

# Pattern-Reversal Visual Evoked Potentials in Patients With Epiretinal Membrane

NICOLE A. M. BEMELMANS, MD, MAURITS A. D. TILANUS, MD,  
MARINUS H. M. CUYPERS, BSC ENG, AND ALFRED J. L. G. PINCKERS, PHD

• **PURPOSE:** To determine the extent of pattern-reversal visual evoked potential parameter alteration by epiretinal membranes and to investigate the use of pattern-reversal visual evoked potential in the estimation of macular function in eyes with epiretinal membrane and in the fellow eyes.

• **METHODS:** In both eyes of 162 patients with epiretinal membrane, 92 of primary and 70 of secondary origin, pattern-reversal visual evoked potentials were recorded. Check sizes of 17', 10', and 7' (minutes of arc) were used. Parameters investigated were N80 and P100 latencies and P100 amplitude.

• **RESULTS:** No significant difference was detected between eyes with epiretinal membrane of primary and secondary origin regarding visual acuity and the pattern-reversal visual evoked potential parameters for the different check sizes. Compared with the fellow eyes, the eyes with epiretinal membrane had a significantly reduced visual acuity, prolonged N80 and P100 latencies, and a reduced P100 amplitude for the different check sizes. Compared with a separate control group (N = 20) with patients 50 to 59 years old, eyes with epiretinal membrane (N = 9) showed the same features as in the total group, but only for the 17' and 10' check sizes. The fellow eyes (N = 9) showed a significant reduction of the P100 amplitude ( $P < .05$ ) for the pattern sizes of 17' and 10',

but no difference in visual acuity or pattern-reversal visual evoked potential latency was found.

• **CONCLUSIONS:** In eyes with epiretinal membrane, pattern-reversal visual evoked potential latencies are prolonged, and amplitude is reduced. Relationships between clinical parameters and pattern-reversal visual evoked potential parameters require further study.

IN 1992, MEHTA AND ASSOCIATES<sup>1</sup> REPORTED PREOPERATIVE pattern-reversal visual evoked potentials in 16 patients with an epiretinal membrane. They concluded that preoperative pattern-reversal visual evoked potential can objectively assess the function of the underlying macula in patients with epiretinal membrane. As in our institute peeling of epiretinal membranes is regularly performed, we wondered if the findings of Mehta and associates were reproducible in our patient population. From a review of the literature, we concluded that no further data on pattern-reversal visual evoked potential recording in patients with an epiretinal membrane were available. We analyzed pattern-reversal visual evoked potential data in 162 patients with either primary (N = 92) or secondary (N = 70) epiretinal membrane. A major goal of the present study was to obtain a sound description of the pattern-reversal visual evoked potential in eyes with epiretinal membrane and in the fellow eyes and to investigate its ability to detect macular pathologic conditions at an early stage. Although subjective tests of visual acuity are by far the most simple and most straightforward index of macular function, an accurate and objective electrophysiologic index of macular function is needed in the clinical treatment of patients with macular pathologic conditions. An advantage of the use of pattern-

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From the Institute of Ophthalmology, University Hospital Nijmegen, Nijmegen, The Netherlands.

Reprint requests to Nicole A. M. Bemelmans, MD, Institute of Ophthalmology, University Hospital Nijmegen, PO Box 9101, 6500 HB Nijmegen, The Netherlands; fax: 31-24-3540522.



reversal visual evoked potential as an index of macular function is that the pattern stimulus elicits electrical signals from the photopic system, and the visual angle of the stimulus is equal to the angle of the retinal area stimulated. The relatively small check sizes (10', 17', and 7') evoke large responses in the region 0 to 3 degrees from the fovea.<sup>2</sup>

## PATIENTS AND METHODS

ONE HUNDRED SIXTY-TWO PATIENTS WITH AN EPIRETINAL membrane underwent pattern-reversal visual evoked potential recording 1 day prior to surgical intervention. Institutional review of the study was obtained. Individual informed consent was also obtained. In addition, a comprehensive routine ophthalmologic examination was administered, including measurement of the refractive error by subjective techniques in adults, corrected visual acuity measurement, Amsler grid testing, slit-lamp examination, and ophthalmoscopy. Pattern-reversal visual evoked potential recording was performed monocularly; both eyes were recorded separately. It was noted whether the epiretinal membrane developed idiopathically (without previous ocular disease or present systemic disease) or secondarily (following previous ocular disease, ocular surgery, or known systemic disease). Fellow eyes had to meet the following inclusion criteria: no history or signs of ophthalmologic disease and visual acuity equal to or better than 20/25.

