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ELECTRORETINOGRAMS EVOKED IN MAN BY LOCAL UNIFORM OR PATTERNED STIMULATION

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SUMMARY

1. We have recorded electroretinograms (e.r.g.s) in normal subjects. Television monitors were used as stimulators. The screens were surrounded by brightly lit white reflecting surfaces to ensure that the responses were developed by defined retinal areas.

2. Various types of stimuli were employed. Either (i) a pattern of dark and bright squares was reversed, to evoke a pattern e.r.g. (p.e.r.g.), (ii) the luminance of the uniform screen was abruptly increased and decreased to evoke a focal on–off e.r.g. or (iii) a pattern was made to appear and disappear from a uniform background. In each of these cases, the sequence of changes of luminance at any one point could be made identical. The aim of the experiments was to determine whether the e.r.g. was modified by the spatial organization of the stimulus.

3. In other experiments a colour monitor was used so that (i) a red–green flicker, (ii) red–green pattern reversal or (iii) the appearance of a red–green pattern from a yellow background could be used as a stimulus. The responses were caused by the changes in hue, since all the colours were equiluminant.

4. With black and white patterns the p.e.r.g. peaks 5 msec later than the focal on–off e.r.g. The largest response is produced by squares of 0·5–1° subtense.

5. The ratio of the amplitudes of the p.e.r.g. to the focal on–off response is largest for stimuli confined to the macula and smallest for those projected onto peripheral retina.

6. The amplitude of responses to chequerboard reversing patterns increases nearly linearly with contrast up to the maximum contrast available.

7. When patterns appear or disappear from a uniform screen, and there is an associated change in the quantity of light entering the eye, recognizable b-waves occur when the average screen luminance increases, independently of whether pattern contrast increases (appearance) or decreases (disappearance).

8. When a pattern appears or disappears with no change in luminance, e.r.g.s are evoked at both 'on' and 'off'. The disappearance of the dark parts of the pattern causes the largest logarithmic increase in local retinal illumination. For patterns of

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square size > 4° the pattern disappearance response is larger than for pattern appearance. As the square size is reduced, the appearance response grows and the disappearance response decreases.The e.r.g.s evoked by the appropriate changes in luminance of a uniform screen are no longer the same as those caused by the appearance and disappearance of the pattern.

9. The responses to change of hue are 70% as large as those produced by black and white patterns. The same ratio occurs for pattern and focal on–off e.r.g.s.

10. When coloured patterns appear from and disappear to a uniform field, the e.r.g.s. evoked are very similar to those recorded when the appropriate changes of hue occur in a uniform field. This result is quite different to the findings for black and white patterns (see 8 above).

11. The results suggest that it is the change in local adaptation caused by the black and white patterns which modifies the e.r.g. and not the presence of contrasting borders.

INTRODUCTION

When the electroretinogram (e.r.g.) is recorded with corneal electrodes, and only a small part of the retina is stimulated directly, most of the response is inevitably produced by stray light (Asher, 1950), unless special precautions are taken. Two techniques have been used to obtain focal e.r.g.s from defined regions of the retina. Brindley & Westheimer (1965) used a large illuminated surround to suppress the response to stray light. Johnson, Riggs & Schick (1966) and Armington, Corwin & Marsetta (1971) used as a stimulus a pattern-reversing chequerboard. With such a stimulus, the quantity of light entering the eye remains constant and therefore the stray light also does not change. Within the retinal image of the pattern there are local changes of illumination each time the pattern reverses and this provides a stimulus for the e.r.g. It is not clear whether the pattern e.r.g. is comparable to the response elicited by uniform flashing fields. Spekreijse, Éstevez & van der Tweel (1973) showed that in man the response to chequerboard patterns was associated with the local increase of luminance, but decreases of luminance did not produce an e.r.g., even when associated with the appearance of a pattern. However Arden & Brown (1965), using micro-electrode recording in the cat retina, investigated the way the local e.r.g. altered as a function of the area of retina illuminated, and concluded that electrical summation of e.r.g. components of opposite polarities could not explain the results obtained. A receptive field organization of the b-wave process was suggested. Nelson, Zrenner & Gouras (1979), and Diehl & Zrenner (1980) showed that the e.r.g. b-wave recorded from the cornea was reduced to a minimum by a stimulus which consisted of light spots of a particular size and spacing. Clinical observations (Arden, Vaegan, Hogg, Powell & Carter, 1980; Arden & Hogg, 1982; Fiorentini, Maffei, Pirchio, Spinelli & Porcaitti, 1981; May, Ralston, Reed & Van Dyk, 1982) show that e.r.g.s produced by reversing patterns are abnormal in a number of clinical conditions where the responses to light flashes are unaffected. Some of these (optic neuritis, amblyopia, glaucoma, and certain congenital defects), are associated with abnormalities of the optic nerve, and suggest that the pattern reversal e.r.g. might be produced at a different retinal locus to the b-wave. Maffei & Fiorentini (1981) have reported that in cat the pattern reversal e.r.g., but not the flash e.r.g., is abolished by section of the optic nerve, but only after a delay which corresponds to the time required for retrograde degeneration.

Such reports suggest that the pattern reversal e.r.g. might be a different type of response, produced in a different way to the well known b-wave. If this were to be the case, altering the stimulus conditions might affect pattern and luminance responses differentially. On the other hand, there might be no specific response to contour. If so, it should be possible to stimulate the eye with the luminance changes associated with, for example, the appearance or disappearance of a pattern, but under conditions where large uniform fields were employed. The resulting e.r.g. should be indistinguishable from a pattern response. The experiments reported below were designed to provide answers to such questions.

METHODS

Subjects. The experiments were performed on the authors and three other subjects. In all cases visual acuity was determined, and the subjects wore appropriate spectacle corrections.

Electrodes. Earth and indifferent electrodes were standard 5 mm silver–silver chloride e.e.g. surface electrodes. The skin under the electrodes was lightly abraded with a blunt syringe needle to reduce the skin impedance below 2 kΩ. The earth electrode was placed centrally on the forehead, and the indifferent electrodes at the lateral margin of each supraorbital ridge. The corneal electrode was a gold foil, placed in the lower fornix (Arden, Carter, Hogg, Siegel & Margolis, 1979). Visual acuity was not affected by the electrodes.

Stimulation. Patterns were produced on television monitors using standard techniques. The pattern generator employed has been described previously (Faulkner, 1978). It produced sine wave or square wave gratings, or chequerboards of variable spatial frequency and contrast. The following modifications and additions were made to obtain the stimuli required.

Pattern reversal. The generator was used with an auxiliary signal source, which controlled the frequency of the reversals, and provided a trigger pulse for each transition.

Focal on–off responses. The pattern could be made so coarse that one half cycle of a grating occupied the screen. Then, as the pattern reversed, the screen flickered, but the luminance across it remained uniform. With such a low spatial frequency, the monitor could not maintain the pattern contrast. In almost all experiments, the right-hand half of the screen was masked off, so one half of a pattern of higher spatial frequency could be seen. Then as the pattern reversed, there was a change in screen luminance unassociated with a pattern change. Note that the triggers were produced both when the screen luminance increased and when it decreased. The pattern reversal and focal on–off modes provide an identical sequence of luminance changes for any one point on the retina. In the pattern reversal mode, half the retinal area is stimulated 180° out of phase with the remaining half.

