ELSEVIER

Ophthal. Physiol. Opt. Vol. 16, No. 1, pp. 42–48, 1996

0275–5408/96 $15.00 + 0.00

0275-5408(95)00043-7

Contrast and luminance as parameters defining the output of the VERIS topographical ERG

Brian Brown[1] and Maurice K. H. Yap[2]

[1] Department of Optometry and Radiography, Hong Kong Polytechnic University, Hung Hom, Hong Kong; and [2] Department of Optometry, University of Auckland, Auckland, New Zealand

Summary

The Visual Evoked Response Imaging System (VERIS I) topographical electroretinogram system (EDI Associates, San Francisco, CA) allows measurement of the response of large numbers of retinal areas simultaneously. This paper examines ERG responses derived with the VERIS system to changes in target contrast and to local reductions in luminance. There is a linear reduction of response with reductions of target contrast. Neutral density filters were placed over part of the display, to mimic the localised reductions in response which occur in glaucoma, age-related maculopathy or diabetic retinopathy. There is a definite reduction in response seen with a 0.4 ND filter, indicating that the system should have similar sensitivity in detection of retinal lesions to the commonly used visual field analysis systems.

Introduction

The conventional electroretinogram (ERG) has been used for many years in the simple flash or flicker mode, and in the pattern mode to provide an objective indication of retinal function. Regan[1] has provided an extensive review of many aspects of human neural electrophysiology, including the ERG. The typical ERG system is, however, limited to providing a single waveform representing the response of the stimulated retinal area. The stimulated area may include the whole retina in the case of the flash ERG, especially in the dark-adapted eye, since light scattered by the optical media or from the optic disc itself will provoke a response[2,3]. The pattern ERG suffers less from scattered light problems since the total light input to the eye is simply redistributed with each successive frame of the stimulus. The focal ERG has been used to examine responses of local retinal areas, but problems of fixation control and the need for sequential recording from different retinal areas has limited its utility. Birch[4] gives a review of the uses and limitations of the focal ERG technique.

The VERIS topographical electroretinogram system is a promising new tool for evaluating local retinal function. It consists of a conventional ERG measurement system coupled to a computer-controlled stimulus generation and response analysis program. It was first described by Sutter and Tran[5] who showed that it is possible to generate high resolution maps of retinal function; some of the stimulus patterns which they used have as many as 241 separate stimulus areas, generating 241 separate ERG waveforms.

The VERIS system can be used in a number of modes. In luminance stimulation mode, the individual elements of the display are simply turned on or off. In this mode each stimulated area produces its own ERG waveform. The stimulus elements may be standard high contrast black and white areas, they may be of specifiable contrast, or they may be colour combinations such as red/green or blue/yellow. All the colours and luminances of the Apple Macintosh display system are available for use as stimuli. Sutter and Tran[5] have shown good concordance between the fall-off of the response to this type of stimulation with eccentricity and cone density measured in human retina by Curcio and colleagues[6].

In pattern stimulation mode, three sets of small circular areas are defined within each of the hexagonal patterns of the array. This stimulus mode is designed to stimulate elements in the visual system with centre/surround organisation, and thus should largely reflect function of the inner retina[7].

