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INTERHEMISPHERIC DIFFERENCES IN PHOTOSENSITIVE EPILEPSY. I. PATTERN SENSITIVITY THRESHOLDS [1]

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Until recently it was generally held that in photosensitive epilepsy discharges are set up in diencephalic structures by direct subcortical inputs (Bickford et al. 1953). When discharges are induced by pattern, however, binocularly innervated orientation-specific units, with complex receptive fields are implicated (Wilkins et al. 1979, 1980). Such units are probably confined to the visual cortex. The fact that cells of this type are involved in triggering the discharges does not necessarily mean that they are themselves the site of origin of epileptiform activity: the visual cortex may function as a relay station, the discharges being set up in thalamo-cortical systems by corticofugal impulses. It is therefore of interest that intermittent photic stimulation can often produce occipital spikes before the onset of generalised discharges (Jeavons and Harding 1975), and that when such discharges are suppressed by sodium valproate focal post-central activity may remain (Binnie et al. 1980). Further evidence for a primary epileptic process located in the visual areas is provided by the following observations that pattern stimulation in the upper, lower and lateral visual fields can produce focal posterior discharges with topography corresponding to the representation of the visual fields in the visual cortex.

Methods

During a 9 month period 57 photosensitive patients were seen in the EEG department of the Instituut voor Epilepsiebestrijding. The criterion of photosensitivity was that intermittent photic stimulation (IPS) elicited at least once a classical generalised photoconvulsive response (Bickford et al. 1952) which outlasted the stimulus (Reilly and Peters 1973). The characteristics of the intermittent light and the stimulation procedure are detailed elsewhere (Binnie et al. 1981). Forty-one of the patients were pattern-sensitive, but, given the requirements of adequate sensitivity, the absence of substantial spontaneous epileptiform activity, good cooperation, and willingness to give informed consent, only 15 participated in the present investigation. All but one of the patients were taking anticonvulsant medication.

Printed patterns of stripes (gratings with a square-wave luminance profile, spatial frequency 2 c/cm, contrast 0.7) were viewed at a distance of 0.57 m. The patterns were circular in outline and bore a central red fixation point (2 mm diameter). Each pattern was mounted on a grey rod and held against a grey screen, 0.6 m square, which was diffusely illuminated by fluorescent tubes run from a 20 kHz power supply. The mean reflectance of the patterns matched that of the screen, and both screen and patterns had a mean luminance of approximately 300 cd/m^2.

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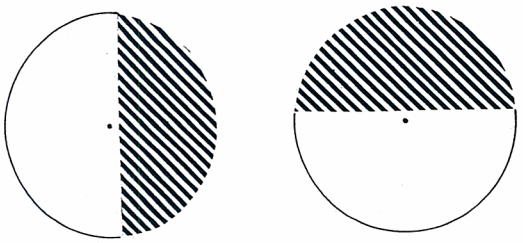

Fig. 1. Schematic diagram of the hemifield patterns, showing the central fixation point.

Patterns were presented for 10 sec or until paroxysmal activity appeared. Commencing with a radius of 3° of visual angle pattern size was increased on successive presentations until paroxysmal activity was consistently elicited. Discs of similar radius were then used to present hemifield patterns. These discs were patterned on one side of a diagonal and grey on the other, with a 5 mm (0.5°) gap between the edge of the pattern and the central fixation point (see Fig. 1). The total number of presentations of pattern or photic stimulation that each patient received varied from 12 to 65. On the rare occasions when patients failed to maintain fixation the trial was discounted.

Results

Figs. 2, 3, 4 and 5 show examples from one patient of the distribution of paroxysmal epi-