Appearance and disappearance with no change in luminance. The generator could cause the appearance of a pattern from a blank screen. If the pattern contrast exceeded 50 %, there were small changes of luminance. These were eliminated by providing a d.c. signal from the auxiliary signal source while the screen was blank.

Appearance and disappearance with change of luminance. In some experiments the pattern was made to appear by causing large increases or decreases of luminance of only parts of the screen. In these, two pattern generators were employed, one of which drove the synchronizing pulse generator (s.p.g.) of the other. The generators were connected to the Red and Green inputs of an RGB colour monitor, and produced a coherent image. The monitor could be operated in monochrome mode. One pattern generator was set to produce focal on–off responses while the other was run in the pattern appearance mode. The d.c. signal produced by the auxiliary source was adjusted till, as the pattern appeared, there was no change in luminance of the screen in the portions occupied by either the dark or the light squares.

Reversal of a coloured pattern. When the colour monitor was operated normally and both pattern generators operated in pattern reversal mode, the subject saw a reversing red–green chequerboard, and internal adjustments of the monitor made it possible to equalize the luminance of the red and green squares. Because the spatial frequency controls on the pattern generators operated independently, it was only possible to use a small range of square sizes. The signal from one generator could be inverted, and then a yellow–black chequerboard was seen.

Appearance of a coloured pattern. If both generators were run in the appearance mode, a red–green pattern could be made to appear from a uniform yellow field. The auxiliary signal source produced two different d.c. voltages during the blanking period to control each pattern generator. This was required to ensure that the yellow and the red and green screen outputs were all equiluminous.

A studio quality monochrome monitor (Melford Electronics), and a RGB colour monitor (Electronic Visuals) were used. The changes in pattern which provided the stimuli were not synchronized to the television frame rate, to reduce mains pick-up, except when colour pattern appearance was studied. At the moment of such transitions, a hue change was seen, which was invisible if the pattern changed during the frame flyback time.

Recording. The subject sat in a comfortable chair, with a head support. He gazed at a small fixation spot on the surface of the screen. The screen was surrounded by a large white card, illuminated by spotlights, whose beams were masked to reduce any direct illumination of the screen. The e.r.g.s were amplified by an electroencephalograph (S.L.E. Ltd.) with bandpass 0·3–50 Hz, and the signals fed into the analogue-to-digital converters of a PDP 11/10 computer system. The averaging programme rejected any response during which the analogue-to-digital converters recorded a maximum or minimum number. This corresponded to a voltage excursion of $\pm 25\ \mu$V. The e.r.g.s were *ca.* 2 μV in size, but large spurious signals due to blinks and eye movements were frequently seen and 'artifact rejection' was essential to obtain good records. The averaging epoch was usually only 120 msec since this reduced the number of responses contaminated by such artifacts. The averaging and display system has been described previously (Arden *et al.* 1979). Each record was the average of 250 accepted responses. In each experiment several records were obtained for each experimental condition. The traces shown are typically the average of 2000–4000 responses. Experiments were carried out by interlacing and reversing the sequence of recording conditions so that any progressive change in response introduced no bias, and proper statistical treatment of the results could be carried out. Responses were recorded from both eyes, and the results combined for analysis. Corneal positivity is plotted as an upwards deflexion (e.r.g. convention).

It was not possible to shield the subjects completely from the electromagnetic artifacts produced by the monitors, but since the patterns changed independently of the television frame rate, 50 Hz interference produced by the coils of the monitor was removed by averaging. Alterations in the gun current, which occurred when the screen brightness changed, could also produce electrical artifacts which were necessarily locked to the triggers. The artifacts were separately recorded in control experiments in which the screen was occluded by opaque card, so that no e.r.g. could be produced. It was found that the artifacts produced by the increase and decrease of luminance were equal in magnitude and similar in wave form, but opposite in polarity. Hence, if the computer was triggered equally at the increase and decrease of illumination, the artifacts (after averaging) cancelled completely. In a few experiments, when the computer was triggered at only the appearance of a pattern, the artifact was troublesome. It could be removed by recording a response in the usual way, then covering the screen with a piece of opaque card, and recording an equal number of sweeps with the amplifier set so that the output signal was reversed in polarity. The artifact was thus subtracted out. The apparent size of the response was thereby halved, since the computer programme summed voltages, and divided the sum by the number of sweeps.

Calibrations. For each experiment, screen luminances were measured in cd/m^2 with a Tektronix J16 photometer. The contrast was calculated in a standard fashion. The controls on the generators permitted the screen luminance during blanking to be adjusted to within 1 % of the luminance during pattern appearance. The bright and dark parts of the pattern changed symmetrically from the mean. The screen output was monitored with fast response photodiodes to ensure that light output remained constant throughout a stimulus presentation. The phosphors of the colour monitor had been measured on a computerized spectrophotometer and the relative emission was known to better than 1 % accuracy at 1 nm intervals over the range 400–800 nm. The chromaticity co-ordinates of the light emitted by the red and green phosphors are given by $X = 0{\cdot}616$, $Y = 0{\cdot}345$ for the red and $X = 0{\cdot}309$, $Y = 0{\cdot}580$ for the green. For bars wider than 2 cm on the screen, the relative intensity of red and green light varied slightly with the size of the pattern, and this was taken into account. The red and green portions of the patterns appeared equally bright to the subjects.

Luminances were measured with the J16 photometer and a UDT photometer. There was a small difference in the relative spectral sensitivities, and an average value was taken.

Interpolations from Éstevez's (1979) calculations of the relative spectral sensitivity of the human colour fundamentals were used to assess the relative degree of excitation of the red and green (cones) by the screen phosphors. Such calculations can only be approximations, since we have no measurements of the preretinal absorption in our subjects' eyes. These calculations were sufficient to determine whether receptor mechanisms are interacting to produce the e.r.g.s evoked by change in hue (see Results). Within the retinal area subtended by the monitor, colour vision for wave-lengths above 500 nm is very similar to that in the fovea (Stabell & Stabell, 1982). The spectral sensitivity of the human pattern e.r.g. has been investigated using a two-colour threshold technique (Korth & Sokol, 1980) and found to be identical with the psychophysically determined spectral sensitivity, which with the technique employed is the π_5 mechanism.

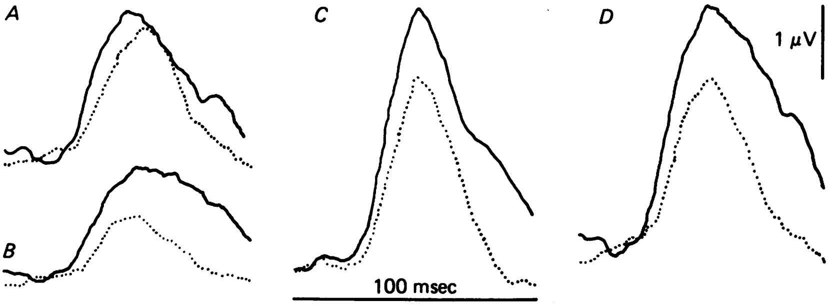

Fig. 1. Comparison of focal on–off (continuous lines) and pattern reversal (dotted lines) e.r.g.s, showing that relative amplitudes vary with retinal location. *A*, stimulus a 50° disk, centred on the fovea, *B*, a concentric annulus of similar area and *C* both disk and annulus. *D* shows the computer sum of $A+B$. Chequerboard stimulus, square sides subtend 40′. L_{max}, 85; L_{min}, 5; and L_{surround}, 75 cd/m^2. For further details see text.

