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VISUALLY-INDUCED SEIZURES

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The following chapter is divided into five sections. The first gives a brief background summary of recent work concerning visually-induced epilepsy. The studies reviewed consider some of the obvious parameters of the visual stimuli responsible for the induction of seizures, and the characteristics of the electroencephalographic response that they evoke. The next three sections are theoretical. They focus in turn on: (1) where in the visual system the seizures are triggered; (2) how the triggering occurs; and (3) some possible reasons as to why. The sixth section returns to practical issues and considers some clinical implications of the previous sections.

1. Background

Studies based on searches of medical records suggest that about one person in every 200 suffers from epilepsy (Ponds *et al.*, 1960), although market research techniques indicate an incidence of the order of 2% (Rose *et al.*, 1973; Gomez and Torrez, 1978). A small proportion of these people (about 3%; Jeavons and Harding, 1975) suffer from seizures

that are induced by visual stimulation (photosensitive epilepsy). Common sources of epileptogenic visual stimulation include television, flickering sunlight, and discotheque stroboscopes. The majority of persons with photosensitive epilepsy are young (the modal age for first referral is 12) and there is a 3:2 preponderance of females. The seizure type is variable, but absences, myoclonic jerks, or tonic clonic convulsions are most typical (Newmark and Penry, 1979, Chapter III). Visually-induced seizures are most common amongst patients with primary generalized epilepsy, and a family history of epilepsy, or more specifically of photosensitive seizures is common.

1.1. Characteristics of the EEG in Photosensitive Epilepsy

Photosensitive epilepsy is usually diagnosed with the help of the electroencephalogram (EEG). The patient is asked to gaze at the centre of the diffusing surface of a gas discharge lamp which delivers trains of flashes at a variety of frequencies. In normal persons flashes at frequencies up to 10 or sometimes 20 Hz elicit EEG activity at the same frequency, often with supra- and subharmonic components ("photic following"). In some 5% of people with seizure disorders, particularly those with seizures that are visually induced, the intermittent light stimulation elicits an anomalous EEG reaction. This "photoconvulsive" response consists of regular or irregular single or multiple spikes interspersed with slow waves. The activity is typically of maximum amplitude in the fronto-central regions, and is fairly symmetrical. It generally has a frequency between 2.5 and 3 Hz and is not phase-locked to the flashes.

The photoconvulsive response is one of a variety of anomalous EEG reactions to intermittent light and unfortunately there exists considerable confusion in the literature concerning the specificity of these responses to epilepsy. This is due in part to inconsistencies in terminology and in part to doubt concerning the normality of various non-epileptic populations which have been studied (see Newmark and Penry, 1979, Chapter 5, for review). Unusual responses to intermittent light which have little or no association with epilepsy include:

(1) "Photomyoclonus", a rhythmic contraction of the muscles of the head and neck producing electromyographic spikes synchronous with the flashes and typically maximal in amplitude over the frontal regions. Photomyoclonus is morphologically distinct from the photoconvulsive response and its occurrence depends on the resting tonus of the muscles concerned. Under optimal conditions it is demonstrable in 50% of normal adults (Bickford *et al.*, 1952).
(2) Conspicuous photic following at supra- and subharmonics of the flash frequency.
(3) Bilaterally-synchronous delta activity (slow waves with a frequency less than 4 Hz), usually generalized, but sometimes confined to the occipital regions.
(4) "Occipital spikes", abnormal spikey components of the visual evoked response with a latency of approximately 85 msec, seen typically during stimulation at frequencies from 4 to 7 Hz (Jeavons and Harding, 1975).

Authors who adopt a broad definition of "photosensitivity" and include responses such as the above find a prevalence of up to 10% in normal adults, and of 15–33% in children (Brandt *et al.*, 1961; Dooze and Gerken, 1973). The photoconvulsive response, on the other hand, is strongly associated with epilepsy. About 90% of persons in whom the photoconvulsive response outlasts the train of flashes may be expected to suffer from some form of epileptic seizures, either spontaneously or during provocative visual stimulation (Reilly and Peters, 1973).* The majority of others are close relatives of people with epilepsy (Jeavons and Harding, 1975).

In so far as this paper reports our own work, it relates exclusively to subjects suffering from epilepsy in whom an optimally provocative stimulus elicited a photoconvulsive

* The extent to which a photoconvulsive response will outlast a train of flashes may depend on the duration of the train and the delay in terminating it once a response has occurred. The effect of such parameters has not been studied.

response. Nevertheless, in many of the studies we have deliberately selected stimulus parameters below the threshold required to give such a response, provoking only localized or transitory disturbances. Both these and the classical photoconvulsive response we have described as "paroxysmal" (i.e. transient) EEG activity, so as to beg no questions as to its clinical significance. We will use this epithet to refer to discharges with spike and slow-wave components that extend beyond occipital regions but that may or may not be generalized. Discharges of spikes confined to the occipital derivations (occipital spikes) have been deliberately excluded because their clinical significance is doubtful (Jeavons and Harding, 1975).

Photosensitivity may be increased by, or may appear after sleep-deprivation (Scollo-Lavizzari and Scollo-Lavizzari, 1974) and is attenuated during the slow-wave phase of sleep. We have observed that, during waking hours, some patients show consistent circadian fluctuations in sensitivity. In women there may also be fluctuations due to the menstrual cycle, but we know of no formal studies that have investigated such effects. Notwithstanding the contribution of the above variables, there are many stimulus parameters that are critical in determining the photoconvulsive response to intermittent light. These will now be reviewed, and readers who are familiar with the literature may wish to turn to Section 2.

1.2. STIMULUS PARAMETERS

A variety of visual stimuli are capable of inducing a photoconvulsive response in photosensitive persons, but diffuse intermittent light is the most commonly used.

1.2.1. *Intermittent light*

The stimulus parameters that affect a patient's response to intermittent light include the colour and mean intensity of the light source; its depth of modulation, frequency and spatial characteristics; the duration of the stimulus train and the interval between successive trains; the area and locus of the retina receiving stimulation; whether one eye or both eyes receive stimulation, and whether the stimulation is given with eyes open or through closed eyelids. Whilst some of these variables have received considerable study, others have attracted little attention. Their effects have been reviewed in detail elsewhere (Jeavons and Harding, 1975; Newmark and Penry, 1979), but the following is a brief summary of the information available.

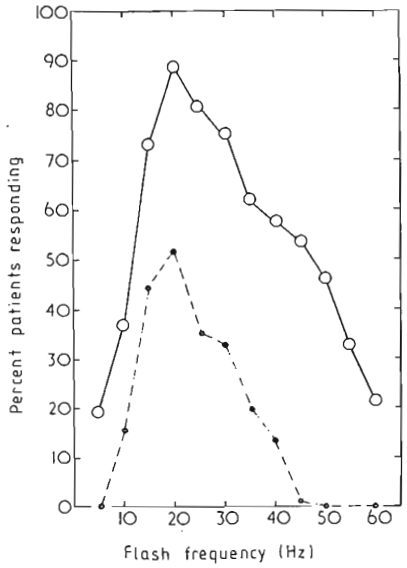

FIG. 1. Percentage of 52 photosensitive patients in whom a photoconvulsive response was obtained, expressed as a function of the frequency of intermittent light. The data are taken from Jeavons and Harding (1975; p. 70; Fig. 26). Open circles: responses obtained with open eyes; filled circles: responses obtained with closed eyelids.

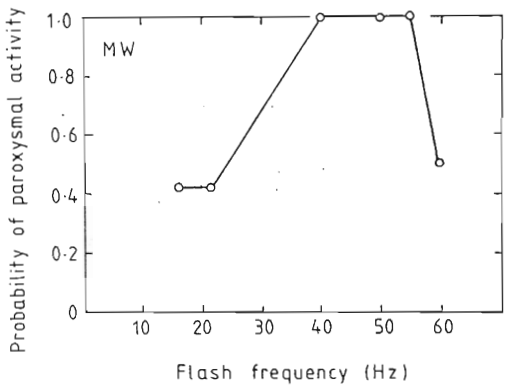

FIG. 2. Probability of paroxysmal EEG activity as a function of the frequency of diffuse intermittent light (1-sec trains of flashes from a Grass photostimulator). The lamp was covered by a diffuser and provided a circular field, diameter 23°, centrally fixated, with a mean luminance of 2×10^2 cd/m^2 (measured with a S.E.I. spot photometer at a frequency of 50 Hz). Data are for one patient MW.

The flicker frequency of the light source has a considerable effect on the probability with which a photoconvulsive response can be obtained. Frequencies in the range 15–20 Hz are widely recognized as being maximally epileptogenic for the majority of patients. Figure 1 shows the proportion of a sample of 52 patients in whom a photoconvulsive response was obtained, expressed as a function of frequency. The data are taken from the large series of patients reported by Jeavons and Harding (1975). Individual patients may show a maximal response at frequencies very different from those at which the majority of patients exhibit a photoconvulsive response. Figure 2 shows the response of a patient who received repeated 1-sec trains of flashes from a conventional photostimulator covered by a diffuser (Wilkins *et al.*, 1979b). The probability of obtaining a photoconvulsive response was estimated by repeated trials in random order (minimum, six). As can be seen, the probability shows a peak at frequencies around 40–50 Hz. It is not usual to present trains of intermittent light repeatedly, owing to the risk of a seizure. Usually the upper limit is obtained by progressively decreasing stimulus frequency trial by trial until a photoconvulsive response is observed. The lower limit is obtained in an analogous manner. Despite the relatively limited number of observations that this procedure involves, the frequency limits obtained can remain remarkably stable across time (Jeavons and Harding, 1975). Usually, patients are sensitive to the entire range of frequencies between the upper and lower limit, although in about 11% of cases no consistent limits are obtainable (Jeavons and Harding, 1975). Occasionally patients are sensitive to more than one discrete range (Forster, 1977; p. 29). The scattergrams in Fig. 3 show the correlation between upper and lower frequency limits in four independent series of patients. Each point represents a patient, and the distance between a point and the diagonal the range of frequencies to which the patient was sensitive. It will be noted that the shape of the distribution is such that with an untransformed frequency scale the variability in the upper limit from patient to patient is far greater than the variability in the lower limit. The variability in the upper limit is also greater than the lower if individual patient's limits are measured repeatedly (Jeavons and Harding, 1975, p. 67). It can be seen from Fig. 3 that the range of frequencies to which a patient is sensitive (the distance from a point to the diagonal) varies with the upper limit more than the lower. It may therefore be inadvisable to use range as a general measure of sensitivity without specifying the limits from which it was derived (cf. Jeavons and Harding, 1975, p. 69).

Although a large number of studies have investigated the effects of the colour of the intermittent light, the results have been inconsistent. It appears that, provided luminance is equated, the colour of the light has little effect on patients' sensitivity, with the possible exception that light at the blue end of the spectrum may be less epileptogenic (see Newmark and Penry, 1979, p. 31, for review).

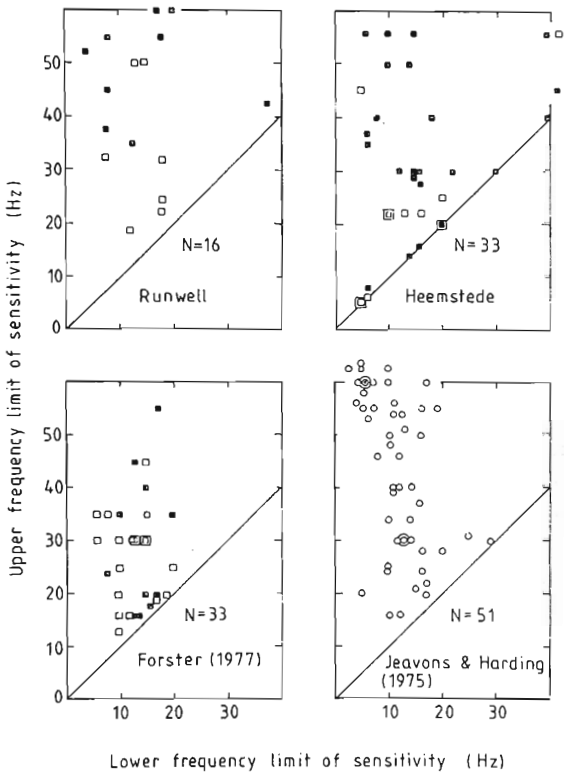

FIG. 3. Upper and lower frequency limits of sensitivity to intermittent light with open eyes in four independent series of photosensitive patients. Patients who were sensitive to static patterns are represented by solid squares, and those who were not by open squares. Open circles represent patients for whom no such data are available. In the Runwell and Heemstede series the intermittent light was diffused (circular field, 20° in diameter, mean luminance about 2×10^3 cd/m^2) and the patterns were stripes (vertical or horizontal gratings with square-wave luminance profile, contrast 0.7, mean luminance at least 300 cd/m^2, spatial frequency 2 cycles/degree, circular in outline with a radius at least 12°). No details are available for the series by Forster (1977).

