Visual evoked cortical potential can be used to differentiate between uncorrected refractive error and macular disorders

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Abstract. The visual evoked cortical potential (VECP) is widely used to verify complaints of reduced visual performance and to identify the site of the disorder. In this study, we investigated the correlation between reduced visual acuity and VECP in volunteers with normal corrected visual acuity and in patients suffering from inherited macular degeneration or from age related macular degeneration (ARMD). Flash evoked VECP was not affected by the visual acuity in the cases of refractive error and in ARMD patients but was reduced in amplitude and delayed in implicit time in the patients suffering from inherited macular degeneration. The VECP elicited by pattern reversal checkerboard (PVECP) was not affected by the quality of the visual image in volunteers with uncorrected refractive error when checks of 60′ or larger were used but were considerably reduced in size and prolonged in implicit time for checks smaller than 15′. In both groups of patients suffering from macular dysfunction, pattern reversal VECP was very subnormal and was characterized by prolonged implicit time compared to values expected from their visual acuity. These findings indicate that the PVECP does not directly correlate with visual acuity but rather with foveal function. Therefore, we suggest that recordings of PVECP can be used to differentiate between refractive error and macular disorders as causing reduction in visual acuity when other clinical signs are missing or not available.

Key words: age related macular degeneration, refractive error, Stargardt's disease, visual evoked cortical potential, visual acuity

Introduction

The practicing ophthalmologist often encounters patients complaining of reduced visual acuity with no satisfying ophthalmologic explanation. These patients may be malingering seeking financial benefits or may be suffering from a functional disorder that can not be detected by routine clinical tests.

These patients are often referred to electrophysiological evaluation in order to verify their complaint, assess the degree of the disorder and try to localize the site of the defect along the visual system.

The visual evoked cortical potential (VECP) is recorded from the scalp and reflects the light-induced electrical activity in the primary visual cortex. The amplitude and temporal pattern of the VECP depend upon the mode of visual stimulation, the quality of the visual image formed on the retina and the functional integrity of the visual system [1–4]. VECPs elicited by pattern light stimuli are commonly used to assess visual acuity while the flash VECP is used to assess potential visual performance prior to surgery (dense cataract or vitreous hemorrhage), to test individuals with poor visual performance and to examine non-cooperating subjects (babies and retarded adults).

Reduction in visual acuity may be caused by a variety of disorders in every level of the visual system. Numerous studies have been conducted in order to correlate VECP parameters and known visual disorders including refractive error, macular degeneration, optic neuritis, multiple sclerosis, amblyopia and more. It is generally accepted that the flash VECP is not a good tool for assessing visual acuity while the pattern VECP is a sensitive test for determination of visual acuity. Differentiation between retinal and post-retinal disorders as underlying reduced visual acuity can be achieved with simultaneous recording of pattern ERG and VECP [5,6]. However, the use of the VECP alone in order to differentiate between different causes of reduced visual acuity is more complex.

This study was designed to test the hypothesis that the VECP is directly related to visual acuity and to assess its relationship to the cause of reduced visual acuity. In order to achieve this goal, we studied three groups of patients with confirmed cause of reduction in visual acuity. One group was composed of volunteers with normal or normal corrected visual acuity. In these subjects, visual acuity was reduced by either adding convex lens (in emmetropes) or by removing their optical corrections (in myopes). The other two groups consisted of patients suffering from different stages of age related macular degeneration (ARMD) or inherited macular degeneration. We found that the VECP elicited by pattern stimuli, composed of reversing checkerboard, depended upon foveal function and did not correlate directly with visual acuity. Thus, for a given visual acuity, the pattern reversal VECP was considerably better when a refractive error underlied reduced visual acuity than in macular disorders.

Materials and methods

Subjects

A total of 63 subjects participated in this study. They were divided into three groups: (1) Twenty nine volunteers with normal corrected visual acuity (6/6); 14 emmetropes and 15 myopes. Age range was 18–30 years old for 28 of them and one was over 60 years old. Uncorrected visual acuity in the myopic group ranged from 6/10 to finger counting from 1.5 m. (2) Twenty patients suffering from different stages of age related macular degeneration (ARMD). These patients were recruited for this study based on clinical examination and fluorescein angiography that indicated unequivocally the presence of ARMD. Age range was 59–83 years with an average of 73 years. Visual acuity ranged from 6/7 to finger counting in front of the eyes. Most of the patients had visual acuity of 6/90 or better in the good eye. Drusen of different patterns were seen in 18 eyes. The remaining eyes were divided into dry (N=16) and wet (N=6) ARMD. (3) Fourteen patients (8 males and 6 females) with confirmed (clinical examination and fluorescein angiography) Stargardt's disease. Age range was 9–46 years with an average of 32 years. Visual acuity ranged from 6/6p to 1/60. All the patients had visual acuity of 6/60 or better in the good eye.

The procedures of the experiments were explained in detail to all the participants and they all signed an informed consent.

Visual evoked cortical potential (VECP)

The VECP was recorded using the bipolar configuration. Two EEG cup electrodes were attached to the skull along the midline with conducting paste. The active electrode was placed about 2 cm above the inion while the reference electrode was placed about 4 cm higher. An ear-clip served for ground electrode.

The signals from the electrodes were amplified by a factor of 500,000 and filtered (1–100 Hz) by a differential amplifier (Grass, Quincy, MA, USA). In most cases a notch filter was needed to remove 50 Hz noise. The output of the amplifier was digitized at a rate of 500 Hz by a computer equipped with a data acquisition board (Scientific Solutions, Solon, Ohio, USA). Fifty responses were averaged on-line by the computer and stored in the hard disk for off-line analysis.

Two types of visual stimuli were presented to the subjects. Flashes were obtained from a PS22 photostimulator (Grass, Quincy, MA, USA) at a rate of 1.1 Hz. The intensity of the light stimuli was controlled by the instrument settings (I_1−I_{16}). Pattern reversal stimuli were obtained from a computer con-

trolled system that was built locally. High contrast black/white check patterns that reversed at a rate of 1.88 Hz were used. The visual angle subtended by the pattern field was 5° vertical and 7° horizontal. Check sizes used were 7.5, 15, 30, 45, 60, 90 and 120 min of arc.

