Responses of human visual cortex following excitation of peripheral retinal rods

Some applications in the clinical diagnosis of functional and organic visual defects

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When sense organs are adequately stimulated, the sensory cortex becomes active, and complex slow potential changes can be recorded from the appropriate regions. These *evoked responses*, which can be sharply differentiated from the ongoing "spontaneous" activity of the brain (the electroencephalogram) can be recorded in man, using electrodes placed on the scalp. However, they are very small and in order to characterize them properly electronic averaging devices are required.

The response of the human visual cortex, the visual evoked response (VER) is of considerable interest in the electrodiagnosis of ophthalmological conditions, for it has been shown that, while light which falls on the fovea and parafovea is effective in evoking cortical responses (VERs), activity of much larger portions of the peripheral retina leads only to very small VERs (Rietveld, Tordoir, and Duyff, 1965; Rietveld, Tordoir, Hagenouw, and van Dongen, 1965; Potts and Nagaya, 1965). Although luminous stimuli of small subtense, falling as much as 50° off the optic axis, have been stated to produce characterizable cortical responses (Eason, Oden, and White, 1967), the dominance of the foveal projection is so great that such "peripheral VERs" may well be produced by stray light stimulation of the central retina. Further, a good correspondence has been shown to exist between the VER and foveal function as regards the area-intensity relationship, spectral sensitivity, and directional sensitivity (DeVoe, Ripps, and Vaughan, 1968).

These properties of the VER are of great interest to ophthalmologists for, even when the light stimulus is not confined to the central retina, the response gives information which is related to subjective visual (*i.e.* foveal) performance (van Balen and Henkes, 1962; Copenhagen and Perry, 1964; Vaughan and Katzmann, 1964; Arden, unpublished). However, the question arises whether the VER can be used as a clinical test in a way which will permit the function of the peripheral retina—and especially the scotopic system—to be separately examined. Various authors have shown that the spectral sensitivity of the VER may agree well with the standard subjective photopic sensitivity curve† (Armington, 1966; DeVoe and others, 1968), as might be expected since these measurements refer to foveal stimulation. Evidence from experiments in which large areas of retina have been stimulated is much less complete. Thus Vaughan and Hull (1965) found that there was a break in the VER latency/light flash intensity curve at a

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†In this paper the spectral sensitivity values of the eye are taken from the Tables of the Commission Internationale d'Éclairage (C.I.E.) as quoted by Le Grand (1968). The values for the eye in the light-adapted and dark-adapted states are distinguished by the usual reference to "C.I.E. photopic" and "C.I.E. scotopic" curves.

level appropriate for the change from scotopic to photopic function. On the other hand, while the VER increases in amplitude and sensitivity during dark adaptation (Perry and Copenhaver, 1966), the change is not quantitatively comparable with that found by psychophysical means. It is possible that in all circumstances the contribution of rods to the excitation which finally evokes a VER might be small. Armington (1964), Eason and others (1966), Monnier (1963), and Bonaventure and Karli (1968) describe changes— increase of blue sensitivity—when the stimulus falls on the dark-adapted peripheral retina, but the results are by no means conclusive, and for this reason it was decided to reinvestigate the subject. In addition, we wished if possible to define a simple technique which would enable (if possible) “rod VERs” to be taken as a clinical routine.

Experimental methods

VERs were recorded in a clinical set-up, using standard electrode placements (Kooi and Bagchi, 1964; Vaughan, 1966). The scalp electrode was placed 2 cm. above the inion, and the other electrodes were connected to the ear lobes. The patient sat in a chair with a headrest. Tektronix 122 preamplifiers were used, with a bandpass of 0.2–250 c.p.s. A modified Tektronix 502A oscilloscope was used to drive a Mnemotron CAT 400C: the CAT output was taken to a simple chart recorder.

