

VARIATIONS IN THE NORMAL ELECTRO-OCULOGRAM*†

BY

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THE existence of an electrical potential in the vertebrate eye, with the cornea positive to the fundus, was demonstrated over a century ago (Du Bois-Reymond, 1849). This potential, the standing or corneo-fundal potential, is often described as a steady potential to distinguish it from the rapidly oscillating potential of the electroretinogram. It is not, however, a truly steady potential, but is constantly changing, and among the factors causing it to vary is a change in illumination. During studies to elucidate the nature of the light-induced change of the standing potential, it was found that in the dark the potential falls to reach a minimum level, the "dark trough level", and on subsequent re-illumination there is a rapid rise in potential to reach a maximum within 8 or 9 minutes, the "first light peak level". The height of the potential rise after darkness depends upon the time in the dark and the intensity of the subsequent re-illumination (Arden and Kelsey, 1962a).

On the basis of these studies, a clinical test was devised as an objective measurement of retinal function, known as the electro-oculogram (EOG). The basis of the test is a comparison of the level of the dark trough with that of the first light peak and to express the result as a ratio (Arden, Barrada, and Kelsey, 1962):

$$\frac{\text{First Light Peak Level}}{\text{Dark Trough Level}} \times 100$$

Other workers had previously used the light-induced change in the standing potential as an index of retinal function (François, Verriest, and de Rouck, 1955, 1956a, b), but they had not employed this sequence of dark and light.

Analysis of a series of normal subjects showed that the EOG ratio is normally over 200 per cent., and that any ratio under 185 per cent. should be considered abnormally low. The histogram showing the frequency of the ratios was positively skewed, with the upper limit tailing off to levels approaching 400 per cent. The ratios of the two eyes were also closely correlated (Arden and Barrada, 1962).

It was not noted whether the EOG of any individual is constant, or whether it may vary from time to time, but subsequent studies have shown that the ratio of an individual can show marked variations (Elenius and Lehtonen, 1962).

If such a variation does occur, then the skewed histogram of EOG levels found by Arden and Barrada could be caused by each individual tending to produce more low ratios than high, rather than by the mean ratios being low rather than high.

A knowledge of individual variations becomes of importance when attempts are made to assess changes in retinal function by serial estimations of the EOG. In the paper describing the technique of the clinical test, Arden and others (1962) noted that certain eye diseases cause a reduction in the EOG, and it would seem that changes in the EOG might be taken to indicate changes in the course of the disease. This

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would not only be of interest in following disease processes, but would also be of importance in anticipating damage due to potentially retinotoxic drugs.

When the Electrodiagnostic Clinic was established at Moorfields Eye Hospital, many requests for serial examinations were made, particularly for patients taking chloroquine. In order to gain some idea as to how the EOG can vary, the following study was undertaken.

Methods

(a) *Subjects*.—These were eight female orthoptic students, aged between 18 and 25 years. All had normal eyes, apart from minor refractive errors, and both eyes were similar. In all cases visual acuity was normal, with correction where necessary.

(b) *Technique*.—This was identical with that described by Arden and others (1962). The only minor variations were that the skin electrodes were S.L.E. silver/silver chloride skin electrodes, and amplification and display by a direct writing Schwartz model PE 4 with a special high gain of the electro-encephalogram type.

(c) *Time of Testing*.—Each subject was tested weekly, five for 10 and three for 11 weeks. As far as possible the test was done at the same time of the same day each week. In all but one subject a further test was done 3 months after the end of the trial. A note was made of the menstrual history of the subjects.

Results

The Table shows that there is a large variation in the ratios of each subject. The mean value for each subject has been calculated as the arithmetical mean of the ratios of the two eyes, and in this small series varies from 196 to 304 per cent. The close

TABLE
EOG RESULTS IN EIGHT NORMAL SUBJECTS AT WEEKLY INTERVALS
WITH FOLLOW-UP EOG 3 MONTHS LATER IN SEVEN OF THEM

Subject ..	A		B		C		D		E		F		G		H		
	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	
Week	1	232	239	219	203	210	203	255	333	225	220	234	218	187	187	240	220
	2	229	228	240	240	212	180	290	313	242	235	240	221	193	196	270	273
	3	235	232	296	275	190	231	250	330	240	226	241	250	190	193	225	205
	4	217	235	220	221	200	195	305	330	226	255	270	243	176	172	255	240
	5	216	225	240	230	193	205	300	324	228	214	230	206	220	226	255	248
	6	246	226	220	220	180	180	270	270	216	210	287	285	222	213	240	254
	7	209	190	249	247	206	181	278	291	215	227	227	237	182	195	220	238
	8	220	205	215	222	155	196	320	320	230	213	252	233	208	215	257	238
	9	193	194	233	255	181	188	280	300	258	230	290	260	211	203	270	220
	10	255	240	250	225	203	197	340	323	215	220	215	220	195	200	235	253
	11	—	—	—	—	217	220	315	347	—	—	—	—	—	—	240	243
Mean	223		236		196		304		228		248		199		243		
Median	227		232		196		309		226		242		195		242		
<i>s</i>	17.5		21.4		16.4		27.0		13.0		23.5		14.9		16.4		
<i>V</i> (per cent.)	7.85		9.0		8.4		8.9		5.7		9.5		7.5		6.75		
Follow-up EOG	225	240	240	230	197	193	325	320	253	229	—	—	225	210	250	240	