Control eyes were selected retrospectively. Most frequently these were the healthy fellow eyes of the patients with the affected eyes, in which pattern-reversal visual evoked potential recordings were also noted. Except for no known or detectable ophthalmologic disease in the control eyes, visual acuity had to be equal to or better than 20/25 in the participating control eyes. Increasing age alters the pattern-reversal visual evoked potential parameters, in particular the N80 and P100 latencies.<sup>3-7</sup> Thus, to minimize the age effect, we selected patients (N = 9; 20 control eyes) in the age range of 50 to 59 years.

The active electrode was placed at position Oz, 2.5 cm above the inion, and the referring electrode was placed at T3, the mastoid process. The grounding was done with an electrode on the earlobe (A1). Impedance, measured at 20 Hz, was kept below 5 k $\Omega$ . The

ambient illumination of the room was not standardized, though kept at mesopic level.

The eyes were optimally refracted for the viewing distance. Pattern-reversal visual evoked potentials were recorded monocularly, using a reversing checkerboard pattern generated by a galvanometer mirror system (Medilog VPS-20). The stimulus consisted of patterns of 17', 10', and 7'. Field size was 9 degrees, the contrast of the checks was 80%, and the mean luminance of stimulus was 40 candelas/m<sup>2</sup>. The ensemble average was obtained from 64 single responses of 500 milliseconds' duration; reversal rate was 2 Hz. After a 100-dB amplification and analog bandpass filtering (fourth order linear phase filter; bandpass, 0.16 to 70 Hz), the evoked response signals were digitized (Keithley DAS-16 ADC; sampling rate, 1,000 Hz); 64 successive sweeps were averaged and stored in a personal computer (Tulip 386 SX MSDOS). In addition, a digital low-pass filter (zero phase), with a cutoff frequency of 40 Hz, was applied to the averaged evoked response.

The N80 and P100 latencies of the pattern-reversal visual evoked potential complex were measured as the time difference in milliseconds between the stimulus reversal and the first negative trough (N80) and the major positive peak (P100) of the response, respectively. The amplitude of the pattern-reversal visual evoked potential is calculated from the difference in microvolts of the N80 trough to the P100 peak. This amplitude is labeled the "P100 amplitude." An example of a pattern-reversal visual evoked potential measurement of a patient with epiretinal membrane is shown in the Figure.

Statistical analysis was performed with the SAS statistical analysis software package (SAS Institute, Inc, Cary, North Carolina). Exploring the distribution of the data in the three groups (eyes with epiretinal membrane, fellow eyes, and control subjects), we found that most of the pattern-reversal visual evoked potential parameters were not distributed in a gaussian manner (Shapiro-Wilk test,  $P < .05$ ). For this reason, the hypothesis test was done with nonparametric methods: a Wilcoxon signed rank test (paired design) for comparison of the data in the eyes with epiretinal membrane and their fellow eyes and a Wilcoxon rank sum test for comparison with the independent control group.<sup>8-10</sup>



