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Two Visual Mechanisms of Photosensitivity

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Summary: *Purpose:* Photosensitive epilepsy is the most common of the "reflex" epilepsies. Precipitated by television viewing, flickering light, or specific visual patterns, it is the cause of seizures in 10% of young people with epilepsy. Photosensitivity is associated with two types of EEG abnormalities: photoparoxysmal responses (PPRs) and occipital spikes (OSs). It is unclear whether these abnormalities are mediated by different mechanisms, and furthermore, the clinical significance of OS is unknown.

Methods: By using our previously established population of patients with photosensitive epilepsy, all showing EEG abnormalities on intermittent photic stimulation or pattern stimulation, we examined the effects of pattern contrast, spatial and counterphase temporal frequency, and colour on these abnormalities.

Results: PPRs and not OSs show linear contrast dependency and are elicited by stationary stimuli and by non–colour-opponent isoluminant stimuli.

Conclusions: PPRs and OSs are generated independently by the parvocellular and magnocellular visual systems, respectively. The results add support to the hypothesis that only PPRs and not OSs are clinically significant. **Key Words:** Photosensitive epilepsy—Magnocellular—Parvocellular—Occipital spikes— Photoparoxysmal response.

Photosensitive epilepsy occurs with an annual incidence of 1.1 in 100,000 of the general population, although its marked prevalence around the age of puberty produces a higher incidence of 5.7 per 100,000 in this age group (1). It is characterized by seizures precipitated by visual stimuli, although some patients also may experience spontaneous seizures. It is more common in women than men, and it appears to have a genetic basis (2). Whereas 25% of patients lose their photosensitivity in their third decade of life (3), the remaining 75% will remain photosensitive throughout life.

In Europe, televised material provides the most common provocative stimuli; >60% of patients experience their first photosensitive seizure while watching television (2). Visual stimuli such as flickering sunlight, stroboscope illumination, the pattern on moving staircases, and high-contrast black-and-white patterns also can cause seizures.

Photosensitive epilepsy can be confirmed only by recording EEG abnormalities in response to intermittent photic stimulation (IPS) or high-contrast pattern stimulation, which may be counterphased. There is some evidence that isoluminant colour combinations, which are processed by colour-opponent pathways, are nonprovocative (4), and that long-wavelength red light may be especially provocative (5). Square-wave gratings are more provocative than are checks (4), and the temporal frequency of the phase reversal is critical (6).

Either photic or pattern stimulation can result in one or both of the following EEG abnormalities. Photoparoxysmal responses (PPRs) consist of spikes and waves that are not usually phase locked to the visual stimulus and that are generalised over the whole head, although they may show a posterior predominance. Occipital spikes (OSs) are always confined to posterior regions of the scalp, are seen most frequently at low flash rates (typically lower than those that elicit a PPR), and often appear to precede PPRs. They are phase locked to the rate of visual stimulation, and when averaged, occur on the descending arm of the P2 component of the flash visual-evoked potential; this suggests either a failure of postsynaptic inhibition or an increase in hyperexcitability of the visual cortex (2). They are not present in the unstimulated EEG, unlike occipital focal spikes.

Two mechanisms of photosensitive epilepsy have been proposed: a (possibly subcortical) primary generalised mechanism, in which a visual stimulus produces generalised discharges (PPRs); and a secondary generalised mechanism, in which a visual stimulus produces

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localized discharges (OSs) in hyperexcitable visual cortex, which then spread to produce secondary generalised discharges (PPRs) (2).

Abnormal excitation of visual cortex may be mediated by either of the two principal pathways of the human visual system: magnocellular or parvocellular. These pathways originate in two predominate types of retinal ganglion cell, termed M and P (7), or P_α and P_β (8). The separation of these cells is maintained through the lateral geniculate nucleus (8,9), and they synapse in different layers of primary visual cortex; M cells in $4C_\alpha$ and P in $4C_\beta$ (10). These two visual pathways have response characteristics that vary in respect of contrast sensitivity, spatial- and temporal-frequency sensitivity, and in chromatic selectivity (e.g., 11,12). In brief magnocellular cells have high contrast gain and respond preferentially to low-spatial-frequency and high-temporal-frequency stimuli, and they are not chromatically selective.

