Electro-oculographic abnormalities in amblyopia

C Williams, D Papakostopoulos

Abstract

Background—Electrodiagnostic tests have been used to investigate retinal function in amblyopia but previous results have been conflicting.

Methods—It was decided to investigate whether the electro-oculogram (EOG) showed any abnormalities in 12 adult amblyopes and 12 age and sex matched controls with normal vision. The mean amplitudes of the EOG recordings from each eye during 12 minutes of darkness and 18 minutes of light were compared.

Results—The mean values from the amblyopic eyes were lower than those from the fellow non-amblyopic eyes. At most time points the difference was significant ($p < 0.05$). After normalisation of the data to minimise intersubject variation, the reduction in EOG amplitudes of the amblyopic eyes at all time points was significant ($p < 0.05$). There was no significant difference between the mean values obtained from the right and left control eyes at any time point, either before or after normalisation.

Conclusion—These results provide evidence for a retinal abnormality in amblyopia and implicate the retinal pigment epithelium as being involved. A deficiency in retinal dopaminergic function in amblyopia is proposed as a possible mechanism causing these results.

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Retinal function in amblyopia has previously been investigated using various techniques. Ikeda and Tremain demonstrated abnormal direct recordings from lateral geniculate nucleus (LGN) cells and from retinal ganglion cells in strabismic cats.^{1,2} Abnormal pattern electroretinograms (PERGs) in strabismic cats have been recorded, reduced in either phase or amplitude or both.^{3,4} In human amblyopia the PERG can also be reduced in amplitude.^{5,6} The amblyopes with reduced PERGs in their affected eyes were those who had failed to respond to occlusion whereas those who had responded to treatment had supranormal PERGs in their amblyopic eyes.⁷ However, other groups have not found significantly more interocular variation in the PERGs of amblyopes than in normal subjects.^{8–10}

The electro-oculogram (EOG) is a test of retinal function, in which changes in the standing potential (SP) of the eye are made manifest.^{11–12} The SP of the mammalian eye is generated primarily by a potential difference between the apical and basal membranes of the retinal pigment epithelium (RPE). In darkness the potential falls to a trough value (the dark

trough; DT). In response to light there is a dose dependent increase in the potential difference, developing over several minutes to a peak value (the light peak; LP) then slowly declining to basal levels. Dopamine has been implicated in the generation of the SP in animal studies¹³ and shown to affect the DT in normal human subjects.¹⁴ There is evidence that systemic dopamine can improve visual function in the elderly¹⁵ and in amblyopic adults¹⁶ and children.^{17,18} It was therefore decided to investigate whether the EOG showed any abnormalities in amblyopic eyes compared with normal eyes.

Materials and methods

The amblyopic subjects were 12 anisometropic or strabismic adults with an interocular difference in visual acuity of at least 2 Snellen lines when wearing full refractive correction. The control subjects were 12 adults with full visual acuity in each eye. The two groups were balanced as far as possible regarding age and sex. All subjects had a full ophthalmic examination including visual field assessment and funduscopy to exclude any ocular disease. No subject was using systemic medication or eye-drops or had had previous ocular surgery. All subjects had normally aligned corneal reflections before dissociation by the prism cover test and had full eye movements. The EOG recordings were carried out by the same operator who was blind to the visual acuity results.

The subjects were seated 1.5 metres in front of a panel on which were mounted eight neon tube bulbs. Two small red bulbs served as fixation lights and were positioned across the centre of the screen such that a 30 degree movement of the eyes were necessary for the subject to change fixation from one to the other. Chlorided silver electrodes were attached to the bridge of the nose and at each outer canthus. An earth electrode was attached to one temple. The resistance of the electrodes was $< 5 \text{ k}\Omega$, measured with a 40 Hz resistance meter. The signals were amplified by an EEG machine (Dantec). The time constant was 10 seconds, the gain $200 \mu\text{V}/\text{cm}$, and the upper frequency response was 100 Hz (3 dB down). The subjects were instructed to make fast eye movements from one fixation point to the other at a rate of once a second. Eight such eye movements comprised a sequence. Sequences were then performed and recorded every 2 minutes. Six sequences were recorded in the dark after an initial 20 minute period of adaptation to room light (room light was 122 lux measured at the subject's face). The room and panel lights were then turned on (1000 lux measured at the subject's face) and

Electrodiagnostic
Department, Bristol
Eye Hospital
C Williams
D Papakostopoulos

Correspondence to:
C Williams, Department of
Ophthalmology, Bristol Eye
Hospital, Lower Maudlin
Street, Bristol BS1 2LX.