LIGHT SOURCE

The usual light source we employ is a stroboscope, $1/4$ J nominal output, 10 μ sec. flash duration. This tube is mounted in front of a parabolic reflector, which subtends 15° at the subject's eye. In front of it can be placed diffusers, neutral filters, and colour filters made of plastic (Cinemoid, Strand Electric Co. Ltd.). In experiments in which near monochromatic radiations were to be used, a similar flash tube was employed, but without a reflector. The housing of the bulb was made much smaller, so that the light passed through a 2 in. diameter interference filter (Schott, Depal), neutral density filters, and a diffuser, before reaching the subject. The diffused light source subtended 5° at the eye. Since interference filters are made for use in parallel beams of light, this crude system caused a deterioration in their performance: this can be calculated from the makers' specifications, and, in the present instance, was small enough to be ignored. All the filters were calibrated on an S.P. 600 spectrophotometer during the experiments.

Results

If the stimulus light intensity is reduced so that it is plausible that the scotopic, but not the photopic, system is stimulated, the VER, as usually recorded, promptly disappears. However, if the subject dark-adapts, after some minutes a small response reappears. In order to increase the sensitivity and the amplitude of the response, it is necessary to increase the area of peripheral retina stimulated. In preliminary experiments, a curved translucent plastic occluder (cut from a ping-pong ball) was fitted over the subject's eye, and the diffuse light shone upon it. The subject reported that, with fairly intense stimulation, the entire field of view appeared uniformly illuminated.

However, if the intensity was further reduced, with neutral filters, the colour of the stimulus flash became less saturated and, with further reduction, all sense of hue vanished: at the same time, the field ceased to be uniform, and the observer became conscious, with each flash, of a central scotoma. Thus the sensation evoked by the stimulus corresponded to stimulation of the scotopic system only. Under these circumstances, the flash evoked a large VER, and some response could still be observed even when the light intensity was reduced by a further 2–3 log units. At this level, the flash could barely be perceived. All the responses recorded in this paper were obtained with such dim flashes of light pre-

sented at a rate of between two and three a second for a period of $1\frac{1}{2}$ minutes. The rate was held constant throughout each experiment. The complex of waves described by other authors (Kooi and Bagchi, 1964; Vaughan, 1966) can be seen. The response is characterized by an extremely long latency (Vaughan, 1966), which is characteristic of the scotopic system at low light intensities (Arden and Weale, 1954).

SPECTRAL SENSITIVITY

Although it is in theory simple to specify some aspect of the VER which alters with stimulus intensity, and then to discover the intensity of monochromatic radiation needed to evoke a criterion response, there are severe practical difficulties. The VER waveform is highly variable from one experimental session to another, even when a trained subject is used, and therefore either the experiment has to be completed in one experimental session (which is quite impossible) or else a more complex experimental plan must be used. We have in fact always measured the sensitivity at only 2 wavelengths in each experiment, one of which was used as a reference; for one subject this was 526 nm, and for the other 569 nm. The reference wavelength was used in every experiment in which the subject took part. In addition, the use of the ping-pong ball has made the accurate calibration of retinal illumination difficult. We have therefore taken advantage of the fact that the spectral sensitivity of the "foveal" VER has been well established, and have measured, at each session, the change in sensitivity of the VER when the eye is light adapted. The subject's pupil was dilated with Mydrilate and an occluder was placed over the eye which then dark adapted. The subject entered the experimental room, which was lit only by a safelight. The occluder was taken off, and placed on the other eye. The dark-adapted eye was then covered with the diffuser, the electrodes were attached, and a series of VERs recorded. An intensity series was obtained at one wavelength, each intensity being employed twice. The wavelength of the stimulus light was then altered, and the procedure repeated. Sometimes, as a check on the stability of the system, further runs were now done at the original wavelength. The diffuser was now removed and the room lights ("daylight" fluorescent tubes) switched on. The subject, who faced a white wall, the illuminance of which was 10 ft. L, was light-adapted, and the entire procedure was repeated. At the end of each session (which took about 2 hours to complete) the relative light intensities were measured with an SEI photometer. The experimenter measured the brightness of the 5° stimulus patch first directly and then with the section of ping-pong ball interposed. To make these measurements the stroboscope repetition rate was increased to 100/sec. This calibration did not, of course, give the absolute retinal illumination under the various experimental conditions, but it did give the *change* in retinal illumination on passing from light of any one wavelength to another. The SEI calibrations were performed at three different intensities, and the error involved is less than 0.1 log unit.