In this series of experiments, the luminance stimulation

Received: 9 January 1995
Revised form: 12 April 1995

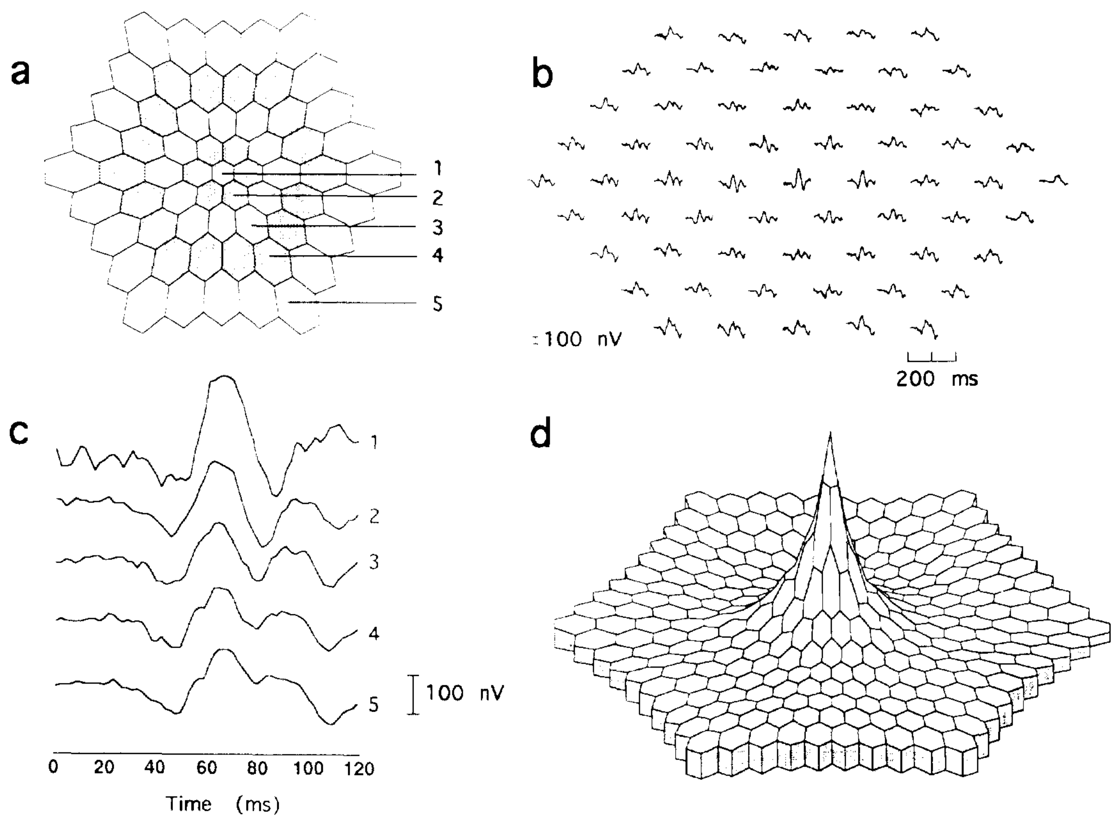

Figure 1. VERIS stimulus and outputs: (*a*) shows the stimulus fields used in these experiments. The fields are hexagonal and the pattern is radially symmetrical. In this pattern the fields are scaled with eccentricity to give responses of approximately equal amplitude across the field. An ERG waveform is derived for each stimulus area (*b*). These can be averaged over selected groups, as shown in (*c*) for the five groups selected in (*a*). (The shading here is simply to indicate which elements are chosen for the averages and does not represent what the subject sees on the display.) Any groups of stimulus elements may be selected and averaged. (*d*) shows the three-dimensional plot of stimulus amplitude corrected for stimulus area for the responses in (*b*).

mode was used. *Figure 1a* and *b* shows the stimulus areas used and the waveforms derived from individual stimulated retinal areas, as well as a three-dimensional plot derived from each set of waveforms (*Figure 1d*). The three-dimensional plot shows the foveal response and a clear decrease in ERG output with increasing eccentricity. The field size in these experiments was 28 × 28 degrees in total extent and so the blind spot depression is not visible, being at the margin of the display. It is possible to average over specified hexagons and, given the radially symmetrical nature of the retina, it is often useful to show the responses of the fovea and the surrounding retinal annuli, as in *Figure 1a*, where the annuli are specified (shown as alternately shaded or non-shaded groups of hexagons), and *Figure 1c* where the average waveforms corresponding to the annuli are shown.

A system such as this, which can map retinal responses, clearly has potential for clinical use in differentiation of retinal, optic nerve or visual cortex dysfunction as is done with the conventional ERG. This system also has potential uses in examination of local losses of retinal function in conditions such as glaucoma, branch retinal vessel occlusion, retinitis pigmentosa and other retinal conditions. In localisation of defects of the retina, this technique will be more specific than visual field plotting, which examines the response of the entire visual pathway.