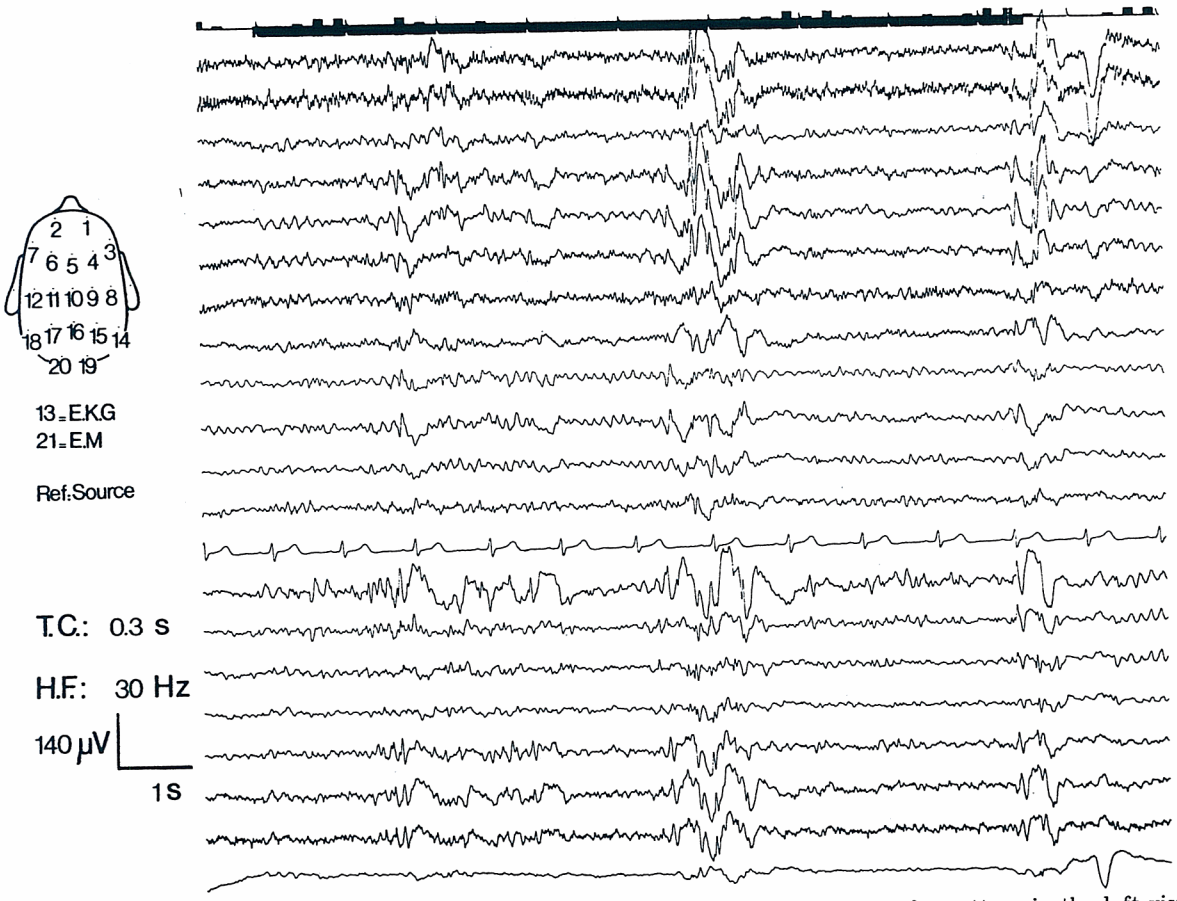

Fig. 2. An example of the paroxysmal activity recorded during the presentation of a pattern in the left visual field. The top channel indicates the period for which the pattern was presented. Initially the discharges are of maximum amplitude at the right posterior temporal electrode; later they become secondarily generalised but remain markedly asymmetrical at the back of the head.