RESULTS

In preliminary experiments we established that when a large surround was illuminated to 10% of the intensity of the maximum screen luminance, stray light responses were suppressed (Brindley & Westheimer (1965)). As a precaution we routinely employed surrounds which were ten times as bright as this. The large bright surrounds scattered light onto the portion of the retina which was stimulated by the pattern, and reduced the effective contrast of the pattern. This reduced the size of the e.r.g.s obtained.

Comparison of pattern reversal and focal on–off e.r.g.s

These two methods of stimulation (see Methods) provide similar stimulation when a single retinal locus is considered, but for pattern reversals, the illumination of half the retina increases at the moment the illumination of the remainder decreases. In the focal on–off condition, the increases and decreases of illumination are synchronous over the entire portion of the retina which is stimulated.

With central fixation, and optimal sizes for the pattern elements, the two responses are similar but not identical. The focal on–off e.r.g. is larger, and peaks slightly earlier than the pattern e.r.g. (Vaegan 1981, and Fig. 1). If the two e.r.g.s are produced by different mechanisms the relationship between them might alter as the stimulus parameters were altered.

Influence of retinal position

Fig. 1 shows the relationship between e.r.g. amplitude and the retinal position stimulated. The screen was masked by a series of annuli and disks, made from pieces of white card. Record *A* was obtained with a 10 cm diameter of the screen viewed at 85 cm, and *B* with a concentric annulus of equal area which, however, produces a smaller response. The records are the averaged results from experiments on two subjects. Both the focal on–off and pattern e.r.g.s are largest (*A*) when the area stimulated includes the macula. The focal on–off response peaks slightly earlier than the response to pattern, and is 0·33 μV larger: the amplitude ratio is 1·20:1. The responses to the annulus (*B*) are 1·48 and 0·80 μV, so that the absolute difference in amplitude is twice that for the disks, and the ratio of amplitudes is 1·62:1. Such differences were observed systematically for a range of disks and annuli. When both were exposed together, the responses shown in *C* were obtained, which are very similar to *D*, the computed sum of *A* and *B*. Thus, when relatively large retinal regions are considered, the responses of adjacent areas simply sum, as described by Brindley & Westheimer (1965).

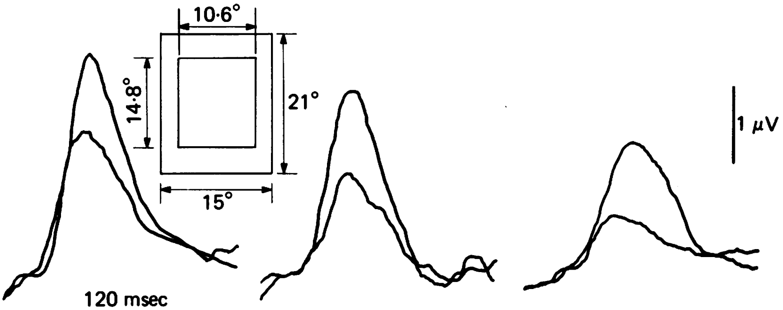

Fig. 2. Comparison of responses of macula and paramacular retina to demonstrate that the amplitudes of focal on–off and pattern reversal e.r.g.s vary independently. In each of the pairs of records, the upper shows the response to a rectangular portion of the screen, fixated centrally, while the lower shows the response of the surrounding retina to a stimulus which occupied an equal area as shown in the Figure. The left-hand records show focal on–off e.r.g.s, the centre responses to 30′ and the right hand to 7·5′ pattern reversing chequerboards. The peripheral region is relatively less sensitive to the small squares, although the responses to luminance are 2/3 the size of the macular responses. $L_{\max}$, 300; $L_{\min}$, 20; and L_{surround} 300 cd/m^2. Average responses from two subjects.

Other experiments were done in which the masks were square, to accommodate the reversing chequerboard. Fig. 2 shows results from such an experiment: note that the responses of the central area are always larger than those of the periphery, as shown in Fig. 1. The ratio of the amplitudes of the e.r.g.s produced by the two retinal regions depends upon the type of stimulus. The on–off response of the central region is only slightly larger than that of the periphery. When 30′ squares are used as a pattern-reversing stimulus, both responses are smaller, but the central response is relatively larger than the peripheral response. When 7·5′ squares are used, the absolute amplitudes of the responses decrease again, but the ratio centre:surround amplitude is considerably increased.

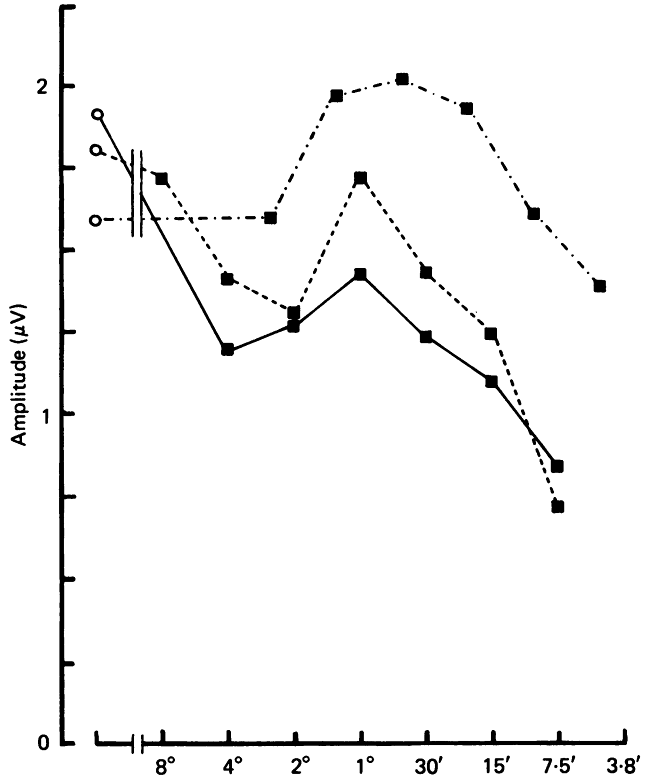

Fig. 3. Alteration of pattern reversal e.r.g. with size of squares, for three different types of target. The dash–dot line joins points obtained with a small field (4·74 × 7·5°) centred on the fovea, with high brightness ($L_{\max}$, 300; $L_{\min}$, 20 cd/m^2) and a relatively low surround intensity (80 cd/m^2). The repetition rate was 3 Hz. Note the peak in the curve for squares of 30′ subtense, and the smaller responses obtained with larger squares. The open circle symbol shows the response to the field flashing uniformly, the focal on–off e.r.g. The dashed line shows similar results for a circular field of 14° diameter, with a lower luminance ($L_{\max}$, 30 cd/m^2) a relatively brighter surround (32 cd/m^2) and a 4 Hz repetition rate. The continuous line shows results for a field consisting of a hollow rectangle, inner dimensions 11° × 15°, and outer dimensions 15° × 21°, with high (300 cd/m^2) screen luminance and surround intensity. Stimulus repetition rate 3 Hz. The rectangular stimuli always contained an integral number of squares. Note that for the larger fields, especially when the macula is excluded, there is a peak in the tuning curve, but that the focal responses to luminance are larger than the pattern response to optimally sized squares. Subject V. The amplitude of the maximal pattern e.r.g. was compared to that of the low frequency minimum, and the results subject to a t test. For the dash–dot line, the number of responses = 12, the smallest response was 1·74 μV, the largest 2·04, and $t = 1·71$, with a significance $0·1 < P > 0·05$. For the full line, $n = 6$, the voltages were 1·12 and 1·69, $t = 2·45$, $0·05 < P > 0·02$. For the dashed line, $n = 18$, the voltages are 2·06 and 2·78. $t = 3·9$, $0·001 < P$. These voltages do not correspond exactly to the points on the graph. The graph points were obtained from records which were averaged in the computer, and measured by hand. The statistics were calculated by the computer which automatically measured each record.