Parvocellular cells respond preferentially to stimuli of higher contrast, higher spatial frequency, and lower temporal frequency than those preferred by magnocellular cells. The majority of these units show some degree of chromatic selectivity, and colour opponency is organized along red/green and blue/yellow axes.

Because PPRs and OSs are elicited most readily by brief light flashes presented at high flash rates, it has been suggested that the abnormal responses are probably mediated along the magnocellular pathway (2). This would, however, be inconsistent with the results of experiments designed to elucidate the role of stimulus contrast: increasing the contrast of simple black-and-white patterns produces an approximately linear increase in the probability of abnormal responses (4). Furthermore, these abnormal responses show dependence on the spatial frequency of the patterned stimulus, occurring most frequently at ~4 cycles/degree (4).

By using our previously established population of patients with photosensitive epilepsy, all showing EEG abnormalities on IPS and/or pattern stimulation, we carried out a number of studies to investigate whether photosensitive epilepsy is mediated by the magnocellular or parvocellular system. These investigations examine the effects of stimulus contrast, spatial and temporal frequency, and colour, on PPRs and OSs. The stimulus dependencies of PPRs and OSs are related to the characteristics of the magnocellular and parvocellular visual pathways, and the clinical significance of these two types of EEG abnormalities are discussed.

METHODS

All patients were drawn from our current photosensitive population and had received a diagnosis of photosensitive epilepsy. All patients had normal or corrected-to-normal visual acuity. All studies received ethical committee approval, and patient consent was obtained on each occasion. EEGs were recorded on a Nihon-Kohden (experiments 1 and 3) or a Nicolet (experiment 2) 16-channel EEG machine by using silver/silver-chloride disk electrodes fixed to the scalp in locations according to the International 10/20 system. Responses were classified according to our usual criteria (2). PPRs consisted of spike/polyspike-and-wave discharges that were generalised, or maximal in parietotemporal derivations, and extended anteriorly beyond the central fissure. OSs occurred at the same rate as the stimulus, were maximal occipitally, and were confined to posterior derivations. Three different experiments were performed to investigate the effects of stimulus contrast and spatial and temporal frequency, as described later.

Experiment 1: Contrast

Thirteen patients participated in the experiment; five were male and eight were female patients; age ranged from 8 to 37 years, and the mean age was 28 years. Stimuli comprised vertical square-wave gratings of 3 cycles/degree, which phase reversed at 1 Hz. The stimuli were generated by an SC Electronics T22 grating generator and were presented on a 50-Hz television screen, which subtended 18 degrees horizontally by 14 degrees vertically at a distance of 1.5 m. Patients viewed the screen binocularly and fixated on a small central target. Stimuli replaced a uniform grey background of mean luminance 190 cd/m^{-2} for a period of 10 s, although if an abnormality was elicited, the stimuli disappeared immediately. The contrast of the gratings was varied between 0 and 90%, and the order of presentation was randomized between patients. The number of patients displaying PPRs and OSs was noted for each stimulus contrast.

Experiment 2: Spatial and temporal frequency

Seven patients participated in the experiment; three were male and four were female patients; their ages ranged from 17 to 28 years, and the mean age was 23 years. The occurrence of PPRs and OSs was noted as a function of stimulus spatial and temporal (counterphase) frequency. Stimuli comprised horizontal sine-wave gratings that varied in spatial frequency (0.5–20 cycles/degree) and counterphase temporal frequency (0–25 Hz). The stimuli were generated by using a Cambridge Research Systems VSG grating generator and were displayed on an Eizo Flexscan T560I monitor with frame rate 100 Hz. The stimuli subtended 16 degrees horizontally by 11 degrees vertically at a distance of 1 m. Patients viewed the stimuli binocularly and fixated on a small central target. The mean luminance of the display was 30 cd/m^2, and the γ corrected display was linear over the range of contrasts used. Stimuli appeared from a uniform grey background for a period of 10 s. If a stimulus elicited an abnormality, it was replaced immediately by the uniform background and then redisplayed

