Changes of cone electroretinograms to colour flash stimuli after successful retinal detachment surgery

M Hayashi, S Yamamoto

Abstract

Aim—To examine the changes in the short wavelength (S) and mixed long (L) and middle (M) wavelength sensitive cone (L,M-cone) electroretinograms (ERGs) after successful retinal detachment surgery.

Methods—Cone ERGs elicited by different colour flashes were recorded from 19 eyes with unilateral rhegmatogenous retinal detachment treated successfully by conventional buckling surgery. Ganzfeld colour flashes on a bright white background were used to elicit S-cone and L,M-cone ERGs. The ratio (operated eye/fellow eye) of the S-cone b-wave elicited by a 450 nm stimulus and the ratio (operated eye/fellow eye) of the L,M-cone b-wave elicited by a 633 nm stimulus were evaluated preoperatively and 1, 3, and 6 months after surgery.

Results—Preoperatively, no significant difference was observed between the ratio of the S-cone ERG amplitudes and the ratio of the L,M-cone ERG amplitudes. Postoperatively, the ratio of the L,M-cone ERGs increased significantly over the preoperative value ($p=0.001$) but the ratio of the S-cone ERG did not improve. There were significant differences between the ratios of the S-cone and the L,M-cone ERGs at 1, 3, and 6 months after surgery. The postoperative recovery of the S-cone ERG was significantly greater in eyes treated within 4 weeks after the onset of the detachment than in eyes treated later than 4 weeks.

Conclusions—These results indicate that the impairment of the L,M-cone system

caused by retinal detachment may be reversible. However, the S-cone system may have more profound permanent damage.

(Br J Ophthalmol 2001;85:410–413)

Rhegmatogenous retinal detachments can be reattached successfully by a single scleral buckling operation.^{1,2} However, there are numerous reports of a discrepancy between the anatomical reattachment and the visual function.^{2–7} It is well known that patients who have undergone successful retinal detachment surgery show a blue-yellow colour vision defect postoperatively.^{5–7} A residual defect in hue discrimination has been reported up to 2 years after surgery in patients whose visual acuity had returned to normal levels within 3 months.⁵

We previously reported that the amplitude of the postoperative short wavelength sensitive (S)-cone ERG b-wave was reduced more than the mixed long (L) and middle (M) wavelength sensitive cone (L,M-cone) ERGs in eyes that had undergone successful retinal detachment surgery.⁸ This indicated that the S-cone system was more impaired than the L,M-cone system after successful retinal detachment surgery. However, because ERGs were not recorded preoperatively, we were not able to state whether the reduced S-cones ERGs were the result of a failure of recovery or of a greater preoperative effect of the retinal detachment on the S-cone system.

In the current study we have examined the changes in the S-cone and L,M-cone ERGs prospectively in patients who had undergone successful retinal detachment surgery.

Department of
Ophthalmology, Toho
University Sakura
Hospital, 564-1
Shimoshizu, Sakura,
Chiba 285-8741, Japan
M Hayashi
S Yamamoto

Correspondence to:
Dr S Yamamoto
shuyama@med.toho-u.ac.jp

Accepted 13 November 2000

Table 1 Summary of preoperative clinical data

Patient No	Age/sex	Retinal detachment			Visual acuity	
		Area (degree)	Macular involvement	Estimated duration (days)	Pre	6 months
1	39/F	300	+	6	20/120	20/50
2	22/M	120	+	7	20/25	20/15
3	61/M	210	+	60	20/120	20/50
4	17/M	360	+	1800	20/400	20/400
5	60/M	180	+	7	HM	20/20
6	63/M	150	–	120	20/15	20/20
7	35/F	120	–	14	20/20	20/15
8	15/M	90	–	5	20/30	20/50
9	16/M	180	+	180	20/400	20/200
10	56/M	180	+	7	20/50	20/100
11	52/F	150	+	6	20/100	20/50
12	40/F	180	+	21	20/30	20/20
13	23/F	210	+	180	20/100	20/60
14	28/F	90	+	90	20/400	20/30
15	44/M	270	+	180	20/40	20/20
16	43/M	90	+	90	20/30	20/60
17	31/F	360	+	6	HM	20/30
18	61/M	120	+	8	HM	20/20
19	46/M	240	+	6	CF	20/200

Pre = preoperative; 6 months = 6 months postoperative; HM = hand motion; CF = counting fingers.

