Non-corneal electroretinogram

Parameters in normal children

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In the investigation of suspected visual disorders electroretinography (ERG) is of considerable clinical value. The ERG is usually recorded from a contact-lens type of electrode placed over the cornea. Although this is possible in co-operative adults using only local anaesthesia, the placement of a contact lens electrode in a young or retarded patient is usually not tolerated without a general anaesthetic. Because of the obvious disadvantages of requiring general anaesthesia for such a test procedure, a method was developed in this department at the beginning of 1968 to record the ERG from an electrode placed between the eyes on the bridge of the nose. The ERG recorded from such an electrode is of small amplitude but can be easily distinguished from larger amplitude background activity using 'averaging' techniques with the aid of a computer. The combined potential change from the retina of each eye is recorded unless one eye is covered during stimulation.

This technique has been used as part of a combined neurophysiological testing procedure in which the ERG, the cortical visually evoked response (VER), and the electroencephalogram (EEG) are simultaneously recorded (Harden and Pampiglione, 1970). This combined approach, which gives information about the level of suspected visual impairment, may be used in babies and young children who are unable to co-operate. No sedation is necessary and where possible the test is carried out in the waking state, with the eyes open.

There are few publications on the normal ERG parameters and usually each laboratory determines its own criteria of normality with its own techniques (Jacobson, 1961). However, because of some doubts as to the reliability of results using non-corneal electrodes in clinical work, the normal range of ERG parameters recorded with our technique is reported in the present paper.

Material and methods

62 children aged 12 mths to 14 yrs without suspected cerebral or visual disorder were selected for this test procedure. All the children were awake (no sedation or mydriatics were given) and, although some of the younger ones were not able to co-operate, it was usually possible to have the eyes open throughout the stimulation period. No selection was made to exclude unco-operative children. When possible a separate record was also taken for comparison with eyes closed during the waking state.

The electrode recording the ERG was a silver/silver chloride disc (as commonly used for EEG) filled with saline jelly and placed on the bridge of the nose between the eyes. The electrode was covered and held in place with elastoplast. A similar electrode placed on the scalp at the vertex was usually used as a reference. The skin resistance between these two electrodes was reduced to 5–10 K Ω .

The ERG signals were amplified and recorded on one of the eight channels of the EEG apparatus (Offner type T), while the EEG, from various regions of the scalp including the occipital region, was also recorded simultaneously on the other channels. A time constant of 0.3 sec. was used and the upper frequency response was linear within 10 per cent. up to 70 c/s. The amplification was usually 10 $\mu\text{V/mm}$. pen deflection. Flashes of light were presented from a gas discharge lamp (S.L.E. photostimulator) as routinely used for photic stimulation in EEG laboratories, held manually at less than 15 cm. from the eyes. A series of 200 flashes were presented at a rate of 2 per second. The room was not darkened for the procedure. If the child became restless or cried, stimulation could be immediately stopped with a push-button device and then restarted at a suitable moment. Following the general electrophysiological convention, negativity of the active electrode was recorded as an *upward* deflection in contrast to more usual ERG recording. The output of the ERG channel was fed in parallel to both the ink recorder of the EEG apparatus and to a Computer of Average Transients (Mnemotron CAT 400B). A Digitimer (Devices) and a homemade programmer were used to control the triggering of the computer and the sequence of stimuli. A permanent record of the averaged signals at the end of each series of stimuli was made either with an ultra-violet recorder or with an X-Y plotter. When monocular stimulation was desirable this was achieved by simply occluding vision from one eye.

Results

All the normal children tested showed an easily recognizable response from the non-corneal electrode and the typical wave form of this ERG is shown in Fig. 1. This response is similar in wave form and latency to the usual ERG recorded from corneal electrodes by other workers showing an initial negative component ('a' wave) followed by a larger positive potential ('b' wave). The ERGs recorded from a corneal electrode (under general anaesthesia) and from a non-corneal electrode on the bridge of the nose (in the waking state) have been compared in an 8-month-old infant (see Fig. 2). Both records were carried out with the same stimulus and amplifying apparatus. The wave form is similar although the amplitude of the response recorded from the cornea is considerably larger (approximately 20

FIG. 1 ERG from non-corneal electrode with both eyes open in a 2-year-old child (A) and a 4-year-old child (B). Negativity recorded as upward deflection. Stimulus at arrow; time marker 25 msec.

FIG. 2 ERG in an 8-month-old patient from electrode placed on cornea of left eye and from non-corneal electrode with stimulation of both eyes. Note difference in calibration signals. Negativity recorded as upward deflection. Stimulus at arrow; time marker 25 msec.

times greater) bearing in mind that the non-corneal electrode is recording the summated response from both eyes.