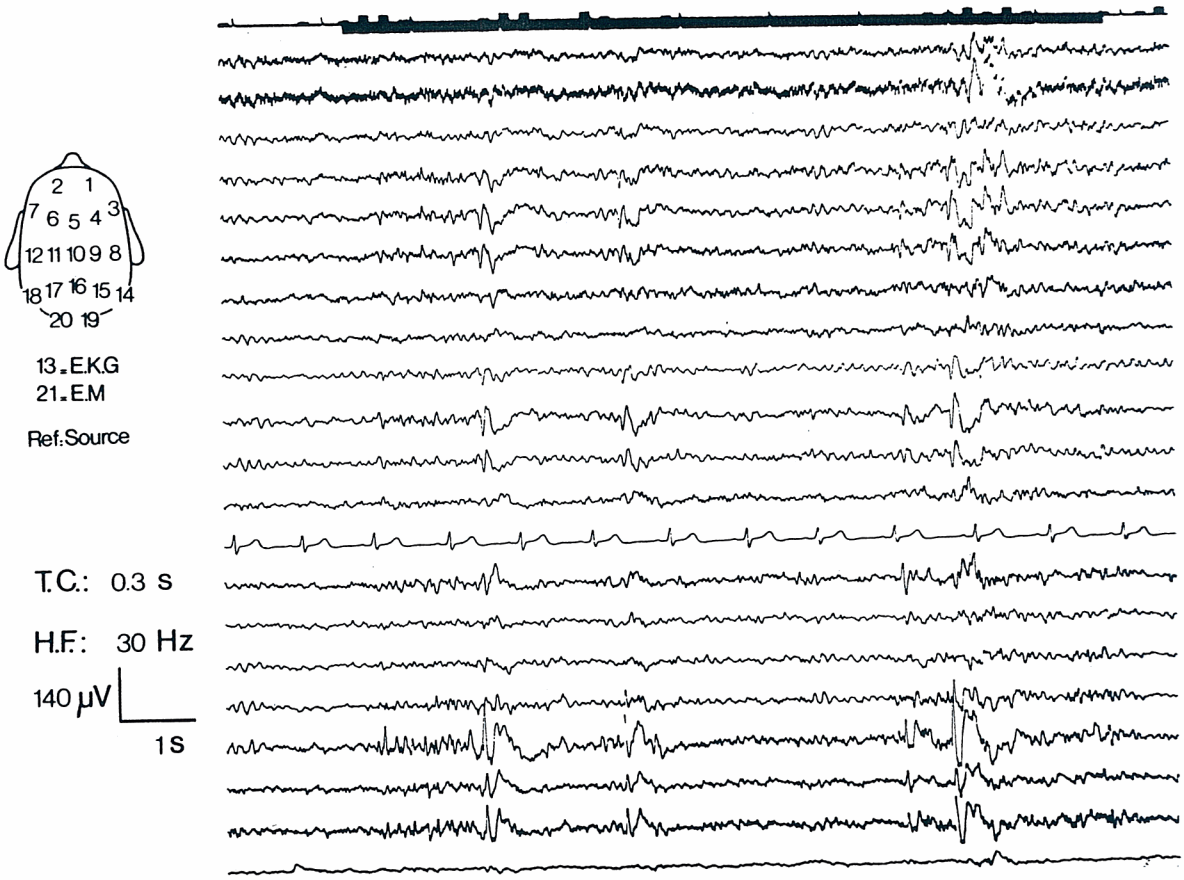

Fig. 3. An example of the paroxysmal activity recorded during the presentation of a pattern in the right visual field.

leptiform activity elicited by a pattern in the left and right, and upper and lower fields respectively. In all the examples either source or common average reference was used, as indicated. In the latter case all the standard electrodes contributed to the average. It will be noted that the activity is maximal contralateral to a unilateral stimulus, and that there is a difference in the vertical distribution of postcentral activity in response to stimulation of the upper and lower fields. The distribution detailed in Figs. 2, 3, 4 and 5 was consistently and repeatedly obtained. When the tracings of this patient were rated independently the dissociation between the responses to the 4 types of stimulus was highly significant (Fisher Exact Probability tests, $P < 0.01$).

Stimulation of the upper and lower fields induced responses in only 9 of the 15 patients. Only 2 of the 9 demonstrated a dissociation similar to that illustrated in the first 6 channels of Figs. 4 and 5. By way of contrast, responses to patterns in the lateral half-fields were obtained in every patient, and the majority of patients demonstrated the contralateral responses exemplified in Figs. 2 and 3. There was a negative association between the side of the stimulus and the side of the response in 13 patients, which reached statistical significance in 8 (Fisher Exact Probability tests). In 7 patients paroxysmal activity was elicited on at least one occasion over the hemisphere ipsilateral to the stimulus, although the association of a lateralised stimu-