When the records were examined it was apparent that the waveform of the VER did not change (in one experimental session) when the wavelength of the stimulus was altered. In the region of 1–2 log units above perceptual threshold, the response grew larger with increase of stimulus intensity. The peak-to-peak amplitudes of the responses were measured directly from the chart records. In the terminology of Vaughan (1966) N_2 – P_2 was measured but, owing to the small size of the near-threshold responses and the inter-session variability, no attempt was made to distinguish the finer details of the responses.

Fig. 1 shows graphs obtained from the results. At the lower light intensities there is a linear relationship between log light intensity and VER voltage (Vaughan and Hull,

1965; Rietveld and Tordoir, 1965; Kitajima, 1967). The slope of the lines was similar in one experiment for both the wavelengths employed, and for both light-adapted and dark-adapted conditions. Thus it appears that the same mechanisms were producing the responses at the two wavelengths, and the measurements can be used to determine relative spectral sensitivity. By interpolation in the graphs of Fig. 1 it is easy to obtain the light intensity corresponding to a VER of any desired amplitude, and thus determine the change in sensitivity at any one wavelength on light adaptation. The linear relationship breaks down when more intense stimuli are used, and in drawing the lines in the graphs of Fig. 1, divergencies at highest intensities were ignored.

FIG. 1 Sample results from an experiment to determine spectral sensitivity of the VER

Above, graphs illustrating relationship between VER peak amplitudes and light intensity. Each point is the average of four runs. The information obtained was collected in one experimental session

Below, sample VERs, one run at 481 nm, at the four intensities indicated in the graph. The stimulus is delivered at the arrow. The averaging time is 0.5 sec. and the stimulus artefact of the following flash can be seen $\frac{2}{3}$ of the way through the record

The intensity values obtained from Fig. 1 do not immediately give the spectral sensitivity of the VER, for in dark- and light-adapted conditions quite different parts of the retina were being stimulated. We have therefore compared the change in sensitivity at the experimental and the reference wavelength. For example, if on light adaptation there was an apparent decrease in sensitivity at 536 nm of 1 log unit, and at 505 nm of 2 log units, then clearly 505 is a more effective stimulus for the dark-adapted eye: and this conclusion is quite independent of considerations of area of retina illuminated, etc.

Fig. 2 shows the final results compared with a theoretical prediction. The points on the graph show the change in spectral sensitivity of the eye which occurs on light adaptation, *i.e.* the Purkinje shift. The points were simply calculated by subtracting the C.I.E. photopic curve from the C.I.E. scotopic curve. Since the values on the ordinate are logarithmic, the points may be moved upwards or downwards. The experimental results (large circles) have been placed in the following way. If we take the observed change in sensitivity at the *reference* wavelength, which is also in log units of light intensity, this point may be adjusted on the ordinate till it fits the theoretical curve—we are merely multiplying the observed value by an arbitrary number. The change in sensitivity of the experimental wavelength, determined at the same session, is now multiplied by the *same* number and plotted. In this way results obtained with different subjects and at different sessions may be compared.