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Table 1 Clinical details of amblyopic subjects

Subject	Deviation at presentation	Refraction at presentation	Diagnosis	Visual acuity at presentation	Occlusion	Deviation on examination	Refraction on examination	Visual acuity on examination
1	Straight	R: Plano/+0.25×80 L: -3.50/+4.50×82	Anisometropic	R 6/4 L 6/24	No	Straight	R: Plano L: -2.00/+2.50×85	R 6/5 L 6/12
2	0.3 m:10 pd 6 m:8 pd	R: +0.50 DS L: +0.50 DS	Strabismic	R 6/18 L 6/5	Yes	0.3 m:6 pd 6 m:8 pd	R: -1.00 DS L: -1.50 DS	R 6/12 L 6/6
3	Straight	R: +2.00/-0.75×10 L: +0.50 DS	Anisometropic	R 6/12 L 6/4	No	Straight	R: +2.00/+0.50×170 L: +1.50 DS	R 6/9 L 6/5
4	Straight	R: +0.50 DS L: +3.75/+1.75×180	Anisometropic	R 6/6 L 6/24	Yes	Straight	R: +0.25 DS L: +1.00/1.25×130	R 6/5 L 6/18
5	0.3 m:14 pd 6 m:14 pd	R: +6.00/+1.00×90 L: Plano	Mixed	R 6/36 L 6/4	Yes	0.3 m:8 pd 6 m: straight	R: +7.00/+1.25×50 L: +1.75 DS	R 6/60 L 6/5
6	Straight	R: +4.50/+1.00×90 L: +0.25/+0.50×60	Anisometropic	R 6/36 L 6/6	Yes	Straight	R: +4.00/+0.75×90 L: -1.00/+0.75×90	R 6/60 L 6/6
7	0.3 m:6 pd 6 m: straight	R: +2.50 DS L: +1.75 DS	Mixed	R 6/60 L 6/6	Yes	Straight	R: +1.75 DS L: +0.75 DS	R 6/36 L 6/5
8	Straight	R: +3.75/+0.75×75 L: Plano	Anisometropic	R 6/18 L 6/4	Yes	Straight	R: +3.50/+1.50×50 L: Plano/-0.50×170	R 6/24 L 6/6
9	0.3 m:6 pd 6 m:8 pd	R: +2.00 DS L: +1.00 DS	Mixed	R 6/60 L 6/9	Yes	0.3 m:6 pd 6 m:10 pd	R: +2.00 DS L: +0.25 DS	R 6/36 L 6/6
10	Straight	R: +4.00/+1.00×60 L: Plano	Anisometropic	R 6/36 L 6/5	Yes	Straight	R: +2.75/+2.00×60 L: Plano	R 6/36 L 6/5
11	0.3 m:10 pd 6 m:14 pd	R: +3.00 DS L: Plano	Mixed	R 6/18 L 6/5	Yes	0.3 m:10 pd 6 m:12 pd	R: +0.75 DS L: +0.50 DS	R 6/12 L 6/6
12	Not available	Not available	Anisometropic	Not available	No	Straight	R: +0.50 DS L: +2.25/+0.50×70	R 6/5 L 6/18

pd=prism dioptres.

another nine sequences were recorded in the light. The amplitude of potential difference for each eye was measured. The head position, eye movements, and pupil diameter were all monitored using an infrared closed circuit TV camera. All results were analysed using the two tailed Student's *t* test, paired or unpaired as appropriate. A *p* value of 0.05 or less was considered significant.