Spatial frequency tuning curves

Fig. 3 shows the relationship between response amplitude and the size of the pattern elements under three separate conditions. For each curve, the left-hand point (open symbol) refers to responses produced by altering the luminance of the entire screen, and obtaining a focal on–off e.r.g. The dashed and dotted line connects points obtained with a small foveally fixated field. The stimulus intensity is high, relative to the large unchanging surround (see Figure legend for details). There is a bell-shaped curve, which peaks for squares of between 30 and 60′ subtense. The e.r.g. produced by a reversing pattern of optimum size is larger than the focal on–off response, and this difference is significant (see legend). When larger stimulus fields are used (dashed line) or only peripheral retina is stimulated (continuous line) similar curves are obtained, but the peak shifts towards larger square sizes, and as shown in the previous Figures, the focal on–off response amplitude is larger relative to the pattern response. Thus, there is a minimum in the curves, for large squares of between 2 and 4° subtense. The difference between the minimal and near optimal amplitudes of the pattern e.r.g.s was subjected to a t test. The differences were significant. Details are given in the Figure legend. The peak of the psychophysical Modulation Transfer Function for sinusoidal gratings is near 3 c/deg for most observers. The maximum cortical evoked

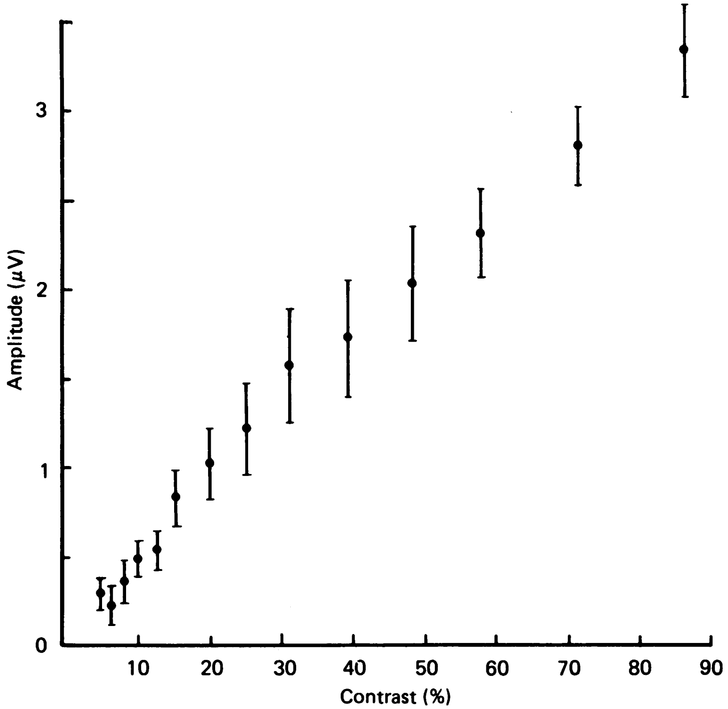

Fig. 4. Relationship between response amplitude and contrast for pattern e.r.g.s. The result is the average of experiments on six subjects, using 1° squares reversing at 4 Hz, the average luminance of the 22° × 16° screen was 50 cd/m². Surround intensity was 5 cd/m².

potential varies with the type of presentation, but for high contrast pattern reversing chequerboards, the largest responses are seen with 30′ squares. In both these cases, the responses are due to activity of foveal and parafoveal retina to a greater extent than is the case for the pattern e.r.g. (Regan, 1972; Celesia & Meredith, 1982).

Relationship between pattern contrast and e.r.g. amplitude

Fig. 4 shows the relationship between pattern e.r.g amplitude and the contrast of the squares in the pattern. The results shown are the average for experiments on six subjects. The vertical bars show ±1 S.E. of the mean. It is noteworthy that the response amplitude increases almost linearly with contrast, up to the maximum available. Since in these experiments the mean illumination was constant, the result shows that there is an approximately linear relationship between the response amplitude and the luminance difference between the dark and light portions of the pattern. When the pattern e.r.g. changes in amplitude as a result of altering some other parameter, it is possible to express the change in terms of the equivalent contrast. (See below for experiments with coloured patterns.)

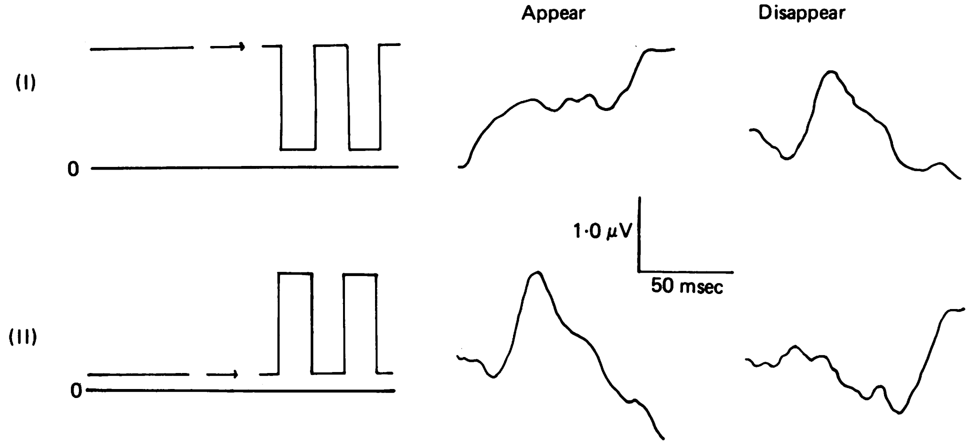

Fig. 5. E.r.g.s evoked by the appearance and disappearance of pattern with an associated change of luminance. In the diagram at the left, the ordinate represents light intensity, and the abscissa, horizontal distance across the screen. In the upper part, a bright uniform screen is changed to a pattern with decrease of mean luminance, and in the lower, a dim uniform screen changes to a brighter pattern. The diagram does not indicate that the pattern was a chequerboard, of 1° subtense. The corresponding e.r.g.s are shown on the right. Subject, S.W. Note that the b-wave is elicited when the luminance increases, regardless of whether the pattern appears or disappears. When bright squares appeared from the uniform screen (11), L_{blank}, 1 cd/m^2; L_{max}, 38 cd/m^2; and contrast 46%. When the dark squares appeared (1), L_{blank}, 24 cd/m^2; L_{min}, = 6 cd/m^2; and contrast 56%.

