974a).

The IPS activation in which a Xenon lamp is used for a light source is apparently too strong in comparison with our visuo-sensory activation. In addition to this, in the IPS activation under the condition of eyes closed, various factors, such as diffuser effect (Brausch and Ferguson 1965; Bickford and Klass 1969; Takahashi 1973b) and red-color effect (Carterette and Symmes 1952; Marshall et al. 1953; Brausch and Ferguson 1965; Takahashi 1973b; Takahashi and Tsukahara 1973) by eyelids, and movement of eyelids and eyes in closing eyes (Robinson 1939; Green 1968; Lewis 1972; Tieber 1972; Takahashi 1973a, b) promote the occurrence of paroxysmal discharges. Because such various factors are concerned with the IPS activation, photoconvulsive response of the same patient sometimes changes from G-type to P-type or vice versa according to whether it is carried out with eyes opened or closed, or according to the difference in frequency of IPS used. Special techniques for giving IPS as described by Jeavons et al. (1972) and Panayiotopoulos et al. (1972) may produce further complex results. On the other hand, the visuo-sensory and oculomotor activations can be an EEG activation in which the factors that are effective for the activation of paroxysmal discharges by the IPS activation are extracted one by one and then each factor or combination of factors is given. And this EEG activation method not only shows a superior activating effect to the effect by the
IPS activation, but it also often brings much information of clinical importance (Takahashi and Tsukahara 1974a, b).

We have reported that the GPDs induced by the visuo-sensory activation bring about distinctly different results according to the difference in parameters of visual stimuli, and that G-type tends to be induced by red-flicker (Takahashi and Tsukahara 1973) and P-type by pattern (Takahashi and Sasaki 1971; Takahashi 1974a). But since the activation was carried out under different conditions of stimulation (red-flicker of less than 40 cd/m² and pattern of 190 cd/m²), we could not immediately conclude that the results are characteristic to red-flicker and pattern. In this study we analyzed the difference of GPD in each of the patients under the controlled conditions by using the “visual stimulator.”

The activating effect of the patterns with white ground was usually greater than that of red-patterns if the brightness of the ground of both patterns was equal. In addition, the patients were more sensitive to the flickering-patterns than to the continuously presented patterns. The latencies of the P-type in response to the flickering-patterns were in general shorter than those in response to the continuously presented patterns. The type of GPD remained the same to the stimuli with “pattern.” Namely, it can be regarded that pattern is one of the important factors in producing the P-type in response to visual stimuli.

Consequently, we largely classified the visuo-sensory activation into two by stimuli, red-flicker and “pattern” of the same brightness, and compared the GPDs induced by them. In 22 (73.3%) of the 30 cases G-type was induced by red-flicker, while 28 (93.3%) of the 30 cases P-type was induced by “pattern.” On the other hand, GPDs induced by the oculomotor activation in 10 cases were all of A-type. These findings may be summarized as follows: GPDs induced by the visuo-sensory and oculomotor activations differ in their types of occurrence according to the kind of activation, with the result that red-flicker, “pattern,” and oculomotor activation tend to induce G-type, P-type, and A-type, respectively.

The findings of the P-type induced by “pattern” support the results of Chatrian et al. (1970) that the paroxysmal discharges triggered by the viewing of line patterns arise within the visual cortex. On the basis of the EEG findings of the G-type induced by red-flicker, namely, simultaneous occurrence of GPDs in all over the scalp, the non-specific thalamo-cortical system can be considered as playing an important role in the precipitation of the G-type of GPD. However, it cannot disregard the finding that the UC GPDs induced by red-flicker were found in 7 cases (23.3%). As shown in the left part of Fig. 4, spikes over the occipital areas slightly preceded the GPD. Such a finding suggests that the paroxysmal discharges induced by red-flicker may primarily arise within the visual cortex in these cases. Thus, the fact cannot be denied that there are some photosensitive patients in whom the occurrence of the GPD with red-flicker is induced by primary participation of the visual cortex. It is a well-known fact that the frontal, occipital, and preoccipital eye fields are concerned with involuntary as well as voluntary eye movements (Crosby et al. 1962; Carpenter 1971). On the
other hand, Wagman (1964) reported that the cerebral cortex of monkey contains large regions concerned with eye movement. The present result of the oculomotor activation was that of 11 cases in which the activation effects were seen, 10 were of A-type and 1 of F-type (right frontal spike). These findings would indicate an important role of the frontal lobe, especially the frontal eye field in the occurrence of the A-type of GPD by the oculomotor activation.

Concerning the electrophysiological mechanism of its occurrence, the GPD of G-type, and the GPDs of P-type, UC and A-type may be considered as identical with the primary bilateral synchrony, and secondary bilateral synchrony (Tükel and Jasper 1952), respectively. For clarification of such hypothesis, further studies by the visuo-sensory and oculomotor activations in different conditions as well as by comparison of the EEGs in resting state, during hyperventilation and sleep of these patients, remain to be done.

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References