With monocular stimulation the amplitude of the whole ERG complex from each eye was approximately half that seen when both eyes were stimulated. When the eyes were closed voluntarily throughout the testing procedure there was always a marked diminution in the amplitude of the ERG response (sometimes becoming nearly unrecognizable). There was also some change in latency and wave form (Fig. 3), but the degree of alteration varied from one child to another.

FIG. 3 ERG from non-corneal electrode stimulating both eyes in an 8-year-old child (A) and an 11-year-old child (B). Upper tracings taken with eyes open and lower tracings with eyes shut. Negativity recorded as upward deflection. Stimulus at arrow; time marker 25 msec.

Under the same testing conditions the results from each child, even on separate occasions, were very consistent, not only in terms of wave form and latency but also amplitude. However there were variations, particularly in amplitude, between individuals and these have been assessed for the whole group and in the different age groups tested with the eyes open.

(a) Amplitude

The amplitude of the first negative component ('a' wave) was measured from a baseline recorded for 25 msec. preceding the stimulus. The amplitude of the positive component ('b' wave) was measured from this same baseline. These values, together with the total amplitude of the 'a/b' complex (peak to peak values which are often regarded by many workers as the 'b' wave amplitude), are listed in Table IA for the whole group of children. The amplitude of the 'a' wave was usually about half that of the 'b' wave and there was a smaller interindividual scatter of values for the 'a' wave than for the 'b' component. If the values are compared at different ages (Table IIA) the mean amplitude of the 'a/b' complex was somewhat smaller in the younger age groups (under 3 yrs). However, when the highest values were considered in each age group, the difference was minimal.

Table I *Non-corneal ERG in 62 normal controls (1-14 yrs)*

Wave	A		B		C	
	Amplitude (μ V)		Peak latency (msec.)		Duration (msec.)	
	Range	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)
'a'	5-18	10 (2.9)	11-15	12 (1.3)	15-24	18 (2.1)
'b'	5-32	20 (7.2)	31-39	33 (2.3)	11-33	23 (4.5)
'a/b' complex	11-45	30 (9.3)			27-52	41 (5.0)

Table II *Non-corneal ERG in 62 normal controls*

Measurement	No. of subjects	Age (yrs)	'a' wave		'b' wave		'a/b' complex	
			Range	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)
A	16	1-2	5-13	9 (2.8)	5-28	15 (7.6)	11-40	24 (9.9)
Amplitude (μ V)	17	3-5	6-15	10 (2.6)	11-28	20 (5.6)	17-41	30 (7.6)
	14	6-9	8-18	11 (2.9)	10-30	22 (5.8)	18-42	33 (7.3)
	15	10-14	7-18	11 (2.7)	13-32	26 (5.3)	21-45	37 (6.7)
B	16	1-2	11-15	13 (1.7)	31-39	34 (2.4)		
Peak latency (msec.)	17	3-5	11-15	12 (1.2)	28-37	33 (2.6)		
	14	6-9	9-13	12 (1.2)	31-39	34 (2.4)		
	15	10-14	11-15	13 (1.1)	31-37	34 (2.0)		
C	16	1-2	16-24	20 (2.8)	13-33	25 (4.8)	37-52	45 (4.6)
Duration (msec.)	17	3-5	15-20	18 (1.6)	11-30	23 (4.1)	27-50	41 (5.1)
	14	6-9	15-22	17 (1.8)	14-33	22 (4.4)	32-50	40 (4.7)
	15	10-14	17-20	18 (1.0)	15-32	24 (4.6)	32-50	42 (4.7)

(b) Peak latency

The values for the peak latency of both 'a' and 'b' components are shown in Table IB and appeared to be remarkably constant with no difference in the younger age groups (Table IIB).

(c) Duration

There was no measurable delay between the stimulus and the onset of the 'a' wave. The duration of the 'a' wave was therefore measured from the stimulus to the point where the descending portion of the 'a' wave crossed the baseline. The 'b' wave duration was measured from this point (the end of the 'a' wave) to where the ascending part of the 'b' wave recrossed the baseline. These values (and their sum) for the whole control group are given in Table IC. The duration of the 'b' wave was somewhat more variable than that of the 'a' wave but there was no marked difference between age groups (Table IIC).

Discussion

Over 30 years ago, Motokawa and Mita (1942) recorded a very small ERG signal from an electrode placed on the skin between the eyes in response to a single flash of light. More

recently, with the increasing use of small computers for 'averaging' techniques, other workers have used non-corneal electrodes of various types placed under the eyelid or near the inner and outer canthus of each eye (Tepas and Armington, 1962; Vaughan and Katzman, 1964; Jacobson, Uchida, and Masuda, 1966; Schmidt, 1969; Jayle and Tassy, 1970; Stephens, Inomata, Cinotti, Kiebel, and Maney, 1971. In babies and unco-operative children, electrodes very near the eye or on the eyelid may be a cause of irritation, but the electrode placed on the bridge of the nose is easily applied and is tolerated very well.