FIG. 2 Spectral sensitivity of the dark-adapted VER. The points $\bullet \bullet$ represent the calculated change in spectral sensitivity which would be expected if the response, which under normal conditions is produced by foveal cones, was in the experimental conditions produced only as a result of stimulation of peripheral rods. The large circles are experimental results, obtained on two normal subjects ($\bigcirc$ and $\bullet$). The line is the regression line obtained from the experimental data

It can be seen that the small points calculated from the C.I.E. curve fall very nearly on a straight line. The line in Fig. 2 is, however, the regression line calculated from the experimental results, using the method of least squares. It almost exactly fits the calculated points. If the dark-adapted VERs had been produced by the photopic mechanism of the eye, there would have been no Purkinje shift: the regression line would then have been parallel to the abscissa. If the Purkinje shift had been partial, *i.e.* both cones and rods contributing to the response, the slope of the line would have been less and would not have fitted the theoretical points. We can therefore conclude that, in the circumstances of the experiment, the responses were entirely produced by the scotopic mechanism.

It is possible to extend the measurements to the short wavelength part of the spectrum, but then additional complications arise. The photopic spectral sensitivity is affected by macular pigmentation, and lens transmission (*via* the Stiles-Crawford effect), while the scotopic spectral sensitivity may be affected by the "scotopic blue mechanism" (Blackwell and Blackwell, 1961). In addition, the C.I.E. scotopic values are too low in the blue. Thus good agreement between a simple theory and experimental result would not be expected, and the divergencies could not easily be corrected. It was therefore considered that the precision of the experiments would not be increased by extending the measurements much below 500 nm.

The power of this method of analysing the results depends upon two factors:

- (a) the convenient finding that logarithmic subtraction of the photopic from the scotopic C.I.E. curve gives values which lie along a straight line;
- (b) that we have measured the *change in spectral sensitivity* on light adaptation.

Thus the results obtained at all wavelengths can be used to estimate quantitatively the magnitude of the Purkinje shift, and day-to-day variations in the VER, which show up on quantitative measurements as changes in light sensitivity, are also eliminated. If the present results had been used to construct a spectral sensitivity curve in a more conventional manner, they would merely have shown that in dark adaptation the maximum response was further in the shortwave part of the spectrum than the light-adapted peak sensitivity. Such results have indeed been previously reported (Monnier, 1963), but the precision is quite insufficient (both in the earlier work and in our own) to demonstrate without further analysis that the VER is totally rhodopsin-based in the dark-adapted eye.

Clinical tests

In routine clinical tests of the dark-adapted VER we have adopted much the same schedule as described above, but interference filters have not been used: the usual “cinemoid” sheets, blue and green combined, have been employed with light levels so low that the central scotoma can be seen, and the flashes appear to be colourless. In fact, as the preceding section shows, any (or no) colour filters could be used provided that the stimulus light was sufficiently dim.

It was found that the “rod-cone” transition was achieved with a blue-green filter and 1 log unit of neutral filter interposed. Fig. 3 shows the responses obtained from a normal subject (Case 1693) under clinic conditions. The increased culmination time and sensitivity of the dark-adapted responses are well shown. In a series of fifteen subjects and patients with normal retinae it was found that very small responses, “threshold responses”, could be observed with 4 log units of neutral filter interposed: thus the range of rod dark adaptation indicated by the VER is about 3 log units in normal eyes. With our clinical dark adaptometer the rod portion of the psychophysical curve extends through 2 log units only. Thus there is no exact correspondence to the VER, which can be explained by a variety of factors (see below), but we have repeatedly recorded VERs from subjects who reported that they could not see the flashes. Such responses are not caused by any noise associated with the stroboscope, for they disappear when the light is completely occluded; in all cases a visual threshold can be established. Since the patient is in the dark, he often

FIG. 3 Normal VERs obtained under clinical conditions. The averaging period is 250 msec. (Case 1693)

tends to doze during the test, and occasionally responses, large by comparison to the threshold response, can be recorded with no light entering the eye. This seems to occur at a particular flash frequency, possibly some sub-multiple of cyclical brain activity. When this artefact is detected, it can easily be eliminated by slightly altering the flash frequency and by alerting the subject.

In assessing patients reported on below, clinical examination was supplemented by the following tests, which are sufficiently widely employed to need only a brief description; other details are discussed in the test.

