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NEUROPHYSIOLOGICAL ASPECTS OF PATTERN-SENSITIVE EPILEPSY

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INTRODUCTION

ABOUT 5 per cent of patients with epilepsy are photosensitive; that is, paroxysmal activity can be elicited in the EEG by conventional intermittent photic stimulation (IPS) using a stroboscope (Jeavons and Harding, 1975, p. 3). In more than half these patients paroxysmal activity can also be induced by the viewing of striped patterns (Stefansson, Darby, Wilkins, Binnie, Marlton, Smith and Stockley, 1977). The present investigation describes the characteristics of a pattern that render it epileptogenic and, on the basis of recent work on the physiology of pattern vision, adduces evidence for the hypothesis that visually-induced paroxysmal EEG activity can be triggered in the striate cortex by the synchronized firing of large numbers of cells, the probability of paroxysmal activity being related to the number of cells stimulated. The hypothesis is an extension of that proposed by Wilkins, Andermann and Ives (1975) on the basis of a single case study.

Three of the studies in this paper report replications of the findings of Wilkins, Andermann and Ives (1975). The remainder provide confirmatory evidence for the hypothesis, and allow the interpretation of their findings to be elaborated.

METHODS

General Methods

Procedure. In all studies the procedure was broadly similar. The procedure for individual experiments will therefore be reported only in so far as it differed from the description that follows.

The patient was seated in a chair while the EEG was recorded, and was instructed to look at a variety of visual stimuli, wearing spectacles if they had previously been prescribed. The stimuli were successively presented in random order, the order constrained so that all stimuli were presented n times before any stimulus received its $(n+2)$th presentation. A stimulus was removed as soon as any paroxysmal activity appeared or when a presentation period had elapsed without any such activity. The period was usually 10 s and there was an interval of at least 5 s between presentations. Every four minutes or so, the patient

was given a longer break in which to rest. Provided the patient was willing, the presentations continued in this manner until a significant variation in the incidence of paroxysmal activity in response to the various stimuli had emerged.

Most of the patients studied were unaware of the occurrence of paroxysmal activity, and only rarely was the activity accompanied by any clinical signs. A major seizure was induced on one occasion only, as a result of conventional IPS.

Patients. The patients who participated in the nine studies are listed in Table 1 which presents the age, sex, type of epilepsy and type of resting EEG activity for each patient. The majority of patients were attending the Instituut voor Epilepsiebestrijding, Heemstede, Netherlands, 7 as outpatients and 3 as inpatients. Five patients were outpatients seen at the EEG Department, Runwell Hospital, Essex, UK and the remaining patient was attending the Montreal Neurological Institute, Canada. The patients were selected on the basis (1) that they were willing to take part in the study, and (2) that photic stimulation and patterns had induced paroxysmal activity during previous routine diagnostic EEG examinations. All of the patients were receiving anticonvulsant medication at the time of examination.

Screening tests. Photic stimulation techniques were standard in so far as every patient received stimulation in a darkened room at frequencies between 6 and 40 Hz (including stimulation in the range 16 to 18 Hz) using an unpatterned photic stimulator which provided a mean luminance of at least 1500 cd/m^2, and which was centrally fixated at a distance of 30 cm from the nasion, subtending at least 28 degrees. Pattern stimulation always included stimulation with square-wave gratings, mean luminance 300 cd/m^2, contrast 0·75, circular in outline and subtending at least 24 degrees, with spatial frequencies including 2 cycles/degree.

EEG analysis. The EEG response to visual stimulation was regarded as positive when bursts of spikes or slow waves or both appeared, with the exception of occipital spikes which were disregarded (Jeavons and Harding, 1975, p. 58). In every patient a response that could broadly be described as spike-wave or multiple spike-wave was elicited by visual stimulation of one kind or another. However, the morphology and topography of the response appeared to depend on the nature of the visual stimulus. It is beyond the scope of this paper to describe in detail the relationship between the visual stimulus and the type of EEG response. Suffice it to say that stimuli that readily elicited paroxysmal activity tended to induce generalized activity, whereas less provocative stimuli would often elicit activity confined to the posterior regions. In no patient was the activity confined to the anterior regions.

Study 1. Effects of Spatial Frequency

At threshold the contrast sensitivity of the human visual system to square-wave gratings is maximal at frequencies of around 4 cycles/degree (Campbell and Robson, 1968). The amplitude of the late positive wave of the evoked potential in response to sine-wave gratings is also maximal at these frequencies (Parker and Salzen, 1977). The question of immediate interest is therefore whether the patterns that are optimal stimuli for inducing paroxysmal EEG activity in photosensitive patients have a similar spatial frequency.

Procedure. Prints of square-wave gratings, circular in outline, 24 cm in diameter, with 0·5, 1, 2, 4 and 8 cycles/cm were dry-mounted on cards. The patient was seated 57 cm from a screen illuminated by a projector and the cards held rigidly against this screen. One centimetre of the pattern thus subtended one degree of visual angle. The gratings had a mean luminance of 300 cd/m^2 and a contrast of 0·75. The following patients took part in the study: M.V.D.H., V.L.N., V.L.P., M.W., D.E., H.V.L.D., H.S. and V.D.U.

TABLE 1. SUMMARY OF PATIENTS' DETAILS

Patient	*Age (yrs)*	*Sex*	*Classification of epilepsy*[1]	*Factors known to precipitate seizures*	*Resting EEG*	*Snellen acuity*
D.E.	9	F	Primary generalized	TV	Generalized and postcentral multiple spike-wave	Not tested
G.F.	16	M	Primary generalized	TV	Brief generalized multiple spike-wave	R 6/6 L 6/6
H.S.[2]	26	M	Secondary generalized	Patterns	Theta dominant	Not testable
H.V.D.[2, 3]	42	M	Secondary generalized	TV	Excess theta activity	R 6/12 L 6/12
H.V.L.D.[2]	28	M	Secondary generalized	TV, patterns, flicker, fluorescent lighting (self-induction)	Slow generalized spike-wave	R 6/18 L 6/18
K.O.	10	F	Primary generalized	TV	Generalized multiple spike-wave	Not tested
K.W.[4]	16	M	Primary generalized	TV	Rare generalized multiple spike-wave	R 6/6 L 6/6
L.D.	12	F	Primary generalized	TV, patterns	Generalized spike-wave	Not tested
M.T.	15	F	*See* Wilkins, Andermann and Ives (1975)			
M.V.D.H.	12	F	Primary generalized	TV	Normal	R 6/7·5 L 6/7·5
M.W.[4]	10	M	Primary generalized	TV	Normal	R 6/7·5 L 6/7·5
S.N.	9	F	Primary generalized	TV	Generalized and postcentral multiple spike-wave	Not tested
S.P.	22	F	Primary generalized	Patterns, fluorescent lighting, cinema	Normal	R 6/6 L 6/6
V.D.U.	18	F	Partial	TV, flicker, patterns	Normal	R 6/6 L 6/6
V.L.N.	10	F	Primary generalized	—	Posterior spike-wave in drowsiness	Not tested
V.L.P.	16	F	Primary generalized	TV	Generalized spike-wave	R 6/5 L 6/5

[1] Merlis (1970). [2] Subnormal. [3] Hemiparetic. [4] Brothers.

