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Pattern reversal electroretinograms in patients with unilateral idiopathic full thickness macular holes

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ABSTRACT: Purpose. *To discover the effect of detachment of the posterior vitreous cortex on pattern electroretinogram (PERG) P50 amplitudes in the uninvolved fellow eyes (FE) of patients with macular holes (MH), and to determine the prognostic value of the PERG in identifying the FE of patients with MH that could be at risk for the development of a MH.*
Methods. *PERGs were recorded using 12' and 46' checkboard stimulus reversing at 5 Hz in 18 patients selected from a cohort of 37 patients with unilateral idiopathic full thickness MH, and in age-matched controls (AMC). Contact lens biomicroscopy with a Goldmann contact lens and kinetic B-scan ultrasonography were performed bilaterally in both patients and AMC.*
Results. *The P50 amplitudes with checks of 12' and 46' were significantly lower in eyes with MH than in the uninvolved FE and AMC. There was a significant reduction in the P50 amplitudes in the FE compared to the AMC with checks of 12', but there was no significant reduction with checks of 46'. In the FE with posterior vitreous detachment (PVD) (eleven cases), the P50 amplitudes with checks of 12' were greater than in the eyes without PVD. With checks of 46', there was no significant difference in eyes with and without PVD.*
Conclusions. *These data suggest that subclinical macular pathology in the FE of MH probably resulting from vitreous traction can be demonstrated by PERG using small check size stimulus. (Eur J Ophthalmol 1999; 9: 37-42)*

KEY WORDS: Idiopathic full thickness macular hole, Pattern electroretinography, Posterior vitreous detachment

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INTRODUCTION

Unilateral idiopathic full thickness macular holes (MH) are characterized by a disk shaped defect which involves the absence of all the layers of the retina. Once a hole develops in one eye, the fellow eye (FE) has been shown to be at risk for the development of the similar condition (1-3). The chance of a hole developing in the FE is affected by certain clinical conditions such as vitreomacular traction (4-6). In some patients in this study, there was a detachment of the posterior vitreous cortex, and it is considered that in PVD, the possibility of traction on the retina is reduced, and, therefore, in such patients the probability of an MH development in the FE is less (6-8). If the pattern reversal electroretinogram (PERG) is of prognostic value, it might be different in these two groups of FE; this would be of interest because it would provide data confirming the clinical findings and providing preliminary evidence of the value of the PERG before a hole develops in the FE.

Therefore, PERGs using small and large checks were recorded in a group of selected patients with unilateral MH and in age-matched controls (AMC) to investigate the correlation of PERG with clinical findings, and to determine the prognostic value of the PERG in those patients with MH that might be at risk for the development of a macular hole in the FE.

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SUBJECTS AND METHODS

A total of 18 patients from a cohort of 37 patients with unilateral MH from my practice who had no detectable systemic or other ocular diseases were the subjects of this study. Patients with a previous history of trauma, intraocular inflammatory disease, age-related macular degeneration, ocular surgery, glaucoma and ocular hypertension, myopia higher than four diopters, retinal vascular occlusive disease either in the affected eyes or in the FE, were excluded from this study. The best corrected Snellen visual acuities were 0.2 or worse in the affected eyes and 0.7 or better in the FE. The diagnosis of a full thickness macular hole was made based on the following criteria: the absence of retinal tissue within the hole as observed biomicroscopically, an increased choroidal fluorescence in fluorescein angiography, and/or a positive Watzke's sign. In addition to the above-mentioned criteria, yellow deposits at the hole base, an operculum in front of the hole, and a retinal detachment surrounding the hole implied the diagnosis of a full thickness macular hole (6). The AMC (18 eyes in 18 subjects) were selected from a cohort of 529 subjects who were examined in the outpatient clinic. The best corrected Snellen visual acuities of these subjects were 0.7 or better, and these patients required reading glasses. Apart from this, these subjects had no detectable systemic or ocular disease. In order to obtain a similar comparison, especially between the FE of MH and AMC, all eyes were divided into two subgroups based on the status of the posterior vitreous cortex: 1) Eyes with a posterior vitreous detachment, either complete or partial (PVD), 2) Eyes without a PVD.