Before the topographical ERG system can be used clinically, an abbreviated protocol needs to be developed, and we need information about the contrast and luminance sensitivity of the system. In this paper we explore the way in which the ERG output of the system varies with reduction of contrast and local reduction of luminance. We report here that there is a linear reduction in response amplitude with decreasing contrast and that local reductions of luminance of 0.4 log units or more produce clear reductions in response.

Methods

We used a VERIS I system which produces a stimulus display on a standard Apple computer monitor. The display used throughout was a 61 hexagon array shown schematically in *Figure 1a*. Luminance modulation of each of the hexagonal elements of the display was produced by the controlling computer program, which simultaneously recorded the raw ERG signal. The subject is simply required to fixate the centre of the display while each of the elements of the display are turned on and off according to a predetermined pseudo-random sequence (see below).

The VERIS system derives the impulse response from each retinal area stimulated using cross-correlation of input (the sequence of on and off transmissions of each of the stimulus areas) and output signal (the ERG response of the retina). Eight samples of the ERG response are acquired on every frame of the display presentation (i.e. at $67 \times 8 = 536$ Hz), giving a sampling interval of 1.87 ms. A binary m-sequence is used to control the on–off transitions of the display elements during stimulation; this pseudo-random sequence allows very rapid computation of the cross-correlation of input and output signal[8]. The system can derive nonlinear components of the response (such as effects of previous stimulation on the current response), although these components are not considered here.

In these experiments, the ERG was recorded with DTL thread electrodes[9]; the ERG signal was amplified 1000 times using Grass P15 amplifiers (with filtering from 0.1 to 300 Hz), and then a further 200 times using custom-constructed amplifiers incorporating a 50 Hz notch filter. The use of the notch filter produces phase shifts among components of the signal, but does not affect signal amplitudes. In the experiments reported here, absolute and relative amplitude measures were made for comparison of the various experimental conditions. Latencies were not considered.

Subjects were volunteers from the laboratory and the authors; informed consent was obtained from all subjects. Subjects had corrected visual acuity of 6/6 or better in the tested eye(s). Four subjects were Chinese and one (author BB) was of European descent; they ranged in age from 24 to 49 years. All had normal ocular health in the eye(s) tested. Pupils were dilated with 0.5% tropicamide and optical corrections were worn, if required. All subjects were corrected for the viewing distance of 35 cm using trial case lenses. Subjects had ERG recorded while they maintained fixation on the centre of the stimulus array, and refrained from blinking. Four or eight stimulus/response epochs of about 2 min in length were recorded for each subject for each condition of contrast or luminance manipulation. In some runs, both eyes of the subject were recorded simultaneously. The pseudo-random sequence used in the VERIS system can be interrupted and broken into segments of tolerable length for recording. Typically segments 15–30 s long were used in the recordings.

Effect of contrast on topographical ERG response

The maximum luminance of the display was 132 cd/m^2, and the minimum was 3 cd/m^2. Luminances of the monitor were measured with a Topcon BM-5 telephotometer; a calibration curve of luminance as a function of the luminance specification value of the Macintosh operating system was derived for the display monitor to allow computation and setting of contrast values. The contrast of the display was changed from run to run, from 96% to 64, 32, 16 and 8%.

ERG data were averaged for the fovea and successive annuli of stimulation (see *Figure 1a* and *c*), and the peak-to-peak amplitude measured between 0 and 66.8 ms from the start of the response.

Effect of local luminance reductions on topographical ERG response

Neutral density filters (2 in $\times$ 2 in) were placed over part of the display. Filters of 0.1, 0.2, 0.4, 0.8 and 1.0 ND were used. The peak-to-peak amplitude of the waveform was measured at the fovea and at the areas shown in *Figure 2b*. The response from the attenuated area and a symmetrically placed control area were compared in the analysis; these are also shown in *Figure 2b*.