The spatial characteristics of the light source appear to influence the likelihood with which paroxysmal activity is induced. Jeavons *et al.* (1972) reported that the safety grid on a certain make of stimulator provided a pattern that enhanced the epileptogenic properties of the intermittent light. The effect of superimposing patterns of this kind is small, and may not be sufficient to offset the reduction in luminance that occurs when a transparency of a pattern is placed over the surface of the light source, given that studies that have failed to control luminance have failed to show an enhancement due to pattern (e.g. Engel, 1974; Kirstein and Nilsson, 1977; see Wilkins *et al.*, 1979b).

The locus of stimulation on the retina has a profound effect on sensitivity to intermittent light. If the fixation on the light source is eccentric, so that the periphery receives maximal stimulation, the photoconvulsive response is attenuated or eliminated (Jeavons and Harding, 1975, p. 75).

The likelihood of obtaining a photoconvulsive response is known to depend on whether the stimulation is given to open eyes or through closed eyelids. When the eyes are closed the intensity of the light is reduced and its wavelength altered; it is diffused so that all the retina receives a similar intensity of flicker; visual stimulation from the surroundings is eliminated; and lastly, sensory input from the periocular region is altered. The EEG shows a shift in favour of lower frequencies, but also a transient change (alpha squeak) immediately after eye closure. The sensitivity to stimulation with eyes open or closed must depend on the way any effects of these variables interact. The interaction may be a complex one and be affected by the intensity of the source of intermittent light. Although the majority of patients are generally more sensitive to intermittent light with the eyes open (Panayiotopoulos, 1974), there are exceptions, and a few patients are

apparently sensitive only with the eyes closed. In one such patient we obtained a photoconvulsive response if the stimulation was given with the eyes open but covered by a white diffuser. In her case at least, differences in periocular sensory feedback were not an important factor.

It has been widely reported that sensitivity to intermittent light is maximal when both eyes are stimulated, and is greatly attenuated, if not eliminated, under conditions of monocular stimulation. This appears to be the case for over 90% of photosensitive patients (Jeavons and Harding, 1975, p. 73). Possible reasons for this difference will be discussed later.

It would not be surprising if the mean luminance, duty cycle (or on–off ratio), and modulation depth of intermittent light were to affect its epileptogenic properties. Owing to the widespread use of high power gas discharge lamps as a source of intermittent light, however, there have been no studies (as far as we know) that have investigated, the effects of these variables independently of one another. A few studies have investigated the effects of the intensity of the light source and the level of background illumination, and both these variables affect the mean luminance and modulation depth. The likelihood of a photoconvulsive response is known to increase with the intensity of the light source for suprathreshold intensities, but the details of the relationship for patients as a whole are uncertain. As has been pointed out elsewhere (Jeavons and Harding, 1979, p. 14) comparison of different studies is made difficult by the variety of units of intensity used. Although it is widely held that high levels of ambient light reduce the effects of intermittent light, with the high intensity light sources conventionally used the effects of normal ambient lighting may be negligible (Van Egmond *et al.*, 1980).

The duration of stimulation varies enormously from study to study, the values that have been used ranging from 2 sec to 20 min. Although the duration may well affect the likelihood of observing a photoconvulsive response during stimulation, if only because near threshold the response is probabilistic, we know of no study that has systematically investigated the effects of this variable.

It is quite likely that the interval between successive presentations of intermittent light has an effect on the likelihood with which the convulsive response is observed, given that either refractoriness or facilitation may be apparent after prolonged or repeated discharges.

1.2.2. *Pattern-sensitivity*

So much for the parameters that affect a patient's sensitivity to intermittent light. Light does not have to be intermittent to be epileptogenic, however. In some photosensitive persons the viewing of static continuously-illuminated patterns will induce paroxysmal discharges in the EEG. Sensitivity to patterns of this kind used to be regarded as a rarity. Bickford and Klass (1969), e.g., found an incidence of only 0.25% in a series of 40,000 epileptic patients. Naquet *et al.* (1976), however, estimated that sensitivity to patterns could be demonstrated in some 17% of photosensitive patients. More recent studies (Stefansson *et al.*, 1977; Wilkins *et al.*, 1979a) suggest that the incidence of pattern sensitivity may be considerably higher. These studies indicate that paroxysmal epileptiform EEG activity can be elicited in some 30% of patients who show a photoconvulsive response to intermittent light and that the incidence rises to 60–70% if the pattern is oscillated in a direction orthogonal to the orientation of its lines. The epileptogenic properties of a pattern are critically determined by the stimulus characteristics (Chatrian *et al.*, 1970; Wilkins *et al.*, 1975, 1979a), and the lower incidence reported in early studies was probably due to a failure to employ optimally-epileptogenic patterns.

An optimally epileptogenic pattern consists of black and white stripes of equal width and spacing—i.e. with a square-wave luminance profile (e.g. Fig. 4). The orientation of the stripes is not usually critical, but their spatial frequency is. The spatial frequency of a pattern refers to the number of cycles of the pattern in one degree of visual angle,* and in

* No reference to the harmonic content is implied, at least in this context.

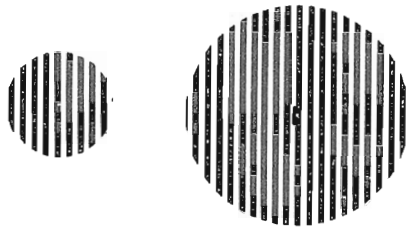

FIG. 4. Examples of gratings with square-wave luminance profile, constant spatial frequency, circular in outline and of different radii.

order to induce paroxysmal activity, patterns usually have to have a spatial frequency between 1 and 4 cycles/degree. In other words, each stripe (black or white) must subtend between 7.5 and 30 minutes of arc at the eye. Figure 5 shows how the probability of paroxysmal EEG activity varies with spatial frequency. The probability was estimated by repeatedly presenting a set of patterns in random order and observing the proportion of trials on which paroxysmal activity was induced. The presentations lasted 10 sec unless paroxysmal activity occurred, in which case they were curtailed.

The luminance of a pattern affects the probability of its inducing a paroxysmal response, but in order to alter the probability appreciably changes in excess of one log unit (a factor of 10) are required. Figure 6 demonstrates this point. The procedure differed from that usually employed in that trials were not randomized but presented as a block at each luminance level so that the patient had a chance to adapt. Fluctuations in sensitivity with time may therefore have influenced the variability of the curves more than is usually the case. The data are nevertheless consistent enough to indicate that pattern sensitivity can be present at levels of luminance at which both rods and cones contribute to vision. The data for patients JH and MVH indicate that smaller patterns require higher levels of illumination to elicit paroxysmal activity with the same probability. The curves for patient AL demonstrate that sensitivity under conditions of monocular presentation is considerably less than that under normal binocular viewing conditions. This effect was earlier demonstrated by Chatrian *et al.* (1970), who asked a

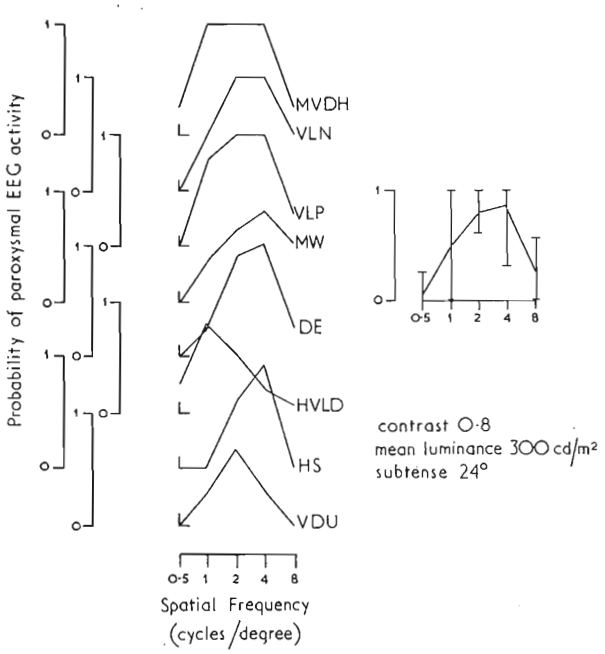

FIG. 5. Probability of paroxysmal activity as a function of the spatial frequency of a pattern of stripes (a grating with square-wave luminance profile, circular in outline, radius 12°, contrast 0.7, mean luminance 3×10^2 cd/m^2, white light). Bars indicate range.

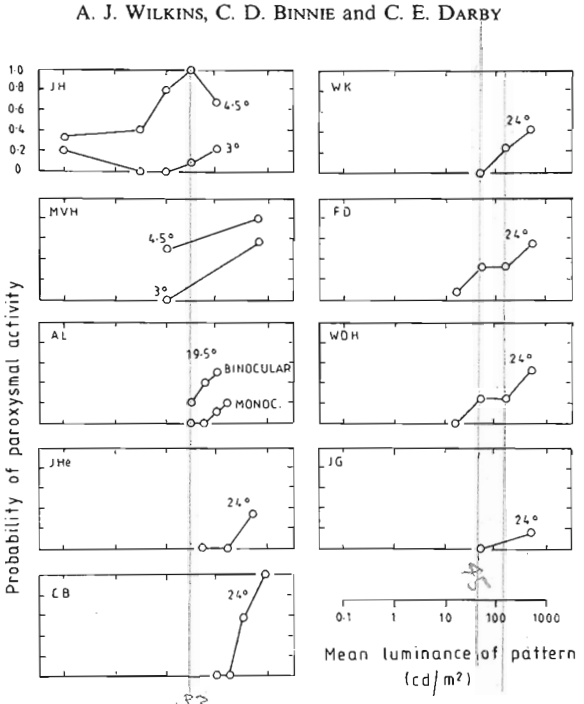

FIG. 6. Probability of paroxysmal activity as a function of the mean luminance of a striped pattern (a grating with square-wave luminance profile, contrast 0.7, circular in outline with radius as indicated). The presentations were binocular except in the case of patient AL in whom the left eye was occluded on some of the trials. The natural pupil was used throughout.

pattern-sensitive patient to view a pattern continuously whilst its luminance was progressively increased. They measured the proportion of the total observation time during which paroxysmal activity occcurred, and their data are reproduced in Fig. 7. It can be seen that under monocular viewing conditions the luminance of a pattern must be increased by about one log unit in order to produce an incidence of paroxysmal activity similar to that occurring under binocular viewing conditions. The data of Chatrian *et al.* have been replotted in Fig. 8 so as to obtain a curve relating the equivalent epileptogenic properties of monocular and binocular patterns at different levels of mean luminance. It can be seen that although monocular stimuli must have a luminance roughly one log unit above that for binocular stimuli in order to induce an equivalent incidence of paroxysmal

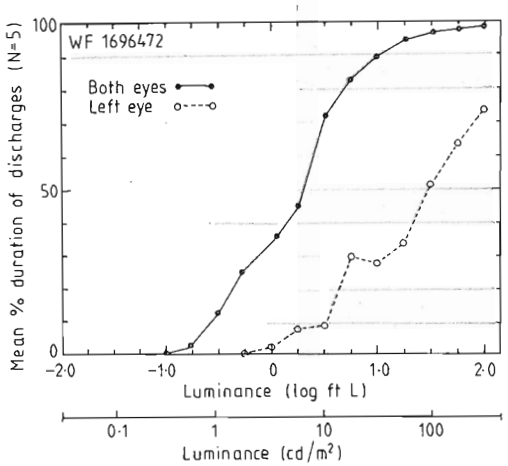

FIG. 7. Percentage duration of paroxysmal activity during uninterrupted pattern viewing in patient WF. The data are from Chatrian *et al.* (1970), and were obtained by progressively increasing pattern luminance throughout the range shown, on five separate occasions. The patient was initially dark adapted and the pupil dilated with neo-synephrine.