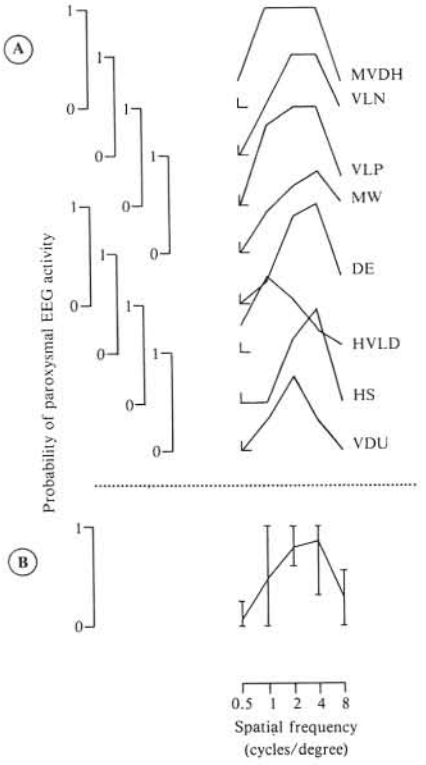

FIG. 1. Probability of paroxysmal EEG activity as a function of the spatial frequency of a square-wave grating, subtense 24 degrees, contrast 0·75, mean luminance 300 cd/m². A, individual patients, B, group data. Bars indicate range.

Results. The incidence of paroxysmal activity for the 8 patients is summarized in fig. 1A. The number of observations per point averaged 9·4 with a minimum of 4. Fig. 1B shows the mean estimates for the patient group with the ranges of values obtained. When the sensitivity to the five spatial frequencies was ranked separately for each individual patient the concordance between patients was highly significant ($W = 0{\cdot}74$, $P < 0{\cdot}01$), the optimum spatial frequency lying between 1 and 4 cycles/degree in all cases.

Discussion. The spatial frequency optimum for inducing paroxysmal activity lay between 1 and 4 cycles/degree for every patient tested. This result for high contrast stimuli mirrors the well-known peak sensitivity of the visual system to gratings at threshold contrast. It also accords well with the subtense at which the maximum amplitude of the late positive wave of the evoked potential is obtained with a 6 degree field using sine-wave gratings (Parker and Salzen, 1977). The functions relating probability of paroxysmal activity to spatial frequency are steep. The slope at the low frequency end is more marked than might be anticipated from

a straightforward model based on the component spatial frequencies of a square-wave grating (Soso and Lettich, 1978). This point will not be discussed in detail here because, given present knowledge, it can tell us little about the locus and nature of the seizure trigger.

Study 2. Effects of Grating Orientation

One of the four cases of pattern sensitivity described by Chatrian, Lettich, Miller and Green (1970) demonstrated a marked orientation selectivity favouring vertical gratings. The second study was therefore designed principally as a preliminary experiment to determine whether for a population of pattern-sensitive patients the vertical orientation was more likely to be epileptogenic. The concern was not to investigate in detail any orientation selectivity that individual patients might show.

Procedure. Square-wave gratings with a spatial frequency of either 2 or 4 cycles/degree were shown in four orientations: horizontal, vertical and the two 45 degree obliques, using procedure and stimuli similar to those of the first study. Patients M.V.D.H., V.L.N., V.L.P., M.W., D.E., H.V.L.D., H.S. and V.D.U. took part.

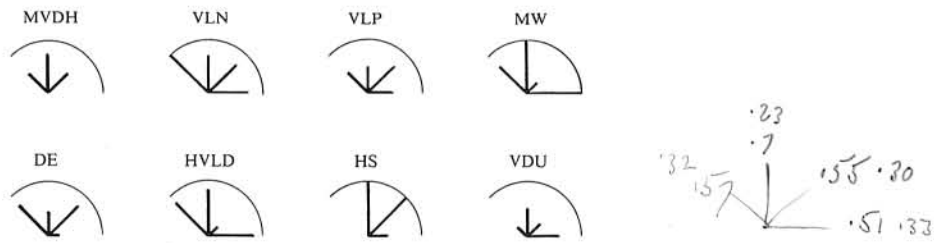

FIG. 2. Probability of paroxysmal EEG activity as a function of the orientation of a square-wave grating, subtense 24 degrees, contrast 0·75, mean luminance 300 cd/m², spatial frequency 2 cycles/degree (V.D.U, 4 cycles/degree). The length of the lines is proportional to the probability and the radius of the arc represents a probability of 1·0.

Results. The incidence of paroxysmal EEG activity for the four pattern orientations is shown separately for each patient in fig. 2. It will be seen that for the group as a whole there is no tendency for one orientation to be more epileptogenic than the others (Kendall's $W = 0{\cdot}036$, $P \geqslant 0{\cdot}05$).

Two patients, H.S. and M.V.D.H. demonstrated a significant difference in sensitivity to the four orientations. Neither of these patients had been prescribed spectacles. In the case of H.S., retinoscopy revealed a marked astigmatism 3·5 D at 170° in the right eye, 1·0 D at 0° in the left. Subjective testing of M.V.D.H. using gratings with a high spatial frequency suggested an astigmatism favouring a vertical over a horizontal axis. Since the probability of paroxysmal activity is reduced when patterns are poorly focused (Chatrian *et al.*, 1970) the astigmatism may be sufficient to account for the orientation specificity, given that in both cases the orientation of the axis was appropriate.

Discussion. For the group as a whole no one orientation was more epileptogenic than the others. Individual patients did, however, demonstrate significant orientation selectivity, possibly as a result of an astigmatism. Cases with orientation selectivity existing independently of astigmatism have yet to be demonstrated and would require more intensive investigation than has so far been attempted. However, the present study is sufficient to emphasize that clinical investigations for pattern sensitivity should include testing with patterns in a variety of different orientations.

The studies described so far have looked at some of the obvious parameters of patterns. These parameters tell us relatively little about mechanisms. The studies that follow take advantage of the information acquired and seek to delimit the number of possible alternative physiological mechanisms, replicating and extending the work of Wilkins *et al.* (1975).

Models of the Photoconvulsive Response

The visual system is conventionally thought of as consisting of a major pathway from the eye to the visual cortex via the lateral geniculate nucleus of the thalamus (LGN), and pathways to the superior colliculus directly from the eye and indirectly via the visual cortex. The major pathway is comprised of X (so-called sustained) and Y (so-called transient) systems. The direct and indirect pathways to the superior colliculus involve only Y neurons. For paroxysmal EEG activity to be evoked by visual stimulation, abnormal neural activity must be precipitated by the action of cells within the LGN, cortex and/or superior colliculus. This is not to say that any component of the visual system itself necessarily functions abnormally.

Bickford, Daly and Keith (1953) in their discussion of the hypothetical pathways for the convulsive response to light proposed three alternatives: (1) a transcortical pathway originating in the visual cortex; (2) a corticothalamic pathway from visual cortex to a thalamic system with diffuse projections to cortex; and (3) a subcortical thalamic pathway from the LGN to the diffuse thalamic system. Bickford *et al.* did not include a pathway from the superior colliculus, although there is no obvious reason for its omission. The first and second of the above alternatives involve the visual cortex, accessed via the normal pathways, and responsible via abnormal pathways for initiating directly in the first case and indirectly in the second, a generalized cortical disturbance. The difficulty with these models is that it is not specified how the abnormal pathways are responsible for the abnormal neural activity.

A simple alternative hypothesis to those proposed by Bickford *et al.* would be that the cortex is for some reason generally hyperexcitable, possibly as the result of the malfunction of a system involving an inhibitory neurotransmitter such as GABA (Meldrum and Balzamo, 1972). Any means of causing large numbers of neurons to fire synchronously may, in such a brain, be sufficient to induce spike trains (Calvin, 1975). However, in *Papio papio*, the photosensitive baboon, inter-

mittent light stimulation triggers bilateral spike and wave discharges specifically in frontal or frontocentral regions. These discharges may spread initially in the anterior cortical areas and the underlying subcortical region, subsequently to the internal capsule, pons and brain-stem and the discharges may ultimately invade all the deep structures except the rhinencephalon. Thus a definite progression of the discharge is seen and the pathways for the spread of the discharge do not involve the visual cortex. Nevertheless the visual cortex appears to be an important link in the pathway from retina in as much as its removal results in the loss of photosensitivity (*see* Naquet, Catier and Menini, 1975, for review).