with a lower contrast. The minimal contrast required to elicit PPRs and OSs was noted for each stimulus condition. For each patient, spatial frequency (using stationary gratings) was investigated first, and temporal frequency (using gratings of 6 cycles/degree) was investigated second; within each condition, the order of the gratings was randomized.

Experiment 3: Colour

Eight patients participated in the experiment, three were male and five were female patients; their ages ranged from 10 to 30 years, and the mean age was 24 years. EEG activity was recorded while patients viewed a cartoon sequence displayed on a 50-Hz television screen, which subtended 18 degrees horizontally by 14 degrees vertically at a distance of 1.5 m. Patients viewed the cartoon binocularly under two conditions: chromatic (known to be provocative) (5), and achromatic. In the chromatic condition, the cartoon comprised primarily red and blue backgrounds of luminance 46 cd/m^2 and 70 cd/m^2, respectively, which alternated at a temporal frequency of 12 fps. In the achromatic condition, the cartoon was matched for the luminance of the chromatic condition, producing an achromatic luminance variation at 12 fps. Each patient viewed both conditions twice; an ABBA design controlled for order effects. The incidence of EEG abnormalities was noted for each condition.

RESULTS

Experiment 1: Contrast

The occurrence of PPRs and OSs as a function of contrast was determined for a group of 13 patients. Ten patients showed PPRs, and three showed OSs, and these abnormalities have different contrast dependencies (Fig. 1): OSs were present at relatively low contrast levels, and the number of patients in which they were elicited saturated at ~20% contrast. The number of patients in which PPRs were elicited by low-contrast stimulus was low, however, and the number increased linearly with contrast, saturating at 60% contrast.

Experiment 2: Spatial and temporal frequency

The incidence of PPRs and OSs as a function of stimulus spatial frequency and temporal phase-reversal frequency was examined in a group of seven patients. Four patients displayed PPRs, two displayed OSs, and one patient displayed both PPRs and OSs, with OSs elicited at lower contrasts than those required for PPRs. For all patients' stationary gratings were less provocative than phase-reversing gratings; four patients showed PPRs, yet no patient showed OSs. It was possible to plot from the PPR data a spatial-frequency tuning curve, which showed bandpass characteristics between 4 and 16 cycles/degree, peaking at 6 cycles/degree (Fig. 2a). There was evidence of bandpass counterphase temporal-frequency tuning between 6 and 25 Hz for both PPRs and OSs, with the most provocative frequency being 16 Hz (Fig. 2b).

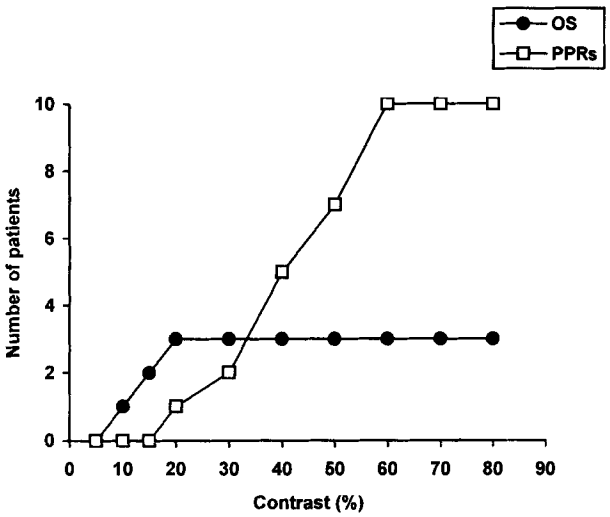

FIG. 1. The number of patients who displayed OSs (solid circles) and PPRs (open squares) as a function of stimulus contrast. The number of patients displaying OSs saturates at 20% contrast, whereas the number displaying PPRs increases linearly, and saturates at 60% contrast.