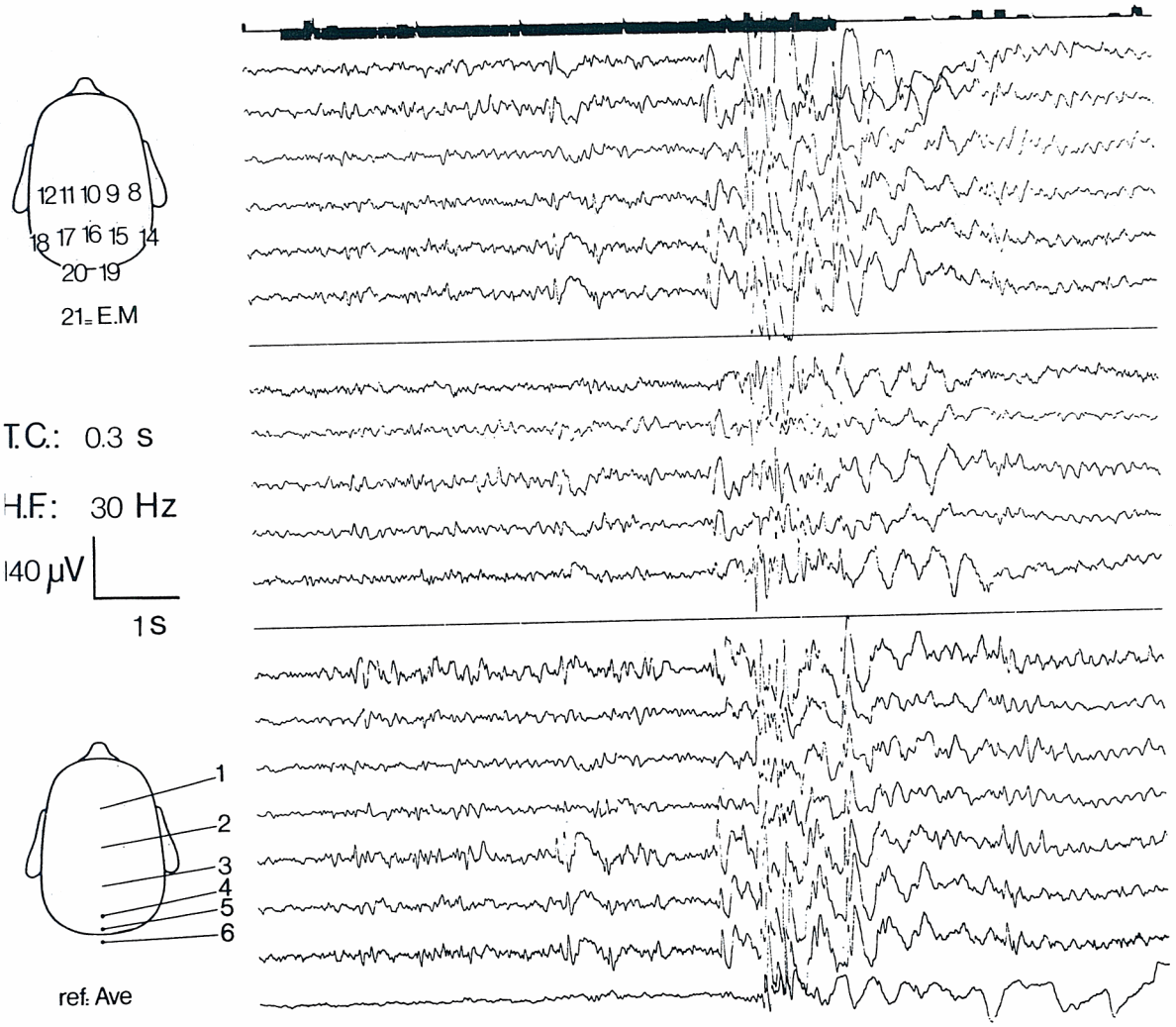

Fig. 4. An example of the paroxysmal activity recorded during the presentation of a pattern in the upper visual field. The first 6 channels include the activity recorded from non-standard midline electrodes in parieto-occipital and occipital regions, and over the inion.

lus with an ipsilateral rather than contralateral response was significant in only one patient.

The probability of a paroxysmal response was not always equal in the two lateral half-fields: sometimes a response could be readily elicited by a pattern in one half-field, but not by a pattern of similar size in the other. This asymmetry in threshold was determined from the association in the 2 × 2 contingency table relating the two categories of paroxysmal response (present, absent) and the two visual hemifields (left, right). The association was measured by the coefficient of association V, advocated by Kendall and Stuart (1967, p. 539) for contingency tables with an empty cell. The value of V varied from −1 when stimulation of the right field was effective and stimulation of the left field was not, to +1 when the reverse was the case.