Procedure

Each subject was tested for visual acuity using a Snellen chart. In the volunteers, belonging to the refractive error group, VECPs were recorded while stimulating the dominant eye. Myopic subjects were tested with and without their correcting glasses. Emmetropic subjects were tested before and after adding convex lens (positive diopter) in order to reach a visual acuity of 6/24–6/36. Flash and pattern reversal VECPs were recorded during sharp and blurred visual image. The sequence of recording differed between the subjects. In some, recording was first done with sharp image using all the different check sizes and flash intensities, then the series was repeated with blur image. In others, the VECP was recorded for each stimulus configuration, once with sharp and once with blur image. In the patients suffering from Stargardt's disease or ARMD, each eye served for VECP recording since in most of them the reduction in visual acuity differed between the two eyes.

Results

Uncorrected refractive error

Figure 1 shows representative VECPs of one myopic subject using pattern reversal checkerboard of different check size. The responses were elicited during sharp (with optical correction) or blurred (without optical correction) vision (upper and lower rows respectively). This myopic subject had a correction of -3 diopters and had a visual acuity of 6/6 with glasses in both eyes and 6/60 in the right eye, 5/60 in the left eye without optical correction. The pattern reversal VECP depended upon the size of the checks used for stimulation and the quality of the visual image. The responses elicited by medium and large checks (30′ and 60′) are similar for sharp and blurred visual image while, with small checks (15′ and 7.5′) blurring the image caused prolongation of the response and reduction in its amplitude. In order to quantify these observations, we measured the implicit time and amplitude of P_{100} (arrows).

The dependencies of the implicit time and the amplitude of the pattern reversal VECP upon check size for sharp and blurred vision (filled and open circles respectively) are shown in Figure 2A and B, respectively. These data were measured from the PVECPs of the subject whose responses are shown in
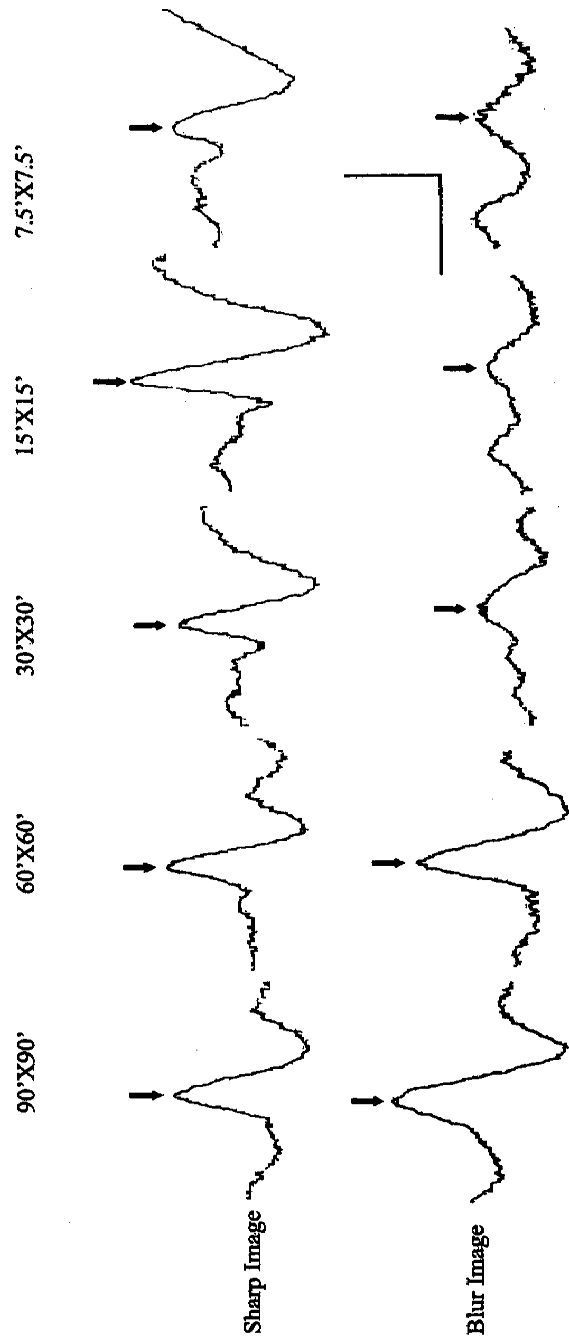
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Figure 1. Visual evoked cortical potentials in a myopic subject elicited by pattern reversal stimuli of different check size. The responses were recorded with (first row) and without (second row) optical correction. In the eye tested in this subject, corrected visual acuity was 6/6 and uncorrected visual acuity was 6/60. The positive wave used for PVECP analysis (P_{100}) is marked in each response by an arrow. Positivity is upward. Calibration bars: vertical 5 μV, horizontal 100 ms.
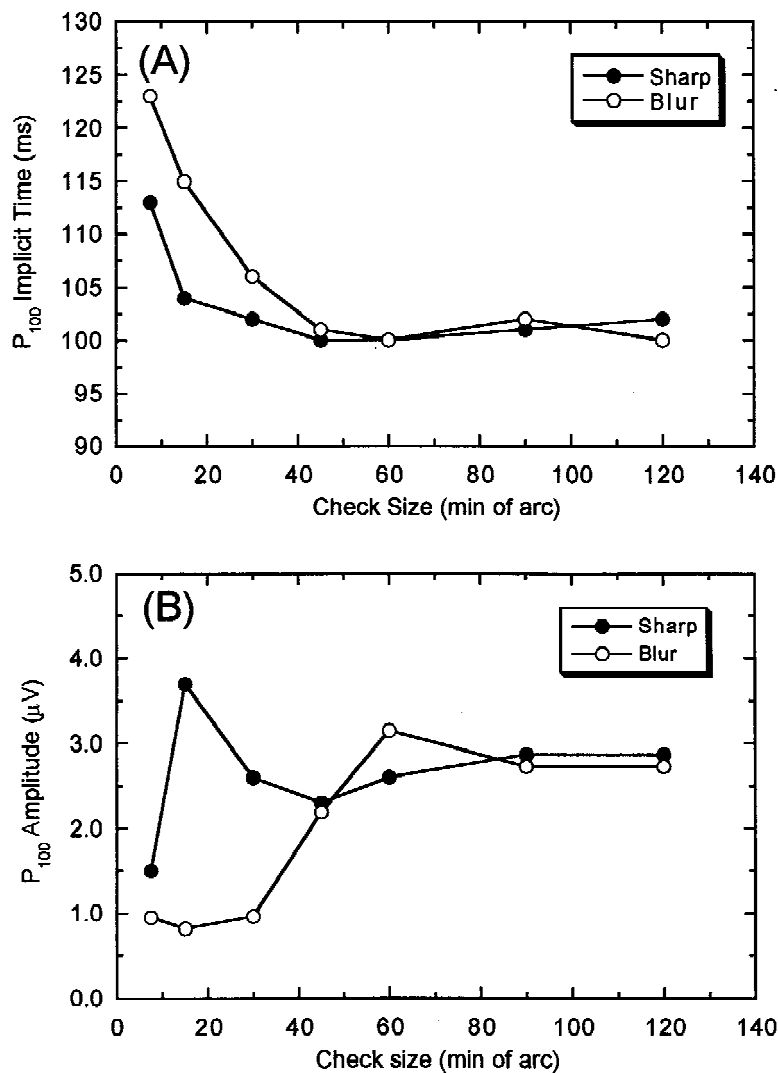
Figure 2. The effects of check size on the implicit time (A) and the amplitude (B) of the PVECP in the myopic subject whose responses are shown in Figure 1. Data are compared between sharp image (using optical correction) and blurred image (without optical correction) (filled and open circles respectively).