Experiment 3: Colour

The incidence of PPRs and OSs to chromatic and achromatic (matched for luminance) versions of the same cartoon was investigated in eight patients. Seven patients showed PPRs or degraded PPRs to the chromatic condition, but no patients showed abnormalities to the achromatic condition (Fig. 3). One patient did not show evidence of EEG abnormalities under either condition.

DISCUSSION

The effects of stimulus contrast, spatial and temporal frequency, and colour on PPRs and OSs were examined in a group of patients with photosensitive epilepsy. The results suggest that PPRs are elicited by parvocellular and OSs by magnocellular visual pathways. Experiment 1 showed that the probability of eliciting a PPR increased linearly with contrast, saturating at 90%, whereas the probability of eliciting an OS saturated at low (20%) contrast (Fig. 3). These different contrast characteristics suggest that the contrast sensitivity of PPRs and OSs resemble those of the parvocellular and magnocellular systems, respectively.

Further support for this hypothesis is supported by the findings of experiment 2, in which OSs were elicited by phase-reversing but not stationary gratings. Magnocellular units are often described as phasic, indicating their inability to respond to slow-moving or static stimuli (13); thus if OSs arise from activity in the magnocellular pathway, they would be difficult to elicit with stationary grat-

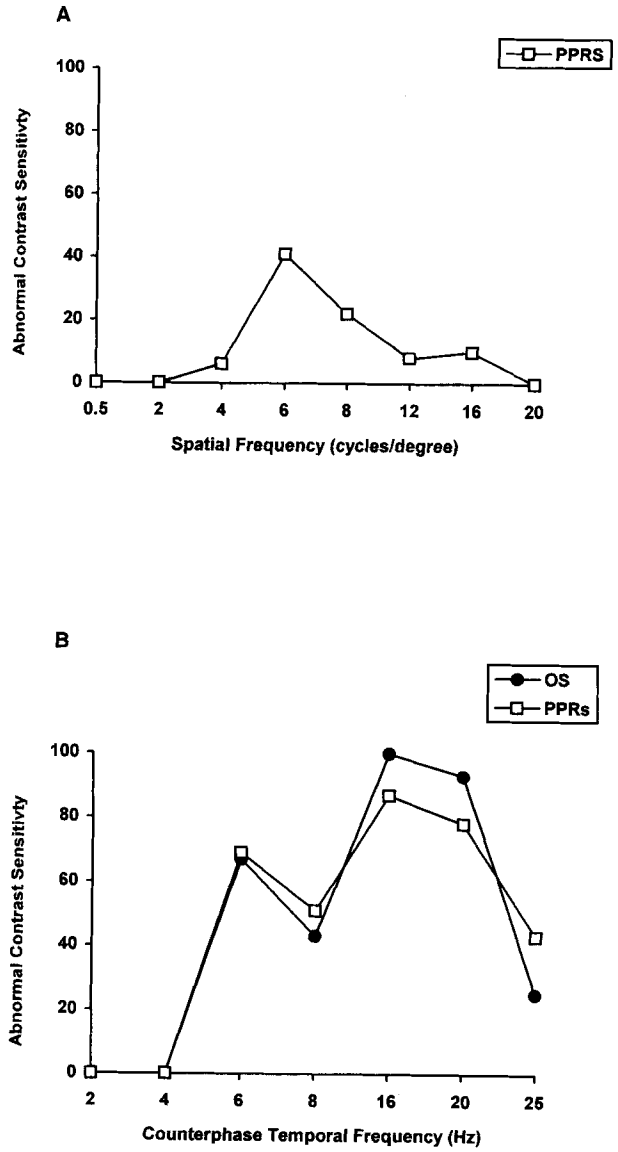

FIG. 2. Abnormal contrast sensitivity (calculated from the mean normalized contrast threshold) of OSs (solid circles) and PPRs (open squares) as a function of stimulus spatial frequency **(A)** and counterphase temporal frequency **(B).** OSs were not elicited by stationary gratings **(A),** and PPRs show bandpass spatial frequency tuning, peaking at 6 cycles/degree. At this peak spatial frequency, **B** shows both OSs and PPRs to have similar bandpass characteristics between 6 and 25 Hz, peaking at 16 Hz.