Pattern appearance and disappearance

Spekreijse *et al.* (1973) demonstrated that luminance, not contrast, was the controlling variable when an e.r.g. was evoked by the appearance or disappearance of a pattern. Fig. 5 shows results similar to theirs, obtained with our equipment under circumstances similar to those of our other experiments (see Methods). The inset to

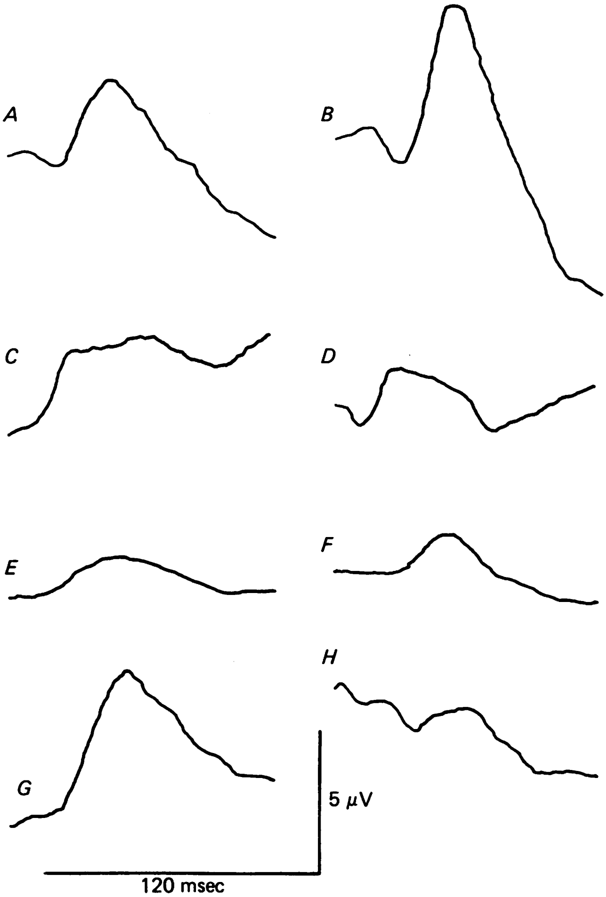

Fig. 6. Pattern e.r.g.s compared to the responses to change in luminance. Records *A*–*F* each represent the average of eight records, each obtained by averaging 250 responses from right and left eyes – 4000 in total. All the records were obtained in one experimental session. *A* shows the e.r.g. obtained when the luminance of a 15° × 11° field increases abruptly from 81 to 156 cd/m^2, and *B* when the luminance increases from 4 to 81 cd/m^2. *C* and *D* show the response obtained when the luminance decreases, for *C* from 81 to 4 and for *D* from 156 to 84 cd/m^2. The luminance changes occurred at a rate of 4 Hz, with a 50% duty cycle. When a pattern appears on the screen, with no change in average luminance, parts of the retinal image brighten (as in *A*) and parts darken (as in *C*). Thus, $A+C$ should average to produce the pattern appearance e.r.g., on the assumption that it is due solely to local changes in retinal illumination. In the same way, $B+D$ should give *F*, the pattern disappearance e.r.g. The lower half of the Figure shows the responses after further averaging and making allowance for the differing screen areas. *E* shows the predicted pattern appearance e.r.g., to be compared with *G*, the response actually obtained. *F* and *H* are the predicted and observed pattern disappearance e.r.g.s. The surround luminance was 250 cd/m^2 with 48′ checks. The computer measured the mean pattern appearance response *G* as 5·15 μV, S.E. of mean = 0·28, $n = 12$. The average of the corresponding luminance responses *E* was 3·09 μV, S.E. of mean = 0·40. For *H* the values are 1·33 μV, S.E. of mean = 0·18, $n = 10$ and for *G* 4·21 μV, S.E. of mean = 0·65. *t* tests performed on these pairs of results give $t = 12{\cdot}3$, which shows that the differences are very highly significant. Subject V.

the Figure shows diagramatically how the screen luminance altered when the stimulus appeared. Provided that the contrast is not greater than 40%, patterns produced by increasing or decreasing the luminance of parts of the screen are difficult to distinguish and evoke the same cortical potentials (Spekreijse *et al.* 1973). However, in the retina, the responses produced by the two types of pattern are very different. It can be seen that when the screen luminance increases an e.r.g. is evoked, regardless of whether a pattern appears or disappears. When the screen luminance decreases, an ill-defined response can be seen, which is similar for both types of pattern.

Synthesis of pattern appearance and disappearance responses

Despite the result shown in Fig. 5 it remains possible that the e.r.g. evoked by a pattern is dependent upon lateral retinal interactions. When the experiment of Fig. 5 was modified so that the pattern appeared and disappeared without change of the average retinal illumination, e.r.g.s were seen both at the beginning and end of the stimulus, but the appearance response was always larger than the pattern disappearance response. This was unexpected. When such a pattern appears, the brighter parts produce on-responses, while some off-response will be developed by areas which dim. When the pattern disappears, the situation is reversed, and the previously bright parts will produce off-responses, while those regions which during the pattern's duration were dim, will brighten and produce on-responses. Since the on-responses are larger than the off-responses, the e.r.g. will be dominated by the former. For pattern appearance, the on-response is produced by an approximate doubling of the light intensity emitted from parts of the screen. When the pattern disappears, the absolute increase in light intensity which produces the on-responses is the same, but it occurs in regions of the retina which were previously dimly illuminated, and therefore represent a many-fold increase in retinal illumination. Therefore, it is plausible that the pattern disappearance response should be the larger. Fig. 6 shows the e.r.g.s produced by altering the entire screen illumination in these ways. It can be seen that as expected, the brightening of the screen from the dim condition produces the largest b-wave. When the entire screen dims, there may be off-responses, but these are confused with a slower drift.

If the appearance and disappearance of a pattern has no other effect than that due to the local increase and decrease of luminance, the onset of a chequerboard pattern, (with 50% of the screen darkening, and 50% brightening), might evoke an e.r.g. comparable to the wave form obtained by summing the records shown in the upper two rows of the left hand column of Fig. 6 and halving the resulting voltage. This prediction is not fulfilled. There is a striking discrepancy between the pattern e.r.g. evoked by the appearance and disappearance of 0·8° squares and the averaged responses to change of illumination. For example, the predicted result is that the largest response will occur at the disappearance of the pattern: in fact, the response is nearly absent. We have considered ways in which stimulation by the uniform screen might differ from pattern stimulation, and provide a trivial explanation of the result. Experiments bearing on this point are presented below and discussed later.