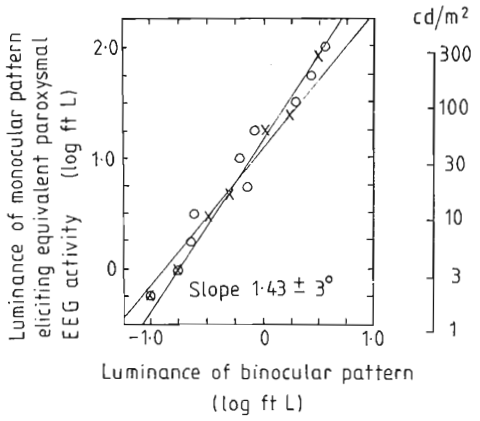

FIG. 8. Data from Fig. 7 replotted so as to show the relationship between binocular and monocular stimulation necessary to induce equivalent amounts of paroxysmal activity. Circles and crosses indicate calculations based on linear interpolation between points on the binocular and monocular curves respectively.

activity, this is only an approximation. There is some suggestion (and given the variability in the original curves, it is only a suggestion) that the higher the level of luminance the greater the difference between monocular and binocular conditions. The linear regression of y on x and x on y are shown in the figure. They lie almost symmetrically either side of a line with slope equal to the square root of two. The significance of the value of the slope is uncertain, and it is an open question as to whether a similar slope would be obtained were the experiment to be replicated.

The spatial frequency and luminance of a grating are but two of a set of parameters that affect its epileptogenic properties. Discussion of the other factors will be postponed because of their relevance to inferences about the trigger mechanism.

1.2.3. *Intermittent light vs pattern*

The relationship between a patient's sensitivity to intermittent light and to static pattern is complex. Whilst it is true that most patients who are sensitive to pattern are sensitive also to intermittent light, this is by no means always so. Several patients with pattern-sensitive epilepsy have been reported who were not sensitive to intermittent light (e.g. four of the 14 reported by Forster (1977)). In general, the detailed characteristics of sensitivity to intermittent light are not strongly predictive of pattern sensitivity. In three series of photosensitive patients (summarized in Fig. 3), some of whom were sensitive also to pattern, there was, overall, a tendency for pattern sensitive patients to have higher upper limits of sensitivity to diffuse intermittent light (with open eyes) than patients who were not pattern sensitive (Chi-square = 7.59, $p < 0.006$). No such difference was evident as regards the lower limits of sensitivity to intermittent light. In the Heemstede series (Fig. 3b), patients who were pattern-sensitive were more likely than those who were not to exhibit generalized polyspike and wave in response to intermittent light. They were frequently diagnosed as suffering from primary generalized epilepsy.

The above characteristics of sensitivity to intermittent light and to pattern tell us relatively little about the physiological mechanisms responsible. For the most part it is difficult to tie together the effects described with any recent knowledge of the physiology of the visual system. The one exception would appear to be the finding of Jeavons and Harding (1975, p. 76), that peripheral intermittent light is less epileptogenic than central. Since peripheral flicker is more visible than central this finding is one of the few examples of a dissociation between factors that affect the visibility and factors that affect the convulsive properties of visual stimuli.

2. Photosensitivity as a Model of Epilepsy

An understanding of the mechanisms of photosensitive epilepsy is important because it enables photosensitive seizures to be prevented, and also because it provides a model of epilepsy. Some of the advantages of such a model will now briefly be considered.

2.1. Advantages of Photosensitivity as a Model of Epilepsy

The first advantage of photosensitivity as a model is that more is known about the physiology of the visual system than any other part of the central nervous system. This information would be of little use if the visual system of photosensitive patients were obviously abnormal. Fortunately, although it is evidently responsible for intermittent neural dysfunction, the visual system appears to function normally at other times. We have examined visual function in over 50 patients with pattern-sensitive epilepsy and with few exceptions they had 6/6 near acuity, as measured by the reduced Snellen chart, normal colour vision (Ishihara plates) and normal stereopsis (Titmus test). Without exception their visual fields to confrontation were full, and their ocular movements apparently normal. Furthermore, Soso *et al.* (1980) have demonstrated a normal perception of gratings at threshold contrast in one patient with pattern sensitivity. Given these data it is reasonable to assume that the visual system is functioning normally up to the point at which paroxysmal disturbance takes place. The only caveat is that the visual evoked potential (VEP) of photosensitive patients shows certain interesting abnormalities (e.g. Jeavons and Harding, 1975, p. 91). The implications of the abnormalities in the VEP will be considered in a later section. For the present it will be sufficient to note that the abnormalities are not confined to the visual system: the somatosensory evoked potentials of photosensitive patients are also abnormal (Broughton *et al.*, 1969).

Another advantage of photosensitivity as a model for epilepsy is that the epilepsy is naturally occurring. The majority of models of epilepsy involve inflicting unusual lesions or administering toxins with the inevitable difficulty of relating the results obtained to epilepsy as it naturally occurs.

A further advantage of photosensitivity as a model is that the nervous system involved is that of man. With this model it is possible to study the initiation of epileptiform discharges in humans with a minimum of risk to the patient. We have never elicited a major attack with patterns in more than 200 patients studied so far, and the incidence of minor attacks is very small owing to the avoidance of stimuli that greatly exceed the threshold at which paroxysmal activity is induced. Although some of the induced discharges may have been associated with transient cognitive impairment, the degree of such impairment is known to depend on the duration of the discharge, the degree of generalization and the voltage (e.g. Hutt, 1979). The paroxysmal activity evoked by pattern in our studies was nearly always less than 3 sec in duration, and was often not generalized. The patient was usually unaware of its occurrence and at worst experienced a sensation described as a shock.

As it will become apparent, the utility of this model of epilepsy is that it has demonstrated how the probability of paroxysmal activity is determined by the degree of neural excitation that a stimulus induces.

Interpretation of the results of the studies that follow requires familarity with the basics of visual physiology and the next section is provided to assist readers who are not familiar with the subject. Those who are may wish to omit the section.

2.2. Outline of the Physiology of the Visual System

Fibres from the retina reach the cortex via the lateral geniculate nucleus of the thalamus (LGN). Although the LGN receives fibres from both eyes, they arrive at different alternate layers between which little or no interaction takes place. Virtually all of the cells are therefore monocular, responding to stimulation of one eye only. The majority of cells are colour-coded and respond differently to light of different wavelengths (Gouras,

1972). The receptive fields have a circular centre-surround organization similar to that of retinal ganglion cells.

Most of the cells in the striate cortex (otherwise known as V1 or area 17) have linear receptive fields and respond best to lines rather than spots of light. Usually the cells are orientation-selective and respond mainly when the line is within 15° of a preferred orientation. They fire maximally when the line is moved, although the optimal speed of movement varies considerably from cell to cell (Sanseverino *et al.*, 1979). Many respond preferentially to one direction of movement more than another (Hubel and Wiesel, 1979). The majority of cells respond to stimulation of either eye, although the ocular dominance varies systematically from cell to cell. Some cells fire only when both eyes are stimulated.

The striate cortex relays information to several discrete areas within the prestriate cortex (V2, V3, V3A, and V4), each with its own separate topographic organization and responsible for the processing of different aspects of the retinal image. The majority of cells in V2, V3 and V3A are orientation-selective, but are not selective for stimulus colour or direction of movement. The area V4, on the other hand, contains a higher incidence of colour-selective cells, and a lower incidence of cells sensitive to orientation (Zeki, 1978).

The superior colliculus is part of the mesencephalon and receives fibres directly from the retina and indirectly via the cortex. The majority of collicular cells are pandirectional and respond to spots of light transversing their receptive fields and to the onset and offset of stationary spots. The receptive fields are much larger than those of retinal ganglion cells and cells in the striate cortex. Collicular cells are generally insensitive to the shape and orientation of stimuli in their receptive fields (Goldberg and Wurtz, 1972).

The fibres connecting the various nuclei can be divided into two major systems, the X-system, sensitive to aspects of the retinal image that are sustained through time, and the Y-system, sensitive to transient aspects of the image. There is some suggestion that these systems remain separate at a cortical level, and that the colliculus receives only Y-fibres. Unfortunately the picture is generally rather confused, and will not therefore be described in detail.

2.3. EXPERIMENTAL METHODS IN THE INVESTIGATION OF HUMAN PHOTOSENSITIVITY

There are two complementary approaches that have been used to investigate the seizure trigger in photosensitive epilepsy. One approach has investigated in detail the characteristics of the stimulus that induces paroxysmal EEG activity whereas the other has examined the electrographic detail of responses that occur.

The advantage of the former approach is that it enables the physiological characteristics of the trigger to be inferred. A good deal is known about the way in which the visual system processes pattern, and this information can be used as the basis for this inferential approach. A disadvantage of the approach is that because so little is known about the way in which the visual system processes the temporal properties of intermittent diffuse light, inferences are confined to the nature of the trigger in pattern-sensitive epilepsy. Of course, the trigger may be similar in all forms of visual sensitivity, but, equally, it may not.

The advantage of the second approach is that once the discharge is of sufficient magnitude to be observable at the scalp, its distribution and spread can be deduced. The disadvantage of this approach is that the activity of cells responsible for initiating the observed discharge cannot be studied.

In the introduction we considered the characteristics of epileptogenic visual stimuli and of the EEG responses they induce. For the most part, these characteristics provided few clues as to the physiological nature of the trigger mechanism.

3. Where Is the Paroxysmal Activity Triggered?

In this section we review further studies of the characteristics of epileptogenic visual

stimuli and of the epileptiform EEG response. We will concentrate specifically on those studies that provide data that may be used as the basis of inferences about the trigger mechanism. The first of these consider the role of movement of the retinal image.

3.1. MOVEMENT OF THE RETINAL IMAGE

Retinal images are continually in motion as a result of the movements of the eye, and these movements appear to be essential for continuous form perception (Riggs *et al.*, 1953). It is therefore reasonable to suppose that the image of a repetitive pattern creates an intermittent stimulation of retinal cells similar to that produced by flashing light. If this is the case the means by which intermittent light and pattern produce a convulsive response may be similar. It is therefore instructive that after-images of patterns fail to elicit paroxysmal activity. After-images are "fixed" on the retina and move with the eye. In seven patients with pattern sensitivity we have created an after-image of a pattern of stripes (with a square-wave profile of luminance) having characteristics appropriate for the induction of paroxysmal activity (spatial frequency 2 cycles/degree, 48° subtense), using a high-power photographic flash gun (120 J) behind a transparency. Despite the darkened surroundings accommodation was ensured by asking the patient to fixate a central luminous fixation point. In none of the patients, even those sensitive to very small patterns and those sensitive at low luminance levels, was paroxysmal activity induced by the afterimage. And this despite the fact that the patients reported seeing it clearly. It can be argued that no paroxysmal activity occurred either because the retina received insufficient stimulation or because movement of the retinal image is essential for the induction of paroxysmal activity.

If movement of the eyes produces an intermittent stimulation of retinal ganglion cells responsible for the induction of paroxysmal activity, patterns that have a large number of brightness contours should induce paroxysmal activity more readily than those with few. Actually, the reverse appears to be the case. Checkerboards that contain a large number of brightness contours are less epileptogenic than stripes of equivalent width (Wilkins *et al.*, 1979a). Furthermore, if checks are progressively elongated in one direction (so as to produce the series of patterns illustrated in Fig. 9), it can be demonstrated that the probability of paroxysmal activity increases with the length of the line contour. Figure 9 shows the results obtained with one pattern-sensitive patient. The probability of paroxysmal activity is a linear function of the logarithm of the ratio of stripe length to width; in other words, as the number of contours decreases, so the probability of paroxysmal

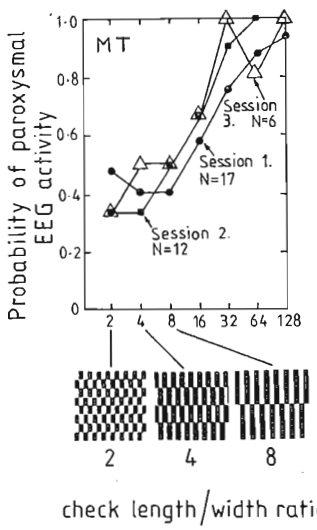

FIG. 9. Probability of paroxysmal activity as a function of the segment length/width ratio in patterns of checks in which the checks have been elongated by varying amounts. Examples of some of the patterns are shown beneath the abscissa. Data are for one patient, MT (Wilkins *et al.*, 1975, 1979).

activity increases. This particular result, and the general finding that checks are less epileptogenic than stripes, together suggest that patients are not sensitive to patterns simply because the brightness contours produce an intermittent stimulation of retinal cells. Evidently there may be spatial as well as temporal aspects of stimulation that are critical.