Figure 1. The implicit time of P_{100} tended to decrease as the check size was reduced from 120′ until a minimum value was reached for 45′. This effect was independent of the quality of the visual image as can be appreciated by comparing data obtained with and without the subject's optical correction. Further reduction in check size caused a gradual increase in the implicit time

Table 1. Mean (S.D.) implicit times and amplitudes of flash VECP and pattern reversal VECP in myopic and emmetropic subjects tested with sharp and blur visual image

| | Myopic Group (N=15) | | | | Emmetropic Group (N=14) | | | |
| | Sharp Vision | | Blur Vision | | Sharp Vision | | Blur Vision | |
	Implicit time (ms)	Ampl. (μV)	Implicit time (ms)	Ampl. (μV)	Implicit time (ms)	Ampl. (μV)	Implicit time (ms)	Ampl. (μV)
FVEP I2	105.0	7.20	107.0	8.20	100.0	7.90	102.0	8.30
	(11.5)	(3.47)	(12.3)	(3.74)	(13.1)	(2.99)	(11.3)	(3.62)
FVEP I16	100.0	6.40	99.0	7.00	98.0	7.60	99.0	6.50
	(15.6)	(3.14)	(11.1)	(3.96)	(12.3)	(2.57)	(12.9)	(3.06)
PVEP 120'	109.6	4.42	110.3	4.52	110.4	6.88#	110.0	6.52#
	(6.9)	(1.42)	(9.2)	(2.34)	(5.4)	(2.00)	(7.2)	(1.50)
PVEP 90'	107.2	5.12	109.8*	5.33	107.2	6.52	108.3*	6.24
	(5.35)	(2.11)	(5.1)	(1.77)	(5.35)	(2.62)	(7.0)	(1.82)
PVEP 60'	107.5	5.00	108.2	5.62	107.6	6.47	108.1	6.21
	(4.0)	(2.36)	(4.93)	(2.32)	(4.3)	(1.77)	(5.9)	(2.26)
PVEP 45'	107.1	5.56	109.8**	5.45	107.8	6.93	107.2	6.18
	(2.90)	(2.57)	(4.04)	(2.39)	(4.8)	(1.40)	(5.6)	(1.99)
PVEP 30"	105.8	5.20	113.1**	3.95**	105.2	6.49	108.4*	6.21#
	(3.16)	(1.89)	(6.45)	(1.86)	(2.0)	(2.29)	(5.2)	(2.23)
PVEP 15|'	108.0	5.88	119.0**	5.19	107.0	6.70	115.4**	5.31
	(4.2)	(1.80)	(9.0)	(2.63)	(4.87)	(3.02)	(4.2)	(2.48)
PVEP 7.5'	117.5	6.18	127.0**	3.52**	114.5	6.62	125.3**	3.74*
	(5.29)	(2.84)	(12.3)	(2.91)	(4.3)	(2.63)	(7.9)	(1.59)

Significant differences between VECP parameter measured with blur image compared to sharp image within each group of subjects using pairted *t*-test; *$p<0.05$, **$p<0.01$.
Significant differences between VECP parameter measured in emmetropic group compared to myopic group using Student *t*-test; #$p<0.05$.

which was considerably more apparent for blurred visual image compared to sharp visual image (Figure 2A).

The amplitude of the PVECP also exhibited a strong dependency upon the quality of the visual image only for small check size (Figure 2B). Reducing the check size from 120' to 60' was expressed in a gradual increase in the amplitude of P_{100} that was similar for sharp and blurred vision. Further reduction in check size caused the PVECP, recorded with sharp image, to increase in amplitude to a maximum at 15' and then to decrease. When the visual image was blurred by removing the subject's optical correction, the amplitude of P_{100} decreased significantly for checks smaller than 30'.

Similar findings to those presented in Figures 1 and 2 were obtained from all 29 volunteers who participated in this study. The average ($\pm$S.D.) values of implicit times and amplitudes are given in Table 1 for both groups of patients; myopic and emmetropic, for each condition of stimulation (flash and pattern reversal). Sharp image represents data obtained from emmetropes without correction and myopes with their own optical corrections. Blurred image includes data obtained from emmetropes with convex lens and myopes without their optical corrections. No significant differences were found between the myopic and emmetropic groups, using a Student t-test, for either implicit time or amplitude of the flash VECP regardless of the quality of the visual image. No statistically significant differences were found between myopes and emmetropes (Student t-test) for the implicit time of the pattern reversal VECP for any check size. The amplitudes of P_{100} were generally larger in the emmetropic group then in the myopic group. However, these differences were statistically significant only for check size of 120' (both sharp and blur image) and for check size of 30' (blur image). Since these differences between the myopic and emmetropic groups are not consistent and represent the minority of the tests used, we grouped all the VECP data (flash and pattern reversal) of all 29 subjects together into two categories according to the quality of the visual image.