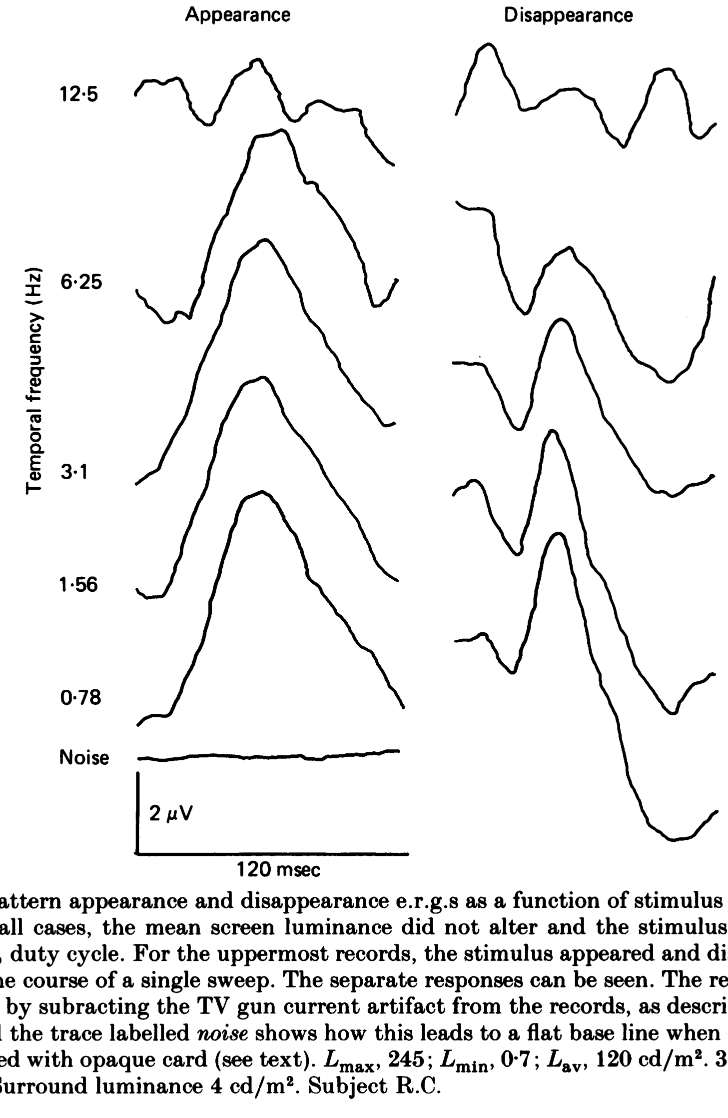

Fig. 7. Pattern appearance and disappearance e.r.g.s as a function of stimulus repetition rate. In all cases, the mean screen luminance did not alter and the stimulus appeared in a 50 % duty cycle. For the uppermost records, the stimulus appeared and disappeared during the course of a single sweep. The separate responses can be seen. The results were obtained by subracting the TV gun current artifact from the records, as described in the text, and the trace labelled *noise* shows how this leads to a flat base line when the screen is occluded with opaque card (see text). $L_{\max}$, 245; $L_{\min}$, 0·7; L_{av}, 120 cd/m^2. 33′ per side checks. Surround luminance 4 cd/m^2. Subject R.C.

The relative size of appearance and disappearance e.r.g.s

Pattern appearance and disappearance e.r.g.s were recorded at repetition rates varying between 12·5 and 0·78 Hz (Fig. 7). For the fastest repetition rate, appearance and disappearance responses occur in the same record. The response wave forms vary somewhat with the stimulus repetition rate, but onset and offset of the pattern clearly produce different responses. This experiment was one in which the gun current artifact was subtracted from the records (see Methods) and for one set of records the entire screen was occluded and voltages recorded to check that the subtraction procedure was satisfactory. The gun current produced a fast initial spike to the record of *ca.* 5 μV, which decayed over about 30 msec. It can be seen that there is no sign of this on the record labelled 'noise'. Note too that the signal-to-noise ratio is high.

The ratio of amplitudes of appearance to disappearance responses is greater for the more rapid stimulation rates.

The experiment was repeated with reduced contrast, and with alterations of surround luminance, and the asymmetry between appearance and disappearance persisted (Fig. 8). The relative amplitude of the response to pattern appearance and disappearance was investigated as a function of pattern size (Fig. 9). It can be seen that for very large squares, the appearance response is smaller than the disappearance response, as is the case for uniform screens: as the pattern size is made finer, the appearance response grows and reaches an optimum at a spatial frequency which approximates to that found for the peak of the pattern reversal tuning curve. The pattern disappearance response becomes progressively smaller as the square size decreases.

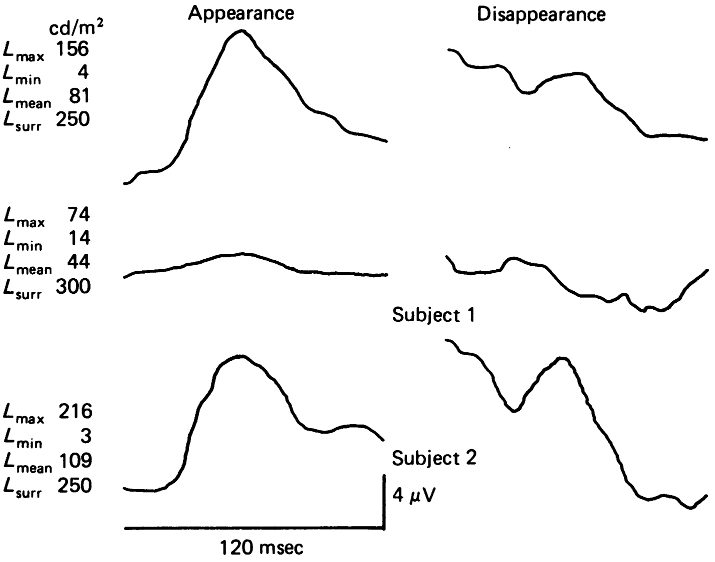

Fig. 8. Appearance and disappearance responses in two further subjects, to demonstrate the asymmetry between appearance and disappearance e.r.g.s with equiluminant screens, and to illustrate that the asymmetry persists with reduced contrast and higher surround intensity, as indicated on Figure.

E.r.g.s produced by colour contrast

Riggs, Johnson & Schick (1966) reported that pattern e.r.g.s could be recorded to changes in hue without change in luminosity. We have confirmed this report, and have also noted that the e.r.g.s evoked by large fields changing from uniform green to red (or red to green) are different in wave form to the responses seen when a red–green chequerboard reverses in hue (Arden & Vaegan, 1982).

Fig. 10 compares the pattern and focal on–off e.r.g.s produced by chromatic and monochrome stimuli. For the responses to colour, the luminance of the stimulus was constant over the area of retina stimulated. For the monochrome stimulus, the bright regions were of the same measured luminance, but the darker parts had a much

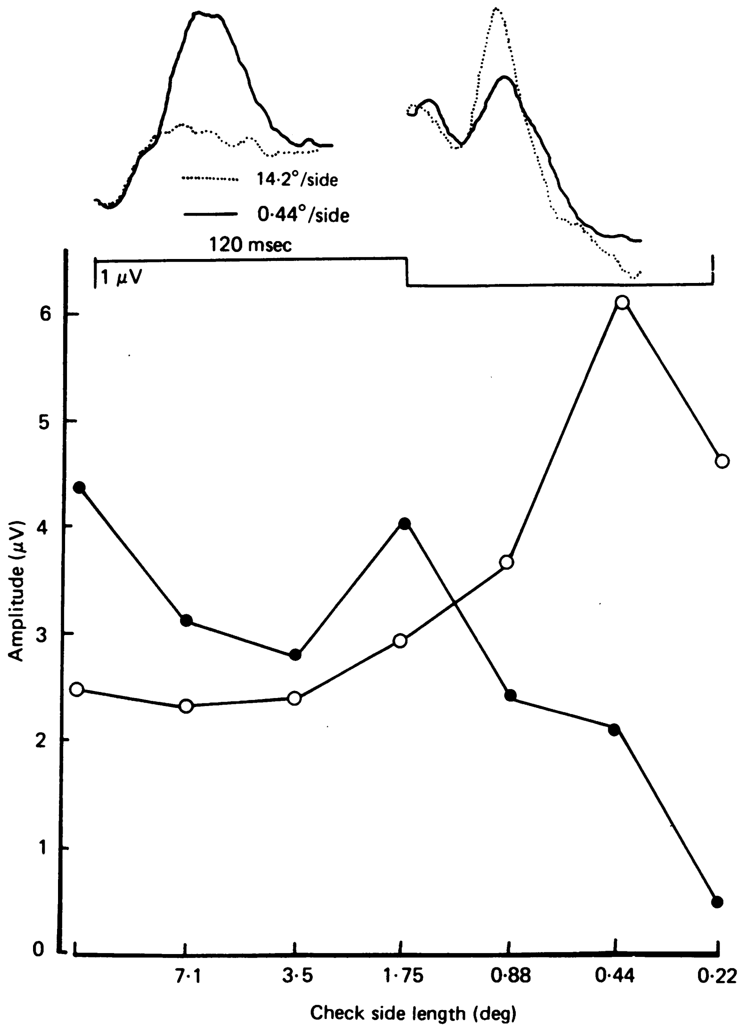

Fig. 9. Effect of altering size of squares on pattern e.r.g. The field size was 23° × 17°, L_{max}, 206 and L_{min}, 4 cd/m^2. Surround brightness was 260 cd/m^2. The pattern appeared for 165 msec. Open circles, pattern appearance, filled circles, pattern disappearance. Records of responses to two pattern sizes are shown above the graph. It can be seen that large squares produce e.r.g.s which are the same as the luminance responses (see Fig. 6) while as the squares become smaller, the e.r.g. changes to resemble the pattern response. Subject R.C.