As mentioned previously, vibrating a pattern at certain frequencies greatly increases its epileptogenic properties. As a rule, nearly all patients who are sensitive to stationary patterns are sensitive also to patterns vibrating in the appropriate manner (Stefansson *et al.*, 1977). Some patients, possibly those who are generally less photosensitive, are mainly sensitive to vibrating rather than stationary patterns. A group of such patients took part in the following study of the effects of pattern movement (Binnie *et al.*, in press (a)).

Patterns were back-projected onto a screen via a surface-silvered mirror mounted on a moving-coil galvanometer. The mirror was vibrated with a triangular waveform at frequencies of 5, 10, 15, 20, 30 and 40 Hz. Five different patterns were used consisting of vertical black-and-white stripes of equal width and spacing (square-wave luminance profile) with the following spatial frequencies: 0.5, 1, 2, 4 and 8 cycles/degree of visual angle. The patterns were vibrated horizontally (across the stripes) with a displacement equal to the width of one stripe or two stripes (i.e. one-half or one complete spatial cycle of the pattern). It was not possible to test all the 60 combinations of the three experimental conditions (spatial frequency, temporal frequency of vibration, and amplitude of movement) in every patient. Ten subjects were tested and Fig. 10 presents the mean results. It is evident that there is little or no effect of the amplitude of vibration. Patterns with a

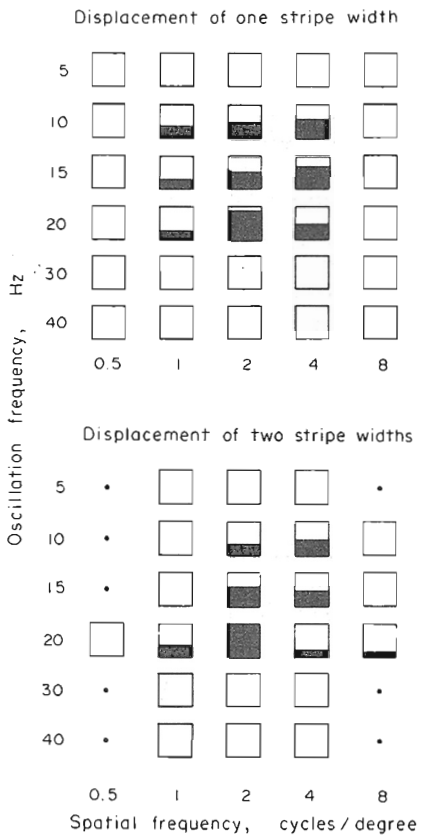

FIG. 10. Probability of paroxysmal activity as a function of the spatial frequency, temporal frequency and amplitude of movement of a vibrating pattern of stripes. The height of the shaded area within each box is proportional to the probability of paroxysmal activity. The pattern had a square-wave luminance profile, and was 15° in radius. The amplitude of movement was equal to the width of one stripe or two stripes (half a spatial cycle or one complete spatial cycle of the pattern) and the results are tabulated separately as shown. The movement was in a direction orthogonal to the stripes and the profile of the displacement against time was triangular.

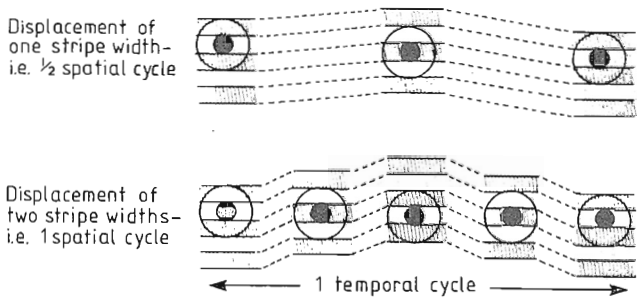

FIG. 11. Illustration of the intermittent stimulation of retinal ganglion cells as a function of the temporal frequency and amplitude of movement of a grating vibrating in a direction orthogonal to its stripes.

spatial frequency of 2–4 cycles/degree were optimal for inducing paroxysmal activity regardless of the frequency of vibration. Vibration at 10–20 Hz was optimal regardless of the spatial frequency. There is no evidence of an interaction between the effects of spatial and temporal frequency: they appear to influence the probability of paroxysmal activity quite independently of one another.

These data cannot be accounted for in terms of an intermittent stimulation of retinal ganglion cells. Figure 11 demonstrates how the effects of spatial and temporal frequency should interact if the intermittent stimulation of these cells were an important consideration. For the cell with a receptive field the size of that shown in the diagram, increasing the amplitude of vibration from one-half to one complete spatial cycle of the pattern (i.e. from one stripe width to two) should double the frequency of intermittent stimulation. The fact that the temporal and spatial aspects of stimulation had independent effects on the probability of paroxysmal activity indicates that the spatial frequency of the pattern must have been having an effect at a point in the visual system where the spatial characteristics of retinal information are analysed independently of retinal position.

The spatial characteristics of retinal input are analysed independently of retinal position at the level of complex cells in the striate cortex. The image of a bar will stimulate such a cell over a range of retinal positions considerably greater than the width of the bar itself. This characteristic is one that distinguishes complex cells from cells at lower levels of the visual system. A trigger mechanism involving complex cells is therefore consistent with the independence of spatial and temporal factors reported in the previous section. This does not, of course, rule out many other possible trigger mechanisms; it does, however, provide one line of evidence in favour of a cortical trigger. Further evidence favouring a cortical locus is provided by the effect of the length/width ratio of stripes illustrated in Fig. 9. The majority of cortical cells have linear receptive fields and a striped pattern presumably stimulates these cells more effectively.

The majority of cortical cells are binocular, and a substantial proportion show summation (the response to corresponding input to the two eyes is greater than that to one eye). If the locus of the seizure trigger is cortical, the response when both eyes see the same thing may be greater than when they do not.

3.2. STIMULI THAT INDUCE BINOCULAR RIVALRY

If patterns are presented in a stereoscope so that one eye sees horizontal stripes and the other eye vertical, the probability of paroxysmal activity is less than if both eyes see the same pattern (Wilkins *et al.*, 1979a). This reduction of the epileptogenic properties of visual stimuli under conditions of binocular rivalry may be attributed either to binocular mechanisms or orientation mechanisms. Either way, the effect can be readily accommodated by the hypothesis that complex cells are involved in the seizure trigger. Such cells are generally binocular and are orientationally-selective. There are however, many other cortical mechanisms that could accommodate the finding. More interesting are the hypotheses that are excluded by the result. Amongst these is the hypothesis advanced by

Bickford *et al.* (1953) in the days when generalized spike-and-wave discharges were attributed to a centrencephalic mechanism (see Gloor, 1978, for review). Bickford and co-workers, in their discussion of the hypothetical pathways of the convulsive response to light, proposed several alternatives, one of which was that of a subcortical thalamic pathway from the LGN to a diffuse thalamic system. According to this conception, paroxysmal activity in response to visual stimulation is triggered by activity at a thalamic level and the cortical involvement is the secondary result of diffuse thalamic input and is not confined to the primary visual areas of the cortex. Cells in the LGN are monocular and not orientationally selective. The above effects of the differential stimulation of the two eyes cannot therefore be accommodated in terms of the model of Bickford and co-workers, or, for that matter, by any other model that postulates a trigger mechanism confined to the LGN.

The effects described in the above study could have resulted from the fact that the visual system received stimulation in more than one orientation, or because the two eyes received different input. Two further studies, now to be described, attempt to separate the effects of orientation from those of differential input to the two eyes. They demonstrate that the trigger mechanism may involve not only orientationally-selective cells, but also binocular mechanisms.

3.3. A Comparison of Plaid Patterns and Stripes

Imagine that two projectors are focussed on a screen so that their images overlap, one projector providing the image of a pattern of vertical stripes, and the other of horizontal. The composite plaid pattern so formed should stimulate cells with linear receptive fields oriented both vertically and horizontally (see Fig. 12 for schematic representation). If energy is summated in the receptive field of an orientationally-selective cell, when the image of the horizontal grating is defocussed so as provide a diffuse uniform field, the stimulation of cells with vertically-oriented receptive fields should be unaffected.

When one projector is defocussed, the effect is similar to that of adding a diffuse uniform illumination, with the same mean luminance as the original pattern, to the image from the other projector. The result is a low-contrast pattern of stripes. Patterns of both kinds, plaid and stripes, were compared in patients who were sensitive to both vertical and horizontal stripes. Despite the greater number and contrast of brightness contours in the plaid, patients were more sensitive to the stripes (Wilkins *et al.*, 1979a; Wilkins, unpublished replication). This finding may be adduced as evidence that cells with orientation selectivity were involved in the seizure trigger as follows. Imagine cells with vertically-oriented receptive fields. They will be unable to distinguish between a vertical grating with appropriately low contrast, and a plaid pattern. The reduced sensitivity to the plaid pattern must therefore have been due to the cells tuned to horizontal orienta-

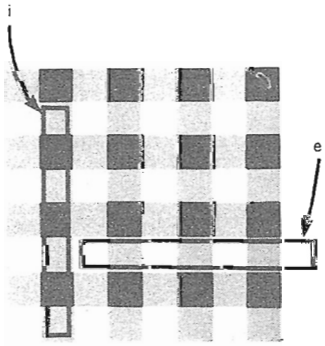

FIG. 12. Schematic illustration of a plaid pattern formed by superimposing the images of two striped patterns. The rectangles represent the receptive fields of cells with inhibitory or excitatory centres, as shown.

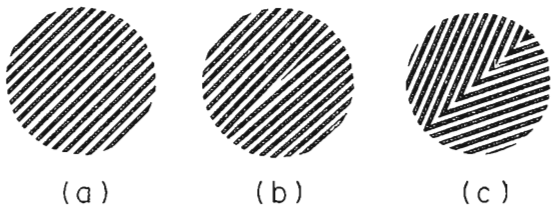

FIG. 13. Schematic representation of patterns composed of square-wave gratings with a spatial frequency of 2 cycles/degree, contrast 0.7, mean luminance 3×10^2 cd/m^2. (a) Unsectored grating; (b) component gratings at an angle of 10 degrees to one another; (c) component gratings at 45°. Pattern orientation varied from trial to trial. Pattern radius was chosen to suit individual patient's sensitivity.

tions. An analogous argument applies for orthogonal orientations. In general, it appears necessary to postulate a trigger mechanism involving orientationally-tuned cells to accommodate the higher convulsive threshold for plaid patterns. The mechanisms of the interaction between orientation-tuned cells sufficient to explain the reduced sensitivity to plaid patterns are obscure. Nevertheless the evidence that the trigger mechanism involves orientationally-selective cells remains, howsoever the apparent inhibitory interaction between them is accommodated.

3.4. VARYING STRIPE ORIENTATION ACROSS THE VISUAL FIELD

It is worth noting at this point that no interaction between orientationally-tuned cells is evident if patterns are composed of stripes in different orientations occupying different areas of the visual field. In five patients tested there was no evidence of any difference in sensitivity to the three patterns represented schematically in Fig. 13. Whereas pattern 13c was designed to stimulate two groups of cells each tuned to different orientations, patterns 13a and 13b were designed to stimulate mainly one group. (The stripes in pattern 13b differed by 10° in orientation. The bandwidth for orientation tuning varies considerably from cell to cell, but is generally greater than 10°.)