Vitreous examination: Contact lens biomicroscopy with a Goldmann contact lens and kinetic B-scan ultrasonography were performed bilaterally in both patients and AMC. A complete posterior vitreous detachment (PVD) was diagnosed when a mobile, thin, continuous membrane without optic disc adhesion was seen, or when the posterior hyaloid membrane containing the peripapillary vitreous condensation ring moved in front of the optic disc. A partial or incomplete PVD appeared as a smooth membranous surface in front of the optic disk and/or paramacular retina. The biomicroscopic detection of a small opacity (pseudo operculum) suspended in front of the foveal retina was also considered to be a sign of vitreomacular separation. The diagnosis of a posterior vitreous traction was made if either a visible attachment of the vitreous at the macular or paramacular area could be observed, or retinal tags, retinal folds and cystic degeneration were noted elsewhere in the retina (7-9).

PERG recording: Transient PERGs were recorded using high contrast (76%) black and white checks reversing in counterphase at five times per second. The entire TV screen subtended 13° at the eye. Mean luminance was 50 cd/m^2. The trace averager was retriggered every 300 miliseconds (ms) and data collection time was 150 ms. Two different check sizes were used: 12' and 46'. Impedance of the skin electrodes was carefully monitored and was <2 Kohm, a measure required to reduce electrical noise and artifacts. Silver silver chloride disk electrodes were placed on the ipsilateral temple (reference) and on the temple (ground). Gold foil electrodes were placed in the lower eyelid as the active electrode. High and low pass filters were set at 1.6-30 Hz and 130-160 responses were averaged and repeated three times. A fixation target 25' in diameter was placed in the center of the TV screen. The amplitude of the positive deflection occurring around 50-55 ms (P50) was measured relative to the baseline. Negative deflection occurring around 90-100 ms (N95) and peak times for both responses (P50 and N95), although recorded in patients and subjects incorporated in this study, were not included.

Full informed consent was obtained from every patient and AMC for both clinical and electrophysiological examinations. Patients' and AMC's electroretinographic testing was done within two weeks following the initial visit, and the whole group was followed at six-month intervals for three years.

The difference between groups (intergroup differences) were analyzed using variance analysis. When there was a significant difference ($p<0.05$) between the groups, Tukey HSD test was used for further multiple comparisons. The difference between the groups with and without PVD was investigated using Kruskal-Wallis one way ANOVA test. The Bonferroni adjusted Mann Whitney U test was used for further analysis when there was a significant intergroup difference ($p<0.05$). Mann Whitney U test was employed to investigate the differences between the groups with and without PVD in each group.

RESULTS

The AMC and MH patients (14 females and 4 males in each group) were aged between 52-66 (mean 60.6 ± 4.0) and 50-67 (mean 60.3 ± 4.4) years, respectively. The status of the posterior vitreous cortex of the eyes incorporated in this study are given in Table I. According to contact lens biomicroscopic and kinetic B-scan ultrasonographic findings, the number of cases with PVD was as follows: 5 of 18 (all females) in eyes with MH, 11 of 18 (9 females, 2 males) in the FE, and 11 of 18 (7 females, 4 males) in the AMC group. The number of cases without PVD was as follows: 13 of 18 (9 females, 4 males) in eyes with MH, 7 of 18 (5 females, 2 males) in the FE, and 7 of 18 (7 females) in the AMC group. Eyes with MH had a significantly lower incidence of PVD compared to the FE and AMC ($p=0.001$), Table I. No patient with clinical evidence of a PVD developed a hole in the FE during the follow-up period, but two female patients aged 65 and 68 years, who had visible attachments of the vitreous at the macular area in the FE, developed a hole after two years. These two patients had reduced P50 amplitudes (1.8 and 1.7 µV) in their FE compared to the rest of the eyes in the FE group.