Subjects and methods

Nineteen patients with unilateral rhegmatogenous retinal detachment who had successful anatomical outcomes after a single surgical procedure without epimacular proliferation and/or cystoid macular oedema were studied. A summary of the preoperative clinical data is presented in Table 1. Patients with a history of ocular trauma or other retinal diseases were excluded from the study. The macula was involved in 16 eyes and the retina was totally detached in three eyes. The duration of the retinal detachment, which was estimated as the time from the onset of the subjective symptoms to the day of surgery, ranged from 5 days to 5 years.

All patients underwent conventional scleral buckling with cryoretinopexy and drainage of subretinal fluid. In 16 eyes surgery with an encircling silicone band was performed in

Figure 1 Cone ERGs elicited by different colour flash stimuli in the presence of bright white background. The ERGs recorded before surgery (left), 6 months after surgery (middle), and from the normal fellow eye of a 22 year old patient whose macula was involved are shown. The numbers on the left indicate the nominal wavelength of maximum transmission of each filter and the numbers in parentheses indicate the neutral density filter used to adjust flash energy to produce approximately equal L,M-cone b-waves. The broken lines indicate the S-cone b-wave that was measured. S = S-cone b-waves; L,M = mixed L,M-cone b-waves. The calibration marker represents 0.62 μ V vertically and 10 ms horizontally.

addition to the segmental buckle. The preoperative visual acuity ranged from 20/20 to hand motion. The difference in the refractive error between the operated and the fellow eye was less than 1.5 D in all patients. No difference was observed in media opacity between the two eyes during the follow up period. Colour vision was tested in 10 patients at 6 months postoperatively with the standard pseudoisochromatic plates part 2 (SPP2). Informed consent was obtained from all subjects after the methods, purpose, and possible consequences of the study were explained.

The method for ERG recordings has been described in detail previously.⁹ The patients' pupils were fully dilated to a diameter of 8 mm with 0.5% tropicamide drops and the ERGs were recorded simultaneously from both eyes with bipolar Burian-Allen contact lens electrodes. ERGs were recorded preoperatively and at 1, 3, and 6 months after surgery. A Ganzfeld stimulator provided full field flash stimuli (5 cd/s/m²) on a white background of 50 cd/m². All patients were light adapted under the same background for 15 min before the recording.

Spectral stimuli were produced by Kodak Wratten colour filters (Eastman Kodak, Rochester, NY, USA) No 98 (450 nm), No 61 (534 nm), No 21 (593 nm) and No 29 (633 nm) on the same white background. The energy of the flash was changed by neutral density filters, usually in 0.1 log unit steps. The stimulus frequency was 5 Hz and 500 responses were averaged using a Neuropack 2 averager (Nihon Kohden, Tokyo). We routinely

obtained responses with the maximum flash intensity available at 450 nm and then dimmed the other spectral stimuli with neutral density filters to produce approximately equal mixed L,M-cone b-waves as shown in Figure 1, because all longer wavelength stimuli had more effective energy for the mixed L,M-cone.^{8,9} In each patient the ratio of the b-wave amplitude of the operated eye relative to that of the normal fellow eye was defined as the change induced by the retinal detachment. This ratio was calculated for the S-cone ERGs elicited by 450 nm stimuli (S_{op}/S_{norm}) and for the mixed L,M-cone ERG elicited by 633 nm stimuli ($L,M_{op}/L,M_{norm}$).

Statistical analyses were performed using the paired Student's *t* test for paired comparisons and the unpaired Student's *t* test for unpaired comparisons.

Results

The cone ERGs, elicited by different spectral stimuli and recorded preoperatively, 6 months postoperatively, and from the normal fellow eye are shown in Figure 1. These ERGs were recorded from a 22 year old patient who underwent surgery for a rhegmatogenous retinal detachment involving the macula. The retina was reattached after the surgery.

In normal eyes the S-cone ERG elicited by the 450 nm stimuli appeared as a separate b-wave riding on a shorter latency mixed L,M-cone b-wave (Fig 1, right column). Middle and long wavelength stimuli (534, 593 and 633 nm) elicited only the mixed L,M-cone b-waves. The S-cone b-wave was measured from its initial appearance, after the peak of the mixed L,M-cone b-wave, to its peak.

Preoperatively, both the S-cone and the mixed L,M-cone b-waves were reduced, and at 6 months after surgery (Fig 1, middle) the L,M-cone b-waves were larger but the S-cone b-wave was still non-detectable in this patient.