reduced luminance to give a contrast which approached 100 %. The colour responses are nearly as large as those evoked by the black–white stimuli. Increasing or decreasing the ratio of red to green light by 25 % increased response amplitude (not illustrated). If the mechanisms responsible for the e.r.g.s had the C.I.E. spectral sensitivity curve, the transition from one colour to another should be a very feeble stimulus. It was calculated (see Methods) that for the human red and green primaries, the transition from red to green on the monitor corresponded to a change in contrast of 13 % for the red mechanism, and 22 % for the green mechanism. Fig. 4 shows that a monochrome contrast of these values, the e.r.g. would be very small, less than 20 % of that obtained with maximum contrast. Thus colour must be a specific stimulus for the focal on-off and pattern e.r.g.

Pattern appearance compared to colour changes

Experiments analogous to those of Fig. 6 were performed using the colour monitor to determine if the responses to colour pattern stimulation were the same as those evoked by changes of colour without pattern. Although the experiment was very similar to the one using black and white illumination, the effects of light scatter and non-uniform retinal adaptation are very different (see Discussion). In one condition, a red-green chequerboard pattern appeared from a uniform yellow field. In the other, uniform yellow fields were changed either to green or to red. In every case, the measured luminance of each small area of the screen did not change. The records (Fig. 11) all show a 50 Hz ripple. Part of this is electromagnetic interference (the stimuli were frame-locked, see Methods) but part is due to the retina responding to the repeated stimulation at mains frequency (Arden *et al.* 1982). The appearance of the pattern produces a response which is 2/3 the amplitude of that to pattern reversal. The disappearance response is about half the size of the appearance e.r.g. and the wave forms of the two are dissimilar. Thus the appearance and disappearance of coloured or black and white patterns produces e.r.g.s with similar wave forms.

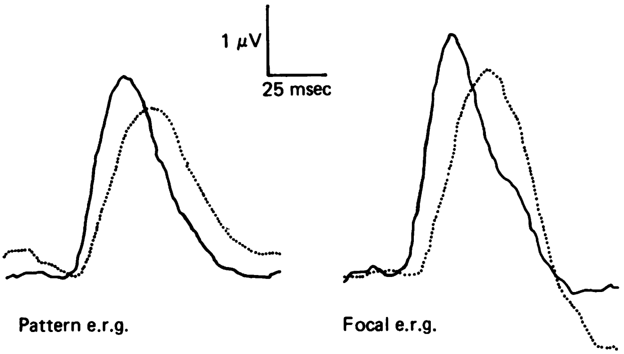

Fig. 10. Pattern and focal e.r.g.s evoked by monochrome changes in illumination (continuous line) or equiluminous changes in colour (dotted line). On the left, pattern e.r.g.s to 1° squares reversing at 4 Hz. On the right, uniform fields change from black to white (contrast 86 %) or from red to green. Mean screen luminance 84 cd/m^2; surround luminance 50 cd/m^2. Subject S.W.

Fig. 11 also shows the responses to transitions of the uniform field from yellow to red or yellow to green and vice versa. As in the previous experiment with black and white patterns, response *A*, to pattern appearance, should be equal to $(B+C)/2$ if the pattern response is due merely to local changes of hue. Record *D* shows such a computer sum compared to *A*. *E*, *F*, *G*, and *H* are for pattern disappearance. The responses are small, and have a 50 Hz component, but it is evident that the result is quite different to that of Fig. 6. The experiment was repeated many times in two subjects, and the results subjected to a *t* test. The pattern appearance and

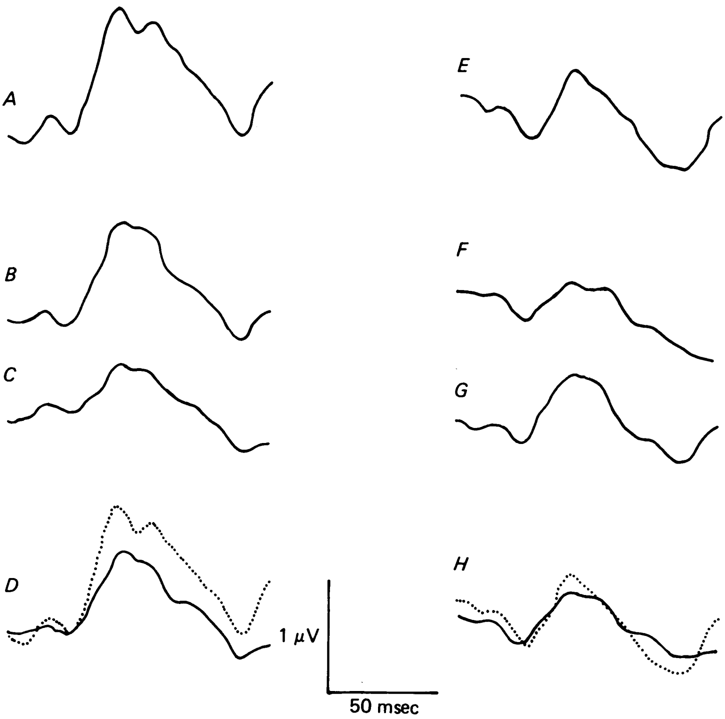

Fig. 11. Comparison of e.r.g.s evoked by coloured patterns and the equivalent changes in hue of a uniform field. The left hand column shows (*A*) a pattern appearance response, evoked by a yellow uniform field changing to a red–green chequerboard. *B* shows the response obtained when the same field changes to a uniform red, and *C* when it changes to green. *D* shows *A* (dotted line) compared with the average of *B* and *C*. Similarly, *E* is the pattern disappearance response, *F* and *G* the changes from red and green respectively to yellow. *H* compares *E* with the average of *F* and *G*. Stimulus repetition rate 4 Hz. Mean luminance 90 cd/m^2. The squares subtended 1°, with a $17 \times 11{\cdot}5$ screen. The pattern generators were frame-locked and the small deflexions on the traces are residual mains interference and also components of the e.r.g. evoked by the TV raster and synchronized to it. The traces shown are the average of two experiments on each of two subjects, S.W. and D.B. *t* tests were performed on the traces in *D* and *H*. For pattern appearance, the voltage = 1·37 μV, while the average of the responses to luminance change = 1·44 μV. For d.f. = 57, $t = 0{\cdot}67$. For pattern disappearance the corresponding voltages are 0·92 and 1·1 μV, $t = 0{\cdot}6$. These values indicate that the differences in amplitude are not significant. The statistics were obtained from records measured by the computer (see caption to Fig. 6).

disappearance responses are not significantly different to the e.r.g.s produced by the appropriate changes in hue in a uniform field. Statistical results are given in the Figure legend.