In the light of the above it is difficult to synthesize a coherent theoretical viewpoint, although as a preliminary hypothesis it might be fair to suppose that pathways from the occipital cortex are responsible for the generation of generalized activity in hyperexcitable cortex. Such a hypothesis would be quite consistent with the known characteristics of the occipital spike, a precursor of paroxysmal activity that often occurs in the EEG of photosensitive patients (Jeavons and Harding, 1975, p. 94).

The remainder of this paper uses the characteristics that render visual stimuli epileptogenic to make inferences about where and how in the visual system the seizures are triggered. The inferences are based in part on the assumption that the characteristics of the receptive fields of cells in the visual system of the photosensitive patient resemble those of cells recorded in monkey or in some instances in cat. This assumption is warranted in so far as there is no evidence to suggest that the visual system of photosensitive patients is itself abnormal: pattern sensitive patients can have quite normal acuity for gratings at threshold contrast (Soso and Lettich, 1978).

Study 3. Effects of Colour Contrast at Isoluminance

Wilkins *et al.* (1975) found that square-wave gratings composed of alternate red and green stripes failed to elicit paroxysmal activity, whereas a pattern of similar dimensions with black and white stripes (luminance contrast 0·8) readily did so. In 7 patients subsequently tested a similar result has been obtained.

Procedure. A vertical square-wave grating, circular in outline and 24 cm in diameter, with 3 cycles/cm, was produced by juxtaposing alternate strips of red and green matt opaque tape (1/16″ Letratape). The pattern was held against a support in the beam of a projector and had a mean luminance of 200 cd/m^2. Seven patients, K.W., M.V.D.H., M.W., V.L.P., V.D.U., D.E. and H.V.L.D., who were known to be sensitive to gratings with spatial frequencies of 2 and 4 cycles/degree were presented with the coloured pattern at a viewing distance of 57 cm, at which distance it had a spatial frequency of 3 cycles/degree.

Results. No paroxysmal activity was elicited by the coloured pattern, despite an average of 7 presentations per patient (minimum 4), and despite the fact that 4 of the patients were sensitive to black and white gratings with mean luminance 130 cd/m^2 and contrast 0·4. Indeed Patients D.E. and M.V.D.H. were sensitive at luminance levels as low as 20 cd/m^2.

Discussion. The failure of patients to respond to a grating with uniform brightness and strong colour contrast is of interest given the recent evidence for separation of colour and form processing by the visual system (*see* Gregory, 1977).

There is some evidence to suggest that the Y system is not colour coded (Gouras, 1969) and the present results may arguably be cited as evidence consistent with a trigger involving the Y system. Such an interpretation is, however, highly speculative. Red light excites not only red-sensitive cones but also to a lesser extent green-sensitive cones. The converse is true for green light. There is thus a physical limit for the amount of excitation that a colour contrast grating can provide (File and Mollon, 1976) and this limit is doubtless considerably less than that for a grating with brightness contrast (*see* Study 8). The limit may account for the absence of any convulsive response to isoluminant gratings.

Study 4. Checkerboards v. Gratings

Wilkins, Andermann and Ives (1975) created a series of patterns of checks in which the check width remained constant while the height increased. They found that the probability of the pattern inducing paroxysmal EEG activity increased linearly with the logarithm of the check length/width ratio; the more the checks approximated a grating the greater the likelihood of paroxysmal activity. Subsequently a number of studies have shown that gratings are more epileptogenic than checkerboards. In the course of an investigation of the mechanisms of television epilepsy we presented a series of photosensitive patients with horizontal and vertical square-wave gratings (spatial frequency of 2 cycles/degree) and a checkerboard (check width 15′). Both patterns were 11 degrees square in outline and had a luminance of 2000 cd/m^2 and a contrast of about 0·9. They were either stationary, or vibrated through one half-cycle of the pattern at frequencies of 10, 15, 18 and 25 Hz. For the patient sample as a whole, stripes were more epileptogenic (Darby, Binnie, Harding, Jeavons, Stefansson and Wilkins, 1977).

The difference between stripes and checks is also obtained when the checkerboard is orientated obliquely with its diagonals horizontal and vertical (*see* Study 5) suggesting that the orientation of the pattern is not responsible for the difference between stripes and checks. Orientation of the pattern has also been found to play little, if any, role in the function relating probability of paroxysmal activity to check length/width ratio. Patient M.T., who was also the subject of Wilkins, Andermann and Ives' study, was retested one year after the original experiments were performed. On this occasion the patterns though similar in form were circular in outline. They subtended 16 degrees with a check width of 8′ and were orientated obliquely. The patterns were presented at a viewing distance of 57 cm, according to the standard procedure, a total of six times each. The incidence of paroxysmal EEG activity is shown as 'Session 3' in fig. 3 which also includes Wilkins, Andermann and Ives' original data for comparison. The new data are more noisy than those previously obtained, doubtless because of the small number of trials, but the shape of the function is essentially similar.

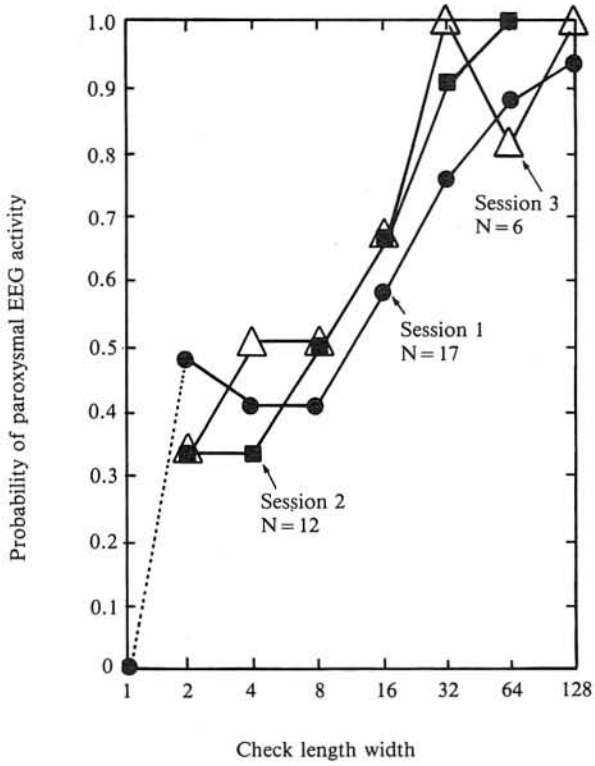

FIG. 3. Probability of paroxysmal EEG activity as a function of check length/width ratio.

Discussion. The increase in the probability of paroxysmal activity with the length of line contour is difficult to interpret in terms of a trigger confined to the LGN where the cells have circular receptive fields, and suggests instead a trigger involving cells with linear receptive fields (Hubel and Wiesel, 1968). Relative to a striped pattern, a checkerboard stimulates such cells ineffectively, but unlike a striped

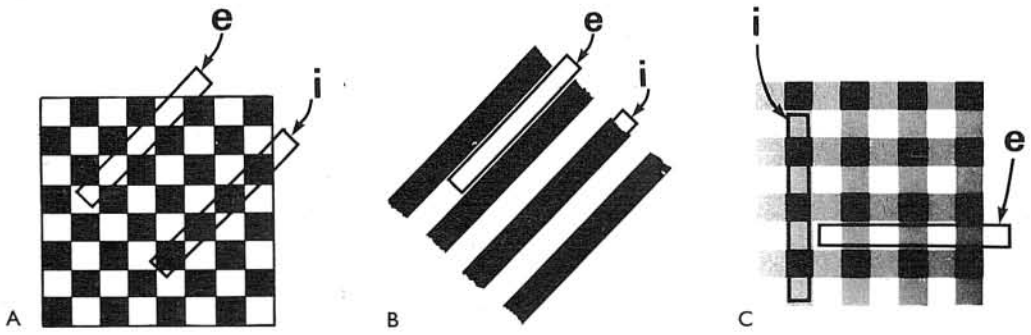

FIG. 4. Stimulation of cells with linear receptive fields and excitatory (e) or inhibitory (i) receptive field centres by A, a checkerboard, B, an oblique square-wave grating and C two superimposed square-wave gratings, one vertical and the other horizontal.