To quantify the changes the ratio of the S-cone b-wave amplitude elicited by the 450 nm stimulus from the detached operated eye to that of the normal fellow eye (S_{op}/S_{norm}) was calculated (Table 2). Similarly, the ratio of the mixed L,M-cone b-wave ($L,M_{op}/L,M_{norm}$) elicited by the 633 nm stimulus was also calculated (Table 2). Preoperatively, the differences between the S_{op}/S_{norm} and $L,M_{op}/L,M_{norm}$ were not significant. At 1, 3, and 6 months after surgery the $L,M_{op}/L,M_{norm}$ increased significantly compared with the preoperative value ($p=0.001$, Student's paired *t* test). This increase in the ratio was a reflection of the increase in the amplitude of the L,M-cone ERGs.

The S_{op}/S_{norm} , on the other hand, did not increase postoperatively and was significantly smaller than $L,M_{op}/L,M_{norm}$ at 1, 3, and 6 months after surgery ($p=0.0002$ at 1 month, $p=0.0004$ at 3 months, and $p=0.0002$ at 6 months after surgery; Table 2).

Plots of the S_{op}/S_{norm} and $L,M_{op}/L,M_{norm}$ 6 months after surgery as a function of the preoperative area of retinal detachment are shown in Figure 2 for each patient. There was no significant correlation between the ratio of the S-cone and the size of the detached area

Table 2 Ratios of S-cone and L,M-cone b-wave amplitude

	Ratio of amplitude (operated eye/fellow eye)			
	Preoperative	1 month postoperative	3 months postoperative	6 months postoperative
S-cone ERG	0.32 (0.26)	0.37 (0.19)	0.41 (0.23)	0.43 (0.24)
L,M-cone ERG	0.44 (0.25)	0.65 (0.19)	0.68 (0.23)	0.74 (0.21)
p value	0.05	0.0002	0.0004	0.0002

Values represent mean (SD).

All analyses were done using Student's unpaired *t* test.

Figure 2 (A) Relation between the ratio of the S-cone ERG b-wave amplitude (S_{op}/S_{norm}) to 450 nm stimuli recorded at 6 months after surgery and the preoperative area of retinal detachment. The linear regression line for all patients was $y = -0.0007x + 0.44$ and the coefficient of correlation was $r = -0.024$, $p = 0.92$. (B) Relation between ratio of the L,M-cone ERG b-wave amplitude to 633 nm stimuli ($L,M_{op}/L,M_{norm}$) at 6 months postoperatively and the preoperative area of retinal detachment. The linear regression line for all patients was $y = -0.0003x + 0.78$ and the coefficient of correlation was $r = -0.25$, $p = 0.61$.

Table 3 Estimated duration of retinal detachment and ratios of S-cone and L,M-cone b-wave amplitude

Estimated duration of retinal detachment	n	Ratio of amplitude (operated eye/fellow eye)	
		S-cone ERG	L,M-cone ERG
≤4 weeks	11	0.53 (0.26)	0.80 (0.12)
>4 weeks	8	0.28 (0.08)	0.62 (0.26)
p value		0.018	0.058

Values represent mean (SD).

All analyses were performed using Student's unpaired *t* test.

($r = -0.024$), nor was there any correlation between the mixed L,M-cone ERG and the size of the detached area ($r = -0.25$).

To examine the effect of the duration of retinal detachment the cases were divided into two groups: those whose estimated duration of retinal detachment was 4 weeks or less and those whose detachment was longer than 4 weeks. The S_{op}/S_{norm} was significantly higher in eyes treated during the first 4 weeks of detachment. No significant difference was observed in the $L,M_{op}/L,M_{norm}$ between the two groups (Table 3).

There was no significant correlation between the ratios of the S-cone and the mixed L,M-cone ERG amplitudes and the number of errors on the B-Y plates of the SPP2 test at 6 months after surgery.

Discussion

In eyes with a retinal detachment both the S-cone and the L,M-cone ERGs were reduced preoperatively. After successful anatomical reattachment the L,M-cone ERG b-wave amplitude increased significantly while the S-cone b-wave did not improve. The reduction of the S-cone ERG in the operated eye was significantly greater than that of the L,M-cone

ERG at 1, 3, and 6 months postoperatively. The area of retinal detachment had no significant influence on the recovery of both the S-cone and the L,M-cone ERGs.