DARK-ADAPTATION

This was tested on a standard Goldmann–Weekers adaptometer. After 5 minutes of standard light adaptation, the dark-adaptation curve obtained with this instrument shows two branches, the first attributable to the return of sensitivity of the cones, and the second to that of the rods. The area of retina tested is a circular patch, 7° in diameter, some 11° superior to the fovea. The essential point of the machine is that the subject is unaware of the operator's movements, and that clues other than visual ones cannot be used by the subject. However, the subject must choose his own threshold criterion.

ELECTRO-OCULOGRAM

This is the record of standard eye movements recorded with periocular skin electrodes. The test consists in determining how greatly the recorded voltages vary with light and dark adaptation. The test used is described by Arden, Kelsey, and Barrada (1962). Abnormalities in the test occur when rods, or pigment epithelium, are pathological. Activity of the entire retina is sampled.

EARLY RECEPTOR POTENTIAL

This is recorded with a contact lens electrode. Intense flashes of light evoke a response from the receptors which occurs without measurable latency: the potentials are generated by charge movements associated with the bleaching of molecules of visual pigment. The intensities of light employed are so great that significant fractions of the pigment are bleached by each stimulus. The ERP merely indicates that pigment is present in the receptors: the membrane activity associated with excitation may be completely absent even when the ERP is present (see Galloway, 1966; Arden, 1969 for review).

ELECTRORETINOGRAM

This is also recorded with a contact lens electrode, using much weaker light flashes. A standard protocol designed to investigate the behaviour of the retina during light and dark adaptation is employed. The *a*-wave of the ERG represents the leading edge of the receptor potential: the *b*-wave which follows is produced by the bipolar (second order) neurones. The ERG responses often, but not always, parallel visual performance. Used in conjunction with the EOG, the ERG gives evidence of the site of a visual disturbance. The activity of the entire retina is sampled. The ERG does not give information about ganglion cell or optic nerve lesions. If more intense stimuli are given oscillations develop in the ERG, which are more closely related to optic nerve activity (Stétiade, 1968).

PERIMETRY

Using the Goldmann perimeter, the subject views a bowl on to which spots of light can be projected. The intensity, colour, and subtense of these stimuli are variable, and the overall illumination of the bowl can also be controlled. Perifoveal vision is also tested with a Bjerrum (or tangent) screen. The patient views a black cloth and reports on the visibility of small white or coloured discs which are placed on the end of a black rod and moved across the cloth. In patients in whom it was suspected that field loss was due to psychiatric disturbances, fields were plotted with targets of different sizes and with the patient at different distances from the tangent screen.

Clinical results

NIGHT BLINDNESS

A 30-year-old man (Case 1359) suffering from familial retinitis pigmentosa had recently complained of difficulty in seeing in the dark.

Examination

The visual acuity was 6/9 in the left eye, and the fundus showed the classical signs of the condition. The peripheral fields were somewhat constricted (Fig. 4). Within the peripheral fields, rod sensitivity was very markedly reduced, for the dark-adaptation curve showed only a single "cone"

branch (Fig. 5). In agreement with the findings of Fishman (1966), a light-adapted VER (Fig. 5) was within normal limits: since central vision was also normal in this patient, this is scarcely surprising. The dark-adapted responses however, were grossly abnormal, no activity being detected with more than 0.5 log unit of neutral filter.

FIG. 5 *Dark-adaptation curve and VERs from same patient as Fig. 4 (Case 1359). The elevated threshold in darkness and the monophasic curve indicate the absence of functioning rods. The VER likewise shows no activity except when intense stimuli are used. Then a short latency (macular) VER is obtained*

Cases like this produce VERs only when the light is bright enough to stimulate cones, as evidenced by the shorter latent period of the responses. These results indicate again the large range of light intensities in which scotopic VERs can be recorded. The decrease in VER sensitivity is about 3.5 log units, while the alteration in sensitivity shown on the dark adaptation curve is only 2 log units (the normal threshold value on the Goldmann dark adaptometer is at the ordinate level 1, Fig. 5). The discrepancy between psychophysical and VER sensitivity could be explained if in the latter test the potential recorded were due to activity over the entire periphery, and not merely to the peri-foveal rods.