ings. Both PPRs and OSs were elicited optimally by a grating that counterphased at 16 Hz. Although the characteristics of the magnocellular system might predict that OSs would be more readily provoked by higher temporal frequencies than PPRs, both magnocellular and parvocellular units can respond to stimuli modulated at this frequency (14), and the difference in optimal stimulus temporal frequency between the two pathways may be small (15), particularly for high-contrast stimuli (11).

The optimal spatial frequencies of PPRs and OSs cannot be compared in this study, as stationary gratings did not elicit OSs. The peak spatial frequency for PPRs was 6 cycles/degree, and although both parvocellular and magnocellular units can respond to this spatial frequency, it is on the upper limit of the latter's sensitivity (11). Because PPRs were observed at spatial frequencies $\leq$16 cycles/degree, it is likely that the PPRs are generated by the parvocellular system.

Interestingly, experiment 2 did not show the same degree of difference between the stimulus contrast required to elicit PPRs and OSs as in experiment 1. The contrasts required to elicit PPRs were similar for the two experiments, but in experiment 1, OSs were elicited at lower contrasts than in experiment 2. This difference may result from the display equipment used; gratings were displayed on a 50-Hz interlaced television (containing high-frequency flicker components of 25 and 50 Hz) in experiment 1, and a 100-Hz noninterlaced monitor in experiment 2. The lower contrasts required to elicit OSs in experiment 1 may be due to the additional flicker components. If this is correct, then as the magnocellular pathway conveys high-temporal-frequency flicker information, this difference also lends support for the hypothesis that OSs and not PPRs are generated by the magnocellular pathway.

Experiment 3 compared the ability of chromatic and achromatic versions of the same cartoon sequence to elicit PPRs and OSs. The chromatic cartoon comprised red and blue backgrounds, alternating at 12 fps, and the achromatic version was matched for luminance. Seven of the eight patients demonstrated PPRs to the chromatic sequence, but not the achromatic sequence, and the final patient did not show abnormalities to either condition. As the luminance was matched between conditions, temporal variations in luminance cannot underlie the observed abnormalities, which must therefore be due to temporal variations in colour. It was suggested previously that red/green isoluminant colour combinations do not provoke epileptogenic activity (4), but it should be noted that the long-wavelength red/blue combination present in the cartoon did not lie along the axes of the colour-opponent pathway, so that, when analysed in terms of the output of these pathways, the stimulus can be considered to have red/black and blue/black components. These are optimal combinations to activate the parvocellular colour-opponent system and result in a lack of spatially opponent inhibition; this probably results in the extreme susceptibility of photosensitive patients to this stimulus, producing the largest number of seizures ever reported for televised material (5). As no abnormalities occurred in the achromatic condition, luminance modulations processed by the magnocellular system cannot cause the observed PPRs. Experiment 3 therefore provides evidence to suggest that PPRs are generated by the parvocellular pathway, and OSs, by the magnocellular pathway.