Fig. 6 shows a scatterplot in which each point (circle or square, filled or unfilled) represents a patient, and the position of the

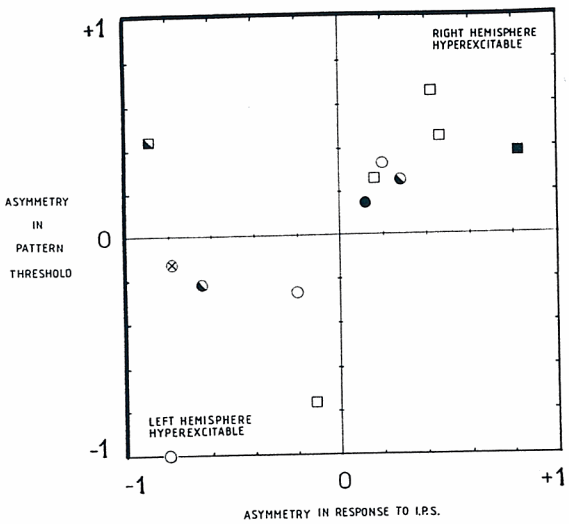

Fig. 6. A scatterplot relating the asymmetry in pattern threshold to asymmetry in response to diffuse IPS. See text for a description of the measures of asymmetry. Each point represents a patient. The circles represent patients in whom only contralateral activity was seen in response to a unilateral pattern. The squares represent patients in whom an ipsilateral response occurred on at least one occasion. Patients with a diagnosis of primary generalised epilepsy are represented by open points, those with secondary generalised by filled points, and those with a partial epilepsy by half-filled points. The patient for whom the diagnosis was uncertain is represented by a point filled with a cross.

varies from −1 for a consistent left hemispheric preponderance to +1 for a right, with a value of zero when all responses are symmetrical, or an equal number are left- and right-maximal. The choice of index can be justified on the basis that the classification of a response as symmetrical may have represented a failure to detect an underlying asymmetry. The index was unaffected by the total number of responses, over the range obtained.

Fig. 6 shows the positive correlation ($rs = 0.59$, $P < 0.05$) between the two measures of hemispheric asymmetry (inequality of pattern threshold, and lateralisation of paroxysmal response to diffuse IPS). The correlation provides support for the argument that in some patients one hemisphere was more hyperexcitable than the other. In other patients (those represented by points near the intersection of the two axes) the two hemispheres appear to be equally hyperexcitable.

The patients in whom a unilateral stimulus elicited at least one ipsilateral response are represented by squares in Fig. 6. It can be seen that they tended to be patients with asymmetric pattern thresholds, or asymmetric responses to IPS. In 5 of the 7 patients the hemisphere over which the paroxysmal activity was observed was that expected on the basis of the asymmetry in pattern threshold or response to IPS. In the two remaining patients ipsilateral activity was observed over both hemispheres.

Although the patients in this study had not all undergone exhaustive neuro-radiological, neuro-psychiatric, and ophthalmological investigation, none had lateralizing signs nor a visual field defect on routine neurological examination (by the authors). In Fig. 6 the patients with diagnoses of primary generalised, secondary generalised, and partial epilepsy are represented by open, filled, and half-filled circles respectively. It can be seen that there is little or no relationship between the diagnostic categories and the degree of hemispheric asymmetry.

Discussion

In previous work we have been concerned to demonstrate that in photosensitive persons excitation of the striate cortex is necessary to induce paroxysmal epileptiform activity in response to patterns. We have shown that the probability of the paroxysmal response is related to the magnitude of excitation in the striate cortex that the patterns produce (Wilkins et al. 1980). On the basis of the present findings it may now reasonably be inferred that excitation confined largely to the striate and prestriate cortex is not only necessary but can perhaps be sufficient to produce a postcentral epileptiform discharge in some patients. The argument runs as follows. The discharges illustrated in Figs. 2, 3, 4