The PERGs in a patient and control subject are given in Figure 1 and the results are given in Figure 2 and Tables II, III. The PERG P50 amplitudes (mean ± SD) of the AMC, MH and FE to 12’ and 46’ of checks were 2.36 ± 0.21 and 2.31 ± 0.13, 1.33 ± 0.22 and 1.38 ± 0.21, 2.08 ± 0.25 and 2.23 ± 0.20 µV, respectively. With checks of 12’, the P50 amplitude was 2.0 µV or better in the FE with PVD, whereas in the FE

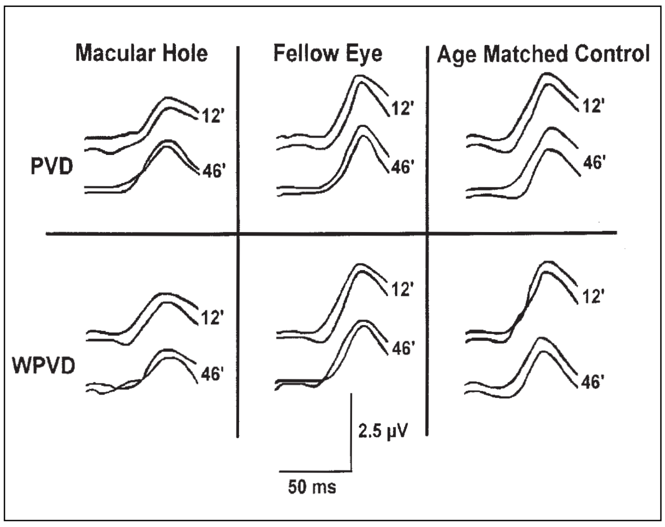

Fig. 1 - *PERG traces from a patient with macular hole and a control subject. Two traces are displayed to show reproducibility.*

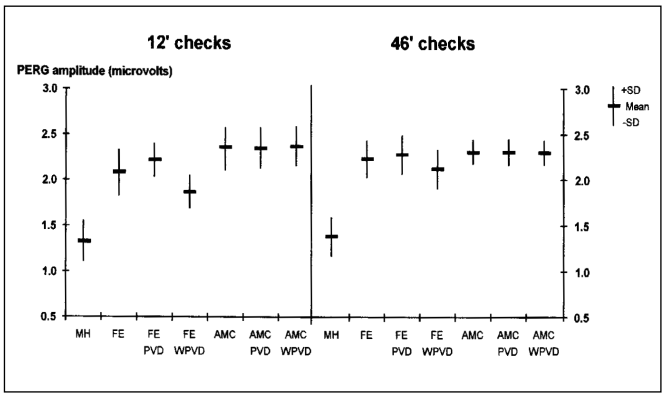

Fig. 2 - *PERG P50 amplitudes in idiopatic full thickness macular holes (MH), fellow eyes (FE) of MH and age-matched controls (AMC). (PVD=Posterior vitreous detachment, WPVD=Without posterior vitreous detachment).*

TABLE I - STATUS OF THE POSTERIOR VITREOUS CORTEX IN EYES WITH MACULAR HOLES (MH) FELLOW EYES (FE) OF MH AND AGE-MATCHED CONTROLS (AMC)

		Eyes, No (%)	
Posterior Vitreous Detachment	MH	FE	AMC
None	13 (72)	7 (39)	7 (39)
Present	5 (28)	11(61)	11(61)
Partial	2 (11)	3 (17)	4 (22)
Complete	3 (17)	8 (44)	7 (39)

without PVD, all amplitudes were below 2.0 µV except in two eyes. With checks of 46', the P50 amplitude was below 2.0 µV only in one eye without PVD. In the AMC, the P50 amplitudes were not different in eyes with and without PVD and were 2.0 µV or better. In one eye, the P50 amplitude was 2.0 µV with checks of 12'. The P50 amplitudes with checks of 12' and 46' were significantly lower in eyes with MH than in the FE and AMC, and in eyes with MH with and without PVD compared to the FE and AMC with and without PVD. There was a significant reduction in the P50 amplitudes with checks of 12' in the FE compared to the AMC, in the FE without PVD compared to the FE with PVD, in the FE without PVD compared to the AMC without PVD, but there was no significant reduction in the FE with PVD compared to the AMC with PVD and in the AMC with PVD compared to the AMC without PVD. With checks of 46', there was no significant reduction in the P50 amplitudes in the FE compared to the AMC, in the FE with and without PVD compared to the AMC with and without PVD, in the FE with PVD compared to the FE without PVD and in the AMC with PVD compared to the AMC without PVD. With checks of 12' and 46', there was no significant reduction in the P50 amplitudes in eyes with MH with PVD compared to the eyes with MH without PVD.