The relationships between implicit time and amplitude of the pattern reversal VECP and check size is shown in Figure 3A and B, respectively, for sharp and blurred visual image (filled and open circles respectively). Each data point denotes mean ($\pm$S.D.) for the entire group (N=29). For clarity of the figure, only one portion of the standard deviation is shown. When the check size was reduced from 120' to 45' the implicit time of the pattern reversal VECP slightly reduced regardless of the quality of visual image. Further reductions in the check size caused prolongation of the implicit time that was considerably more pronounced with blurred image compared to sharp one. The differences between blurred and sharp image were tested for statistical significance using a paired t-test. No differences were found for medium and large checks ($>$45') while significant differences were found for small checks as indicated in Figure 3A (**p<0.01). The implicit times of the pattern reversal VECPs were also tested for differences within each group of subjects (Table 1). In the myopic group significant differences (p<0.01) between sharp and blurred image were found for check size of 45' or smaller. In the emmetropic group differences at this level of significance were found only for small checks (15' and 7.5') and a smaller degree of difference (p<0.05) when checks of 30' were used. With large checks (60' and larger) no significant differences were found between sharp and blur image in either of the groups.
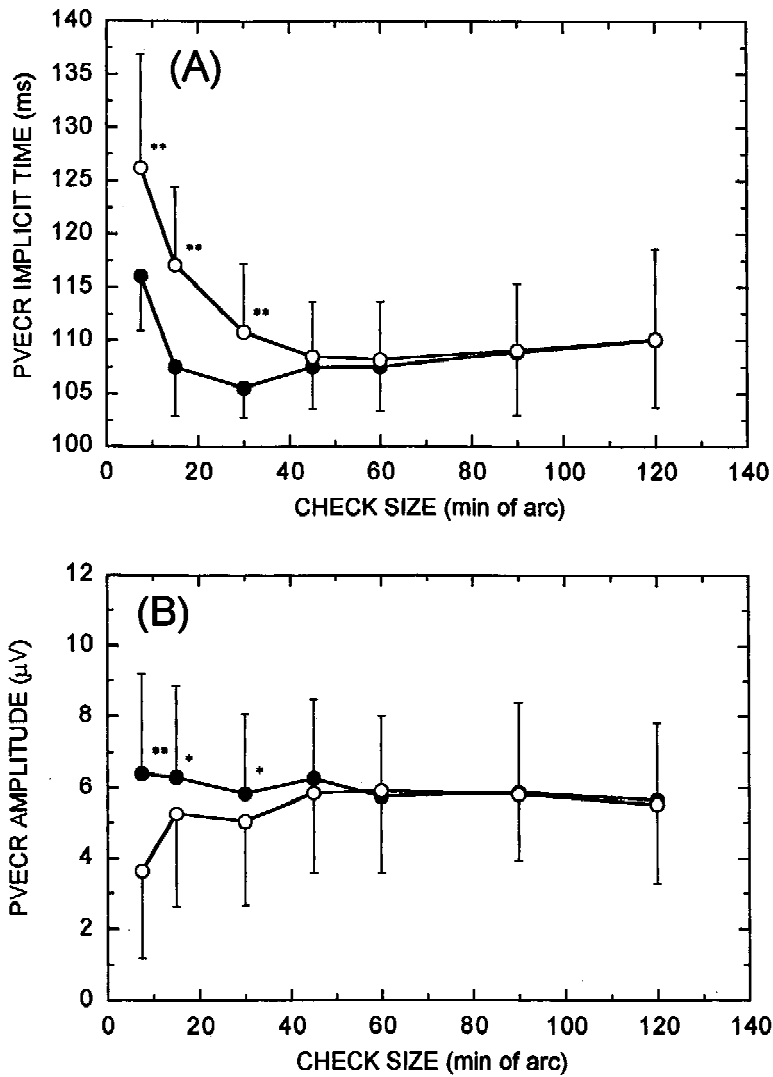
Figure 3. Average (±S.D.) implicit time (A) and amplitude (B) of P_{100} in the pattern reversal VECP of all the subjects in the group of uncorrected refractive error ($N=29$). The VECPs were elicited with pattern reversal stimuli of different check sizes with sharp or blurred image (filled and open circles respectively). For clarity of the figure, only one part of the standard deviation is plotted. Statistically significant differences are marked by one ($p<0.05$) or two ($p<0.01$) asterisks.

The mean ($\pm$S.D.) amplitudes of P_{100} are plotted in Figure 3B as a function of check size for all subjects tested during sharp and blurred image (filled and open circles respectively). The amplitude measured with sharp image slightly increased when the checks size was reduced from 120′ to 7.5′. The PVECP recorded with blurred image exhibited similar dependency upon checks size in the range 120′ down to 45′. Further reduction in checks' size caused reduction in the PVECP amplitude. The differences between sharp and blurred visual image were highly significant ($p<0.01$) for the smallest checks (7.5′) and less significant for checks of 15′ and 30′ ($p<0.05$). When the amplitudes of the P_{100} wave were tested within each group of subjects between blurred and sharp image, a highly significant difference was found in both groups only for the smallest (7.5′) check size (Table 1).

Macular disorders (ARMD and Stargardt's disease)

Two groups of patients with clinically confirmed macular disorders were tested in this study. One group consisted of patients suffering from different degrees of age related macular degeneration (ARMD). The second group consisted of patients suffering from inherited macular degeneration (Stargardt's disease).

Figure 4 shows representative VECPs from one ARMD patient. This patient suffered from drusen in the left eye with relatively good visual acuity (6/9) and from the wet form of ARMD in the right eye with poor visual acuity (finger counting from 1 m). The flash VECP is of similar pattern in both eyes though the response elicited by stimulating the good eye appears to be of larger amplitude. The pattern reversal VECPs are very subnormal in the more diseased eye (upper row). In this eye, a PVECP of normal pattern could not be obtained even with checks of 90′ in visual angle. In the good eye, reliable PVECPs were obtained even when the check size was reduced to 15′ however, they were characterized by prolonged implicit times. VECPs, similar to those shown in Figure 4, were observed in all other ARMD patients that were studied here.