pattern it stimulates cells tuned to a variety of different orientations, particularly those parallel to the diagonals of the checks. Fig. 4A illustrates how a cell with an on-centre and off-surround (e) will be excited by the diagonal of a checkerboard. The mean illumination within the excitatory centre of the cell is greater than that in the surround and so the cell is caused to fire. An exactly analogous process occurs for cells with off-centres (i). The degree of excitation of cells tuned to one particular orientation can never be as great for a checkerboard as for a grating consisting of stripes of similar contrast and appropriate orientation, because in a grating the boundaries of pattern contrast correspond to the borders of the receptive field (*see* fig. 4B). But a grating, unlike a checkerboard, can only excite cells tuned to one particular orientation. Thus a checkerboard differs from a grating in two important respects: first it stimulates cells tuned to a variety of different orientations and second, it stimulates each orientation system relatively ineffectively. The finding that checkerboards and checkerboard-like stimuli were less effective at eliciting paroxysmal activity may have resulted either because cells were stimulated ineffectively or, conceivably, because of some complex 'inhibitory' interaction between cells tuned to different orientations.

To separate the effects of stimulation of several orientations from those of the effectiveness of that stimulation, the fifth study used patterns in which the number of orientations stimulated was allowed to vary while the effectiveness of stimulation in any one particular orientation remained constant.

Study 5. Effects of Mixing Gratings

Patterns were produced by adding to an image of a grating either an image of a diffuse field with the same mean luminance or an image of another grating, similar to the first in every respect except orientation. Fig. 4C illustrates schematically the result of superimposing the images of two orthogonal gratings. Such a stimulus should excite more cells than the stimulus obtained by adding a diffuse field to a grating simply because it contains twice as much modulation of light. As can be seen, the pattern will stimulate cells with linear receptive fields orientated along both a vertical and a horizontal axis. Cells with differently orientated linear receptive fields will not be stimulated so effectively.

Stimuli were produced by two methods. One involved the physical superimposition of the images from two projectors (Experiment (i)). As a result the contrast of the images varied with the ambient illumination. The second method (Experiment (ii)) used a semisilvered mirror to achieve the optical superimposition of the images of two fields, one viewed by transmission through the mirror, the other by reflection from its surface. In both cases the mean luminance of the two component fields was equal.

The two patients who took part in this study were selected on the basis that they were sensitive to patterns in a variety of orientations.

Study 5, Experiment (i)

Method. Patient K.O. was seated in a well-lit room in front of a 25 cm square white card at a viewing distance of 104 cm. Two 35 mm slide projectors matched for luminous intensity were mounted behind the patient so that their images filled the card. Each projector could display a slide of a square-wave grating or a slide containing a neutral density filter with the same average transmittance. When both projectors were brought to focus on the card, one providing a grating and the other a diffuse uniform field, the image of the grating had a spatial frequency of 1·6 cycles/degree, a mean luminance of 90 cd/m^2 and a contrast of 0·2. Two such gratings were used, one horizontal and one vertical. Their effects were compared with those of a third stimulus obtained by overlapping the images of a vertical and a horizontal grating, one from each projector. There was little change in mean luminance at pattern onset or offset.

Twelve series of 3 to 11 presentations, each separated by at least 10 s were given. One stimulus was presented throughout each series and the series alternated between the two superimposed gratings and one or other of the two single gratings chosen at random.

Results. The incidence of paroxysmal EEG activity in response to the vertical grating was 8/19 trials (42 per cent) as compared with 12/22 (54 per cent) in response to the horizontal grating. The incidence in response to the two superimposed gratings was 8/41 trials (19 per cent), significantly lower than for the single gratings ($\chi^2(1) = 6{\cdot}56$, $P < 0{\cdot}02$).

Study 5, Experiment (ii)

Apparatus. A box measuring 30 × 30 × 30 cm contained a diagonal semisilvered mirror positioned so that when the patient looked through an aperture in the front of the box he saw not only the back of the box (visible by light transmitted through the mirror) but also one of the sides (visible by reflection). The two visible surfaces each contained a central circular aperture, 10 cm in diameter, optically superimposed, subtending 15 degrees. A stimulus field mounted 9 cm behind each aperture was illuminated by 10 'festoon' tungsten bulbs. The bulbs were arranged in a ring concentric with the aperture but 4 cm greater in diameter, mounted between the aperture and the stimulus field and thus hidden from view. The two rings were wired in series. Two sheets of polarizer with axes of polarization orthogonal to one another, one across each circular aperture, enabled the two simulus fields to be mixed in varying degrees depending upon the orientation of a third polarizer placed between the patient and the mirror.

Procedure. Ten types of pattern stimuli were presented and they are shown schematically in Table 2.

TABLE 2. INCIDENCE OF PAROXYSMAL EEG ACTIVITY IN RESPONSE TO MIXED PATTERNS

Stimulus	Field 1	Field 2	Incidence of paroxysmal activity	%
a			0/9	0
b			1/9	11
c			1/9	11
d			0/9	0
e			2/9	22
f			5/9	55
g			4/4	100
h			3/5	60
i		Occluded	5/9	55
j		Occluded	0/9	0

Stimuli a–e were produced by a vertical square-wave grating (3·4 cycles/degree, contrast 0·6) in one field, and a similar grating in the other with orientation 90, 45, 22, 11 and 6 degrees to the vertical respectively. For stimuli f, g and h, a vertical, oblique, or horizontal grating was shown in one field, while the other contained a uniform grey patch with the same mean reflectance as the grating. For all the above stimuli (stimuli a–h) the third polarizer was orientated with its axis of polarization at 45 degrees to the other two so that the two fields were mixed in equal proportion. As a result the contrast of the single grating was 0·3. The remaining stimuli (i–j) were produced by orientating the polarizers so that one field was occluded. The other field contained a vertical grating (stimulus i) or an oblique checkerboard with check width 9′ (stimulus j). The use of polarizers ensured that for every stimulus the mean luminance remained constant. Stimulus onset and offset were associated with a considerable change in luminance because the patterns were not illuminated during the interval between presentations.

Patient L.D. acted as subject. After a few initial trials it was established that at a mean luminance of 34 cd/m^2 the patient was sensitive to some patterns and not to others, and this luminance was used for the remainder of the experiment. Presentations lasted a maximum of 10 s and the intertrial interval was approximately 20 s although the patient was given a rest of several minutes between blocks of ten trials. In order to limit the occurrence of generalized spike and wave activity stimuli g and h were omitted halfway through the session.

Results. The incidence of paroxysmal activity for mixed gratings (stimuli a–e) was 4/45 (*see* Table 2). This incidence was significantly lower than that for single gratings, whether full contrast (stimulus i, $P < 0{\cdot}01$, Fisher exact probability test) or reduced contrast (stimuli f–h, $P < 0{\cdot}001$, Fisher exact probability test). The checkerboard was significantly less epileptogenic than the single full-contrast gratings ($P < 0{\cdot}05$, Fisher exact probability test), confirming the results obtained earlier with patient M.T.

Discussion. Even though the superimposed gratings modulated twice as much light as single gratings they were less epileptogenic. This finding suggests the hypothesis that cells with orientation selectivity are involved in the triggering of paroxysmal activity. Such a hypothesis would be quite consistent with the finding of Study 2 that selective sensitivity to some grating orientations is rare and possibly attributable to astigmatism; presumably large numbers of orientationally selective cells with a wide variety of orientation tunings are involved.