The clinical details of the amblyopic subjects are shown in Table 1 where 'mixed' denotes amblyopia associated with both anisometropia and strabismus. The details of the normal controls are shown in Table 2.

Results

Twelve adult amblyopes and 12 normal control subjects were examined. The amblyopes comprised eight females and four males; the controls were nine females and three males. The mean ages were 23.7 (SD 4.2) years for the amblyopes and 23.8 (SD 2.4) years for the normal controls. For each subject, 15 values were obtained from each eye, corresponding to the amplitude of potential recorded

during each 2 minute sequence of eye movements. Mean values were calculated for all the affected and unaffected eyes (amblyopes) and all the right and left eyes (controls). Comparisons were made using Student's two tailed paired *t* test.

The mean values obtained from the amblyopic eyes were lower than those from the fellow normal eyes at all times in dark and light. The difference was significant ($p < 0.05$) in most cases as shown in Table 3. There was no difference between the mean values obtained from the right and left control eyes. The data from Table 3 are shown in Figures 1 and 2.

In order to reduce the intersubject variation in the absolute values obtained, the results were normalised by expressing each value as a percentage of the maximum value obtained from the subject. The statistical comparisons between affected and unaffected eyes of the amblyopes, and the right and left eyes of the controls were then repeated using the normalised data. The results are shown in Table 4 which illustrates that the difference between the amblyopic and non-amblyopic eyes became significant at all times during the recording and the significance was increased. There remained no significant difference between the right and left eyes of the control subjects. The data from Table 4 are shown in Figures 3 and 4.

Further comparisons were carried out using the normalised data. The values from the amblyopic eyes were compared separately with those from either the right or left control eyes using Student's unpaired two tailed *t* test. In all cases the mean values from the amblyopic eyes were significantly lower ($p < 0.05$) than those from the right or left control eyes. There was no significant difference between the values from the non-amblyopic eyes and either the right or left control eyes. As a further check, an analysis of variance (ANOVA) was performed to compare the normalised results from all four groups of eyes for the light peak and for the dark trough. There was a significant difference

Table 2 Clinical details of control subjects

Name	Deviation	Refraction	Visual acuity
1	Straight	R: -0.50/+0.75×160 L: -0.5/+1.00×5	R 6/4 L 6/4
2	Straight	R: Plano L: Plano	R 6/5 L 6/5
3	Straight	R: -3.25/+0.75×70 L: -4.50/+1.25×160	R 6/6 L 6/6
4	Straight	R: -0.50/+0.25×60 L: -0.50/+0.50×120	R 6/5 L 6/5
5	Straight	R: -1.25 DS L: -1.25 DS	R 6/5 L 6/5
6	Straight	R: -0.50 DS L: -0.50 DS	R 6/5 L 6/5
7	Straight	R: -2.50/+4.00×170 L: -5.00/+2.00×170	R 6/5 L 6/5
8	Straight	R: Plano L: Plano	R 6/6 L 6/5
9	Straight	R: -1.00 DS L: -1.00 DS	R 6/5 L 6/5
10	Straight	R: -3.75/+0.75×70 L: -3.75/+0.50×180	R 6/6 L 6/6
11	Straight	R: Plano L: -0.25/+0.50×90	R 6/5 L 6/5
12	Straight	R: -8.50/+0.50×15 L: -5.75 DS	R 6/5 L 6/5

Table 3 Mean (SD) amplitude (μV) of EOG recordings from affected and non-affected eyes (amblyopes) and right and left eyes (controls)