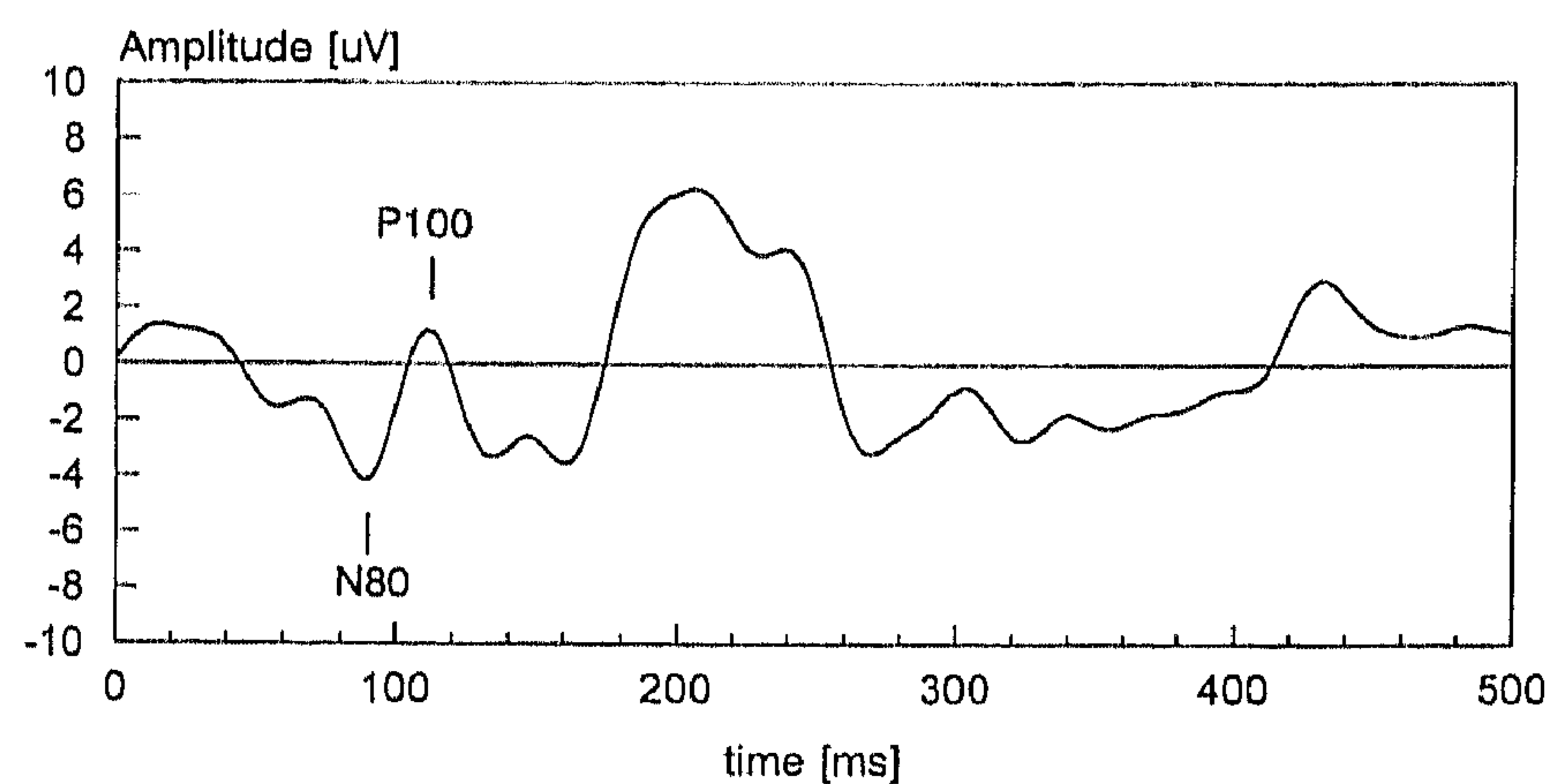