agreement between the mean and the median in all cases indicates that the ratios are distributed symmetrically about the mean value.

The standard deviation of the ratios has been calculated from the equation:

$$s = \sqrt{\frac{\sum (x - \bar{x})^2}{n}}$$

The standard deviation shows a marked variation between the subjects, from 13 to 27, but seems to be greater where the mean is larger. In order to make the standard deviations comparable Pearson's Coefficient of Variation is given as:

$$V = \frac{100 \cdot s}{\bar{x}}$$

The range here is less than that of the standard deviation, from 5.7 to 9.95 per cent.

The relation of the EOG changes to time is shown in Fig. 1 (opposite); it is apparent that the wide fluctuations follow no pattern, although the two eyes change in much the same way. Despite the close relation between the two eyes, in several instances the ratios are markedly different, and it appears that the differences are greater where the ratio is greater. In order to make the differences comparable, they have been expressed as a ratio of the difference between the two eyes at each recording divided by the mean of the two eyes at that recording, multiplied by a hundred. The frequency of the differences is shown as a histogram in Fig. 2. As would be expected, most of the differences form a very small percentage of the mean of the two eyes, but almost 10 per cent. of the differences are more than 12 per cent. of the mean of the two eyes.

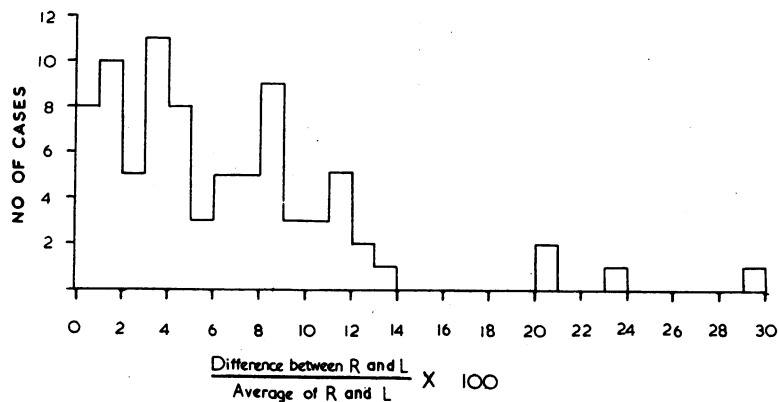


FIG. 2.—Frequency of difference in ratio between the two eyes.

The results of the follow-up EOG done on seven of the subjects 3 months later are also shown. In no case did the result fall outside the limits previously established. No longer-term studies have yet been reported, but since the inception of the test 6 years ago the EOG of the author has stayed the same.

The menstrual cycle of each subject is also shown on Fig. 1, the date of ovulation being taken to be 14 days before the first day of the menstrual period (Hamilton, Boyd, and Mossman, 1945). On this weekly recording neither event appears to influence the EOG.