Illumination	Time (minutes)	Amblyopes (n=12)			Controls (n=12)		
		Affected (μV)	p Value	Unaffected (μV)	Right (μV)	p Value	Left (μV)
Dark	0	336 (195)	0.076	367 (191)	411 (114)	0.85	414 (121)
Dark	2	304 (200)	0.007	342 (193)	379 (156)	0.76	384 (119)
Dark	4	274 (177)	0.018	314 (183)	344 (104)	0.61	351 (111)
Dark	6	249 (160)	0.030	278 (165)	314 (96)	0.56	322 (106)
Dark	8	228 (140)	0.029	255 (144)	290 (100)	0.70	296 (106)
Dark	10	216 (130)	0.044	242 (123)	284 (99)	0.94	285 (106)
Light	12	237 (140)	0.067	267 (134)	307 (93)	0.79	311 (111)
Light	14	325 (195)	0.066	364 (180)	399 (130)	0.96	399 (120)
Light	16	459 (264)	0.078	508 (255)	523 (156)	0.71	534 (145)
Light	18	536 (305)	0.047	592 (293)	615 (170)	0.69	623 (169)
Light	20	555 (322)	0.046	613 (309)	641 (178)	0.56	654 (190)
Light	22	518 (310)	0.039	575 (298)	604 (175)	0.63	614 (187)
Light	24	437 (287)	0.017	495 (290)	528 (167)	0.34	545 (191)
Light	26	352 (241)	0.028	402 (252)	441 (159)	0.42	455 (178)
Light	28	290 (210)	0.022	335 (222)	378 (140)	0.61	382 (162)

Figure 1 Mean (SE) EOG amplitude (μV) for affected and unaffected eyes of amblyopic subjects.

Figure 2 Mean (SE) EOG amplitudes (μV) for right and left eyes of control subjects.

in the dark trough values between the four groups (F ratio 4.943, $p=0.005$). Tukey's pairwise comparison showed that the DT values from the amblyopic eyes were significantly lower than those from the right ($p=0.008$) and left ($p=0.010$) control eyes but not from the fellow eyes ($p=0.172$). There was also a significant difference in the light peak values between the four groups of eyes (F ratio 5.690, $p=0.002$). Tukey's pairwise comparison

showed that the light peak values from the amblyopic eyes were significantly lower than those from the fellow eyes ($p=0.003$), the right ($p=0.008$) and left ($p=0.002$) control eyes.

The light peak/dark trough ratio was calculated for each subject and was normal ($>170\%$) in all cases. The mean value for the amblyopic eyes was 216% (SD 130%) and for the non-amblyopic eyes was 243% (SD 123%), there was no significant difference ($p=0.43$). Similarly the mean ratio for the control right eyes was 234% (SD 35%) and for the left eyes was 241% (SD 45%); there was no significant difference between them ($p=0.45$).

The time course of the EOG changes was normal in all subjects. The individual amplitudes of the dark trough, light peak and the time taken to reach these points for each subject are given in Table 5 for the dark trough and Table 6 for the light peak. The mean time until the dark trough was 9.17 minutes for amblyopic and fellow eyes; there was no significant difference (paired t test, $p=1.0$). The corresponding times for the right and left eyes of the controls were right eye 8.50 minutes and left eye 9.33 minutes; there was again no significant difference ($p=0.096$). Similarly the mean time until the light peak was 19.50 minutes for the amblyopic, fellow and right control eyes and 19.67 minutes for the left control eyes. There was no significant difference in the time until light peak between the amblyopic and fellow eyes ($p=1.0$) or the right and left control eyes ($p=0.338$).

The potential measured in the EOG is dependent on eye movement as well as on retinal function. The eye movements of all subjects were recorded on videotape as the EOG was being carried out. The eye movements were subsequently studied and measured using freeze frame examination of the videotape. The eye movements were measured on the screen from limbus to inner canthus at the point of maximal abduction of each eye. A mean of 4–6 measurements was calculated for each eye. The mean values were compared between amblyopic and fellow eyes for the amblyopes and the right and left eyes for the controls. There was no significant difference between the means for the amblyopic and fellow eyes ($p=0.50$) or between the right and left eyes of the controls ($p=0.17$).