DISCUSSION

Differences between pattern and focal e.r.g.s

The television screens used as stimulators in our experiments had large bright surrounds to minimize the effect of stray light (Brindley & Westheimer, 1965). Control experiments (Fig. 1) showed that we obtained the linear spatial summation of response amplitudes expected under such circumstances. Therefore in each condition we compared the responses of similar retinal areas to focal and pattern stimulation. Because of the light adaptation caused by the surrounds the e.r.g.s recorded were very small. Prolonged averaging was required to characterize their wave forms and relative amplitudes.

Pattern responses are distinguishable from those produced by unpatterned stimulation. The time-to- peak of the e.r.g. evoked by black-and-white reversing patterns is some 5 msec longer than for the focal on–off e.r.g. The timings are different for red–green stimulation; again, there is a difference between the responses to a uniform or a patterned stimulus. The relative amplitude of the pattern and focal on–off e.r.g.s vary with the location of the stimulus on the retina. However, these differences are small and much of the experimental work was devoted to discovering conditions which would emphasize the differences between the responses evoked by patterned and uniform stimuli. The most important are those in which the size of the pattern elements was varied. Thus in Figs. 3 and 9 it can be seen that the largest pattern responses are obtained with squares whose sides subtend 0·5–1°. Holden & Vaegan (1981) and Holden (1982) have reported a similar finding in the pigeon. Korth (1981) who uses a rapidly responding optical stimulator, has reported a maximum in the tuning curve for the large wavelets of the pattern e.r.g. which his technique elicits. The fact that larger squares produce smaller e.r.g.s is difficult to explain unless it is accepted that changes of the spatial distribution of illumination within the retinal image can influence the e.r.g. Other experiments (see below, Fig. 6) reinforce this conclusion. Some authors have not found this peak of the tuning curve (Armington, 1982).

Do units with antagonistic centre and surround receptive field organization generate the pattern e.r.g.?

The experiments of Figs. 3 and 9 show that the pattern e.r.g. is largest for squares subtending 0·5–1°. This is reminiscent of what is found for other visual functions. For example, the cortical evoked potential is maximal for similar square sizes, and the contrast sensitivity function peaks at 2–3 c/deg. It is considered that such optima occur because there is a correspondence between the pattern size and the size of the most common receptive field centres. Therefore centres and surrounds are maximally excited. Larger patterns inhibit surrounds, and this is the cause of the 'low frequency fall-off'. Fig. 5 shows differences between the e.r.g. and the responses generated further upstream. Increases in light intensity produce much larger responses than decreases in luminance or changes in contrast. For cortical cells, change in contrast is by far the strongest stimulus (Spekreijse *et al.* 1973). In addition, ganglion cells and higher level responses saturate for fairly low contrast, while (Fig. 4) for the pattern e.r.g. the response grows up to the highest contrast available. This is more in keeping with the e.r.g. being generated by local changes in luminance.

The experiment of Fig. 6 was devised to resolve the matter. The result shows that the pattern appearance response is larger than the sum of the e.r.g.s produced by the appropriate spatially uniform changes of luminance. Thus this experiment, and the others considered in this section, are consistent with the idea that lateral retinal interactions help generate the pattern e.r.g. Alternative explanations are possible.

An objection can be raised to the experiment of Fig. 6. When (for focal on–off e.r.g.s) the luminance of any single point on the retina increased, the quantity of light entering the eye increased. When the pattern appeared, the quantity remained constant. Thus not every aspect of the stimulus was the same in the two cases. For this reason, experiments were performed with coloured patterns, and a different result obtained (Fig. 11). This finding, which at first seemed paradoxical, and consideration of the significance of the responses to coloured stimuli, lead to another hypothesis, discussed below.

The excitatory and adaptive fields of the units producing the pattern e.r.g. have different extents

Fig. 10 shows that responses to a red–green alternating chequerboard are 70% of the size of those produced by black–white reversals. The phosphors of the TV screen produce relatively desaturated colours, and were adjusted to be isoluminant. If the mechanism responding to pattern reversal had the C.I.E. spectral sensitivity, there should have been no response. If only one set of receptors generated the response, it should have been very small (see Results). Therefore there must be interactions (colour coding) between different classes of receptors before the site of generation of the e.r.g. Since the amplitudes of pattern reversal and focal on–off e.r.g.s are similar (Fig. 10) no lateral interactions need be postulated to account for the size of the pattern e.r.g. When the yellow field changes to a red–green pattern, total retinal illumination remains unaltered as does the illumination of every point within the stimulus area. The changes of hue evoke the e.r.g. Pattern appearance and disappearance e.r.g.s are smaller than the average response to change in hue. Thus, when the experiment of Fig. 6 is refined so that no change in retinal illumination occurs the results suggest that there is no specific response to pattern.

Such findings may be reconciled by assuming that the pattern e.r.g. is produced by local changes in luminance, but the amplitude is also dependent on a mechanism which samples retinal illumination over a region which subtends several degrees of visual angle, and integrates for a brief period before and after any change. Then, for example, when a pattern disappears, the e.r.g. produced by the squares which brighten would be small because the adaptational level would be set by the average luminance, of dark and white squares. If the pattern is sufficiently coarse, the amplitude of the response is governed to a greater extent by the minimum light level. If this hypothetical mechanism has a spectral sensitivity similar to the C.I.E. curve, it would remain unchanged in activity by change in hue, which acts as a powerful stimulus for the e.r.g.

Retinal layers which may generate the pattern e.r.g.

These experiments do not locate the cellular origin of pattern e.r.g. The elements of pattern and colour coding in cold blooded retinas are laid down as a result of horizontal cell feed-back onto receptors (Baylor, Fuortes & O'Bryan, 1971). Other lateral interactions may occur at subsequent synapses. In the goldfish (Kaneko, 1973) true colour coding can be seen in bipolar cells. In primates, colour coding occurs in tonic ganglion cells (Gouras & De Monasterio, 1975; Gouras, De Monasterio & Tolhurst, 1975; Gouras & Zrenner, 1979), but information about earlier stages is lacking. Thus, the demonstration of colour specificity is compatible with the response being generated as a result of bipolar cell activity. Horizontal cells, which sample receptor activity over considerable areas, and which in many cases are not colour coded, could account for the failure of luminance changes in uniform fields to minic the pattern appearance and disappearance response for black and white patterns.

If local changes in retinal illumination produce the pattern e.r.g., it could be a more sensitive index of local retinal disturbances than are focal flashes. Deposits of abnormal material such as may be seen in maculopathy could affect it specifically. Alterations to the gross anatomy of the inner retinal layers might also affect the ability to record local retinal responses (Arden *et al.* 1980; Vaegan *et al.* 1982). The pattern response may be modified to some degree by factors which do not affect the focal on-off e.r.g. However, luminance responses should be produced by pattern reversal and there is no indication in the present experiments that pattern and focal on–off e.r.g.s are separate phenomena. In the pigeon, both responses are recorded at similar retinal depths (Holden & Vaegen 1981). The report that sectioning the optic nerve abolishes one, but not the other, remains to be explained.

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