Figure 5 shows VECPs of two patients with Stargardt's disease, the first one with early stage of the disease (left part of Figure 5) and the other suffering from an advanced stage (right part of Figure 5). The flash-evoked VECPs that were elicited by stimuli of moderate intensity (Figure 5A) and the pattern reversal VECP that were elicited by check size of 60′ (Figure 5B) are compared. In both patients, the degree of the disease differed between the two eyes as expressed by the different visual acuity noted to the right of each response. The patient suffering from an early stage of the disease is characterized by FVECP of normal amplitude but prolonged implicit time. The second patient
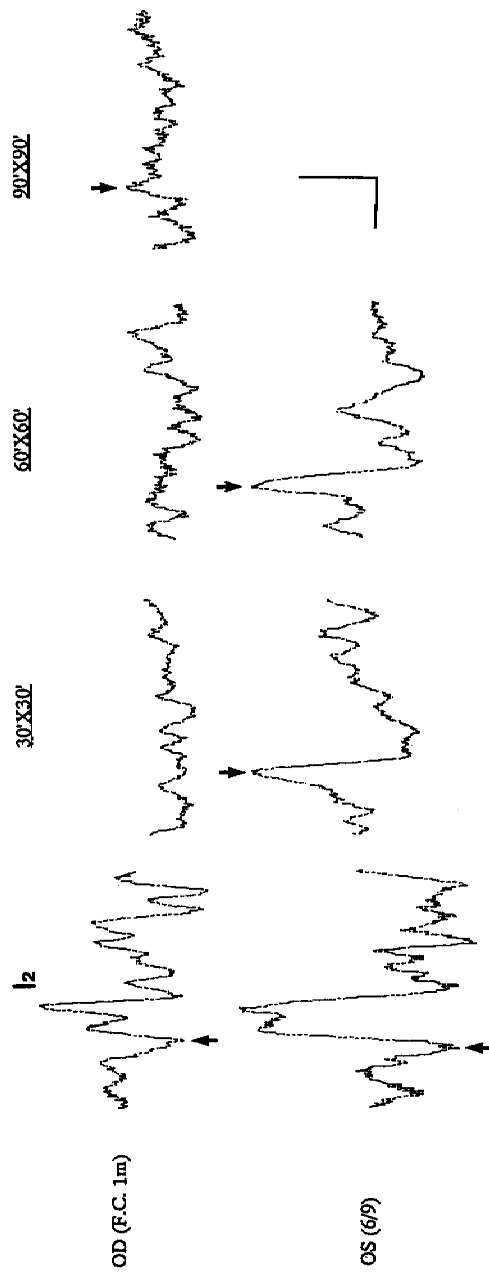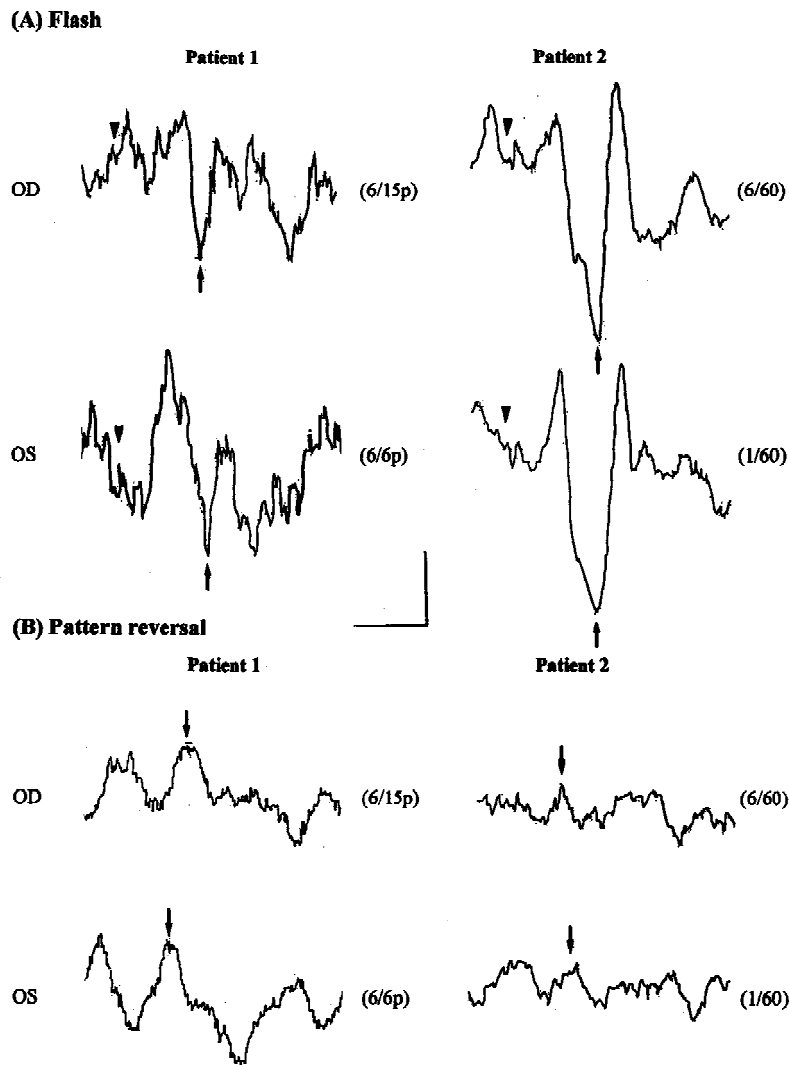
Figure 4. Pattern reversal VECPs and flash VECPs of one ARMD patient. The responses were recorded by stimulating each eye separately. The visual acuity of each eye is denoted to the left of each row of responses. P_{100} in the PVECP and N_1 in the FVECP are marked by arrows. Positivity is upwards. Calibration bars: vertical 5 μV, horizontal 100 ms.

(A) Flash

Patient 1   **Patient 2**

OD   (6/15p)   (6/60)

OS   (6/6p)   (1/60)

(B) Pattern reversal

Patient 1   **Patient 2**

OD   (6/15p)   (6/60)

OS   (6/6p)   (1/60)

Figure 5. Flash evoked VECPs (A) and pattern reversal VECPs (B) of two patients suffering from Stargardt's disease. The visual acuity of each eye is denoted to the right of the traces. The flash VECPs were elicited with intensity I_2 of the photostimulator and the pattern VECP by stimuli composed of 60$'$ check size. P_{100} in the PVECP and N_1 in the FVECP are marked by arrows. An arrowhead denotes flash timing in the FVECPs. Positivity is upwards. Calibration bars: vertical 5 μV, horizontal 100 ms.

is characterized by FVECPs of normal amplitude but abnormal pattern as indicated by the prolonged implicit time and the wide negative wave.

The pattern reversal VECPs of these patients, elicited by check of 60′ are compared in Figure 5B. In the patient with the mild form of the disease, the PVECPs are of normal pattern but the implicit time is significantly prolonged even in the eye with normal visual acuity (OD). In the patient with advanced stage of the disease, the PVECPs are very abnormal and only a small P_{100} can be identified at a very prolonged implicit time. The VECPs of all 14 patients suffering from Stargardt's disease that were studied here, were qualitatively similar to those shown in Figure 5.