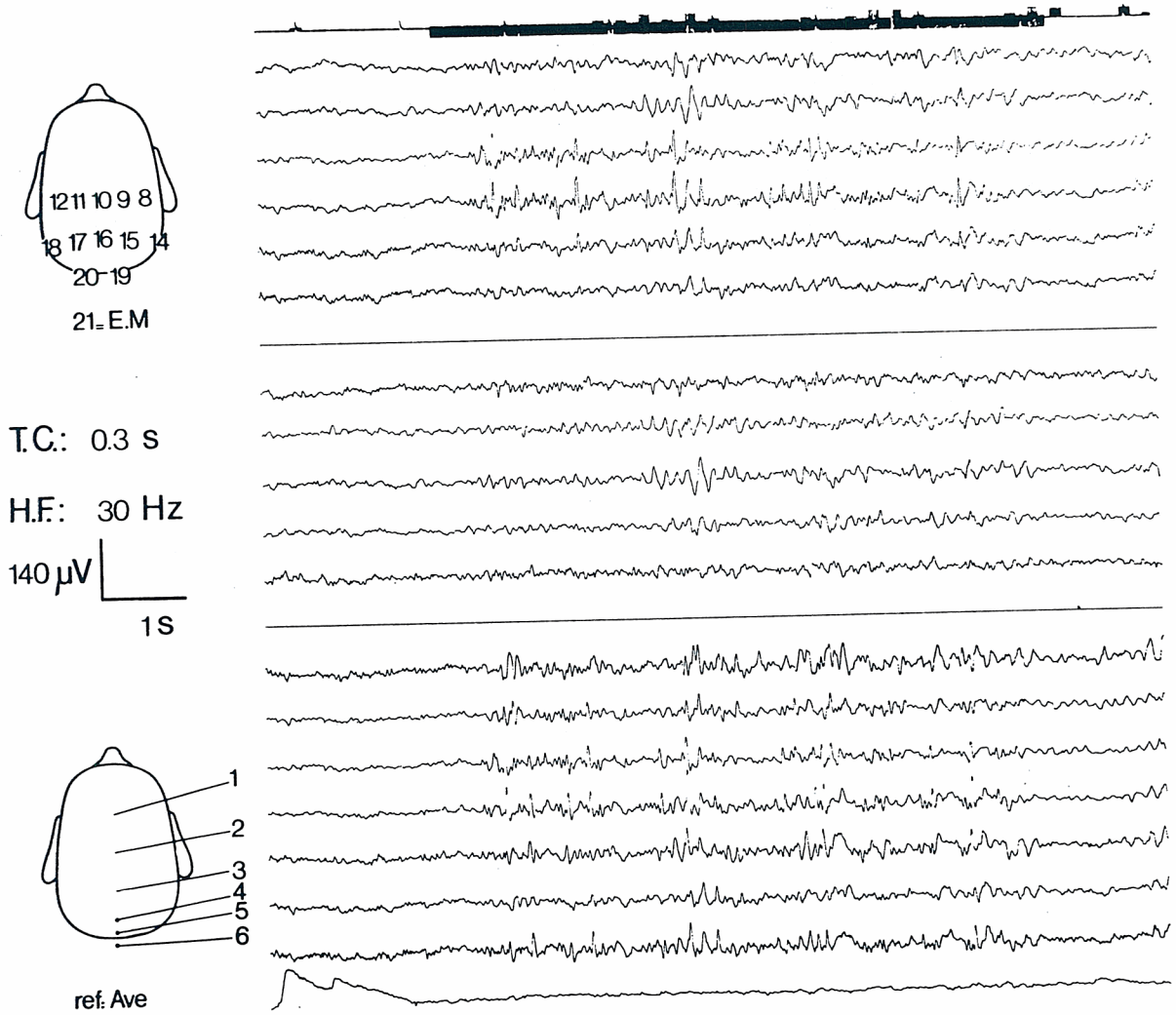

Fig. 5. An example of the paroxysmal activity recorded during the presentation of a pattern in the lower visual field.

points relative to the ordinate is determined by the degree of asymmetry in pattern threshold, V. (In two patients all pattern presentations elicited a response, and so the asymmetry of threshold could not be determined. These patients are not represented in the scatterplot.)

The asymmetries in pattern threshold were paralleled by a unilateral preponderance of epileptiform discharges to (bilaterally symmetrical) diffuse IPS. The asymmetry in the response to IPS forms the abscissa of the scatterplot in Fig. 6 and was determined as follows. Each response to IPS was classified as left maximal, right maximal, or symmetrical on the basis of the amplitude of the epileptiform components. The following index of asymmetry of response to IPS was calculated:

$$(R - L)/(L + R + S)$$

where L, R, and S are the number of trials with left maximal, right maximal, and symmetrical responses respectively. The index