Results

ERG amplitude and contrast

ERG amplitude decreases linearly with decreasing contrast; this is true for all areas of the retina. There do not appear to be any marked deviations from linearity for the foveal response or for any of the peripheral retinal annuli. Typical data are shown in *Figure 3*; this figure shows a typical set of averaged waveforms for one subject for foveal stimulation and for the annular regions for 96, 64 and 32% contrast. *Figure 4a* shows a comparison of the peak-to-peak amplitude measured from these waveforms for a single subject; *Figure 4b* shows mean data from all subjects used in these experiments. The reduction of response with reducing stimulus contrast appears to be similar for the fovea and the periphery. The slope of the function relating ERG amplitude to contrast varies from subject to subject; however the apparent difference in slope evident in the data of a single subject in *Figure 4a* is not seen in the data of the group shown in *Figure 4b*.

ERG amplitude and local luminance reduction

In these experiments we found that the 0.2 ND filter placed over the display shows measurable attenuation of response, while a 0.4 ND filter produces substantial effects. Results for a single subject are shown in *Figure 5*; the left panels of the figure show the response of the retina to each

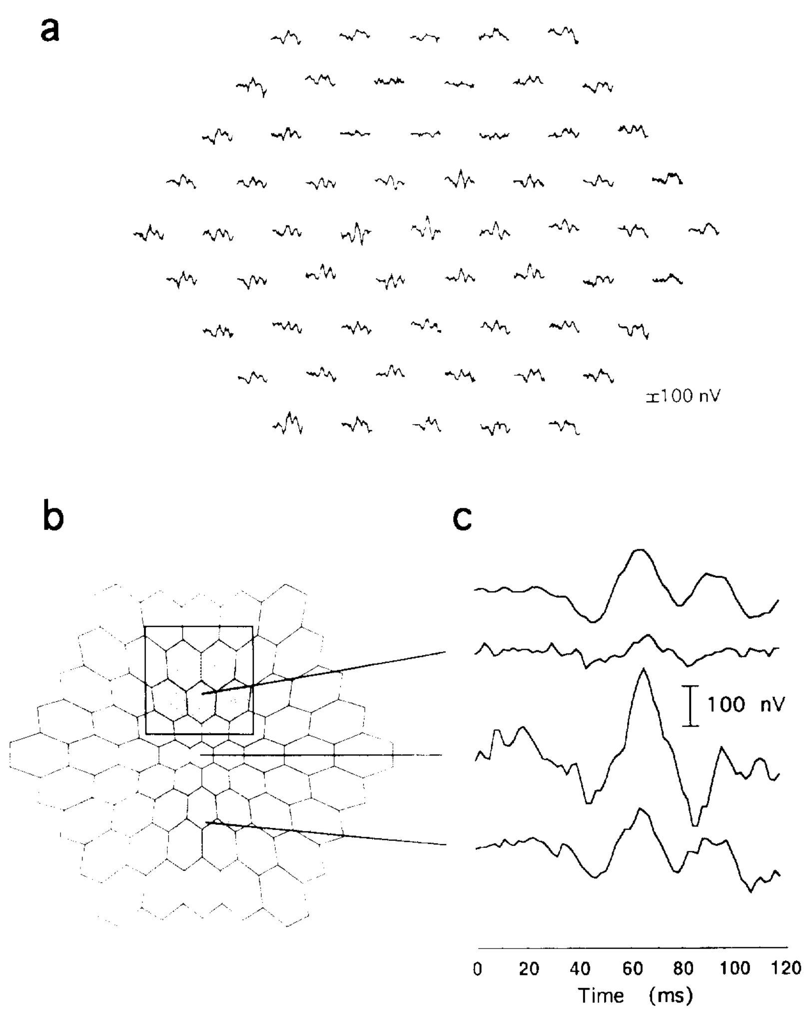

Figure 2. Areas of the display masked with ND filters (upper central elements in (*a*) showing reduced response. (*b*) and (*c*) show (from the top) the average response from the unselected elements, the response from the five elements in the upper part of the display which were masked with a 0.8 ND filter, the foveal response, and the response of the five elements in the lower part of the display which were selected as a control for the upper peripheral elements.