Comparing refractive error and macular disorders

In order to assess the correlation between the VECP and reduced visual acuity resulting from different etiologies, the flash VECPs and the pattern reversal VECPs of a myopic subject (63 years old), an ARMD patient of similar age and a patient with Stargardt's disease are compared in Figures 6 and 7 respectively. All three patients had similar uncorrected visual acuity – 6/36. The flash VECPs of the subject with uncorrected refractive error are of normal amplitudes and implicit times. Those from the ARMD patient are also of normal patterns and amplitudes while, the FVECPs recorded from the patient with Stargardt's disease are of small amplitudes and abnormal temporal properties.

Pattern reversal VECPs of the same three subjects are compared in Figure 7. The responses that were recorded from the myopic subject with no optical corrections were normal as long as the stimuli consisted of checks larger than 30′. Only the VECPs elicited by stimuli of small checks (15′ and 7.5′) were of subnormal amplitudes and delayed implicit times. In the ARMD (2nd row) and the Stargardt's (3rd row) patients, the VECPs elicited by pattern reversal stimuli were subnormal and delayed regardless of check size.

Findings, similar to those illustrated in Figures 6 and 7, were obtained from all the patients that were suffering from uncorrected refractive error or from macular malfunction. Figure 8 shows the dependency of implicit time (A) and amplitude (B) of the flash VECPs upon visual acuity for uncorrected myopia (filled circles) and for patients with macular degeneration (ARMD, open squares; Stargardt's disease, open triangles). The normal range denoted by the two dashed horizontal lines was calculated from measurements in 10 volunteers with normal visual acuity of the same age group as the ARMD patients (50–70 years). Most of the myopic subjects were characterized by flash VECPs of normal implicit times (Figure 8A) and normal amplitudes (Figure 8B). The ARMD patients also exhibited FVECPs of normal implicit times and normal amplitudes. In fact, some of the ARMD patients were