The origin of the apparent 'inhibitory' interaction between the two gratings is difficult to interpret. While it is true that most intracortical connections are inhibitory, recent evidence would suggest that this inhibition is maximal when the component orientations of a complex stimulus are similar (Fries, Albus and Creutzfeldt, 1977). No effects of similarity were apparent in Experiment (ii).

Whatever the interpretation of the 'inhibitory' interaction, the results of the present study indicate that the difference between checks and gratings discussed in Study 4 is at least partly due to the fact that a checkerboard stimulates cells tuned to a variety of different orientations. The effects of binocular rivalry, now to be described, may also be due to the different component orientations of a pattern presented in rivalry.

Study 6. Effects of Binocular Rivalry

Wilkins *et al.* (1975) used a stereoscope to present horizontal or vertical gratings separately to the two eyes. They found that the probability of paroxysmal activity was greater when both eyes saw similarly orientated gratings than when the orientations were different for each eye. This finding has now been replicated with two patients, D.E. and H.V.D.

Procedure. A stereoscope with a binocular field subtending 15 degrees was used to present prints of square-wave gratings with a spatial frequency of 2 cycles/degree and mean luminance of approximately 20 cd/m^2. Horizontal and vertical gratings were presented to the right and left eyes in all four of the possible combinations, according to the standard procedure. Maximum presentation time was 12 s.

TABLE 3. INCIDENCE OF PAROXYSMAL EEG ACTIVITY IN RESPONSE TO STEREOSCOPIC PATTERNS

Left eye	*Right eye*	*D.E.*	*H.V.D.*
▥	▥	5/9 (55%)	8/14 (57%)
▤	▤	8/8 (100%)	15/19 (79%)
▥	▤	2/7 (29%)	8/16 (50%)
▤	▥	4/9 (44%)	7/18 (39%)

Results. Table 3 shows the incidence of paroxysmal activity. Patterns that fused were significantly more epileptogenic than those that were in rivalry ($P < 0{\cdot}05$ in both cases, Fisher exact probability tests).

Discussion. Patterns that fuse in binocular vision are more epileptogenic than those that do not. This effect could be due to the greater stimulation of binocular cells by patterns that fuse (Wilkins *et al.*, 1975) but it is also possible that an interaction between the two orientations reduced patients' sensitivity in a manner analogous to that of the previous study (Study 5), quite independently of any binocular effect. Whichever was the case, the results are difficult to reconcile with a trigger confined to the LGN because geniculate cells are monocular and they are not orientation selective. Cells in the superior colliculus are binocular, but few are orientation selective (Goldberg and Wurtz, 1972). It is only in the cortex that the majority of cells are both binocular and orientation selective. It would therefore be interesting to assess the possible role of binocular cells independently of the confounding effects of orientation. For this reason the following study investigated the effects of interocular phase on the response to diffuse flicker.

Study 7. Effects of Counterphase Interocular Flicker

As Sherrington (1904) observed 'Ordinarily when the binocular gaze is directed upon an object intermittently illuminated, successive phases of illumination affect the corresponding areas of the two retinae synchronously. The question rises, will the rate of repetition necessary for visual fusion of the successive light phases be altered if those phases fall upon corresponding retinal points not synchronously

but alternately?' He found that 'the light phases at the one eye practically do not . . . interfere or combine at all with the coincident dark phases at the other' and concluded that the 'right and left corresponding retino-cerebral points do not when tested by flicker reactions behave as though combined or conjugate to a single mechanism'. Since the majority of pattern-sensitive patients are sensitive not only to pattern but also to a diffuse flickering field (IPS), Sherrington's technique was applied to the induction of paroxysmal EEG activity by flicker in order to assess the contribution of monocular and binocular mechanisms. The probability of paroxysmal activity was plotted as a function of (temporal) frequency and the peak of the resulting 'tuning curve' for monocular flicker compared with that for alternate stimulation of the two eyes.

Apparatus. The light from a frosted 100W tungsten filament bulb passed through a system of prisms and lenses and was brought into Maxwellian view at two lenses, one for each eye. This created a diffuse binocular 8 degree field. The field was bisected by horizontal and vertical lines, 0·6 degrees wide, that formed a fixation cross. Due to the large surface area of the light source, the field remained uniformly illuminated at all head positions permitted by a face mask, and so a bite bar was not needed.

The light path was interrupted near its source by a sectored disc mounted in a plane orthogonal to the light path. The disc rotated about a central axle, belt-driven by an electrostatically screened 6V DC motor at a speed that could be controlled by a rheostat and measured from a magnetic tachometer attached to the axle.

The surface of the disc was covered by a neutral-density filter with a transmission equivalent to that of two type HN 32 polarizers (Polarizers UK Limited) with orthogonal axes of polarization. In two 6 degree sectors of the disc, spaced 180 degrees apart, the neutral filter was replaced by a polarizer. The axes of polarization of the four polarizers were identical. With suitably orientated polarizers placed in front of each eye the disc could be made to produce alternate flashes first to one eye and then the other. The flash duration was, of course, determined by the speed of rotation of the sectored disc, but the pulse to cycle fraction (duty cycle) of stimulation remained constant at 6/180 = 3·3 per cent.

The disc could be slid in and out of the light path whilst it rotated, and when out of the beam its place was taken by a static neutral density filter with approximately the same average transmission as provided by the rotating disc. This allowed sudden onset of modulation with little change in time-averaged luminance. The luminance of the field was 2000 cd/m² for the duration of the flash and 25 cd/m² otherwise. The flicker frequency was sufficient to render the use of an artificial pupil unnecessary. The detail of the alternate eye condition is summarized in fig. 5. The monocular conditions were identical but for the occlusion of one eye.

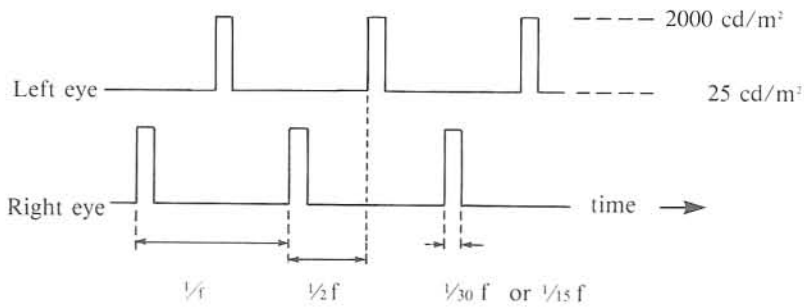

FIG. 5. Parameters of flicker stimulation at frequency f in the alternate eye condition of Study 7.

Procedure. Patient M.T. took part in the study. Like the majority of pattern-sensitive patients she was sensitive not only to patterns but also to diffuse flicker (IPS). She was seated so that her head rested in the face mask and was instructed to look at the centre of the cross. The rotating disc was then slid into the light beam causing the diffuse field to be temporally modulated with a frequency and interocular phase selected according to a schedule in which a 10 s presentation of flicker (terminated if paroxysmal EEG activity appeared) was followed by an interval of at least 20 s. The presentations were grouped so that all the frequencies were tested in random order either once or twice within a block and the patient was allowed to rest between blocks. Blocks of trials under the three conditions of stimulation were ordered within a testing session so that any effects of practice or sensitization would be equated for the three conditions.

The data were collected on three days. On the first two days the flicker had a duty cycle of 3·3 per cent (measured at one eye). On day 1 the data for right eye, left eye and alternate eyes were collected; on day 2 further observations were collected for the alternate eye condition. On the third day the disc was replaced by one with four 6 degree sectors spaced 90 degrees apart, providing a 6·6 per cent duty cycle. Further data were then collected for all three conditions of presentation.