Several electrophysiological studies have shown that the ERG responses recover gradually after retinal detachment,^{10,11} with no suggestion that the recovery of the three cone systems is different. We have previously reported that the reduction in the S-cone ERG b-wave is significantly greater than that of the L,M-cone ERG b-wave postoperatively.⁸ The present study not only confirmed our previous results, but also demonstrated that such postoperative differences between the S-cone ERG and the L,M-cone ERG were not the result of preoperative differences but resulted from differences in the postoperative recovery of the three cone systems.

The preoperative duration of retinal detachment was a significant factor in the recovery of the S-cone ERG which showed a significantly greater improvement postoperatively in cases treated within 4 weeks after onset than in those with longer preoperative duration. The L,M-cone b-wave amplitude also showed a greater recovery in cases with a shorter preoperative period but the difference was not significant. These findings confirm those of previous studies that have reported a significant relation between the duration of the detachment and recovery of such functions as visual acuity and colour discrimination.^{1-3,5}

Macular detachment is also well known to be a prognostic factor for functional recovery.¹⁻⁶ In our study no significant difference was observed between the "macula-on" and "macula-off" eyes; however, only three of 19 eyes were in the "macula-on" group.

Retinal detachment is rapidly followed by degeneration of the photoreceptors that initially affects the outer segments and later the receptor cell bodies.¹² An ultrastructural study by Kroll and Machemer¹³ showed marked degeneration of the outer segments of rods and cones in an experimental retinal detachment study in rhesus monkeys. Surgical reattachment resulted in rapid regeneration of the outer segments of both rods and cones. Because the L,M-cones make up about 90% of the cone population in the rhesus monkey, they were presumably observing changes mostly in the L,M-cones. Nork *et al*¹⁴ examined retinas from eyes with traumatic retinal detachment immunohistochemically and found a complete dropout of the S-cones, a homogeneous loss of about half the rods, and a mild reduction of the L,M-cones. These findings were found even in retinas that had suffered retinal detachment for only a few days before the examination. However, they could not draw any conclusion about whether the L,M-cones were injured because their study was limited to observing only significant morphological changes visible by light microscopy. These two earlier reports agree reasonably well with our results of the postoperative recovery of the L,M-cone ERGs.

There have been many psychophysical studies reporting acquired colour vision defects along the blue-yellow axis in eyes with retinal

detachment,¹⁵ and in eyes after successful retinal detachment surgery.⁵⁻⁷ The hue discrimination examined with the Farnsworth Munsell 100 hue test reportedly showed a blue-yellow defect in eyes without macula detachment and a generalised deficiency in all axes in eyes in which the macula was involved preoperatively.⁶ The "macula-on" eyes showed a significant improvement in colour discrimination 3 months after surgery but there was only marginal improvement after 12 months. The "macula-off" eyes continued to show improved colour discrimination up to 12 months after surgery. Recovery from the blue-yellow defect after retinal detachment surgery, as evaluated by the pseudoisochromatic test, was similar to that of visual acuity as the number of errors on the B-Y plates decreased significantly from 2 weeks to 2 months after surgery.⁷

In our study the amplitude of the L,M-cone b-wave had increased significantly at 6 months after surgery but the S-cone b-wave remained at the preoperative level even at 6 months post-operatively. We also examined colour vision by SPP2 in 10 patients 6 months after surgery and found that there was no significant correlation between the number of errors on the B-Y plates in SPP2 and the reduction in the S-cone and mixed L,M-cone ERG b-wave amplitudes. The differences between the results from SPP2 and those from ERGs may result from the fact that colour vision tests mainly reflect foveal cone function while the S-cone ERG reflects the entire retina. This type of discrepancy was also observed in the complete type of congenital stationary night blindness as the S-cone ERGs elicited by Ganzfeld flash stimuli were undetectable but the S-cone function at the fovea measured psychophysically was normal.¹⁶ Topographical differences in S-cone function have also been reported in this disease.¹⁷ It will be interesting to know if there is a difference in the recovery of S-cone function after retinal detachment surgery at the fovea and in the extrafoveal regions.