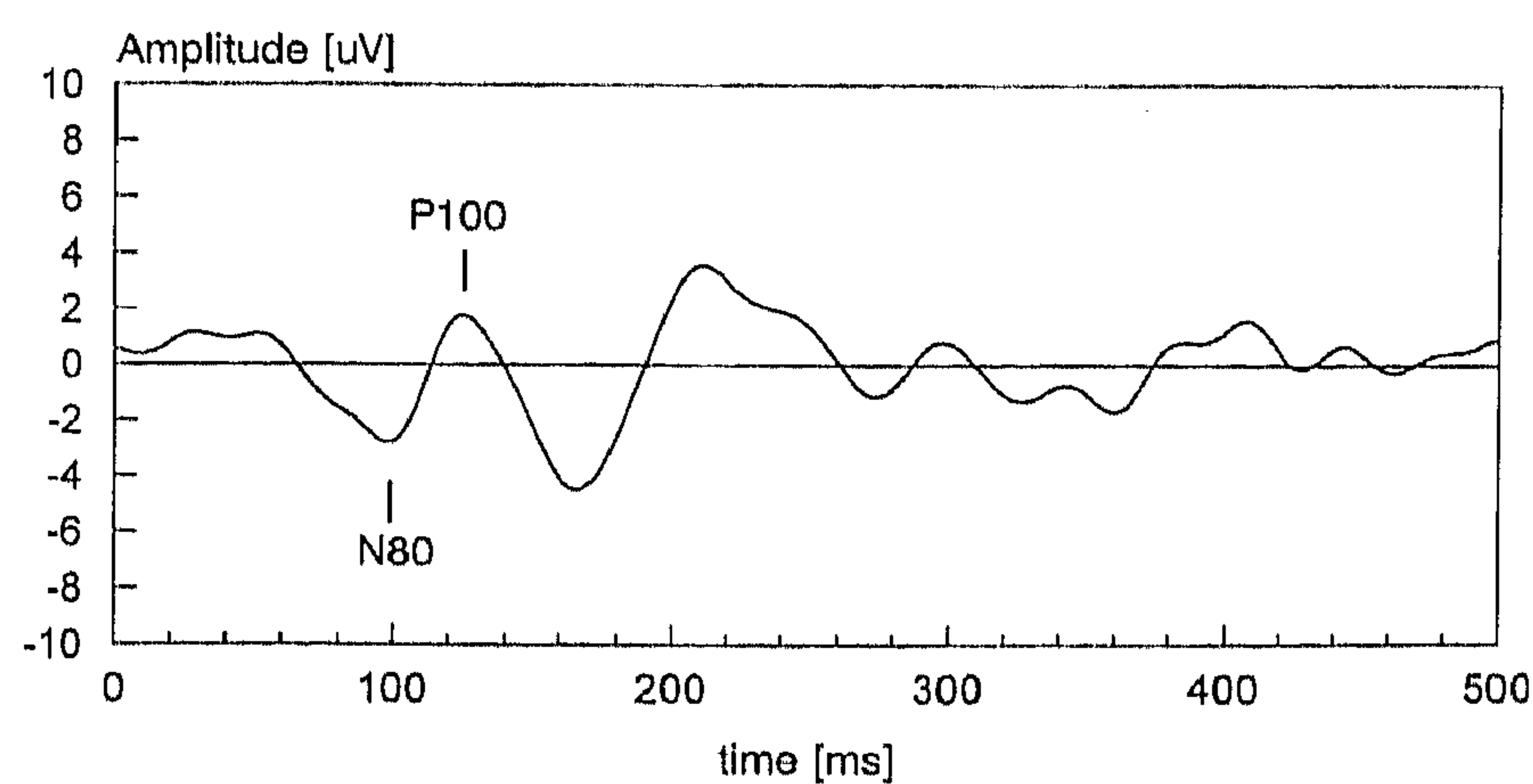