TABLE 4. INCIDENCE OF PAROXYSMAL EEG ACTIVITY AS A FUNCTION OF THE FREQUENCY AND DUTY CYCLE OF MONOCULAR FLICKER AND ALTERNATE INTEROCULAR FLICKER

Eye	*Duty cycle* (%)	*Flash frequency at one eye (Hz)*							
		5	*7·5*	*10*	*15*	*20*	*25*	*30*	*40*
Right	3·3	—	—	0/5	2/5	2/3	—	1/4	—
	6·6	—	—	0/5	1/5	2/5	3/5	1/5	0/5
Left	3·3	—	—	0/4	1/4	5/5	—	4/5	0/4
	6·6	—	—	0/5	1/5	5/5	4/5	3/5	0/5
Alternate	3·3	0/12	1/13	2/25	15/19	7/17	—	—	—
	6·6	—	—	2/10	6/10	5/10	2/10	0/10	—

Results. The incidence of paroxysmal EEG activity under the various conditions of flicker frequency, duty cycle and eye stimulated are shown in Table 4. It can be seen that, for the values used, the effects of duty cycle are negligible compared with those of frequency. For this reason the data for the two conditions of duty cycle have been combined to form the data points shown in fig. 6. The curves in this figure were obtained by fitting the probability of paroxysmal activity at a given frequency, P(A|f), by a three-parameter logit-linear model

$$\text{logit } P(A|f) = \alpha(f-\mu)^2+\gamma$$

where μ is the frequency at which the probability of paroxysmal activity is greatest, α determines the 'sharpness' of the peak and γ the overall height of the curve. The model is a natural extension of standard dosage-response curve-fitting methods (Nimmo-Smith, in preparation).

Maximum likelihood solutions were obtained for different values of μ, allowing the other two parameters, α and γ, to attain their optimum. Iterative techniques

were then used to obtain the optimum value of μ. In other words the value of μ giving the best fit regardless of the other parameters of the model was obtained (Nimmo-Smith, in preparation).

The values of μ for monocular stimulation were very similar: 22·4 Hz for the right eye (95 per cent confidence limits: 19·5, 26·0) and 23·5 Hz for the left (confidence limits: 22·5, 25·5). The value of μ for stimulation of alternate eyes was significantly lower: 17·1 Hz (confidence limits: 15·5, 18·5). Lest it be argued that the above curve-fitting procedures beg too many questions about the physiological nature of the data they describe, it is worth noting that the incidences of paroxysmal activity in response to monocular stimulation and stimulation of alternate eyes differ significantly at the 15, 20, 25 and 30 Hz points ($P < 0{\cdot}05$, Fisher exact probability tests).

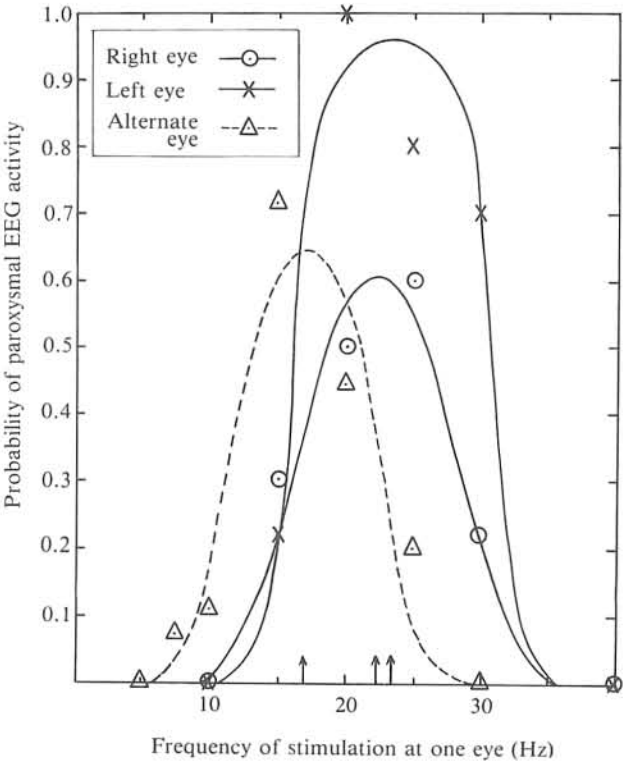

FIG. 6. Probability of paroxysmal EEG activity as a function of the frequency of monocular flicker and alternate interocular flicker.

Discussion. The results of Study 7 clearly implicate binocular interaction in the induction of paroxysmal activity by flicker, an interaction that occurs independently of orientation. If there were no binocular interaction the peak of the tuning curve for monocular and alternate eye stimulation should have been identical. If the

interaction were complete the peak for alternate eye stimulation should have been half that for monocular (that is, about 11·5 Hz). The result in fact obtained is evidence for a partial interaction between the two eyes, as would occur if populations of (predominantly) monocular and (predominantly) binocular cells were stimulated. Simple models of the possible interaction between monocular and binocular components would predict a bimodal tuning curve for alternate eye stimulation. The data are insufficient to distinguish a bimodal from a unimodal curve.

If the mechanisms for the induction of paroxysmal activity by flicker are similar to those of pattern induction, and there is at present no reason to suppose that they are not, the findings of the present experiment may be combined with those of the other experiments described so far. The picture that obtains is entirely consistent with the hypothesis of a seizure trigger in the striate cortex, where the majority of cells are orientation selective and have a degree of binocularity. Neurons in the LGN are monocular and although there is evidence of some binocular interaction in the cat (*see* Sanderson, Darian-Smith and Bishop, 1969) which may arise from corticofugal fibres (Schmielau and Singer, 1977) the interaction is not extensive. It is therefore unlikely that a trigger confined to the LGN could have produced the considerable interaction between the two eyes observed in fig. 6. A subcortical pathway from LGN to the diffuse thalamic system is therefore unlikely.

The next experiments attempt to address the question as to how the probability of paroxysmal EEG activity relates to the general level of excitation that may be assumed to be occurring as a result of pattern stimulation.

Study 8. Effects of Brightness Contrast

In cat cortex the rate at which cells fire is determined by the contrast across the boundaries of the receptive fields. The rate of firing increases with increasing contrast up to contrasts of between 0·1 and 0·3, at which most cells have either saturated or have begun to do so (D. J. Tolhurst, J. A. Movshon and I. D. Thompson, personal communication). If the probability of paroxysmal activity shows a similar relationship to contrast it might be reasonable to hypothesise a direct relationship between the general level of activation in the cortex and the paroxysmal activity that results.

Study 8, Experiment (i)

Procedure. Two projectors were mounted side by side so that their beams were coincident on a distant screen. One projector contained a slide of a vertical square-wave grating; the other was used to provide a diffuse uniform field. A mask with a central circular aperture was mounted parallel to the object plane of each projector but slightly displaced so that the superimposed images of the grating and field had a common but indistinct circular boundary. The beams from the projectors each passed through a polarizer, and the two polarizers were mounted rigidly with orthogonal axes of polarization. The beams emerging from the polarizers were adjusted to have the same luminous flux. The beams then passed through different sections of a large disc of polarizer that could be rotated in a plane perpendicular to

the beams. As it rotated the angle between the axes of polarization of the disc and the two stationary polarizers changed by an exactly equivalent amount, the intensity of one beam being reduced as the other increased. Thus by rotating the disc the contrast of the image of the grating on the screen could be manipulated whilst the mean luminance remained constant.

When the polarizer was orientated to provide an image of maximum contrast, the actual contrast of the image was measured by taking several readings with a spot photometer (Salford Electrical Instruments Ltd). Lower contrast levels produced by rotating the polarizers were calculated on the basis of the theoretical reduction in maximum contrast. Contrast values are therefore limited in accuracy to ± 5 per cent.

The grating had a mean luminance of 55 cd/m^2, a spatial frequency of 2 cycles/degree and a total subtense of approximately 35 degrees. Patient M.V.D.H. was seated 57 cm from the screen and instructed to fixate a 1 cm black square attached to the screen at the centre of the concentric circular overlapping images from the two projectors. The gratings were presented by rapidly increasing the contrast from zero to one of the four values: 0·08, 0·28, 0·41 and 0·52. Pattern presentations were not, therefore, accompanied by any change in mean luminance.