The fact that patients are usually sensitive to stripes in a variety of different orientations does not detract from the notion that cells with orientation selectivity are involved in the seizure trigger; a large number of columns of cells may be involved, each tuned to a different orientation. There are a few patients who are sensitive only to a narrow range of stripe orientations, but these patients generally turn out to have an astigmatism such that the orientations to which the patients are insensitive are those that are poorly focussed on the retina. We have, however, seen one case of an 11-yr old boy, who was consistently sensitive only to a limited range of orientations, as shown in Fig. 14. We were unable to find any evidence of astigmatism either by retinoscopy or subjective

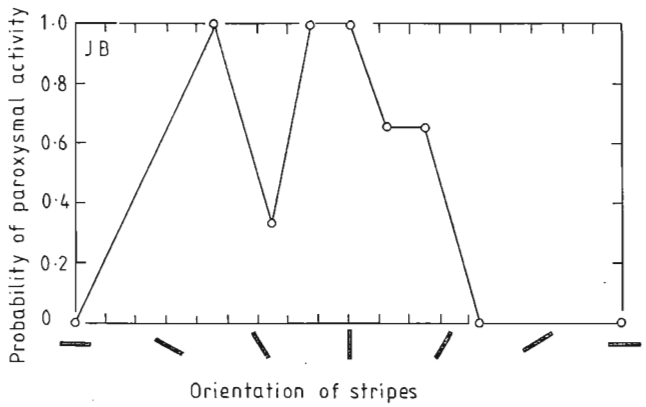

FIG. 14. Probability of paroxysmal activity as a function of the orientation of a striped pattern (square-wave grating, spatial frequency 2 cycles/degree, circular in outline, radius 20°, contrast 0.7, mean luminance 3×10^2 cd/m^2). Data are for one patient, JB.

testing. This case provides further evidence that orientationally-selective cells may be involved in the seizure trigger. If orientationally-selective cells are involved, the seizure trigger cannot be confined to the LGN, where there are no orientationally-selective cells. A similar story holds for a trigger in the superior colliculus. None of the sample of collicular cells studied by Goldberg and Wurtz (1972) was sensitive to the shape or orientation of stimuli.

3.5. ALTERNATE STIMULATION OF THE TWO EYES

Unlike the monocular cells in the LGN, the majority of collicular cells respond to the stimulation of either eye. It may therefore be important to separate the binocular components of the seizure trigger from those of the orientation selectivity of the component cells. We have attempted to do this in one patient. She was sensitive to patterns and also to diffuse intermittent light, and it was her sensitivity to diffuse light that was studied in an attempt to separate the effects of binocular and orientational mechanisms. A diffuse field provided a train of flashes to one eye, or alternately to one eye and then the other. The frequency of flicker (measured at one eye) at which the patient was maximally sensitive differed in the two conditions (monocular and alternate eye), suggesting that some binocular aspect of the trigger mechanism integrated the input from the two eyes (Wilkins *et al.*, 1979a). This binocular mechanism may help to explain why the majority of photosensitive patients (239 of the 244 studied by Jeavons and Harding, 1975) are more sensitive to binocular than monocular stimulation.

4. How is Paroxysmal Activity Triggered?

In the previous sections we have described evidence suggesting that paroxysmal activity is triggered by the action of cells that have linear receptive fields, that are orientationally-selective and possibly binocular, and that analyse spatial features independently of precise retinal position. It is therefore reasonable to conclude that the cortex is the site of the trigger mechanism because the majority of cells in the primary visual cortex possess these properties.

The question remains as to how the action of these cells gives rise to the paroxysmal activity. In the first instance it would be interesting to know how the number of cells stimulated by a pattern affects the probability with which paroxysmal activity is induced. In the studies now to be described, the number of cells stimulated was varied by using patterns of different size. In the first of three studies pattern size was varied by changing the radius of a pattern of stripes circular in outline. In the second study, size was altered by changing the pattern area uniformly for all retinal eccentricities, and in the third study, pattern area was increased separately for both peripheral and central retina.

4.1. VARYING PATTERN RADIUS

Figure 15 shows the way in which the probability of paroxysmal activity increases with the radius of a centrally-fixated pattern, circular in outline, and composed of stripes with a constant and uniform spatial frequency (see Fig. 4). Each curve is for a different patient. Each patient appears to have a different threshold size below which no paroxysmal activity appears and above which the probability of paroxysmal activity increases with pattern radius over a limited range. These data are consistent with the notion that paroxysmal activity occurs when a critical number of cells is excited, the threshold varying from patient to patient. As can be seen in Fig. 15, the radius of a pattern has to double to increase the probability of paroxysmal activity from near zero to near one.

4.2. VARYING SECTOR SIZE

Both in the retina and the striate cortex the number of cells devoted to the analysis of the centre of the visual field is greater than the number devoted to the periphery. The

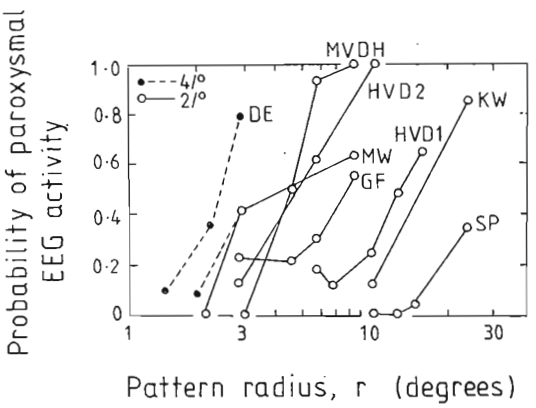

FIG. 15. Probability of paroxysmal activity as a function of the radius of a pattern of stripes (square-wave grating, circular in outline, contrast 0.7, mean luminance 3×10^2 cd/m^2, spatial frequency 2 or 4 cycles/degree, as shown). The data are for seven patients one of whom (HVD) was tested twice.

number of cells stimulated by a pattern cannot therefore be expected to increase uniformly with pattern radius. In order to manipulate the size of pattern in such a way as to reduce the confounding effects of eccentricity, the patterns shown in Fig. 16 were used. The patterns were composed of diagonally-opposed sectors shaped like slices of a cake, the "cake" consisting of concentric rings with a spatial frequency of 2 cycles/degree. The patterns comprised two or four sectors, and the pattern area was manipulated by varying the sector angle. Changing the pattern area in this manner had the advantage that both large and small patterns could be increased in size, in such a way that it was reasonable to assume that there was an equivalent increase in the number of neurons excited for both types of pattern. Of course, as the sector angle increased so did the length of the curvilinear pattern segments. It is unlikely, however, that the increase in length of the segments would, of itself, have resulted in a more effective stimulation of line detectors, owing to the curvature of the segments. As can be seen in Fig. 17, the probability of paroxysmal activity was a linear function of pattern area, different patients giving functions with similar slopes but different intercepts. The excitation responsible for the paroxysmal activity involved a more restricted activation when two-sector patterns were presented than when four-sector patterns of similar total area were used. This appeared to make little difference to the probability of inducing paroxysmal activity. Figure 17 also shows the data for two- and four-sector patterns plotted as a function of the total pattern area, so that each value of sector angle for the two-sector patterns corresponds to a value half as large as for the four-sector patterns. It can be seen that, with the exception of two patients, CB and JH, the functions for two- and four-sector patterns overlap. This would suggest that the probability of paroxysmal activity is a function of the number of cells stimulated, regardless of whether they are confined to one part of the visual cortex or are

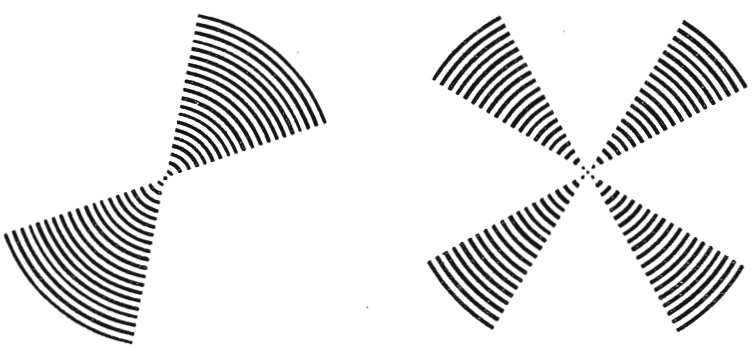

FIG. 16. Diametrically-opposed sectors of concentric annuli with diagonal axes of symmetry, square-wave luminance profile and constant spatial frequency (radial measurement).

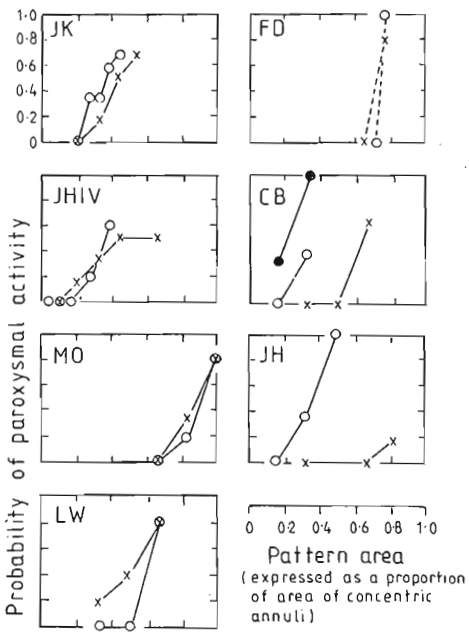

FIG. 17. Probability of paroxysmal activity as a function of the area of patterns composed of diametrically-opposed sectors of concentric annuli (contrast 0.7, mean luminance 3×10^2 cd/m^2). Pattern area was manipulated by varying the sector angle. Patterns with a "twenty minutes to two" orientation are represented by open circles, and those with a "twenty minutes past ten" orientation by filled circles. Patterns with four sectors are represented by crosses. The spatial frequency (radial measurement) was 2 cycles/degree and the sector radius 24°, except for patient FD who was tested using patterns with a spatial frequency of 3.5 cycles/degree and radius 15°.

distributed more widely, an inference that will require qualification later. The fact that the functions failed to overlap in two cases is hardly surprising considering the large number of factors such as orientation selectivity that could have contributed to differences between the patterns. We did not expect to obtain an overlap of the curves in so large a proportion of patients.

Both the above studies indicate that each patient has a different threshold amount of excitation below which no paroxysmal activity is induced. Above this threshold the probability of paroxysmal activity increases with increasing excitation, and the rate of increase is similar from one patient to another. If fluctuations in cortical hyperexcitability are responsible for the probabilistic nature of the paroxysmal response, the similar rates of increase from patient to patient would suggest that these fluctuations in hyperexcitability are also similar from patient to patient. The site of excitation within the cortex appears not to be a critical factor. To adapt (and perhaps abuse) Lashley's terminology (Lashley, 1929; Lashley and Wiley, 1933), the cortex appears to be equipotential, and paroxysmal activity the result of the mass action of neurons, a critical mass being required to initiate the discharge. If the site of excitation is not critical the type of cell stimulated may not be critical either. The next study compared the effectiveness of peripheral stimulation with that of stimulation in the centre of the visual field so that the action of different types of cell could thereby be compared.

4.3. VARYING CENTRAL AND PERIPHERAL STIMULATION SEPARATELY

Not only is the number of cells devoted to the analysis of a given area of the peripheral visual field less than that analysing central areas, the types of cell involved differ at every level. In the retina the ratio of cones to rods changes with eccentricity, as does the number of cells sensitive to transient, as opposed to sustained aspects of the visual scene. If it can be shown that the probability of paroxysmal activity is a function of the number of cells stimulated whether centrally or peripherally, and that the changes in cell types

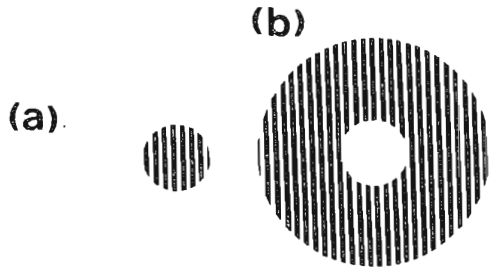

FIG. 18. Schematic illustration of (a) a disc and (b) an annulus of a vertical square-wave grating The spatial frequency and size varied as described in the text.

are relatively unimportant, further data in support of the hypothesis of mass action and equipotentiality will have been obtained. There are, of course, immediate problems with any analysis of this kind. It is necessary to assess the effects of the spatial frequency of a pattern separately for peripheral and central stimulation, because the size of the receptive fields of cells increases with eccentricity.