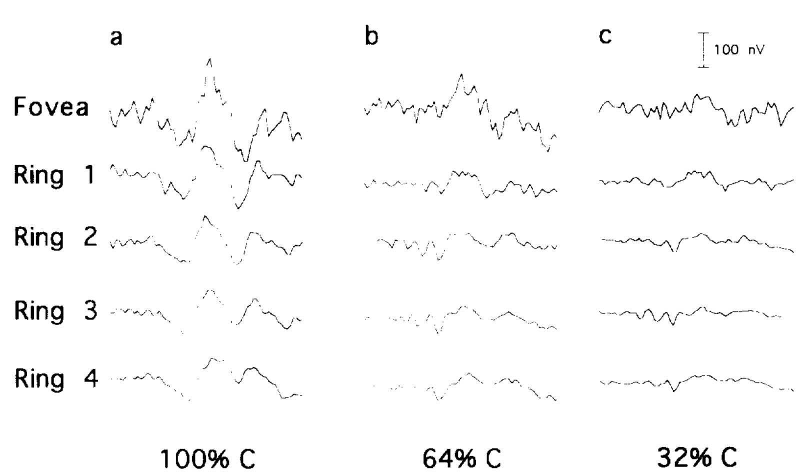

Figure 3. Responses for the fovea and averaged responses for successive stimulus annuli for stimuli of maximal and reducing contrast.

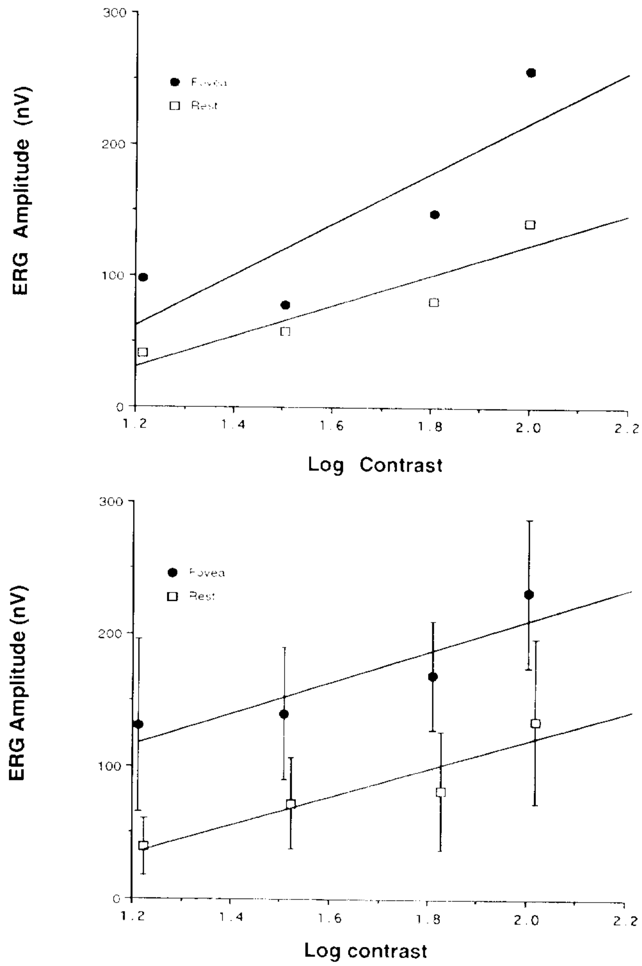

Figure 4. Peak-to-peak ERG amplitudes as a function of contrast with the foveal response in the upper data set (filled symbols) and averaged responses over all other elements (open symbols) in the lower set of each panel. The upper panel shows data for one subject, the lower panel shows the average of seven data sets derived from five subjects. Error bars show ± 1 SD; the points are slightly displaced to show error bars more clearly.

stimulus element. The five upper waveforms (shown circled) are those with the ND filter in place; the five symmetrically placed lower waveforms (also shown circled) are selected as a control area. The foveal response is also circled. Response waveforms for the fovea and average response waveforms for these areas (ND and control) and the rest of the elements are shown in the right panels of this figure.

Data for seven eyes of five subjects averaged across the luminance attenuated hexagons are shown in *Figure 6*. The reduction in amplitude appears to be linear with increasing density of the applied filter. The variability in these data can be reduced if they are normalised with respect to the amplitude of response in another part of the retina (fovea or periphery) in the same record. *Figure 7* shows the ERG amplitude change relative to the average peripheral response which shows this reduction in variability.