MACULAR DEGENERATION AND ABIOTROPHY

In cases such as this, one would expect that VERs produced by the foveal projection would be affected, but that the “dark-adapted” responses, being produced by the peripheral retina, would be unchanged. Such a syndrome can easily be observed, as indicated in the following reports.

A 28-year-old man (Case 1734) had normal vision until he reached the age of 15 years. In the next 3 years, his vision dropped to “counting fingers” in each eye and has since remained stationary.

Examination

The fundus showed pigmentary disturbance at both maculae and in the periphery; there was bilateral narrowing of retinal arteries and pallor of the optic discs. The fields (Fig. 6) showed a dense central scotoma. The peripheral fields were full. The EOG and ERG were reduced. The latter is shown, together with the ERP in Fig. 7. In the light-adapted condition, the VER (right eye) was absent (Fig. 8), although the area of retina directly stimulated by the stroboscope was larger than the scotoma. The dark-adapted response was present, but the threshold was raised by 2 log units. Visual threshold, determined on the Goldmann adaptometer, was raised by 0.5 log unit, though naturally fixation could not be maintained.

FIG. 6 Central visual fields, re-plotted from tangent screen results, of a patient with macular degeneration (Case 1734). The blind spots are indicated

FIG. 7 Responses to high intensity flashes from same patient as Fig. 6 (Case 1734). The stimulus (arrow) is followed by a downwards (cornea-negative) deflection, the early receptor potential; neural activity (the electroretinogram) follows. With lights of this intensity, the ERG consists mostly of the “receptor potential”. Upper trace, first stimulus. Lower, second similar flash, delivered 30 sec. later. Note decreased size of ERP due to bleaching of rhodopsin

FIG. 8 VERs from the same patient as in Fig. 6 (Case 1734). Note absence of photopic responses and preservation of long latency scotopic responses

A 53-year-old woman (Case 1725) had suffered deterioration of vision over the past 2 years. The visual acuity was 6/60 in the right eye and 6/36 in the left.

Examination

Bilateral macular degeneration was seen, but the vessels and discs were normal. An abnormal EOG was recorded, but ERGs of normal waveform and amplitude were obtained from both eyes. In a subjective test of dark-adaptation (Goldmann adaptometer) thresholds 0.5 to 1.0 log unit above the average were recorded. The peripheral fields were full but central scotoma could be detected (Fig. 9, overleaf). The VERs in light-adapted conditions were very small, but normal dark-adapted VERs were seen (Fig. 10, overleaf).

FIG. 9 Tangent screen fields from a patient with macular degeneration (Case 1725)

FIG. 10 Photopic and scotopic VERs in same patient as Fig. 9 (Case 1725)

HYSTERIA

One of the main reasons why we developed the dark-adapted VER as a clinical test was that a large group of patients was referred to the clinic, complaining of loss of vision, in whom the ERGs and EOGs were normal, whereas dark-adaptation and visual fields were abnormal. In general, gross constriction (to well within 10° of fixation) of the peripheral fields was accompanied by apparent night blindness, and the final thresholds on the Goldmann dark adaptometer were raised between 2 and 6 log units. These cases closely resemble the "hysterical amblyopia" described by Krill (1967) and Krill and Newell (1968).

A girl aged 10 years (Case 0958) was first seen in 1967 because she was unable to read from the blackboard. Her parents had previously noted symptoms suggestive of night blindness.