In the study now to be described, patterns of striped lines (gratings), with a uniform spatial frequency, varied not only in their external radius but also in the radius of a concentric circular unpattered region with the same mean luminance as that of the pattern (see Fig. 18b). Sensitivity to these annular patterns was compared with sensitivity to patterns having no central unpatterned central region (i.e. complete gratings, or "discs"; see Fig. 18a). The curves in Fig. 19 show how the probability of paroxysmal activity varied with spatial frequency in three patients. The pattern radii (both inner and outer) are shown beside each curve. It will be noted that the spatial frequencies optimal for inducing paroxysmal activity do indeed differ for discs and annuli, annuli being epileptogenic at lower spatial frequencies than discs. (The spatial frequency optimal for the induction of paroxysmal activity by discs is higher than shown in Fig. 4, presumably because far smaller stimuli were used.) Annuli producing paroxysmal activity with a probability similar to that of discs have a far larger surface area than the discs. This is to be expected if the probability of paroxysmal activity is a function of the number of cells stimulated, owing to the smaller number of neurons devoted to analysis of peripheral vision.

Drasdo (1977), in a re-analysis of data from a variety of published sources, has estimated that the percentage of striate cortex subserving a centrally-fixed circular region of the visual field is given by Q in the equation

$$Q = 100[1 - \exp(-0.0574\,A)] \qquad (1)$$

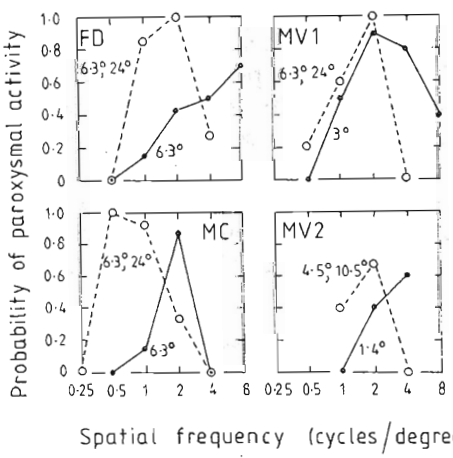

FIG. 19. Probability of paroxysmal activity as a function of the spatial frequency of discs (solid circles, solid lines) and annuli (open circles, broken lines) of a vertical square-wave grating, contrast 0.7, mean luminance 3×10^2 cd/m^2. The radii of the patterns are shown beside each curve. The data are for three patients, one of whom (MV) was tested twice.

where A is the angular radius of the circular region. The density of cortex is uniform (Daniel and Whitteridge, 1961), and so Q may be regarded as an estimate of the proportion of cells in the striate cortex available for analysis of the region of visual field determined by A. From Q can be determined the percentage of striate cortex devoted to the region of visual space occupied by the pattern, be it disc or annulus. Of course, not all the cells capable of analysing the region will be stimulated by a particular pattern. The proportion of available cells that the pattern actually stimulates is unknown and cannot be estimated given present knowledge. It is likely to vary with spatial frequency, and cannot be assumed to be the same for annuli and discs, even if the optimum values of spatial frequency are separately determined.

Despite these problems, the notion of mass action with equipotentiality appears to hold up. Eleven patients were presented with discs and annuli of various sizes, and those patterns that induced paroxysmal activity on some trials but not others were selected for each patient. The percentage of striate cortex (Q) subserving the region of visual space occupied by the patterns was calculated separately for each pattern and the values for discs and annuli averaged for each patient. The mean values have been used as the basis of the plots in Fig. 20a, in which each point represents a patient, and the position of the point is determined by the mean values of Q obtained for the discs and annuli used with that particular patient. The data show a significant positive correlation ($r_s = 0.64$, $p < 0.05$). In Fig. 20b the mean areas of the discs and annuli rather than their values of Q have been used as the basis of the plot. The correlation is not significant ($r_s = 0.32$). Taken together, Figs 20a and 20b suggest that pattern area is not of itself a critical variable, whereas the number of cells stimulated by a pattern is. The correlation between the values of Q for annuli and discs is high, given that the proportion of available cells actually stimulated by a pattern cannot be estimated. The correlation suggests that the effects of the different types of cell stimulated with peripheral and central patterns may be less important than the number of cells stimulated regardless of type.

Drasdo's equation for the cortical magnification factor applies to the cortex. No equivalent data are available for the superior colliculus, but it is unlikely that a similar

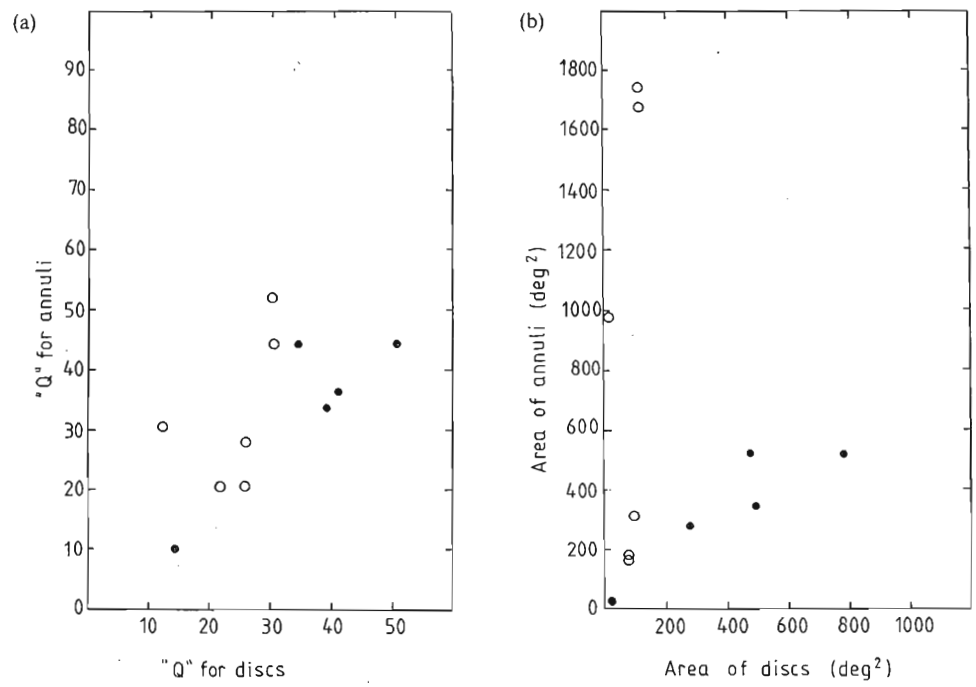

FIG. 20. (a) The value of Q for discs and annuli eliciting paroxysmal activity with approximately similar probability in 11 patients. (b) The area of the discs and annuli used in (a). Solid circles are for patients tested with annuli having an inner radius of 1.5° and open circles for patients tested using annuli with a larger inner radius.

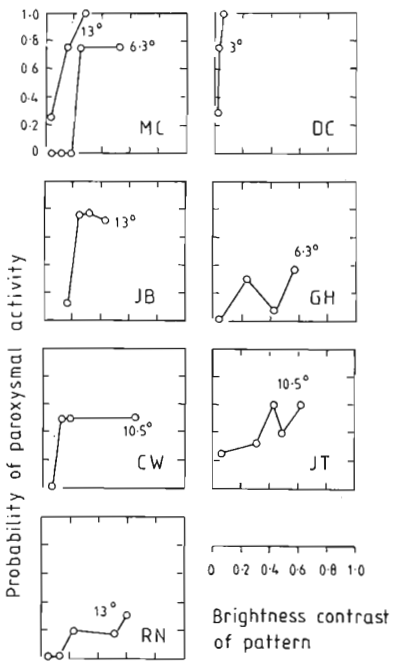

FIG. 21. Probability of paroxysmal activity as a function of the brightness contrast of a striped pattern (square-wave grating, spatial frequency 2 cycles/degree, mean luminance 3×10^2 cd/m^2, circular in outline with radius as indicated). Contrast is here defined as $(L_2 - L_1)/(L_2 + L_1)$, where L_2 and L_1 are the luminance of the light and dark stripes, respectively.

function is applicable. In so far as Drasdo's estimate fits the data, it may be taken as evidence in favour of a cortical rather than a collicular trigger.

4.4 PATTERN CONTRAST

The luminance contrast of a pattern can be defined as

$$(L2 - L1)/(L2 + L1) \qquad (2)$$

where $L2$ and $L1$ are the luminance of the bright and dark regions of the pattern respectively. Tolhurst *et al.* (personal communication) have recorded from units in the striate cortex of cats and found that for a limited range of values, usually below 0.3, the firing rate of a cell increases with the contrast of a stimulus. At contrasts greater than about 0.3, most cells have either saturated or have begun to do so.

Figure 21 shows how the probability of paroxysmal activity increases with pattern contrast. As can be seen, the probability shows a rapid initial increase for most patients for values between 0 and 0.3, and a plateau thereafter. On the basis of the data of Tolhurst and co-workers, the relationship between contrast and probability of paroxysmal activity may be interpreted as suggesting that paroxysmal activity occurs when the firing rate of cells excited by the pattern exceeds a critical threshold. Increasing the contrast of a pattern may also, of course, increase the total number of cells excited, but as yet we have no information on this point. The curves for patient MC (Fig. 21) demonstrate that paroxysmal activity can be elicited at lower contrasts if the size of the pattern is increased. They indicate that the threshold for paroxysmal activity can be expressed in terms of total excitation, and that the firing rate and the number of cells stimulated may have additive effects.

4.5. EXCITATION WITHIN A HEMISPHERE

In all the experiments described so far, the pattern has been symmetrical about a central fixation point. This reflects a deliberate attempt to equate the degree of excitation

FIG. 22. Schematic illustration of a unilateral square-wave grating. The fixation point was displaced 0.5° from the vertical border.

of the two cerebral hemispheres. Having obtained evidence suggesting that the probability of paroxysmal pattern activity is related to the degree of excitation, and is independent, at least to some extent, of the type of neuron stimulated, the question arises as to whether these relationships hold between, as well as within, cerebral hemispheres. In recent studies, still in progress, we have presented a variety of patterns to one or other visual half-field (e.g. see Fig. 22), and have discovered that, initially at least, the mass excitation appears to remain confined to the hemisphere stimulated.

We have been finding that when a pattern is presented to either visual half-field the threshold diameter is similar to that for a bilateral pattern. (There are, however, patients who demonstrate a marked asymmetry between the two visual fields; a difference that may turn out to reflect aetiology, but for which we have as yet no explanation.) There is therefore no evidence of any additive effect between half-fields. Instead, it appears that mass action can occur independently within each hemisphere. Consistent with this finding is the fact that when the paroxysmal activity is confined to the posterior regions (which, with our techniques, it often is), it is seen over the hemisphere contralateral to the stimulus. On those occasions when the paroxysmal activity is seen in anterior regions, both hemispheres are involved.

The above findings are very preliminary and need replication, but they are consistent with what might be expected on the basis of Zeki's studies of monkey cortex. Zeki (1978) has shown that in areas V1, V2, V3, V3A and V4 of one hemisphere, only the visual field contralateral to the hemisphere is represented. Callosal fibres occur only at the junction between one visual area and another, and apparently serve to "sew together" the corresponding areas of each hemisphere. In the superior temporal sulcus, however, both visual fields are represented and callosal fibres are widespread. The fact that the paroxysmal activity remains contralateral whilst only the posterior regions are involved is consistent with the view that callosal fibres are involved in the spread of paroxysmal activity from one hemisphere to the other.

5. A Synthesis

Until now we have considered the seizure trigger in terms of the immediate physiological precipitants. We will now enlarge the frame of reference and begin with considerations of the underlying pathology.