Discussion

The reduction of the ERG with decrease in contrast confirms the findings of Hess and Baker[10] for the pattern ERG. The stimulus used here, although designated 'luminance' stimulation by Sutter and Tran[5], is quite similar to a conventional pattern ERG in that local retinal areas are stimulated with an alternating on–off stimulus. There are retinal responses to both the absolute luminance change and the edge component of this stimulus (see, for example, Sutter and Vaegan[11]).

Hess and Baker[10] found a linear relation between ERG amplitude and contrast level over almost the entire range of contrasts examined, from about 10 to 100%, but in many cases they found an intercept with the response axis at about 20% contrast. They found that the slope of the function varied as a function of the spatial and temporal characteristics of the stimulus. Hess and Baker[10] also reported a similar dependence of ERG amplitude on luminance of the stimulus, with the response amplitude increasing over two log units from 2 to 200 cd/m^2. Over this range, the signal increased from 5 to 15 times, depending on the spatial frequency of the stimulus. In their experiments, eccentricity was an important determinant of the ERG response amplitude: the peak response density decreased to about 20% of the amplitude at the fovea at 15 degrees eccentricity and to 10% of the foveal amplitude at 34 degrees eccentricity. This is a loss of amplitude of about 1 log unit in 32 degrees. Hess and Baker were only able to examine peripheral responses by masking out the foveal areas and did not have the advantage of being able to examine responses from the same retina at the same time.

The topographical ERG system is comparable in many respects with conventional visual field testing, although it is specific for retinal function. If it was to be used in conjunction with conventional visual field testing, it would provide additional diagnostic information to narrow down the sites causing visual dysfunction to the retina or elsewhere. It also indicates the location of defective areas of the retina.

The topographical ERG system examines responses of retinal area, rather than testing specific points separated (typically) by about six degrees as in visual field testing. The commonly used Humphrey Visual Field Analyser (VFA) has a stimulus range of five log units (50 dB) and, under clinical conditions, would expect to reliably detect 2–4 dB losses. The threshold procedure in the Humphrey VFA works in 2 dB steps at the end of the threshold determination procedure and the screening function 'flags' 6 dB losses. The topographical ERG has comparable sensitivity when scaled for individual variability in subject's responses in these experiments, and if this sensitivity can be maintained for clinic patients, the topographical ERG could be used as an objective visual field screener for retinal lesions. The topographical ERG has significant