When looked at individually there were

Table 4 Mean values (SD) obtained using normalised data (% maximum from each subject) for EOG recordings from affected and non-affected eyes (amblyopes) and right and left eyes (controls)

Illumination	Time (minutes)	Amblyopes (n=12)			Controls (n=12)		
		Affected (μV)	p Value	Unaffected (μV)	Right (μV)	p Value	Left (μV)
Dark	0	50.7 (9.0)	0.041	57.6 (7.9)	61.4 (8.0)	0.98	61.5 (6.3)
Dark	2	44.8 (9.7)	0.041	53.2 (7.4)	56.1 (7.4)	0.78	56.8 (6.6)
Dark	4	40.4 (8.7)	0.009	48.6 (7.8)	50.8 (6.2)	0.65	51.7 (5.9)
Dark	6	37.0 (8.2)	0.013	43.1 (7.5)	46.5 (5.6)	0.62	47.4 (6.3)
Dark	8	34.3 (7.6)	0.021	39.7 (7.0)	42.6 (5.8)	0.68	43.4 (6.8)
Dark	10	32.5 (7.0)	0.034	38.4 (7.5)	41.7 (6.1)	0.92	41.5 (7.4)
Light	12	35.1 (8.4)	0.041	42.1 (7.0)	45.5 (6.3)	0.96	45.6 (6.8)
Light	14	48.0 (9.8)	0.044	57.1 (9.5)	58.7 (8.9)	0.95	58.8 (7.3)
Light	16	68.7 (12.1)	0.044	79.3 (9.8)	78.0 (7.7)	0.64	79.2 (6.6)
Light	18	80.3 (11.8)	0.029	92.6 (7.6)	91.3 (7.8)	0.68	92.4 (5.4)
Light	20	82.9 (13.4)	0.031	95.6 (6.2)	95.1 (6.9)	0.59	96.6 (5.4)
Light	22	77.1 (14.0)	0.029	89.6 (7.7)	89.5 (8.5)	0.68	90.8 (7.5)
Light	24	64.3 (16.4)	0.014	76.5 (12.6)	77.9 (9.1)	0.41	79.9 (9.6)
Light	26	51.6 (15.6)	0.020	61.7 (13.9)	64.6 (9.8)	0.51	66.2 (10.1)
Light	28	42.3 (14.3)	0.015	51.1 (12.8)	54.6 (9.2)	0.76	55.3 (10.4)

Figure 3 Mean (SE) normalised EOG amplitudes for affected and unaffected eyes of amblyopic subjects.

Figure 4 Mean (SE) normalised EOG amplitudes for right and left eyes of control subjects.

interocular differences in EOG amplitude for most of the control subjects as well as for the amblyopes. Nine of the amblyopes had recordings consistently smaller from their amblyopic eyes, two had recordings consistently greater from their amblyopic eyes, and for one there was no difference between the eyes. In the control group, five control subjects had recordings consistently smaller from their left eyes, six had recordings consistently lower

in their right eyes, and for one subject there was no difference between the eyes. In order to explore the interocular variation for all subjects, a mean value of the interocular difference ('IOD index') for all 15 recordings was calculated for each subject ($R-L/R\%$ for the controls and non-affected-affected/non-affected % for the amblyopes). These values are shown in Figures 5 and 6. The mean IOD index for the control subjects was -2.12% (SD 13.27%) and for the amblyopes was 13.52% (SD 20.02%). A one sample t test was carried out on the IOD indices for the control group and the mean was not significantly different from 0 ($p=0.59$). The same test carried out on the IOD indices from the amblyopes shows that the mean is significantly different from 0 ($p=0.015$).

The data from the normal subjects can be used as a normal range with which to compare the values from the amblyopes. Five amblyopes have IOD indices greater than 2 SD from the control group mean; all such that the affected eye has smaller EOG amplitudes. The amblyopes with an abnormally large IOD index were subjects 2, 3, 5, 6, and 9. If the individual values for IOD in the light peak are considered in the same way ($NA-A/NA\%$ for the amblyopes and $R-L/R\%$ for the controls) a similar distribution is seen. The same five amblyopes have an IOD in the LP values greater than 2 SD from the control mean. There was more variability in the DT values such that only three amblyopes had DT IOD outside 2 SD of the control group mean (subjects 3, 8, and 9).

The normalised data were used to compare DT and LP with the visual acuity for the amblyopic eyes. Such a comparison would be inappropriate for the unaffected eyes or the control subjects' eyes as all visual acuities were normal. Correlation coefficients for the logarithm of the reciprocal of the Snellen acuity compared with the DT ($r=-0.37$) or the LP ($r=0.0045$) were not statistically significant, although a trend was observed towards worse visual acuities being associated with lower DT values.