5.1. UNDERLYING PATHOLOGY

In some animal models of epilepsy there is evidence that an imbalance of excitation and inhibition inducing seizures can result from a failure of inhibitory mechanisms. In penicillin foci there is a reduction in the number of interneurons subserving recurrent inhibition (Anderson and Rutledge, 1979), and in alumina gel foci a reduction has been reported in the number of nerve endings staining for glutamic acid decarboxylase (GAD), the cerebral enzyme responsible for the production of GABA, an inhibitory neurotransmitter (Ribak *et al.*, 1979). Both foci involve large destructive lesions, however, and in the case of Ribak's study the destruction may not have been specific to GABA-ergic termin-

als. Perhaps the best evidence is pharmacological. Administration of drugs, such as allylglycine, that inhibit GAD enhance the natural syndrome of photosensitive epilepsy in the baboon *Papio papio* (Meldrum *et al.*, 1975). On the other hand, sodium valproate is an effective anticonvulsant in both baboon and man, and there is some suggestion that it enhances GABA-ergic inhibition. It is conceivable, therefore, that the pathology underlying photosensitive epilepsy is a failure of GABA-ergic inhibitory mechanisms (but see Kuhnt (1972), for an alternative viewpoint). The failure of such mechanisms need only be minimal. It is not apparently sufficient, under typical levels of visual excitation, to interfere with normal visual function. It may be that it is only when the level of excitation is excessive that the partial failure of inhibitory mechanisms has any consequences.

It is arguable as to which parts of the brain are affected. There is some suggestion that the disturbance may be diffuse, at least in so far as somatosensory evoked potentials are abnormal in photosensitive patients (Broughton *et al.*, 1969). This abnormality may or may not be a reflection of abnormal inhibitory mechanisms, of course.

In this paper we have argued that the triggering of paroxysmal activity by patterns involves cells with characteristics typical of single units in the striate and prestriate areas of monkey cortex. The probability of paroxysmal activity appears to be dependent on both the number of cells stimulated, and possibly also their firing rate. It does not appear to be influenced by the particular region of visual cortex stimulated, simply the total area. The curves relating the probability of paroxysmal activity to excitation are steep; over a restricted range small changes in excitation give rise to large changes in probability.

The probabilistic nature of the occurrence of such activity may possibly be a reflection of fluctuations in cortical hyperexcitability, conceivably related to fluctuations in the responsiveness of cortical units that are frequently encountered during microelectrode recordings (Robson, personal communication). Were it not for these fluctuations, the occurrence of paroxysmal activity might be an invariable result of a stimulus above a given size. Be that as it may, it is not only the occurrence of paroxysmal activity that is variable, but also the head regions affected when the activity does occur, and it is these changes in topography that may provide clues as to the way in which a discharge spreads.

Careful examination of the EEG tracings obtained with pattern stimuli close to the threshold of the photoconvulsive response sometimes shows focal parieto-occipital discharges, sometimes generalized spike–wave activity, and sometimes disturbances that are initially focal and suddenly become generalized. We have never seen a discharge gradually spreading from the occiput to the central regions but no further. Patterns presented to one visual field produce a contralateral response unless or until anterior regions are involved, in which case the response is generalized. We have yet to see a response involving the anterior regions of only one hemisphere.

5.2. AN HYPOTHESIS

The stimulus characteristics of pattern sensitivity and the topographic distribution of paroxysmal activity combine to suggest that epileptiform disturbances originate in occipital regions, and are sometimes responsible for the induction of generalized activity. There is no reason to assume that subcortical regions are involved in the generation of the occipital discharge, but they may be responsible for its anterior spread. The generalization of a discharge as assessed by the scalp EEG appears to have an all-or-none character at least in so far as gradual generalization of an initially local event is rarely seen.

There therefore appear to be two stages in the generation of a photoconvulsive response. When normal physiological excitation exceeds some (slightly variable) limit, paroxysmal disturbance is triggered. When the disturbance exceeds some topographic limit, complete generalization occurs. The notion of a critical level of excitation appears to apply to both stages. The critical excitation is physiologically normal in the first stage,

and abnormal in the second. In the first stage, variability in threshold may reflect fluctuations in excitability. In the second stage the threshold appears to be all-or-none.

5.3. LIMITATIONS OF THE HYPOTHESIS

The two-stage hypothesis outlined above has been advanced to account for paroxysmal activity induced by pattern stimulation. Considerations of parsimony would lead one to suppose that the hypothesis may also apply to paroxysmal activity evoked by other forms of retinal stimulation, notably diffuse intermittent light. Parsimony aside, there is some evidence to support this view. Occipital abnormalities, such as occipital spikes, have been reported in response to intermittent diffuse light at frequencies below those at which a photoconvulsive response is induced, and also after the response has been eliminated by administration of sodium valproate (Jeavons and Harding, 1975; Binnie *et al.*, in press). Sensitivity to intermittent light is reduced, if not eliminated, under conditions of monocular stimulation, a finding that suggests a binocular mechanism and is consistent with a cortical locus. Against these considerations are set the poor correlation between sensitivity to pattern and to diffuse intermittent light (see Section 1.2.3) and the fact that single cortical units are not strongly excited by flashing spots of light.

It is possible that, although diffuse intermittent light can trigger paroxysmal activity as a result of the stimulation of units in the visual cortex, other nuclei within the visual system may also play a role. In other words, the trigger mechanism may be less specific than that underlying pattern sensitivity. It may also, therefore, be more diffuse, and less consistent from time to time and from patient to patient.

A diffuse flickering field may not stimulate a large number of cortical units, but it is likely to cause those that it does stimulate to fire at similar times. Stationary pattern stimuli, on the other hand, may fail to produce excitation that is as synchronized. The majority of cells respond better to moving than to stationary images of bars, and the response is usually more marked for movement in one direction than another. These properties should mean that the image of a pattern, displaced on the retina when the eye moves, stimulates a large population of cells at the same time as the movement. The cells making up that population should, however, change with the direction, amplitude and velocity of movement. If the direction of movement is repeatedly changed, as in the case of a rapidly vibrating pattern, the degree of synchronization may be greater. It is possibly for this reason that sensitivity to vibrating patterns can be greater than to patterns whose only retinal movement is a result of the motion of the eye. It is difficult, nevertheless, to separate out the effects of synchronization from those of the magnitude of excitation, given that variables that affect one also affect the other.

There are several further shortcomings of the two-stage hypothesis outlined above. Firstly, it cannot accommodate the differences in the epileptogenic properties of plaid and striped patterns (Section 3.2). Secondly, it cannot account for sensitivity to gratings in some orientations and not others, in the absence of any evidence of astigmatism. Perhaps the trigger can be confined to those dimensions of the striate cortex devoted to the analysis of a limited range of orientations. Despite the evidence for equipotentiality described earlier, it is quite possible that in some patients certain parts of the cortex are more hyperexcitable than others. As mentioned above, we have recently found that some patients are more sensitive to pattern stimulation in one visual field than in the other.

5.4. RELATIONSHIP WITH OTHER MODELS

Gabor and Scobey (1975) used an animal model of epilepsy in which small amounts of penicillin were applied to circumscribed areas of cat visual cortex, rendering the cells within the area hyperexcitable. Visual stimuli (flashing spots) within a region of the visual field corresponding to the affected cortex were capable of triggering a paroxysmal wave. The probability of occurrence of the paroxysmal wave was directly related to the size of the stimulus used, regardless of where in the affected region the stimulus was placed. The critical threshold size varied with the eccentricity of the affected region in such a way as

to suggest that the probability of a paroxysmal wave was a function of the number of units stimulated.

The similarity between the results of Gabor and Scobey, and those that we have obtained with photosensitive patients, is interesting, and suggests that it may be a general property of hyperexcitable cortex to exhibit an excessive response to excitation above a certain level, with little regard to how or where this excitation is achieved.

The most widely-used model of photosensitive epilepsy is the photosensitive baboon, *Papio papio*. There are several grounds for believing that the trigger mechanism in *Papio papio* may differ from that in man, and although these have been extensively reviewed elsewhere (Newmark and Penry, 1979) it is perhaps worth emphasizing the following points. As described above, a substantial proportion of photosensitive patients are sensitive to patterns. The paroxysmal activity evoked by patterns often has a postcentral emphasis and is never confined to anterior regions. Postcentral activity is also occasionally produced by intermittent light stimulation. The baboon appears not to be pattern-sensitive, although this may simply be a reflection of the difficulty in persuading the animal to look at a pattern for a prolonged period (B. Meldrum, personal communication). The EEG paroxysms first appear over fronto-rolandic areas and are never confined to posterior regions. In *Papio papio* rapid fluttering of the eyelids is seen during stimulation with intermittent light, and there is evidence that these movements may act to potentiate the effects of the retinal stimulation (Menini *et al.*, 1974). In man, stimulation with patterns is hardly ever associated with any fluttering of the eyelids; the only movements of the eyelids that do occasionally occur appear to be part of an attempt to self-induce seizures (see Section 6.3). Stimulation with intermittent light is sometimes accompanied by a screwing up of the eyes, particularly if the light is intense. This response does not usually resemble the eyelid fluttering seen in *Papio papio*, however. As has been pointed out elsewhere, there are many features of the response in *Papio papio* that resemble the human photomyoclonic response (Newmark and Penry, 1979, Chapter 13).

The work of Gloor and collaborators (Gloor, 1979) has strongly suggested that in feline penicillin-induced epilepsy, the spike-and-wave pattern recorded from surface electrodes is an expression of rhythmic activation of a recurrent intracortical inhibitory pathway. The waveform appears to be a reaction of abnormal cortex to thalamo-cortical volleys, particularly those that give rise to spindles in normal cortex. These thalamo-cortical volleys presumably have the property that they stimulate large populations of cortical neurons, and it may be this aspect of thalamo-cortical afferents, rather than their thalamic origin that is critical for the induction of spike and wave. Any other means of synchronizing large populations of cortical neurons may have an effect similar to that of thalamo-cortical afferents.

5.5. IMPLICATIONS FOR VISION

If patterns induce paroxysmal activity as the result of a critical mass of excitation in equipotential cortex, the way in which the probability of paroxysmal activity is influenced by variables such as spatial frequency and contrast acquires a new significance. Apparently the excitation that a (square-wave) pattern evokes is maximal for spatial frequencies in the range 1–4 cycles/degree. Apparently excitation is little affected by pattern contrast for values in excess of 30%. Evidently the luminance of a pattern has little affect on the cortical excitation that it induces, except, perhaps, at high levels of luminance (see Fig. 6).

When the area of a circular square-wave grating was manipulated in terms of its radius, the rates of increase in the probability of paroxysmal activity were similar from patient to patient when pattern radius (and hence pattern area) were expressed logarithmically (see Fig. 15). When pattern area was manipulated in such a way as to avoid the confounding effects of a differential contribution from the periphery the rates of increase were similar when pattern area was not so transformed (see Fig. 17). Taken together

these findings suggest that as the radius of a circular square-wave grating is increased, the excitation it produces is a logarithmic function of pattern area.

6. Clinical Aspects of Photosensitivity

6.1. TELEVISION EPILEPSY

The most commonly recognized clinical manifestation of photosensitivity is television-induced convulsions, often known as "television epilepsy". Many people spend hours every day watching television, so that a history of consistent association between attacks and television viewing, together with the finding of photosensitivity on EEG investigation, is necessary to establish the diagnosis. Although attention was first drawn to television-induced epilepsy by the occurrence of seizures when the television was grossly malfunctioning (e.g. due to loss of vertical hold) or when the patient was changing channels (Richter, 1960; Dummermuth, 1961; Pallis and Louis, 1961; Mawdsley, 1961), it now appears that the majority of seizures occur when the set is working normally (Binnie *et al.*, 1973).

The mechanism whereby television induces seizures is not immediately obvious. The television picture is composed of lines drawn by a spot that varies in intensity as it zig-zags down the screen. The frequency with which the spot scans from the top to the bottom of the screen is close to that of the domestic electricity supply. The supply frequency in most countries is 50 Hz, although in a few countries, mainly on the American continent, the frequency is 60 Hz. As a result of the scan the entire screen flickers. Figure 1 shows the proportion of patients sensitive to intermittent light at 50 Hz and 60 Hz, and it will be noted that, with eyes open, some 50% of the patients in the sample were sensitive at 50 Hz, whereas only about 20% were sensitive at 60 Hz. Jeavons and Harding (1975) explain the lower incidence of television-induced seizures on the North American continent on the basis of this difference. Their sample may not be representative of photosensitive patients in general, however. There is some suggestion that people can adapt to the flicker from a television: the flicker from a set which scans from top to bottom in the normal manner is less perceptible than that from a set that scans from bottom to top (Corbett and White, 1976). If people can adapt to the direction of the scan it is possible that they may also adapt to its frequency. It is therefore conceivable that the convulsive effects of intermittent light in persons who have had the opportunity to adapt to televisions with a 50 Hz scan (e.g. European patients) may be different from those in persons who have not (e.g. patients in North America). A difference in the incidence of sensitivity to intermittent light at 50 and 60 Hz obtained in a European sample of patients may not perhaps provide a sufficient explanation of the difference in the incidence of television epilepsy in the European and American continents. Be that as it may, many of the patients in Jeavons and Harding's sample had a history of television-induced attacks but were not sensitive to intermittent light at 50 Hz. This suggests that a mechanism other than the diffuse flicker of the screen may have been responsible for their attacks.