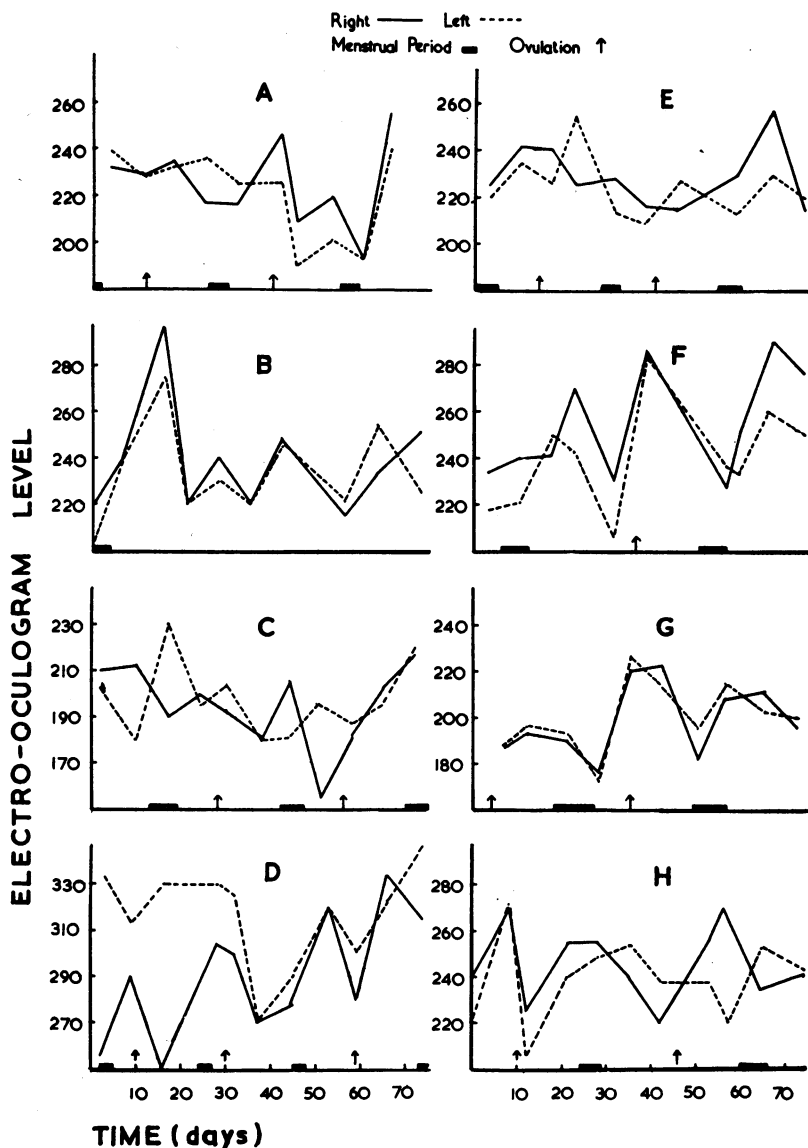


FIG. 1.—Variations in EOG with time. Abscissa—time in days. Ordinate—level of EOG.

Discussion

The findings in this series confirm that the EOG varies greatly from person to person, and that the preponderance of low ratios giving the positively skewed histogram of Arden and Barrada (1962) is due to the fact that most people have a lower ratio, rather than to the fact that each individual produces more low than high ratios. As shown in Fig. 1, the individual variation is a haphazard affair, the change between consecutive recordings being very small or swinging between the limits of

the series. None the less, spurious trends can be detected in some of the records. In Subject A a fall may be discerned over the first 60 days, while in Subject D an equally definite rise may be seen over the last 40 days. What other trends would have been made evident if the times of testing had been changed is a matter for speculation, but it must be accepted that large swings in the EOG, and apparent trends over a period of time cannot be taken to indicate pathological changes in the retina.

A further point is the interpretation of a low result, assuming that 185 per cent. should be taken as the lower limit of normal. Subjects C and G in this series both had mean values under 200 per cent., and both gave several readings below the limit of normal and yet there was no evidence of retinal disease.

This does not mean that retinal changes cannot be followed by this technique, but a large number of cases will have to be followed so that the random variations may be compensated statistically. This was attempted in a series of subjects taking large doses of chloroquine, but it was not possible to predict retinopathy by changes in the EOG (Kolb, 1965). This is because the EOG is significantly lowered only when clinical evidence of retinopathy is present (Arden, 1965).

Such wide variations are not common in physiological tests, but it is of interest to note that the electroretinogram has also been shown to have similar wide variations in the same individual from time to time (Spivey and Pearlman, 1963), although other workers have claimed that reproducible results are possible with this technique (Rendahl, 1961).

The similarity of the two eyes in most recordings is a feature of this study, indicating that where the two eyes are structurally similar then similar EOGs may be expected. This is not a constant phenomenon, unfortunately, and a few wide differences were found, the cause of this not being determined. On the other hand, a wide difference was an uncommon event, and in general it may be considered that the one eye serves as a control for the other. This makes the test a useful tool in the investigation of unilateral eye disease, particularly where the retina is invisible because of opacities of the media, or where the fundus picture is equivocal or even apparently normal.

It was not the object of this study to determine the cause of any variation that might be found. In view of the fact that the menstrual cycle influences many metabolic activities, and the light-induced change in the standing potential is a metabolic activity (Arden and Kelsey, 1962b), it was thought worth while to note the menstrual history of the subjects. On the basis of the weekly tests no relation was evident with either the menstrual period or the time of ovulation, but more frequent recordings might have given more information.

Summary

Electro-oculograms were performed weekly in a series of eight normal subjects for a period of 10 or 11 weeks, with a follow-up 3 months later. In each subject, a wide variation of results was found distributed symmetrically about the mean value.

Such wide individual variations with time in the normal subject prevent the use of this test to assess changes in retinal function in any one subject, although its use in a series of subjects is possible.

The EOGs of the two eyes tend to be similar, and the normal eye may thus serve as a control in the assessment of unilateral eye disease.

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