Discussion

The results from this study demonstrate that the normalised mean EOG amplitudes

Table 5 Individual dark trough (DT) amplitudes (μV) and time to DT (minutes) for all subjects

Amblyope number	Aff DT (μV)	Time (minutes)	p Value	Unaff DT (μV)	Time (minutes)	Control number	Right DT (μV)	Time (minutes)	p Value	Left DT (μV)	Time (minutes)
1	321	10		325	10	1	162	10		162	10
2	150	12		200	8	2	200	8		225	10
3	112	6		175	6	3	475	6		487	10
4	237	8		175	10	4	337	8		312	8
5	125	6		175	8	5	162	8		150	10
6	87	8		112	10	6	287	8		300	10
7	312	10		337	8	7	275	10		387	8
8	125	12		200	12	8	262	10		162	10
9	87	10		150	8	9	300	8		300	8
10	237	8		237	10	10	375	10		325	10
11	537	10		575	10	11	187	8		187	10
12	250	10		225	10	12	375	8		412	8
Mean		9.17	1.0		9.17			8.50	0.096		9.33
SD		1.99			1.59			1.24			0.98

obtained from a group of amblyopic eyes were significantly lower than the normalised mean amplitudes from the fellow eyes at all time points during the EOG recording. There was no significant difference at any time point between the right and left eyes of age and sex matched controls who underwent an identical recording procedure. The reduction in EOG amplitude was consistent in all conditions of light and dark adaptation tested. This is illustrated by the fact that the LP/DT ratios for all subjects were normal. In the nine out of 12 amblyopes who had reduced EOG amplitudes in their affected eyes, the DT and the LP were equally affected, therefore the LP/DT ratio remained normal. From the available clinical information on the amblyopes there are no distinguishing features to explain why the other three were different. There was no significant correlation between the LP amplitude and visual acuity, refractive error, or treatment history. It may be that the normal intersubject and intrasubject variation is too great to allow the observation of subtle differences between subjects, or that too little information is available on the presenting features and treatment history of the amblyopes. The amblyopes were mainly anisometropic or mixed anisometropic/microstrabismic. This was due to the inclusion criterion specifying no previous ocular surgery, as it was suspected that surgery would have resulted in abnormal eye movements which would affect the EOG. The amblyopic group, however, is heterogeneous with respect to the aetiology of their amblyopia. The two amblyopes who had larger EOG amplitudes in their affected eyes (amblyopes 4 and 12) were both straight eyed anisometropes, as was the amblyope whose EOG amplitudes were equal in both eyes (amblyope 10). Amblyopes 4 and

10 had received occlusion therapy with some improvement in visual acuity, but amblyope 12 had no recollection of any occlusion and no medical notes were available to exclude other forms of treatment such as atropinisation. It has been suggested that previous partially successful treatment of amblyopia can result in increased amplitude PERGs in the affected eyes.^{5 7 19} It may be that previous treatment is a relevant factor in the atypical results from amblyopes 4, 10, and 12, but we do not have adequate previous records to assess this possibility fully.

In our results the LP values (both actual and normalised) show less variability between subjects than do the DT values. This phenomenon was also described by Anderson and Purple in their paper on circadian rhythms and variability in the clinical EOG.²⁰ They suggest that this may reflect the dose dependent relation of the LP to the level of illumination and the period of dark adaptation, both of which are fixed in the procedure for recordings. The DT, however, is an absolute value for each individual and displays a diurnal fluctuation. While diurnal changes would not affect interocular differences, they may explain the greater variability in DT values. However, all recordings were carried out in normal working hours and not at the times of the most pronounced diurnal changes, which occur in the late evening and early morning. Other sources of error such as variations in facial asymmetry, electrode placement, and measurement error affect both the recordings from the amblyopes and from the controls. These errors cannot explain the significant interocular difference between the amblyopic and non-amblyopic eyes, as there is no such difference between the control eyes. Asymmetry of eye movements