Results. For the four levels of contrast compared (0·08, 0·28, 0·41 and 0·52) the incidence of paroxysmal EEG activity was 0/5 (0 per cent), 2/16 (13 per cent), 9/13 (69 per cent) and 13/14 (93 per cent) trials respectively. The results are shown in fig. 7.

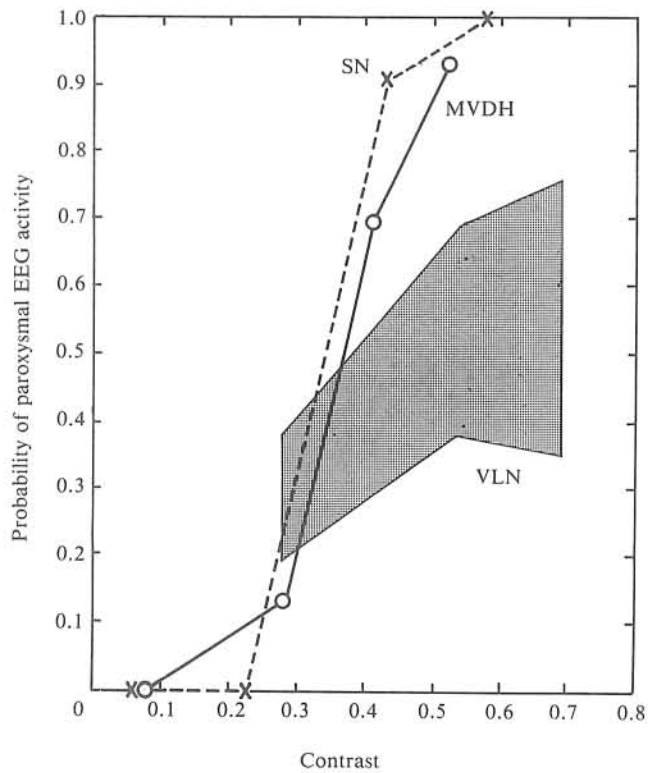

FIG. 7. Probability of paroxysmal EEG activity as a function of the contrast of a square-wave grating.

Study 8, Experiment (ii)

Procedure. The procedure was similar to that for Experiment (i) except that the following levels of contrast were compared: 0·28, 0·54 and 0·69. Patient V.L.N. took part.

Results. The paroxysmal activity was difficult to assess. The proportion of unequivocally positive trials was 3/16 (19 per cent), 5/13 (38 per cent), 6/17 (35 per cent) for the three levels of contrast respectively. If equivocal trials are included as positive the proportions are 6/16 (38 per cent), 9/13 (69 per cent) and 13/17 (76 per cent). The shaded area in fig. 7 is bounded by these proportions.

Study 8, Experiment (iii)

Procedure. The grating was viewed from a distance of 114 cm at which distance it had a spatial frequency of 4 cycles/degree and subtended about 16 degrees. The mean luminance was 100 cd/m^2. Patient S.N. took part in the experiment. The following contrasts were compared using the usual randomized procedure: 0·06, 0·23, 0·43 and 0·58.

Results. The incidence of paroxysmal activity was 0/10, 0/11, 10/11 and 11/11 for the four levels of contrast respectively.

Discussion. Fig. 7 provides a summary of the results of the three experiments. It can be seen that the increase in the probability of paroxysmal activity shows a very steep ascent for values near 0·3. This sudden ascent does not mirror the progressive increase in firing rate with increasing contrast observed in cat cortex by D. J. Tolhurst, J. A. Movshon and I. D. Thompson (personal communication). If the paroxysmal activity is triggered in the cortex, and if the response of the human cortex to pattern contrast is similar to the cat's, then the present results would suggest that the probability of paroxysmal activity is not directly related to the general level of excitation. Rather the probability appears to increase abruptly only when the majority of cortical cells are firing at or near saturation. These are tentative inferences and further evidence is desirable. A more direct way to examine the effects of the level of excitation was employed in the next study in which the number of cells stimulated was varied by manipulating pattern size.

Study 9. Effects of Pattern Size

Procedure. Prints of vertical square-wave gratings were prepared with a spatial frequency of 2 cycles/cm, contrast 0·78, circular in outline with radii of 2, 3, 4·5, 6, 8, 10, 12·5, 15 and 24 cm. A red fixation point 1 mm in diameter was placed at the centre of each pattern, on the boundary between a black and a white stripe. The patterns were mounted on grey rods and could be placed at the centre of a vertical grey screen which had the same mean reflectance as the pattern. The screen was illuminated by two projectors mounted either side of the patient and the patterns and screen had a mean luminance of 600 cd/m^2. The patient was usually seated at a distance of 57 cm from the screen so that the grating had a spatial frequency of 2 cycles/degree. The patients were instructed to fixate the red dot when the pattern was placed before them. Only one patient (H.V.D.) had difficulty complying with the instructions. All patients were observed during the presentation of the patterns, and trials accompanied by an obvious deviation of gaze were eliminated. The patterns were presented in ascending order of size until paroxysmal EEG activity appeared, and patterns near the threshold size were then repeatedly presented in random order. Maximum presentation time was 10 s with a minimum interval between presentations of 10 s.

Results. Figure 8 shows the way in which the probability of paroxysmal activity varied with the size of pattern. The mean number of observations per point averaged 10 with a minimum of 7. Points connected by a broken line were obtained using patterns with a spatial frequency of 4 cycles/degree. In the case of the most sensitive patient (D.E.) the viewing distance was increased to 114 cm because at 57 cm there were no patterns to which she failed to respond. In the case of patient M.W. the 4 cycles/degree point was obtained at a viewing distance of 57 cm using a 4 cycles/cm pattern. (Note that the 2 cycles/degree and 4 cycles/degree patterns with a radius of 2 degrees contained four and eight cycles respectively; Kelly, 1975.)

One patient, H.V.D., was tested on two occasions. On one occasion the resulting EEG contained spontaneous paroxysmal EEG activity (H.V.D. 1); on the other it did not (H.V.D. 2). Patient G.F. also had spontaneous paroxysmal activity. In both cases the incidence of this activity indicated that in a period of 10 s duration (the presentation period) the probability of observing paroxysmal activity was about 0·3.

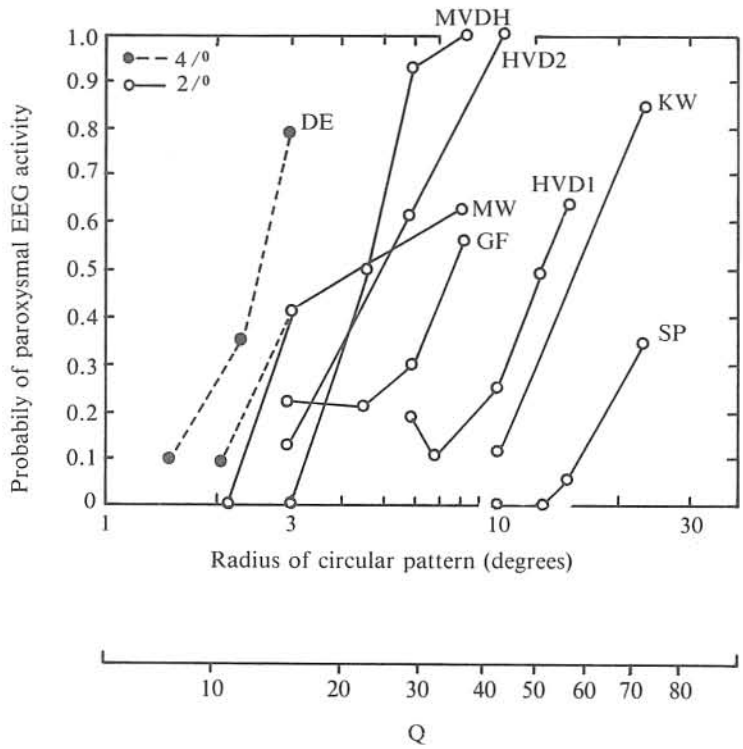

FIG. 8. Probability of paroxysmal EEG activity as a function of the subtense of a square-wave grating, contrast 0·78, mean luminance 600 cd/m², spatial frequency 2 or 4 cycles/degree, as shown.