Examination

The visual acuity was 6/24, and a clinical examination revealed no abnormality. Perimetric investigations showed constriction of peripheral fields to within 10° of the fovea. The ERG and EOG were normal. Colour vision testing revealed a medium strength red/green defect. The dark-adaptation curve (Fig. 11) was a simple, monophasic type, and the final threshold was 4 log units above normal—i.e. the "cone" sensitivity was reduced, as well as complete loss of the scotopic portion of the curve. The dark adaptation and visual fields were examined several times over a period of approximately 6 months, and similar results were obtained on all occasions. The edges of the visual fields were sharply defined. The field angle was considered to be independent of the distance the subject was placed from the tangent screen. The dark-adaptation curve was continued for long after the final threshold had been achieved, and variation in the patient's responses was very small, and certainly no greater than in normal subjects.

Krill (1967) described an "exhaustion" phenomenon in dark adaptation of hysterical patients—if the test is prolonged, the eye apparently becomes progressively *less* sensitive. This obviously did not occur in this patient, and we have only once observed this phenomenon. Thus all examinations gave no indication that the patient had a functional complaint and a tentative diagnosis of retinal abiotrophy had been made. However, the VER was normal, in both the light-adapted state and dark-adaptation (Fig. 12). Thus there was a sharp discrepancy between the subjective and objective methods of measuring visual sensitivity. The subsequent course of this patient confirmed the diagnosis of hysterical amblyopia. The visual acuity improved over the next 18 months to 6/12, and the visual fields became full to confrontation. However, in perimetric measurements the constriction remained unaltered.

FIG. 11 Dark-adaptation curve obtained from a patient with hysterical amblyopia (Case 0958). From 0 to 5 min. the patient was light-adapted

FIG. 12 Normal VERs obtained from same patient as Fig. 11 (Case 0958)

There was no evidence of any psychiatric disturbance in this case, and the defects spotted by other observers seemed typical of organic lesions. The ERG and EOG tests ruled out the possibility that receptors of bipolar cell lesions caused the night blindness and constricted fields, but the reproducibility of the results of these subjective tests was such that a central lesion was suspected, although the tests themselves lent no support to this idea. The normal foveal VER (light-adapted) is consistent with the moderate reduction in visual acuity. The scotopic VER however demonstrates that retinal information from large areas of retina is reaching the optic cortex, and at least some data-processing is occurring there. Thus the night blindness demonstrated so convincingly on the dark-adaptometer must be due to a disturbance still further “upstream” in the visual pathway.

Many similar cases have been investigated, a considerable proportion being in children (approximately 50 per cent.). These are to be reported separately (Behrman, in preparation). We have, however, also found puzzling correspondences between the VER and subjective tests in cases in which a functional basis was clearly demonstrable.

A 43-year-old woman (Case 1261), who was in good general health, was first seen in the Electrodiagnostic Clinic in September, 1967, with a 6 months’ history of poor visual acuity and limitation of the field of vision of the right eye only.

Examination

No abnormality was found in the anterior or posterior segment at any time, and the ocular tension remained normal. Peripheral and central fields tested at this time showed an increasing generalized constriction and the visual acuity had fallen from 6/6 to 6/18 in the right eye. The left eye was normal.

History

There was no relevant family history or previous illness. She was not receiving any medicaments and did not smoke. The patient’s daughter volunteered the information that her mother had recently been under some emotional stress.

Before attending Moorfields, she had seen several consultant ophthalmologists who strongly suspected the possibility of a functional disorder, but ultimately abandoned this diagnosis because

of her social position [!] and the apparent stability of her personality. Neurological examination revealed no abnormality apart from the gross field defect.

Progress

The patient was sent to the Electrodiagnostic Clinic for further evaluation and was seen on three occasions.

On October 18, 1967, the visual acuity was 6/18 in the right eye and 6/6 in the left. The EOG and ERG were normal (Fig. 13). Central and peripheral fields of the right eye were severely constricted when tested on the Goldmann perimeter. Visual fields obtained on a tangent screen at 1 and 2 metres did not indicate a functional disturbance. Testing with H.R.R. plates revealed total achromatopsia in the right eye and normal colour vision in the left.