The exact mechanism(s) for the selective reduction of the S-cone system in retinal detachment has not been determined. The S-cone pathway is thought to be more vulnerable to hypoxia than the L,M-cone system,¹⁸ so detachment from the retinal pigment epithelium may cause selective damage to the S-cone photoreceptors. Scleral buckling reportedly reduces ocular blood flow, probably because this procedure increases choroidal vascular resistance.^{19, 20} This may lead to hypoxia in the outer retina resulting in selective impairment of the S-cone system. It

has also been reported that constriction of the eye by an encircling band causes chronic ischaemia, a diminished ocular pulse, and obstruction of the choroidal venous outflow.²⁰ In our study 16 eyes underwent encircling surgery with a silicone band in addition to the segmental buckle, and three eyes had only segmental buckles. No difference in the recovery of the S-cone ERGs between the two groups was observed, although the number of eyes without encircling was not sufficient for statistical analysis. Further studies are needed to clarify the mechanisms for the selective and somewhat permanent impairment of the S-cones in eyes with retinal detachment.

- 1 Tani P, Robertson DM, Langworthy A. Prognosis for central vision and anatomic reattachment in rhegmatogenous retinal detachment with macula detached. *Am J Ophthalmol* 1981;92:611-20.
- 2 Kreissig I. Prognosis of return of macular function after retinal reattachment. *Mod Probl Ophthalmol* 1977;18:415-29.
- 3 Gundry MF, Davies EWG. Recovery of visual acuity after retinal detachment surgery. *Am J Ophthalmol* 1974;77:310-4.
- 4 Friberg TR, Eller AW. Prediction of visual recovery after scleral buckling of macula off retinal detachments. *Am J Ophthalmol* 1992;114:715-22.
- 5 Foulds WS, Reid H, Chisholm IA. Factors influencing visual recovery after retinal detachment surgery. *Mod Probl Ophthalmol* 1974;12:49-57.
- 6 Chisholm IA, McClure E, Foulds WS. Functional recovery of the retina after retinal detachment. *Trans Ophthalmol Soc UK* 1975;95:167-72.
- 7 Ueda M, Adachi-Usami E. Assessment of central visual function after successful retinal detachment surgery by pattern visual evoked cortical potentials. *Br J Ophthalmol* 1992;76:482-5.
- 8 Yamamoto S, Hayashi M, Takeuchi S. Cone electroretinograms in response to color stimuli after successful retinal detachment surgery. *Jpn J Ophthalmol* 1998;42:314-7.
- 9 Gouras P, MacKay CJ, Yamamoto S. The human S-cone electroretinogram and its variation among subjects with and without L and M-cone function. *Invest Ophthalmol Vis Sci* 1993;34:2437-42.
- 10 Blach RK, Behrman J. The electrical activity of the eye in retinal detachment. *Trans Ophthalmol Soc UK* 1967;87:263-6.
- 11 Hamasaki DI, Machermer R. Experimental retinal detachment in the owl monkey. *Graefes Arch Clin Exp Ophthalmol* 1969;177:212-21.
- 12 Foulds WS, Ikeda H. The effects of detachment of the retina on the induced and resting ocular potentials in the rabbit. *Invest Ophthalmol Vis Sci* 1966;5:93-108.
- 13 Kroll AJ, Machermer R. Experimental retinal detachment and reattachment in the rhesus monkey. *Am J Ophthalmol* 1969;68:58-77.
- 14 Nork TM, Millecchia LL, Strickland BD, et al. Selective loss of blue cones and rods in human retinal detachment. *Arch Ophthalmol* 1995;113:1066-73.
- 15 Yokoyama M. Blue sensation in eye disease. *Jpn J Clin Ophthalmol* 1979;33:111-25.
- 16 Kamiyama M, Yamamoto S, Nitta K, et al. Undetectable S-cone electroretinogram b-wave in complete congenital stationary night blindness. *Br J Ophthalmol* 1996;80:637-9.
- 17 Terasaki H, Miyake Y, Nomura R, et al. Blue-on-yellow perimetry in the complete type of congenital stationary night blindness. *Invest Ophthalmol Vis Sci* 1999;40:2761-4.
- 18 Smith VC, Ernest JT, Pokorny J. Effect of hypoxia on FM 100-hue test performance. *Mod Probl Ophthalmol* 1976;17:248-56.
- 19 Yoshida A, Fekke GT, Green GJ, et al. Retinal circulatory changes after scleral buckling procedures. *Am J Ophthalmol* 1983;95:182-8.
- 20 Yoshida A, Hirokawa H, Ishiko S, et al. Ocular circulatory changes following scleral buckling procedures. *Br J Ophthalmol* 1992;76:529-31.