I2 **I16**

Refractive error

ARMD

Stargardt's disease
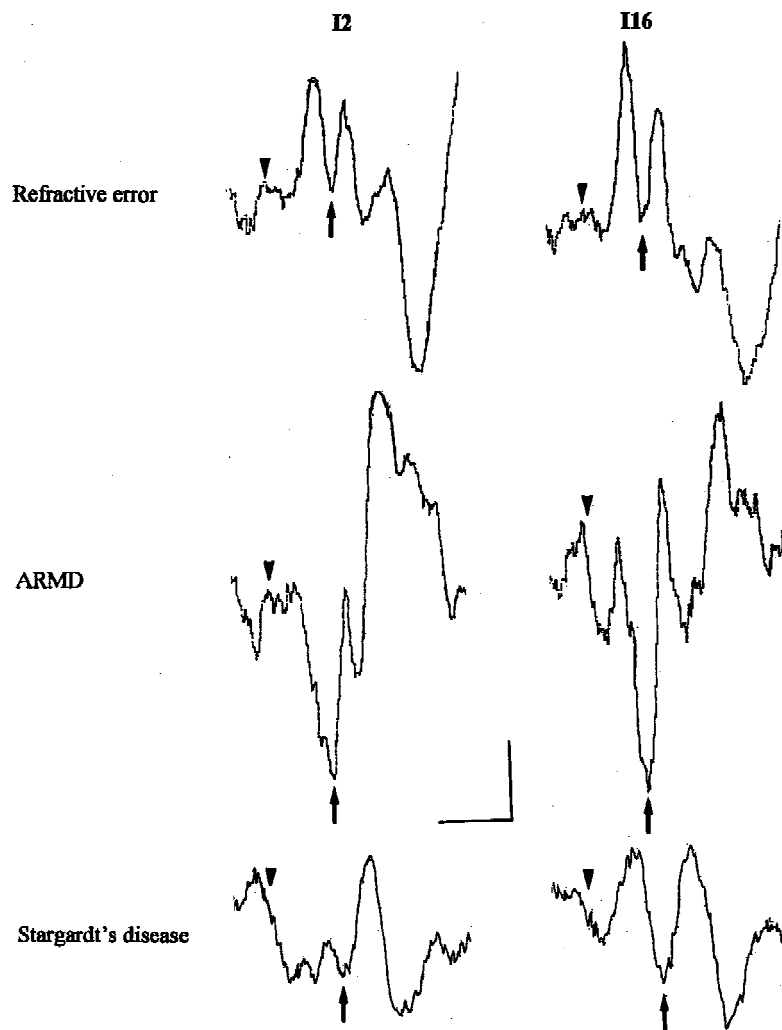
Figure 6. Comparison of flash VECPs elicited by two intensities between a myopic subject that was tested without optical correction (1st row), an ARMD patient (2nd row) and a patient suffering from Stargardt's disease (3rd row). All three subjects were characterized by similar visual acuity (6/36). Flash presentation is marked by an arrowhead. The first negative (N_1) in the FVECP is marked by an arrow. Positivity is upwards. Calibration bars: vertical 5 μV, horizontal 100 ms.
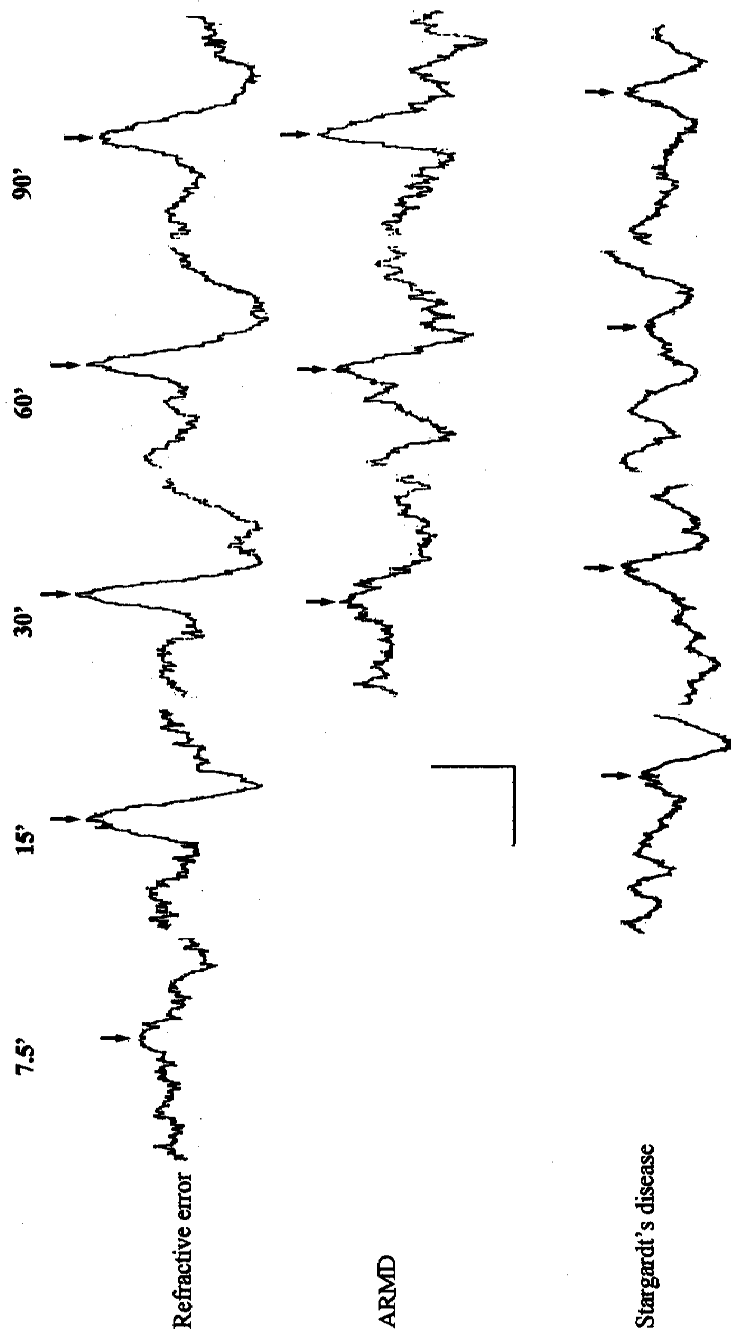
Figure 7. Comparison of pattern VECPs elicited by stimuli composed of checks of different sizes between a myopic subject that was tested without optical correction (1st row), an ARMD patient (2nd row) and a patient suffering from Stargardt's disease (3rd row). All three subjects were characterized by similar visual acuity (6/36). Arrows mark P_{100} in the PVECPs. Positivity is upwards. Calibration bars: vertical 5 μV, horizontal 100 ms.
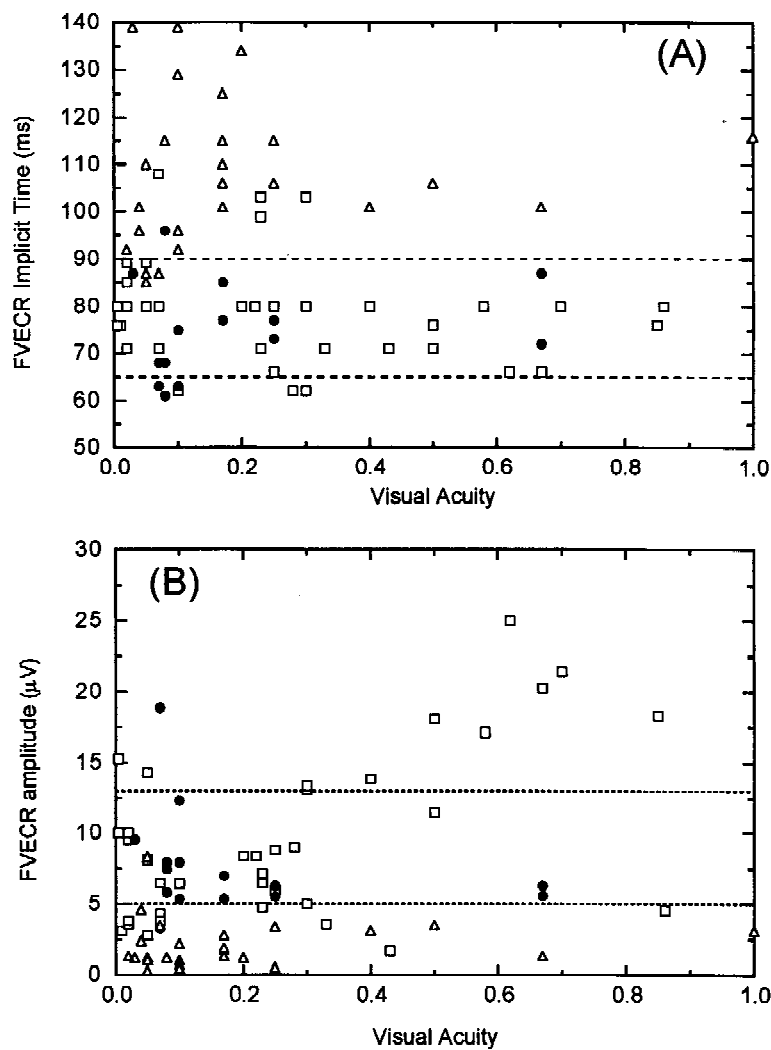
Figure 8. The relationship between flash VECP and visual acuity in uncorrected myopic sub-
jects (filled circles), ARMD patients (open squares) and in patients suffering from Stargardt's
disease (open triangles). Implicit time (A) and amplitude (B) of the first negative wave (N_1)
are compared to visual acuity. The two horizontal dashed lines represent the normal range as
determined for 10 subjects (50–70 years old) with normal (6/6) visual acuity.