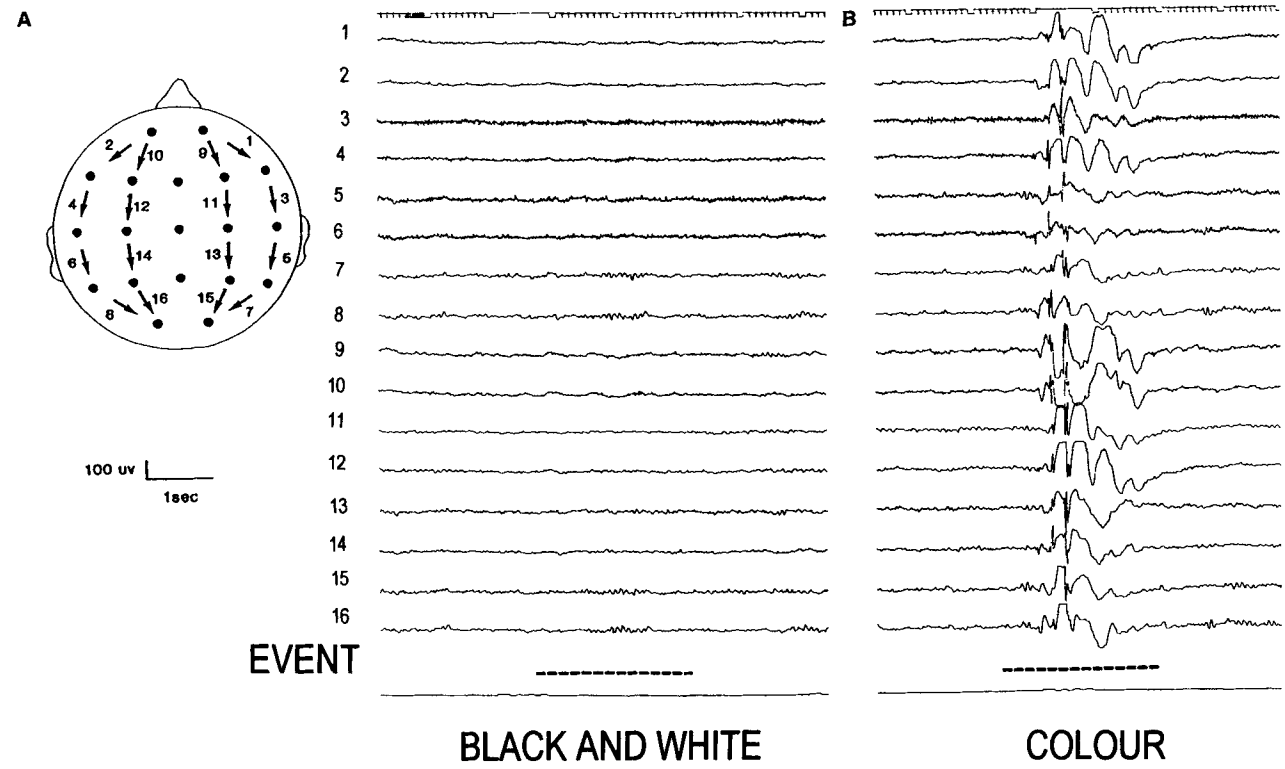

FIG. 3. EEG activity recorded while a patient viewed luminance-matched black-and-white **(A)** and chromatic **(B)** versions of the same cartoon. The achromatic version does not elicit EEG abnormalities, whereas the chromatic version elicits a clear PPR. Chromatic and not luminance variations in the cartoon therefore underlie the PPR in **(B)** (From Harding 1998).

The results of the three experiments described here provide evidence to suggest that the two types of abnormalities seen in photosensitive patients (PPRs and OSs) are indeed separate phenomena, showing different stimulus dependencies, and that PPRs and OSs may be indicative of activity in the parvocellular and magnocellular pathways, respectively, of the human visual system. OSs typically precede PPRs, and so it has often been assumed that the two phenomenon are linked causally, OSs representing a focal abnormality in the visual cortex, which then becomes secondarily generalised, resulting in PPRs. These studies suggest that the temporal relation is fortuitious and may result only from the faster speed of the magnocellular pathway (16,17). This study suggests, therefore, that photosensitive epilepsy is primarily generalised.

It has been known for many years that PPRs predict clinical photosensitivity (18) and that OSs are seen in other conditions and are not predictive of clinical photosensitivity (19). Furthermore, the most effective antiepileptic drug, valproic acid, is effective on PPRs and has absolutely no effect on OSs (20).