Discussion. Drasdo (1977) has calculated the percentage surface area of striate cortex (Q) corresponding to a concentric region of visual space. He finds

$$Q = 100\,(1 - \exp\,(-0{\cdot}0574\theta))$$

where θ is the angular radius. Since the density of cortex is uniform (Daniel and Whitteridge, 1961), Q may be taken to be the proportion of cortical cells available for analysis of the area of the visual field determined by θ. The scale for Q is shown beneath that for pattern radius in fig. 8. Any pattern will stimulate a certain proportion of the cells available for the area of visual field that it covers. The proportion of the available cells that are actually stimulated will vary with attributes of the pattern such as its spatial frequency. A 2 cycles/degree grating will not stimulate the same proportion of cells in all areas of the visual field given the increase in receptive field size with increasing eccentricity. If the data in fig. 8 are replotted against Q the curves decrease in slope as the x-intercept increases. This may be interpreted as indicating that the probability with which paroxysmal activity is evoked by a pattern is lawfully related to the number of cells that the pattern activates. The decrease in the slope of the curves with increasing intercept may be attributed to a reduction in the proportion of available cells actually stimulated by a 2 cycles/degree pattern as more of the periphery of the visual field is involved. This being the case, the simplest interpretation of the present data would be that paroxysmal activity occurs when a given number of visual cells are activated, and subsequently increases in probability with the number of cells activated in excess of this threshold.

If the probability of paroxysmal activity is indeed a simple function of the number of cells firing in excess of threshold it should not matter which areas of striate cortex are stimulated. An annular grating should be as effective as a complete grating provided it stimulates the same number of cells. Experiments along these lines are being conducted at the time of writing and preliminary findings suggest that the probability of paroxysmal activity is indeed independent of retinal location stimulated.

The results of Study 9 are preliminary in many respects. For a meaningful comparison of slopes more data points on each curve are required. However, the data are sufficient to demonstrate three important facts:

(1) The increase in the probability of paroxysmal activity with increasing pattern size is extremely steep.

(2) Patients have very different curves. This point is of considerable interest given the remarkable degree of consistency between patients as regards the effects of spatial frequency, colour contrast, checkerboards, binocular rivalry and brightness contrast. It suggests that whereas the manipulations involved in the majority of experiments described in this paper affect large numbers of neurons, manipulations of pattern size affect relatively few.

(3) Large patterns may be necessary to detect pattern sensitivity. It will be suggested elsewhere (Wilkins, Darby and Binnie, in preparation) that the routine

testing for pattern sensitivity may be of clinical value in the assessment of patients referred with suspected epilepsy. There are three grounds for supporting this position. First, some 50 per cent of patients sensitive to IPS are also sensitive to patterns; secondly, pattern sensitivity cannot reliably be determined from characteristics of the response to IPS; thirdly, a pattern-sensitive patient is liable to attacks induced by the large number of striped patterns in the modern urban environment. It might be argued that a pattern subtending 48 degrees has no counterpart in the normal environment and is therefore an unnecessarily provocative stimulus with which to assess sensitivity to environmental pattern. Such an argument ignores the fluctuations in a patient's sensitivity that can occur (*see* H.V.D., fig. 8).

The differences between patients have a theoretical significance in terms of the numbers of neurons needing to be excited in order for paroxysmal activity to occur. The use of patterns with a variety of sizes may therefore provide a useful model for assessing the effects of anticonvulsants on photosensitivity.

GENERAL DISCUSSION

Wilkins, Andermann and Ives (1975), in their discussion of the nature and locus of the trigger mechanism in pattern-sensitive epilepsy, concluded that seizures appeared to be triggered in the striate cortex, possibly by the firing of complex cells. The results of the present series of studies have replicated their findings with other pattern-sensitive patients, and provided further data consistent with the notion of a cortical locus for the trigger mechanism. The results do not, however, rule out a trigger in the superior colliculus.

Wilkins *et al.* used the evidence for binocular involvement in the trigger mechanism to argue that binocular neurons (for example, complex cells) were involved. This hypothesis is still tenable but, given the present evidence that the trigger arises from the mass action of cells, a more parsimonious hypothesis is simply that paroxysmal EEG activity arises when neural activation reaches a threshold level; the activation resulting from cells of a wide variety of types. The mass action of cells with varying degrees of binocularity, such as are known to occur in the striate cortex, some responding more to one eye, some more to the other, would give effects that could not, on the basis of present evidence, be distinguished from those of predominantly binocular cells.

Given the present evidence for mass action it is intriguing to speculate whether the mass action occurs within orientation columns or between them. Recent evidence from penicillin foci in cat cortex would suggest that the action is confined to cells within a column (Gabor and Scobey, 1977).

The relation between flicker-induced and pattern-induced paroxysmal activity appears to be a close one. Patients who are more sensitive to one form of stimulation are more sensitive to the other (Wilkins, Darby and Binnie, in preparation). It is quite possible that intermittent temporal stimulation of retinal cells by the

microsaccades that occur during fixation may be necessary for patterns to induce paroxysmal activity; such movements are certainly necessary for continuous form perception (Riggs, Ratliff, Cornsweet and Cornsweet, 1953). This is not to say that intermittent stimulation of the retina is a sufficient explanation of the trigger mechanism: the seizure discharge is most unlikely to occur solely as the result of abnormal neural activity at the level of the retina (Green, 1969). Whatever the role of such retinal intermittence, it cannot impair the inference made from Study 7 which, in implicating a considerable degree of binocular interaction in the seizure trigger independently of any possible contribution from eye movements, makes a seizure trigger confined to the lateral geniculate nucleus unlikely. In the present paper no attempt has been made to disentangle spatial from temporal factors in the induction of paroxysmal activity by patterns. It remains to be seen whether spatial attributes alone are sufficient.

SUMMARY

The capacity of striped patterns (square-wave gratings) to induce paroxysmal EEG activity in a group of pattern-sensitive epileptic patients is shown to depend on:

1. The spatial frequency of the pattern. The optimum spatial frequency lies between 1 and 4 cycles/degree in every patient tested.

2. The orientation of the pattern. Although, for the patient group as a whole, no one orientation is consistently more likely to induce paroxysmal activity than any other, the responses of individual patients can show marked orientation selectivity.

3. The brightness contrast of the pattern. The probability of paroxysmal EEG activity increases dramatically as contrast is increased from 0·2 to 0·4. Red/green gratings at isoluminance fail to induce paroxysmal activity.

4. The size of the pattern. There is considerable variation between patients in the subtense of a centrally-fixated circular pattern necessary to induce paroxysmal activity with a given probability. However, for every patient an increase in the probability of paroxysmal activity from near zero to near unity is effected by an increase in the angular subtense of the pattern by a factor of two.

Patterns other than square-wave gratings are capable of inducing paroxysmal activity but, in general, patterns that stimulate more than one orientation system are less epileptogenic.

The above findings are compatible with the hypothesis of a seizure trigger in the striate cortex and are incompatible with a trigger confined to the lateral geniculate nucleus of the thalamus. Further evidence against a geniculate trigger is obtained from an investigation of the response of a pattern-sensitive patient to a diffuse (unpatterned) flickering field in which it is shown that the effects of counter-phase interocular flicker implicate binocular mechanisms.

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