FIG. 13 ERGs and EOGs (normal) obtained from a patient with hysteria (Case 1261)

FIG. 14 Dark-adaptation curves obtained from same patient as Fig. 13

Dark adaptation was investigated on the Goldmann-Weekers dark adaptometer (Fig. 14). Initially the patient could scarcely see the test light, and was unable to perceive the fixation light. Over the next 40 minutes the threshold slowly fell and the patient then volunteered the information that she could see the fixation light; this corresponds with what we know should occur in patients with reduced visual sensitivity, but in normal subjects the delay is only a few seconds, not 20 minutes. For the next 20 minutes the threshold remained unaltered, but then sensitivity started to increase once more, finally reaching normal values after 70 minutes. The dark-adaptation curve of the normal left eye, is shown for comparison.

When sensitivity had reached the scotopic level, the patient volunteered the information that her visual field had increased in size, and also that the hue of the fixation spot had altered so that now it appeared red. The foveal VER was normal. The peripheral VERs, taken after 30 minutes, showed a loss in scotopic sensitivity of about 3 log units, consistent with the dark-adaptometry (Fig. 15).

We therefore believed that this patient had a unocular lesion and that her peripheral retina ceased to function when she was light-adapted; the level of the block would have to be the ganglion cells, since the normal ERG and EOG were normal. Therefore we dark-adapted the patient and plotted visual fields in a modified Goldmann perimeter, with no background light whatsoever. We also determined visual thresholds to both white and monochromatic light in various portions

of the peripheral field. Normal results were obtained as we anticipated from the previous investigations. Following this, we put a very dim background illumination on to the perimeter bowl and repeated the investigation (*i.e.* we attempted to perform increment thresholds). Normal results were obtained as the background was gradually raised to the maximum illumination obtainable with the Goldmann perimeter. The fields remained full, and sensitivity and colour vision were normal. After the test was over the patient left the test room and entered a relatively ill-lit corridor, and immediately her symptoms returned. During the following months they waxed and waned in severity, and occasionally both eyes were involved (Fig. 16). It is therefore clear this case can be classified as one of “hysterical amblyopia”.

FIG. 15 Absence of scotopic VERs in same patient as Fig. 13

FIG. 16 Variation in size of peripheral fields in same patient as Fig. 13

The VERs shown in Fig. 15 were obtained between the second field (October, 1967) and the third (January, 1968)

The interest of this case lies in the facts that the patient can mimic the signs of organic disease to the extent of producing an abnormally slow dark-adaptation curve, and that her scotopic VER shows a loss of sensitivity. It is impossible to prove that the patient was not consciously malingering. She could, for example, have closed her eyes during the VER and developed some trick so that she increased her retinal illumination progressively during the dark-adaptation test. However, we believe this possibility can be discounted. The patient was unfamiliar with the apparatus and the tests, and the testers were alive to the possibility of this type of “cheating” and took steps to prevent its occurrence (though admittedly such steps cannot totally exclude trickery). In addition, only two tests showed any abnormality, and both these pointed to a lesion in the central optic pathway: it is unlikely that our patient had expert knowledge of neuro-ophthalmology

as well as of neurophysiology. It therefore seems that a hysteric may be able to cause a block in the flow of visual information at a subcortical level. Thus, although in most cases of functional disturbance, the VER is normal, it is impossible to be sure that an abnormal VER proves the presence of an organic lesion.

Summary

The change in spectral sensitivity of the eye on dark adaptation—the Purkinje shift—can be reliably measured with the VER. Over a large range of stimulus intensities, the results indicate that the responses are due solely to the activity of the rods. Thus the dark-adapted VER can be used as a sensitive test of peripheral retinal function. Abnormal dark-adapted VERs were found in patients with night blindness, while the light-adapted VER was normal. In patients with disease of the macula, the reverse is true. In patients with “hysterical” amblyopia, who suffer from constricted visual fields and night blindness, both light- and dark-adapted VERs are characteristically normal, but exceptions may exist.

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