Table 6 Individual light peak (LP) amplitudes (μV) and time to LP (minutes) for all subjects

Amblyope number	Aff LP (μV)	Time (minutes)	p Value	Unaff LP (μV)	Time (minutes)	Control number	Right LP (μV)	Time (minutes)	p Value	Left LP (μV)	Time (minutes)
1	662	22		687	22	1	387	20		387	20
2	300	20		437	20	2	425	18		525	18
3	300	18		450	18	3	875	20		912	20
4	600	20		487	20	4	712	18		700	18
5	275	18		362	20	5	400	20		387	20
6	275	18		375	18	6	600	20		650	20
7	812	20		925	18	7	862	22		962	22
8	387	20		475	20	8	712	18		600	18
9	262	20		387	20	9	662	18		675	20
10	887	18		850	18	10	837	20		750	20
11	1300	20		1430	20	11	487	20		475	20
12	700	20		612	20	12	800	20		887	20
Mean		19.50	1.00		19.50			19.50	0.34		19.67
SD		1.24			1.24			1.24			1.15

Figure 5 IOD indices for the amblyopic subjects.

could cause abnormalities of the EOG, but there was no significant difference between the degree of excursion of the amblyopic eyes compared with the normal fellow eyes. Abnormal drift in eye movements has been described in amblyopic eyes during monocular fixation but movements were normal during binocular fixation.²¹

The consistency of our results during dark and light adaptation suggests the involvement of the RPE, which is the main generator of the SP. Abnormal RPE function in amblyopia could be either a primary retinal phenomenon or secondary to central influences. There is little direct evidence of a corticofugal retinal input in mammals, although this has been well described in birds, fish, and reptiles.²² A primary retinal abnormality could involve the RPE or any part of the retina which affects RPE function. Dopamine has been proposed as affecting the changes in the depolarisation of the RPE which leads to the LP.¹³ This is based on observations that dopamine causes a dose dependent increase in the SP in both the perfused mammalian eye²³ and the intact chicken eye.^{13, 24} These effects are blocked by halo-

peridol.²⁵ After blockade of catecholamine and serotonin synthesis an increase in the SP occurs in the chicken eye, suggesting that the SP may be affected by a balance between catecholamines and indolamine.²⁶ Furthermore, the EOG is reported to be abnormal in cases of dopaminergic loss such as Parkinson's disease²⁷ and in depression.²⁸⁻³⁰ Dopamine levels in the retina exhibit a diurnal fluctuation with peak levels in the day and reduced levels at night.³¹ The SP similarly has a diurnal periodicity with the greatest dark adapted potentials being those recorded between 1230 and 1430.²⁰

Dopamine has already been implicated in the pathophysiology of human amblyopia. Dopamine improves visual function in amblyopic adults^{16, 32} and children.¹⁷ Thus, one can hypothesise that in human infants and children, retinal dopaminergic elements may be affected by visual abnormalities during the sensitive period of visual development. There is experimental evidence in support of this from animal models of amblyopia in which levels of retinal dopamine and tyrosine hydroxylase are reduced in the amblyopic eye.³³⁻³⁵ The visual deficits in amblyopia are more marked in photopic conditions when retinal dopamine activity should be high. As dopamine improves both visual function and increases the SP, a reduction in dopaminergic retinal function in amblyopia would fit with the experimental and clinical evidence, as well as the results of this study. Against this hypothesis, it has been shown that a large dose of levodopa caused a reduction in the DT in subjects with normal vision.¹⁴ However, the use of a peripheral decarboxylase inhibitor would have prevented the RPE cells from receiving any extra dopamine from the choroidal circulation. It may be also that the effects of levodopa on the human EOG vary with different doses as they do in the animal models.

Our findings demonstrate that the EOG is abnormal in some amblyopic subjects. Further work is necessary to characterise these findings in more detail and in a larger, more uniform sample, but our results support a retinal abnormality in amblyopia and the literature suggests that dopaminergic mechanisms may be involved.

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Figure 6 IOD indices for the control subjects.

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