and 5 show a clear dissociation, the response to an upper field stimulus having a lower surface topography than the response to the lower field, and the responses to stimulation of the lateral fields having a contralateral distribution. Despite the complex nature of the interacting electrical fields in the vicinity of the calcarine fissure (Jeffreys 1977; Blumhardt et al. 1978), it seems unlikely that the correspondence between the distribution of paroxysmal activity on the scalp and the topography of the underlying visual areas is fortuitous or even anomalous. It is true that electrode placement was of obvious importance as regards the measurement of the response to upper and lower fields, as inspection of the activity recorded from the non-standard midline electrodes will confirm. It is also true that the responses to upper and lower fields, when obtained, did not invariably show a dissociation. Nevertheless the fact that the dissociation did occasionally occur, and that when it occurred it was consistent from trial to trial is instructive. The dissociation may well have been a reflection of the manner in which the upper and lower visual fields are represented in the striate and prestriate cortex, particularly in areas 17, 18 and 19. It seems unlikely that more anterior visual areas were appreciably involved. In monkeys these areas generally show a lack of retinotopic organisation, the vertical meridian can be multiply represented, and in the visual centres of the temporal cortex there are many interhemispheric connections (Zeki 1970, 1978, 1980; Desimone and Gross 1976).

Given that the visual areas of the two cerebral hemispheres are largely symmetrical, and that the placement of electrodes was likewise symmetrical, it is difficult to explain the lateral asymmetries in paroxysmal activity other than by assuming that the neural discharges within each hemisphere differed. The asymmetry of the discharge can be influenced by the side of presentation of the stimulus, as first noted by Soso et al. (1980). It may perhaps be inferred that the paroxysmal activity occurs independently in the two hemispheres. Such an inference would help explain why the upper and lower field stimuli were less epileptogenic: the level of excitation induced in either hemisphere was less for upper and lower field patterns than for left and right.

The response asymmetry induced by a unilateral stimulus appears to be superimposed on an underlying asymmetry that is best attributed to an inequality in the hyperexcitability of the two cerebral hemispheres. This inequality is evident when a symmetrical stimulus (such as IPS) produces an asymmetrical response. The above evidence for a difference in the hyperexcitability of the hemispheres has implications for the pathophysiology of epilepsy which are discussed in the paper that follows (Binnie et al. 1981).

Summary

A group of 15 volunteers with both photosensitive epilepsy and pattern sensitivity were shown patterns of stripes in the left and right visual hemifields. In the majority of patients the resulting paroxysmal epileptiform EEG activity was maximal in the posterior temporal and occipital regions contralateral to the stimulus. Patterns in the upper and lower hemifields were also presented and in two patients there was a difference in the vertical distribution of the response such as to suggest that in these patients the discharges were largely confined to the striate and prestriate cortex.

The probability with which paroxysmal activity was evoked was usually different for the two lateral hemifields. This difference between the hemifields (which was dramatic in some patients) was mirrored in a lateralisation of the responses to diffuse intermittent photic stimulation. The association between the asymmetries in pattern sensitivity and in the responses to photic stimulation suggests that the two cerebral hemispheres often differed in hyperexcitability. It is therefore interesting that the putative differences in hyperexcitability were observed in patients

with primary generalised epilepsy as well as those with other types.

Résumé

Différences interhémisphériques dans l'épilepsie photosensible. I. Seuils de sensibilité au pattern

On a présenté à un groupe de 15 volontaires qui avaient à la fois une épilepsie photosensible et une sensibilité au pattern, des patterns de bandes dans les hémichamps visuels gauche et droit.

Chez la majorité des patients l'activité EEG épileptiforme paroxystique qui en a résulté était maximale dans les régions temporales postérieures et occipitales, contralatérales au stimulus. On a également présenté des patterns dans les hémichamps supérieurs et inférieurs: chez 2 sujets existait une différence dans la distribution verticale de la réponse, ce qui suggère que chez ces patients les décharges étaient essentiellement restreintes au cortex strié et préstrié.

La probabilité pour qu'une activité paroxystique soit évoquée différait en général pour les deux hémichamps latéraux. Cette différence entre les hémichamps (très importante chez certains patients) se retrouvait dans une latéralisation des réponses à la stimulation lumineuse intermittente diffuse. L'association des asymétries de la sensibilité au pattern et de celles des réponses à la stimulation lumineuse suggère que les deux hémisphères cérébraux n'ont souvent pas la même hyperexcitabilité. Il est donc intéressant que des différences présumées d'hyperexcitabilité aient pu être observées chez des patients atteints d'épilepsie généralisée primaire tout autant que chez des patients présentant un autre type d'épilepsie.

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