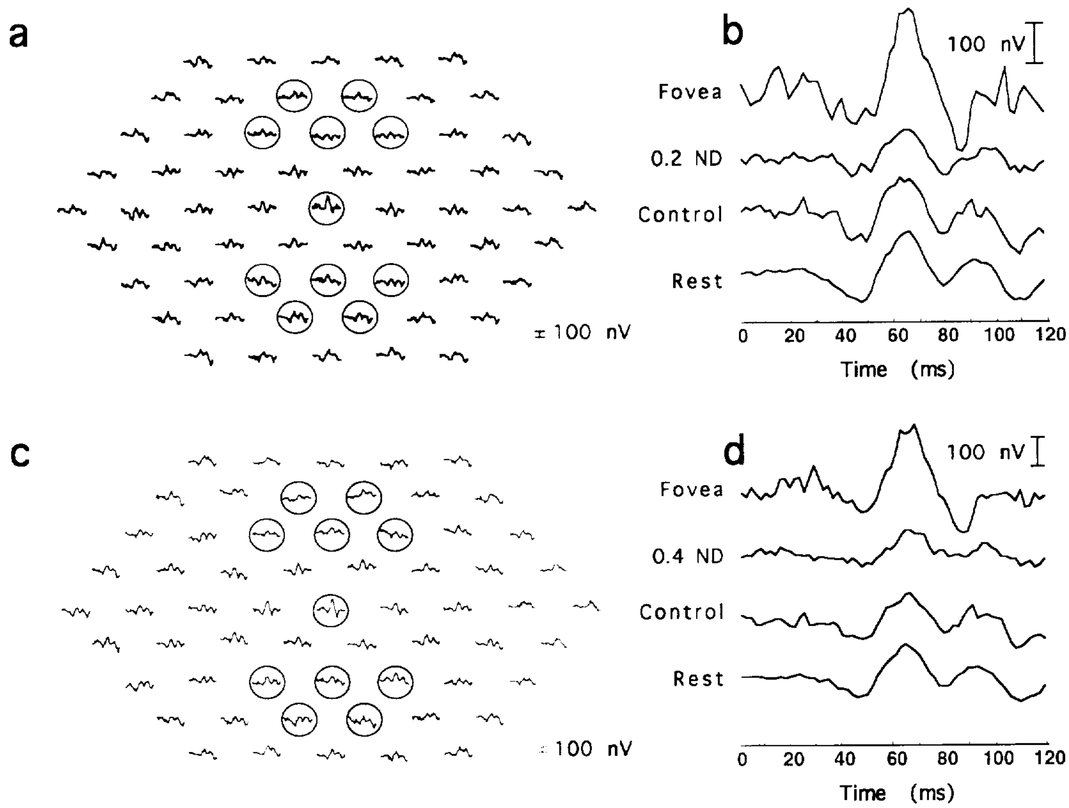

Figure 5. Topographical ERG response and ND filter/local luminance reduction. In panels (*a*) and (*c*), the five upper waveforms (shown circled) are those with the ND filter in place; the five lower waveforms (shown circled) are selected as a control area. The foveal response is also circled. Response waveforms for the fovea and average response waveforms for these areas (ND and control) and the rest of the elements are shown in panels (*b*) and (*d*), for 0.2 ND filter and 0.4 ND filter, respectively.

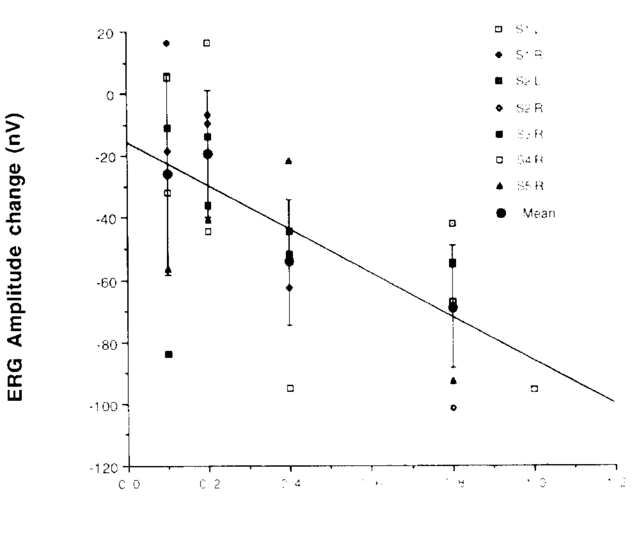

Figure 6. Absolute change in peak-to-peak ERG response as a function of the density of the locally applied ND filter. Data are shown for seven eyes of five subjects, and the data averaged over all seven eyes. The regression line is fitted to the mean data; error bars show ±1 SD.

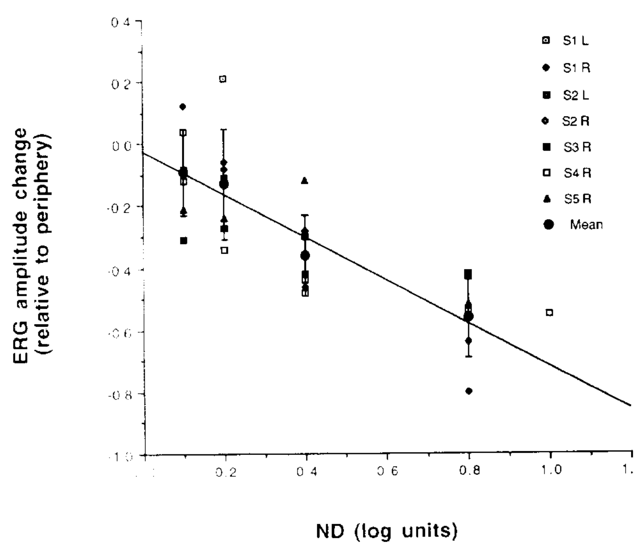

Figure 7. Change in peak-to-peak ERG response as a function of the density of the locally applied ND filter. These data have been normalised with respect to the average peak-to-peak ERG response in the periphery (i.e. excluding fovea and the areas with ND filter applied) and show the proportional change with added ND filter; error bars show ±1 SD.