The peak latencies and duration of the 'a' and 'b' components are very consistent in all age groups studied, although there are considerable variations in amplitude. It is known that the newborn child shows only a small amplitude ERG which gradually assumes adult size (Zetterström, 1969). However, this evolution may not be very uniform, as François and de Rouck (1968) found some babies with an ERG amplitude of adult value at 3 months and others 'subnormal' till after 1 year. For this reason normal findings under 1 year of age have not been included in the present paper. The somewhat smaller amplitude ERG responses found in some of the younger children aged 1 to 2 years may have been due not so much to the "immaturity" of the ERG as to the fact that the children's eyes were not always fully open throughout the test. As has been shown in this study, eye closure may reduce very greatly the amplitude of the ERG, presumably by altering the intensity of light falling on the retina. Considerable care is needed in assessing this factor at the time of the test.

However, even the corneal ERG may show wide interindividual variations in amplitude in adults as has been noted by Jacobson (1961) (normal limits of 125–440 μV) and Finkelstein and Gouras (1969) (normal range of 280–550 μV) with their techniques. On the other hand, for a single subject, Finkelstein and Gouras maintained that the ERG amplitude should not vary more than 10 per cent. from day to day. It seems likely, therefore, that the range of amplitudes found in the present normal series using non-corneal electrodes reflects the same interindividual variations and is not primarily the result of the techniques used.

Noonan, Wilkus, Chatrian, and Lettich (1973) have shown that direction of gaze influences the size of the ERG response from periorbital electrodes in different positions around the eye and the polarity was reversed when the response was recorded in lateral gaze from the temporal electrode. By stimulating both eyes simultaneously, with the technique described in this paper the ERG is probably not so greatly affected by eye movements.

We have aimed at recording a fairly maximal response (with proportionately large 'a' component) by using a high-intensity flash close to the eyes. However, no special attempt has been made to separate cone and rod components. The room was not darkened in order not to frighten the child and true dark adaption would be difficult to achieve when a fairly large number of responses must be averaged in a short period. However, it is possible to carry out stimulation with faster flash frequencies to determine flicker fusion and also with different intensities and wavelengths of stimulus if and when necessary.

The technique has now been satisfactorily carried out on a variety of patients ranging from babies to adolescents with suspected disorders of vision. Experience has shown that the method appears to give reliable and useful information for clinical problems at all ages and is especially useful when combined with VERs and EEG (Harden and Pampiglione, 1970). There are also other advantages in carrying out this technique by workers primarily concerned with electrophysiological measurements. If the records are to be relatively artefact-free, skillful handling of unco-operative patients is essential. This can often best be done by staff who are used to managing active, young and retarded patients in the waking state for this type of test procedure.

References

- FINKELSTEIN, D., and GOURAS, P. (1969) "Visual electrophysiology. An introduction to the ERG, EOG, ERP and VER", in "Electrical Responses of the Visual System", ed. S. J. Fricker. Little, Brown, Boston. *Int. Ophthalm. Clin.*, **9**, 857
- FRANÇOIS, J., and ROUCK, A. DE (1968) "Electroretinography in the diagnosis of congenital blindness", in "ISCERG Symposium: The Clinical Value of Electroretinography", p. 451. Karger, Basel (20th int. Congr. Ophthalm., Munich, 1966)
- HARDEN, A., and PAMPIGLIONE, G. (1970) *Lancet*, **1**, 805
- JACOBSON, J. H. (1961) "Clinical Electroretinography". Thomas, Springfield, Ill.
- , UCHIDA, S., and MASUDA, Y. (1966) *Jap. J. Ophthalm.*, **10**, Suppl. p. 204
- JAYLE, G. E., and TASSY, A. F. (1970) *Brit. J. Ophthalm.*, **54**, 51
- MOTOKAWA, K. and MITA, T. (1942) *Tohoku J. exp. Med.*, **42**, 114
- NOONAN, B. D., WILKUS, R. J., CHATRIAN, G. E., and LETTICH, E. (1973) *Electroenceph. clin. Neurophysiol.*, **35**, 495
- SCHMIDT, B. (1969) *Ber. dtsch. ophthalm. Ges.* 1968, **69**, 558
- STEPHENS, G. M., INOMATA, K., CINOTTI, A., KIEBEL, G. and MANEV, I. (1971) *Vision Res.*, **11**, 1213
- TEPAS, D. I., and ARMINGTON, J. C. (1962) *Invest. Ophthalm.*, **1**, 784
- VAUGHAN, H. G., and KATZMAN, R. (1964) *Ann. N.Y. Acad. Sci.*, **112**, 305
- ZETTERSTRÖM, B. (1969) *Int. Ophthalm. Clin.*, **9**, 1039