Figure. (Top) Pattern-reversal visual evoked potential of eye with epiretinal membrane (visual acuity, 20/20). (Bottom) Pattern-reversal visual evoked potential of fellow eye. N80 and P100 latencies of the pattern-reversal visual evoked potential are considerably prolonged with respect to the fellow eye (N80 latency, 99 vs 89 milliseconds in fellow eyes; P100 latency, 125 vs 112 milliseconds in fellow eyes). P100 amplitude of eye with epiretinal membrane is reduced.  $\mu\text{V}$  indicates microvolts, and ms, milliseconds.

## RESULTS

THE DATA OF 92 EYES WITH EPIRETINAL MEMBRANE OF primary origin and 70 eyes with epiretinal membrane of secondary origin were compared statistically (Table 1). The analysis (Wilcoxon rank sum test) revealed no significant difference on preoperative visual acuity and pattern-reversal visual evoked potential latency and amplitude. As a consequence of this outcome, we concluded that, for statistical analysis, eyes with epiretinal membrane of primary and secondary origin can be considered as one group regarding the pattern-reversal visual evoked potential parameters.

The pattern-reversal visual evoked potential data of the eye with epiretinal membrane and the fellow eye were compared (Table 2). The number of patients for whom pattern-reversal visual evoked potential data

Table 1. Data on Eyes With Epiretinal Membranes

Type of Epiretinal Membrane	History	No. of Patients
Primary	Idiopathic	92
Secondary	Extracapsular cataract extraction and intraocular lens	27
	Retinal detachment	22
	Vitrectomy	2
	Extracapsular cataract extraction and intraocular lens/retinal detachment	1
	Extracapsular cataract extraction and intraocular lens/vitrectomy	1
	Other	15
	Extracapsular cataract extraction and intraocular lens/other	1
Retinal detachment/other	1	
Total		162

were available for comparison depended on the number of recordable pattern-reversal visual evoked potentials in eyes with epiretinal membrane. In other words, when the pattern-reversal visual evoked potentials in the eye with the epiretinal membrane were not reliably recordable, the comparison with data of the fellow eye was impossible. In the eyes with epiretinal membrane, the pattern-reversal visual evoked potential was recordable in 67%, 58%, and 41% for the check sizes of 17', 10', and 7', respectively.

Preoperative visual acuity was significantly ( $P < .001$ ) lower in the eye with the epiretinal membrane compared with the fellow eye. For all check sizes, N80 and P100 latencies were significantly prolonged ( $P < .02$ ), and P100 amplitude was significantly ( $P < .0001$ ) reduced in the affected eye.

To be able to compare the eyes with epiretinal membrane and the fellow eyes with a separate control group, we selected control subjects between 50 and 59 years of age, thereby avoiding confounding by age. Eight eyes with epiretinal membrane could be compared with the 20 control eyes (Table 3). Preoperative visual acuity in eyes with epiretinal membrane was



Table 2. Mean and SD of Pattern-Reversal Visual Evoked Potential Parameters for Eyes With Epiretinal Membranes and Fellow Eyes\*

Check Size	Parameter	Eyes With Epiretinal Membranes		Fellow Eyes		P Value
		Mean (SD)	N	Mean (SD)	N	
—	Visual acuity	0.3 (0.2)	162	0.9 (0.1)	113	.0001
17'	N80 latency (ms)	89.6 (12.8)	108	82.6 (6.6)	105	.0001
10'		95.1 (11.7)	94	86.3 (6.2)	102	.0001
7'		101.9 (12.3)	66	94.8 (9.9)	98	.0013
17'	P100 latency (ms)	115.3 (13.4)	108	108.2 (9.3)	105	.0001
10'		121.9 (12.4)	94	111.2 (8.2)	102	.0001
7'		127.9 (15.0)	66	122.9 (14.7)	98	.0139
17'	P100 amplitude ( $\mu$ V)	4.9 (3.7)	108	6.1 (3.9)	105	.0001
10'		5.0 (4.1)	94	6.1 (3.7)	102	.0001
7'		3.8 (3.2)	66	4.9 (3.6)	98	.0001

\*Statistical significance was analyzed with a Wilcoxon signed rank test.

significantly lower than in the control eyes. P100 latency was significantly prolonged for the 10' check size; P100 amplitude was significantly reduced for the 17' and the 10' check sizes.

We compared the nine fellow eyes of the patients with epiretinal membrane with the 20 control eyes of patients 50 to 59 years old. Pattern-reversal visual evoked potential latency was comparable, and there was no statistically significant difference between the groups ( $P = .1142$  for the 17' pattern size and  $P = .2186$  for the 10' pattern). However, the pattern-reversal visual evoked potential amplitude was significantly ( $P < .05$ ) lower in the fellow eyes.

The Figure shows the pattern-reversal visual evoked potential of the eye with epiretinal membrane (visual acuity, 20/20). N80 and P100 latencies of the pattern-reversal visual evoked potential response are considerably prolonged with respect to the fellow eye (Figure, bottom) (N80 latency, 99 vs 89 milliseconds in the fellow eyes; P100 latency, 125 vs 112 milliseconds in the fellow eyes). P100 amplitude of the eye with epiretinal membrane was reduced.