We suggest, then, that photosensitive epilepsy is mediated by the parvocellular pathway, and that stimuli that activate this pathway are the most critically epileptogenic (5) and that OSs, although representing some form of hyperexcitibility in the visual cortex, may not be clinically significant.

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REFERENCES

1. Fish DR, Quirk JA, Smith SJM, et al. *National survey of photosensitivity and seizures induced by electronic screen games: interim findings.* London: Department of Trade and Industry, 1993.
2. Harding GFA, Jeavons PM. *Photosensitive epilepsy* (new edition). London: MacKeith Press, 1994.
3. Harding GFA, Edson A, Jeavons PM. Persistence of photosensitivity. *Epilepsia* 1997;38:663–9.
4. Wilkins AJ, Darby CE, Binnie CD. Neurophysiological aspects of pattern-sensitive epilepsy. *Brain* 1979;102:1–25.
5. Harding GFA. TV can be bad for your health. *Nat Med* 1998; 4:265–7.
6. Fylan F, Harding GFA, Webb RM. Spatio-temporal analysis of epileptogenic patterned stimuli. *Electroencephalogr Clin Neurophysiol* (in press).
7. Kaplan E, Shapley RM. The primate retina contains two types of retinal ganglion cells with high and low contrast sensitivity. *Proc Natl Acad Sci* USA 1986;83:2755–7.
8. Perry VH, Oehler R, Cowey A. Retinal ganglion cells that project to the dorsal lateral geniculate nucleus in the macaque monkey. *Neuroscience* 1984;12:1101–23.
9. Leventhal AG, Rodieck RW, Dreher B. Retinal ganglion cells

classes in the old world monkey: morphology and central projections. *Science* 1981;213:1139–42.
10. Hubel DH, Wiesel TN. Laminar and columnar distribution of geniculocortical fibres in macaque monkey. *J Comp Neurol* 1972; 146:421–50.
11. Merigan WH. P and M specialization in the macaque. In: Valberg A, Lee BB, eds. *From pigments to perception.* New York: Plenum Press, 1991:117–25.
12. Schiller PH. The colour-opponent and broad-band channels of the primate visual system. In: Valberg A, Lee BB, eds. *From pigments to perception.* New York: Plenum Press, 1991:127–32.
13. Kaplan E, Lee BB, Shapley RM. *New views of primate retinal function.* In: Osborne N, Cohaden J, eds. *Progress in retinal research.* Vol 9. New York: Pergamon Press, 1990:273–336.
14. Derrington AM, Lennie P. Spatial and temporal contrast sensitivities of neurones in the lateral geniculate nucleus of macaque. *J Physiol* 1984;357:219–40.
15. Purpura K, Kaplan E, Shapley RM. Background light and the contrast gain of primate P and M retinal ganglion cells. *Proc Natl Acad Sci USA* 1988;85:4534–7.
16. Nowak LG, Munk MHJ, Bullier J. Visual latencies in areas V1 and V2 of the macaque monkey. *Vis Neurosci* 1995;12:371–84.
17. Givre SJ, Schroeder CE, Arezzo JC. Contribution of extrastriate area V_4 to the surface recorded flash VEP in the awake macaque. *Vision Res* 1994;34:415–38.
18. Waltz S, Christen H-J, Doose H. The different patterns of the photoparoxysmal response: a genetic study. *Electroencephalogr Clin Neurophysiol* 1992;83:138–45.
19. Maheshwari MC, Jeavons PM. The clinical significance of occipital spikes as a sole response to intermittent photic stimulation. *Electroencephalogr Clin Neurophysiol* 1975;39:93–5.
20. Harding GFA, Herrick CE, Jeavons PM. A controlled study of the effects of sodium valproate on photosensitive epilepsy and its prognosis. *Epilepsia* 1978; 19:555–65.