DISCUSSION

Vitreoretinal traction in the macular region is the major cause of the development of idiopathic full thickness macular holes (8, 10). The risk of developing a hole in the fellow eye is greatly increased in the presence of a posterior vitreoretinal traction, and greatly decreased in the presence of a posterior vitreoretinal separation (10, 11). Since posterior vitreous attachments and macular abnormalities may be important in predicting macular hole formation in the FE of MH cases (12, 13), contact lens biomicroscopy and

TABLE II - PERG P50 AMPLITUDES IN MACULAR HOLES (MH), FELLOW EYES (FE) AND AGE-MATCHED CONTROLS (AMC) WITH 12' AND 46' OF CHECKS. MEAN± STANDARD DEVIATION OF PERG P50 AMPLITUDES ARE GIVEN IN MICROVOLTS

Eyes with	Check Size	MH	FE	AMC	MH-FE	MH-AMC	FE-AMC	SM
PVD+WPVD	12'	1.33 ± 0.22	2.08 ± 0.25	2.36 ± 0.21	*	*	*	(1)
	46'	1.38 ± 0.21	2.23 ± 0.20	2.31 ± 0.13	*	*		(1)
PVD	12'	1.30 ± 0.29	2.22 ± 0.18	2.35 ± 0.22	*	*	-	(2)
	46'	1.46 ± 0.23	2.28 ± 0.21	2.31 ± 0.14	*	*	-	(2)
WPVD	12'	1.34 ± 0.20	1.87 ± 0.18	2.37 ± 0.21	*	*	*	(2)
	46'	1.35 ± 0.20	2.16 ± 0.17	2.30 ± 0.13	*	*	-	(2)

SM = Statistical Method; PVD = Posterior vitreous detachment, WPVD=Without posterior vitreous detachment; * $p<0.05$, - $p>0.05$; (1) Tukey HSD test; (2) The Bonferroni adjusted Mann Whitney U test

TABLE III - PERG P50 AMPLITUDES IN EYES WITH AND WITHOUT PVD. MEAN ± STANDARD DEVIATION OF PERG P50 AMPLITUDES ARE GIVEN IN MICROVOLTS

		PVD	WPVD	p
MH	12'	1.30 ± 0.29	1.34 ± 0.20	-
	46'	1.46 ± 0.23	1.35 ± 0.20	-
FE	12'	2.22 ± 0.22	1.87 ± 0.18	0.004
	46'	2.28 ± 0.21	2.16 ± 0.17	-
AMC	12'	2.35 ± 0.22	2.37 ± 0.21	-
	46'	2.31 ± 0.14	2.30 ± 0.13	-

MH = Macular hole; FE = Fellow Eyes; AMC = Age Matched Controls; PVD = Posterior Vitreous Detachment; WPVD = Without Posterior Vitreous Detachment; p = Significance level (Mann Whitney U test); - $p>0.05$

kinetic B-scan ultrasonography have proven to be very useful in detecting the status of the posterior vitreous cortex (9, 14, 15). In the patient population studied, no FE with a clinically diagnosed PVD acquired a macular hole in the follow-up period of three years, and the PERG P50 amplitudes of the FE with PVD were 2.0 μV or better. The PERG P50 amplitudes with small and large checks in the FE with PVD were not significantly different from the AMC with and without PVD. With large size checks (46'), the P50 amplitudes in the FE without PVD were also not significantly different from the AMC with and without PVD, but with small size checks (12'), the P50 amplitudes were significantly attenuated, suggesting possible subclinical macular pathology.

Previous electrophysiological studies in patients with MH have shown that the implicit time of the b-wave in the affected eyes were significantly delayed when a small size stimulus was used (16) and the amplitude of the foveal cone electroretinograms were significantly correlated with the hole diameter (13). Also with small check size (15'), a reduction in pattern reversal electroretinogram or visual evoked potential amplitude was shown in eyes with macular holes as compared to control eyes (17, 18) and the FE of eyes with MH may also show electrophysiologic abnormalities (13).

The results of this study indicate that subclinical macular pathology in the FE of MH probably resulting from vitreous traction can be demonstrated by PERG using small check size stimulus since the proportion of PERG arising from parafovea and macula increases when pattern is small (19). The P50 amplitudes were below 2.0 μV in cases of vitreoretinal traction and this evidence may lead us to use the PERG in cases of MH to pick up those FE which might be at risk for developing a hole where clinical findings may fail to demonstrate vitreoretinal traction.

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