## DISCUSSION

EPIRETINAL MEMBRANES WITH INDICATIONS FOR SURGICAL removal are usually located in the premacular area. These membranes are likely to influence the pattern-reversal visual evoked potential, as this examination obtains its information almost exclusively

from the central 10 degrees of the visual field,<sup>11</sup> the area in which P100 latency and P100 amplitude are maximally influenced by pathologic disease or abnormalities.

The results show that N80 and P100 latencies are prolonged and that P100 amplitude is reduced in eyes with epiretinal membrane compared with the fellow eyes. This confirms the earlier findings of Mehta and associates.<sup>1</sup> Eyes with epiretinal membrane compared with control eyes, both groups in patients who were 50 to 59 years old, showed prolongation of P100 latency for the 17' check size and reduction of P100 amplitude for the 17' and 10' check sizes. The finding that only P100 latency showed a significant ( $P < .05$ ) prolongation in eyes with epiretinal membrane for the 10' check size probably resulted from the small numbers of eyes that could be compared.

The fellow eyes, when compared with the control eyes in a comparable age range (50 to 59 years old), showed a significant reduction of the P100 amplitude for the 17' and 10' check sizes, whereas no significant prolongation of the N80 and P100 latencies was found. This finding is remarkable but is comparable to the findings in an earlier study<sup>12</sup> in which the P100 amplitude of the fellow eyes of patients with unilateral macular hole was also reduced. The altered pattern-reversal visual evoked potential P100 amplitude in the fellow eyes of patients with unilateral epiretinal membrane may be an indication that, in these eyes, despite



Table 3. Comparison of Eyes With Epiretinal Membranes, Fellow Eyes, and Separate Control Group in 50-to-59-Year Age Range

Check Size	Parameter	Eyes With Epiretinal Membranes (Group 1)		Fellow Eyes (Group 2)		Control Eyes (Group 3)		P Value*	
		Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Group 1 vs 3	Group 2 vs 3
—	Visual acuity	0.19 (0.15)	12	0.98 (0.07)	9	0.99 (0.01)	20	.0001	.7232
17'	N80 latency (ms)	83.4 (7.2)	8	79.0 (3.6)	8	81.3 (2.8)	20	.5235	.1142
10'		90.7 (10.3)	9	81.8 (2.9)	8	83.3 (2.6)	20	.1026	.2186
17'	P100 latency (ms)	110.7 (10.0)	8	107.7 (18.8)	8	104.5 (3.7)	20	.1938	.1462
10'		116.3 (9.8)	9	106.0 (2.0)	8	107.9 (3.6)	20	.0264	.1687
17'	P100 amplitude ( $\mu$ V)	5.9 (5.0)	8	6.2 (3.0)	8	10.1 (4.0)	20	.0088	.0157
10'		5.2 (4.7)	9	6.3 (3.6)	8	9.8 (3.5)	20	.0020	.0168

\*Significance is achieved if  $P < .05$ .

the normal visual acuity and the absence of symptoms, a certain similar underlying process in an earlier stage may be present. In 21% of patients, bilateral epiretinal membrane will develop sooner or later.<sup>13</sup> Therefore, follow-up consultation would be advisable. A long-term follow-up study will be necessary to investigate whether the fellow eyes with abnormal amplitude develop an epiretinal membrane later.

A disadvantage of using small check sizes is the difficulty in obtaining a reliable pattern-reversal visual evoked potential response in subjects with reduced visual acuity. The 17' check size resulted in a recordable pattern-reversal visual evoked potential in 67% of the patients with epiretinal membrane. For the 10' and 7' check size, this percentage was 58% and 41%, respectively.

With the exception of the study of Mehta and associates<sup>1</sup> on a small number of patients, objective prognostic parameters have not been investigated. In the past, several indicators of postoperative good visual results after the surgical approach of epiretinal membrane peeling were suggested. Preoperative visual acuity of 20/100 or better would be favorable, as would be a short duration of symptoms before surgery.<sup>14</sup> Thin and transparent membranes,<sup>15</sup> which do not automatically implicate a certain content of cellularity or amount of collagen,<sup>16</sup> would gain better results. Also, the absence of posterior traction retinal detachment<sup>14</sup> would lead to better postoperative visual acuity. The absence of cystoid macular edema