advantages over conventional visual field testing: it requires only that the patient be able to maintain fixation; it is capable of testing the function of the retina in as little as 4–8 min (plus preparation time); and both eyes can be examined at the same time. It gives an objective, quantifiable output which can easily be averaged over different regions for comparison with control areas elsewhere in the retina.

While the topographical ERG shows promise for detection of reduced amplitude responses from central and peripheral retina, as with the more commonly used visual field measurement systems, strategies for examination of variability in response and decision rules for detecting areas of loss remain to be developed. The Humphrey VFA uses indices of overall variability and various strategies for examining local losses[12]. These strategies are used to identify changes due to glaucoma and other neurological conditions. These techniques can also be applied to topographical ERG data although the technique, as implemented in the VERIS I software, does not yet give easy access to all of the individual waveforms; this is a needed development before the technique can be routinely applied in the clinic.

The topographical ERG system provides potential for a completely objective method of assessing the visual pathway. In its current state the topographical ERG system is intended for use in examining response of the retina. It can also be used to examine responses of the visual cortex, although because of the re-mapping of the retina to cortex, and variations in cortical anatomy between subjects, the topographical response will be 'distorted' in many respects. Single or multiple waveforms which represent primarily foveal function can be obtained and, since the VERIS system will record two channels simultaneously, both ERG and VEP could be recorded at the same time. Simultaneous topographical ERG and topographical VEP recordings could provide a very fast and objective means of assessing the integrity of the retina and visual pathway.

Acknowledgements

Supported in part by a grant from the University Grants Commission, Hong Kong.

References

1 Regan, D. *Human Brain Electrophysiology: Evoked Potentials and Evoked Magnetic Fields in Science and Medicine*. Elsevier, New York, USA (1989)

2 Asher, H. The electroretinogram of the blindspot. *J. Physiol.* **112,** 40P (1951)

3 Boynton, R. M. and Riggs, L. A. The effect of stimulus area and intensity upon the human retinal response. *J. Exp. Psychol.* **42,** 217–226 (1951)

4 Birch, D. G. Focal electroretinography. In: *Principles and Practice of Clinical Electrophysiology of Vision* (ed J. R. Heckenlively), Mosby Year Book, St Louis, MO, USA, pp. 334–338 (1991)

5 Sutter, E. E. and Tran, D. The field topography of ERG components in man. I. The photopic luminance response. *Vision Res.* **32,** 433–446 (1992)

6 Curcio, C. A., Sloan, K. R., Kalina, R. E. and Hendrickson, A. E. Human photoreceptor topography. *J. Comp. Neurol.* **292,** 497–523 (1990)

7 Dowling, J. E. *The Retina: An Approachable Part of the Brain*. Belknap Press, Cambridge, MA, USA (1987)

8 Sutter, E. E. The fast m-transform: a fast computation of cross-correlations with binary m-sequences. *SIAM J. Computing* **20,** 686–694 (1991)

9 Dawson, W. W., Trick, G. L. and Litzkow, C. A. Improved electrode for electroretinography. *Invest. Ophthalmol. Visual Sci.* **18,** 988–989 (1979)

10 Hess, R. F. and Baker, C. L. Human pattern electroretinogram. *J. Neurophysiol.* **51,** 939–951 (1984)

11 Sutter, E. E. and Vaegan. Lateral interaction component and local luminance nonlinearities in the human pattern reversal ERG. *Vision Res.* **30,** 659–671 (1990)

12 Lieberman, M. F. and Drake, M. V. *Computerized Perimetry: A Simplified Guide*. Slack Inc., Thorofare, NJ, USA (1992)