On one traverse of the flying spot from the top to the bottom of the screen the odd lines are drawn (top line, third from top, fifth from top etc.) so as to create one "half-frame" or field. The even-numbered lines are drawn on the next traverse, and the two types of traverse, odd and even, alternate. Since the fields are drawn at a frequency similar to that of the domestic electricity supply (50 or 60 Hz) the spot takes nearly 1/50th or 1/60th sec to traverse from the top to the bottom of the screen, and each line is drawn 25 or 30 times per second. The pattern of interlacing lines that results is similar to a pattern of stripes "vibrating" at 25 or 30 Hz. The lower of these frequencies is very close to that optimal for the induction of paroxysmal activity by a vibrating pattern (see Section 2.4.). The effects of the pattern should depend not only on its temporal frequency, but also on its spatial frequency. When the patient is close to a large television screen the spatial frequency of the line pattern may be low enough (i.e. the stripes may be large

enough) for paroxysmal activity to be induced. At distances where the line pattern cannot be resolved the diffuse flicker remains, due to the repetition of each field. The sensitivity of patients may therefore depend critically on the distance at which they view the set. This has been shown to be the case.

Wilkins *et al.* (1979b) asked patients to watch television whilst their EEG was monitored. They found that patients who were sensitive to intermittent light stimulation at 50 Hz were also sensitive to the television at normal viewing distances (> 1 m). Patients who were only sensitive to intermittent light at frequencies less than 50 Hz were also sensitive to the television, but only at close viewing distances. No such relationship between threshold viewing distance and sensitivity to intermittent light occurred when the intermittent light was patterned, suggesting that the above finding was not simply a reflection of some non-specific degree of photosensitivity.

In a further study, Wilkins *et al.* (1979b) compared patients' sensitivity to three types of television screen: one small (266 mm, diagonal measurement), one approximately twice the size, and a third comprising the large screen covered by a mask the same size as the small screen (see Fig. 23). Both the size of a television screen and its component lines change with viewing distance, but by comparing sensitivity to the three types of screen (small, large and masked) over a range of viewing distances it was possible to study the effects of these variables independently. It turned out that for patients who were sensitive at normal viewing distances, the size of the image of the screen on the retina predicted the probability of paroxysmal activity. For patients who were sensitive only at close viewing distances, the size of the screen was unimportant and the retinal size of the component lines predicted the probability of paroxysmal activity. This was true except when the viewing distance was very small when presumably the accommodative mechanisms of the eye were unable to maintain a sharp retinal image of the lines. All patients were very much less sensitive to the small screen than to the large at all viewing distances, as a result of both the small screen size and the small size of the component lines. Patients who suffer television-induced attacks may therefore be well advised to change their set for one with a smaller screen.

Some patients, mainly those sensitive to intermittent light at 50 Hz, will be sensitive to a small-screen television (albeit to a lesser extent than a large), and a change to a small screen may be insufficient to control their seizures. There will undoubtably be other patients who find such a change impracticable. For these patients there may yet be one alternative to pharmacological treatment. If a sheet of polarizer is placed over the television screen, and the patient is given a pair of spectacles to wear, one lens of which is polarized at an angle orthogonal to that of the sheet, binocular viewing of the television is selectively and cosmetically prevented. As reported earlier, the convulsive effects of retinal stimulation are greatly attenuated, if not eliminated, under conditions of monocu-

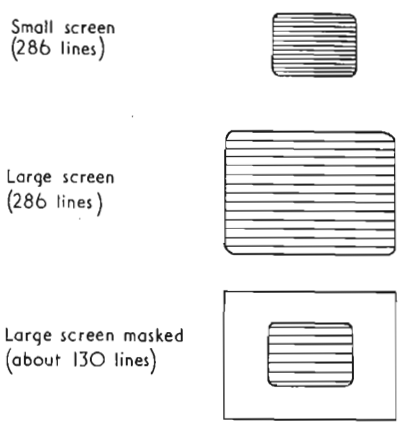

FIG. 23. Schematic illustration of three types of television screen used to distinguish the effects of the angular subtense of the screen from those of the subtense of its component lines.

lar viewing. A few patients have found this a successful treatment, although the majority complain of eyestrain (Wilkins *et al.*, 1977).

Increasing ambient illumination by placing a lamp on top of the television, advocated by Jeavons and Harding (1975) as a technique for reducing the chances of a seizure, may actually serve to increase, rather than decrease the chances, according to recent electrographic studies (Binnie *et al.*, in preparation).

6.2. PATTERN-INDUCED SEIZURES

Patients, their relatives, and their doctors, are presumably far more likely to notice a relationship between television and seizures than they are a relationship between patterns and seizures. At the moment we have no reliable estimate of the incidence of pattern-induced seizures. In our own small and highly selected series of photosensitive patients the incidence of seizures recognised as being pattern-induced (excluding those due to the television raster) exceeds 30%. Epileptogenic environmental stimuli include grills, fences and venetian blinds, and stripes on wall paper, clothes and furnishing fabrics. Arguably the most epileptogenic of common environmental patterns is that of the metal stair tread on a certain make of escalator in widespread use.

It may be possible for the patient to avoid exposure to those patterns that have major epileptogenic properties; he or she can, e.g., be advised to cover epileptogenic furnishing fabrics, change curtains or wallpaper, etc. But for the highly sensitive patient even these precautions, restrictive as they are, will be insufficient. For such patients the only alternatives are anticonvulsant therapy or special glasses. Anticonvulsant therapy is the obvious choice, and will be reviewed briefly in the next section, but for those patients for whom such treatment is inappropriate or ineffective, spectacles with one frosted lens may prove effective. In two (severe) cases (Wilkins *et al.*, 1975, 1977), long-term EEGs were recorded and demonstrated that when glasses of this kind were worn the incidence of paroxysmal activity was reduced by over 80%. Figure 24 shows the results obtained from one of the patients. The reduction in paroxysmal activity is testimony to the number of potentially epileptogenic patterns in the modern urban environment.

6.3. SELF-INDUCED SEIZURES

Some photosensitive patients deliberately induce seizures or epileptiform EEG discharges. One method, seen mainly in mentally-subnormal patients, is to produce intermittent retinal stimulation by waving the outstretched fingers in front of the eyes (Rodovici *et al.*, 1938; Andermann *et al.*, 1962). Less easily recognized, but considerably more common, even amongst patients of normal intelligence, is a slow closure of the eyelids

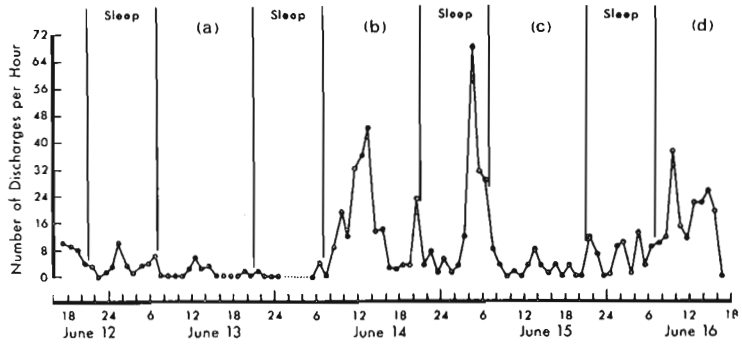

FIG. 24. Incidence of EEG discharges during continuous 4-day monitoring of a pattern-sensitive patient. The four conditions were as follows: (a) the patient wore glasses with the right lens frosted and the other plane; (b) the patient wore "placebo" glasses with an upper and lower portion of both lenses frosted; (c) the patient wore glasses with the left lens frosted; and (d) no glasses were worn. Note the decrease in the incidence of discharges under conditions of monocular viewing, (a) and (c).

with a marked upward rotation of the eyeball (Green, 1966; Darby *et al.*, 1980; Binnie *et al.*, in press, b.). In studies that have used prolonged EEG monitoring with the eyes open in well-lit surroundings the phenomenon has been found in about 25% of photosensitive patients (Binnie *et al.*, 1980). The characteristic eye movement precedes epileptiform EEG activity and its occurrence is often reduced under conditions of low illumination when the association with paroxysmal activity often disappears. Slow eye-closures, can, however, be associated with paroxysmal activity in darkness, suggesting a possible contribution from some conditioning mechanism (Darby *et al.*, 1980). Patients who self-induce seizures are often psychiatrically disturbed, and the slow eye-closures generally become more frequent under conditions of stress. Patients are often unwilling or unable to discuss the phenomenon, and may angrily deny that it occurs. Later, when their confidence has been gained, many describe either a pleasurable sensation or a compulsive urge to make the inducing movement. In some instances a clear advantage derives from the self-induced seizures, which may be used to manipulate relatives. Often, however, there is no obvious gain, and one is struck by the similarity with the behaviour of experimental animals with electrodes in the medial forebrain bundle (Olds, 1958). The mechanisms underlying self-stimulating behaviour in animals are apparently domapinergic or serotonergic, and for this reason the treatment of this (generally intractable) condition by antidopaminergic drugs has been attempted. Preliminary results suggest that such drugs are indeed effective in most patients (Overweg *et al.*, in preparation). And this despite the convulsant properties reported for some of these drugs.

6.4. ANTICONVULSANT THERAPY

Not all anticonvulsant drugs suppress photosensitivity in man. The most effective are the benzodiazepines, suxinimides and sodium valproate. These probably have the common pharmacological property of potentiating the action of GABA-ergic inhibitory synapses. Until recently, photosensitive epilepsy was generally considered to be resistant to anticonvulsant therapy (Livingston and Torres, 1964; Troupin, 1966). However, sodium valproate now appears to offer effective control in many patients (Herrick, 1978; Harding *et al.*, 1978). The mode and site of action of sodium valproate are unknown, but both acute and chronic studies have shown that after suppression of the generalized photoconvulsive response by sodium valproate, an abnormal response to photic stimulation may persist over the occipital regions (Herrick, 1978; Binnie *et al.*, 1980). These findings are consistent with the evidence that photosensitivity involves a trigger in the striate cortex, and suggest that valproate suppresses the generalization of the initial discharge, possibly by increasing the threshold in the second stage hypothesized in Section 5.1. The range of frequencies at which intermittent light will elicit a photoconvulsive response has been used as a measure of sensitivity in several studies that have assessed the time-course of the action of sodium valproate. Thus, Rowan *et al.* (1979) and Binnie *et al.* (in press, c.) have shown that, although the drug has a short biological half-life and rapidly passes the blood–brain barrier, its suppressant effects are seen several hours after peak serum concentrations have been reached. Following termination of sodium valproate therapy, photosensitivity usually returns, but over a period of several months (Harding *et al.*, 1978).

7. Conclusion

All the available evidence is consistent in suggesting that in photosensitive epilepsy the paroxysmal disturbance evoked by patterns is initiated in the visual cortex. (The disturbance evoked by intermittent light may have a less specific and less consistent locus of onset.) The discharge appears to occur when a critical level of excitation is reached, and the locus of the excitation within the visual cortex is not critical; i.e. there is some degree of equipotentiality. This abnormal reaction to massive excitation is possibly the result of a failure of inhibitory mechanisms which is insufficient to disturb function under normal

conditions of excitation. There are some preliminary indications that, once a discharge has been initiated, as the result of massive excitation, it may remain confined to one cerebral hemisphere unless or until anterior cortical regions are involved.

Hopefully the notions of a critical level of excitation, mass action and equipotentiality will be quickly superceded by more specific concepts, just as Lashley's ideas have been overtaken by recent evidence for the localization of cerebral function. For the present, however, these notions have some explanatory utility, and it seems likely that they will continue to do so until we have far more detailed evidence than we do at present about the way in which seizures are initiated.

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