preoperatively was described as favorable and as having no influence on final visual outcome.<sup>15,17</sup> Except for the latter, all of these factors have been described as favorable for obtaining good postoperative visual results with a reduction of metamorphopsia. However, some are subjective measurements, either by the patient or by the ophthalmologist. Search for objective parameters would be welcome. Pattern-reversal visual evoked potential recording is an objective method to investigate the functioning of the macula, provided no other ocular, neurologic, or vascular entities influence the pattern-reversal visual evoked potential. Even in an eye with an epiretinal membrane and normal visual acuity, pattern-reversal visual evoked potential can be abnormal, as shown in the Figure.

In eyes with epiretinal membrane, pattern-reversal visual evoked potential latency is prolonged and amplitude is reduced. Relationships between clinical parameters and pattern-reversal visual evoked potential parameters require further study. In a future study, with sufficient follow-up duration, in which preoperative pattern-reversal visual evoked potential recordings can be related to postoperative visual acuity improvement, reduction of metamorphopsia, and the surface of the area from which the epiretinal membrane has been removed, it can be investigated whether pattern-reversal visual evoked potential has prognostic value for postoperative visual acuity in a membrane peeling procedure. However, in a future



study with clinical aspects, it will be necessary to separately analyze results for primary and secondary membranes.

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# CORRESPONDENCE

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## Retinal Arterial Occlusions in Young Adults

EDITOR:

IN THE ARTICLE "RETINAL ARTERIAL OCCLUSIONS IN young adults," by C. M. Greven, M. M. Slusher, and R. G. Weaver (*Am J Ophthalmol* 120:776-83, December 1995), the authors discuss various associated factors leading to a hypercoagulable state or embolic condition in patients less than 40 years old with retinal arterial occlusions. However, hyperhomocysteinemia, a newly recognized risk factor for the occurrence of premature arterial occlusive disease, was not excluded in the patients. From a study published in *THE JOURNAL*, we concluded that hyperhomocysteinemia predisposes to the development of premature retinal artery and retinal vein occlusion.<sup>1</sup> It should be recognized that the prevalence of hyperhomocysteinemia is much higher than that of homocystinuria, which is another disorder associated with central retinal artery occlusions in young adults.<sup>2,3</sup>

JOHAN R. M. CRUYSSBERG, M.D.  
AUGUST F. DEUTMAN, M.D.  
*Nijmegen, The Netherlands*

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### AUTHOR REPLY

WE APPRECIATE THE COMMENTS OF DRS. CRUYSSBERG and Deutman. Their paper describing hyperhomocys-

teinemia as a treatable risk factor in young people with retinal vascular occlusions facilitates our understanding of these events. The patients in our series were treated before 1993 when their article appeared, and therefore our patients were not examined for hyperhomocysteinemia. However, in the future we will use the information they have provided in examining young patients with retinal vascular occlusive disease.

CRAIG M. GREVEN, M.D.  
M. MADISON SLUSHER, M.D.  
RICHARD G. WEAVER, M.D.  
*Winston-Salem, North Carolina*

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EDITOR:

IN THEIR VALUABLE RECENT ARTICLE, "RETINAL ARTERIAL occlusions in young adults", by C. M. Greven, M. Madison Slusher, and R. G. Weaver (*Am J Ophthalmol* 120:776-83, December 1995), the authors describe retinal artery occlusions in 27 eyes of 21 patients under 40 years of age. Cardiac valvular disease, present in four (19%) patients, was the most commonly recognized etiologic factor. Emboli were identified in seven (33%) patients, five of whom had cardiac or cerebrovascular sources. The authors note that their incidence of detectable emboli is higher than in previous studies.

The presence of visible emboli in retinal artery occlusions is important for many reasons. In older patients, although central retinal artery occlusion can occur in the setting of temporal arteritis and primary vasospasm, it more commonly results from emboli from atherosclerotic carotid arteries or diseased cardiac valves to the central retinal artery. Likewise, in Greven and associates and other studies of patients younger than 40 years, three of five patients with central retinal artery occlusion had visible emboli; one had an atrial myxoma and one had an internal carotid artery thrombus. Also, some studies have