characterized by responses of supernormal amplitudes. In contrast, the pa-
tients with Stargardt's disease were characterized by FVECPs of subnormal
amplitude and prolonged implicit time. These effects were more apparent as
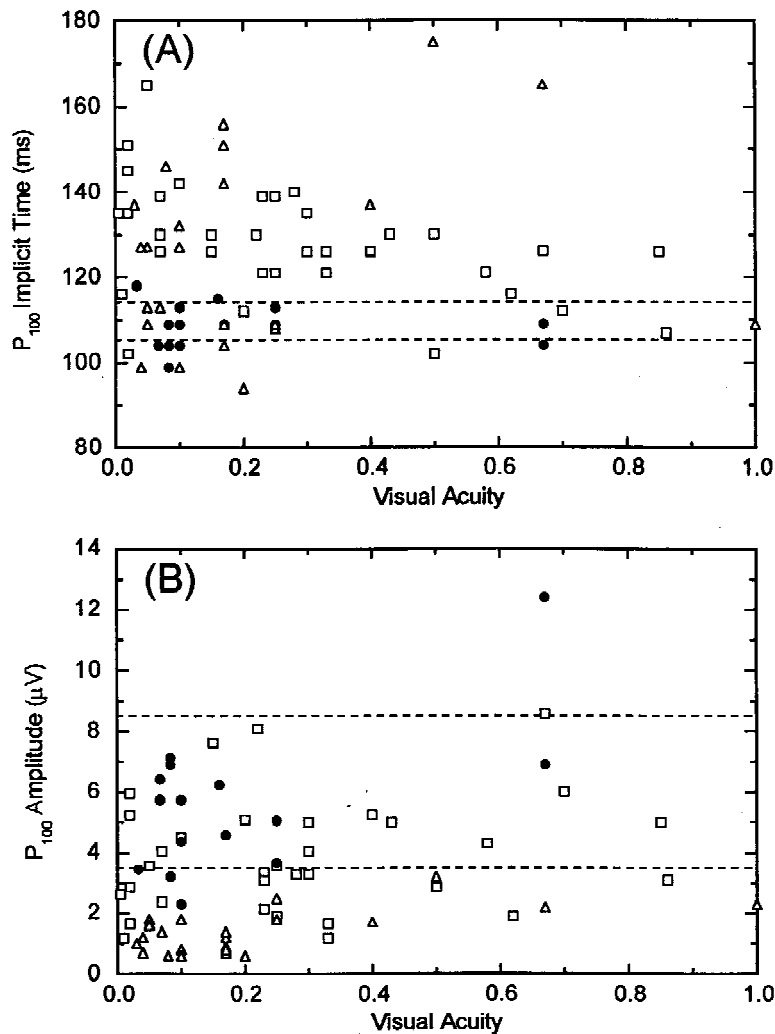visual acuity was reduced.

Figure 9. The relationship between pattern reversal VECP elicited by check size of $60'$ and visual acuity in uncorrected myopic subjects (filled circles), ARMD patients (open squares) and in patients suffering from Stargardt's disease (open triangles). Implicit time (A) and amplitude (B) of P_{100} are compared to visual acuity. The two horizontal dashed lines represent the normal range as determined for 10 subjects (50–70 years old) with normal (6/6) visual acuity.

In order to examine the relationship between pattern reversal VECP and visual acuity, we chose the responses elicited by check size of $60'$. This check size was chosen because it was the smallest one that could be used to elicit measurable responses in most of our patients with macular disorders (age related or inherited) and was found to be unaffected by visual blur due to

Table 2. Average (±S.D.) VECP parameters and visual acuity of three groups of patients suffering from reduced visual acuity

	Myopia (without corrections)	ARMD	Stargardt's disease
FVECP (I_2) implicit time (ms)	74.3±10.6	78.4±11.2	107.6±15.2
FVECP (I_2) Amplitude (μV)	7.62±3.75	9.46±5.95	2.18±1.63
PVECP (60′) Implicit time (ms)	108.2±5.1	127.9±13.1	125.6±22.5
PVECP (60′) Amplitude (4μV)	5.61±2.41	3.95±1.95	1.41±0.69
Visual acuity	0.192±0.200	0.262±0.239	0.188±0.217

refractive error (Figures 2 and 3). In Figure 9, the implicit time (A) and the amplitude (B) of P_{100} are compared to visual acuity for uncorrected myopia (filled circles) and for macular degeneration patients (ARMD, open squares; Stargardt's disease, open triangles). The implicit times of the myopic subjects are in some cases shorter than the normal range (filled circles in A). This probably reflects the prolongation of the P_{100} with age as has been demonstrated by previous reports [7–10]. The age range of the myopic group was 18–30 years while the normal range in Figure 9 was constructed for age group 50–70 years. The amplitudes of the PVECPs are within the normal range for most myopic subjects who were tested without their glasses regardless of visual acuity (filled circles in Figure 9B). The parameters of the VECPs measured in patients with macular degeneration (ARMD and Stargardt's disease) are abnormal in most cases even in patients with relatively good visual acuity. The implicit times are prolonged and the amplitudes are subnormal (open symbols in Figure 9).

In order to obtain a semi-quantitative comparison between the three groups of subjects studied here, the visual acuity and VECP parameters were averaged and are summarized in Table 2. We did not perform any statistical tests in order to compare the different groups since they were of different sizes, not homogenous and in neither we could obtain a complete set of parameters

from all the patients. However, it is quite clear that visual acuity was similarly reduced in all three groups with the ARMD group having on the average the best acuity. The FVECPs are similar in the myopic subjects and the ARMD patients but subnormal and delayed in the patients suffering from Stargardt's disease. The PVECPs elicited by checks of 60′ are of prolonged implicit times and of smaller amplitudes in the two groups of patients suffering from macular disorders compared to the myopic subjects.

Discussion

In this study, we investigated the VECP in three groups of patients with different underlying causes for reduction in visual acuity. The flash VECP was found to be independent of visual acuity in the subjects with uncorrected refractive error (Figure 8). This observation is expected since the flash VECP reflects mainly the integrity of the cone photoreceptors in the macular region, the conduction of the optical pathways and the functional integrity of the primary visual cortex. These are normal in myopic subjects. In the ARMD patients with confirmed macular malfunction, the flash VECP was within the normal range and in some patients, responses of supernormal amplitudes were recorded. In contrast, patients suffering from inherited macular degeneration, especially those with advanced stage of the disorder, were characterized by FVECPs of subnormal amplitudes and delayed implicit times (Figure 8). The difference between the two groups of macular dysfunction probably reflects the source of the disorder. In ARMD, macular function is normal and starts to deteriorate around the 5th–6th-decades of life. Therefore, the functional integrity of foveal cones is probably compromised leading to reduced visual acuity but the photoreceptors (cones and rods) in more peripheral retinal regions that contribute to the FVECP may retain normal function leading to normal FVECPs. In contrast, patients with Stargardt's disease suffer from inherited disorder that is expressed in malfunction of cones in areas larger than the fovea itself and therefore, the FVECP is also affected by the disorder.

We therefore, support previous reports [10–12] and conclude that the flash VECP is not a good test for visual acuity. In fact, in most maculopathies, acquired or inherited, the flash VECP is relatively normal in the early stages of the disease and becomes abnormal only in advanced stages [13]. This can be accounted for by the size of the stimulus and the region contributing to the FVECP. With large stimuli, contributions from non-diseased areas result in a FVECP of normal amplitude and pattern. One exception has been reported in a recent study on Cone–Rod Dysfunction [14]. However, in these cases the disorder was not restricted to the foveal area, but rather was expressed as diffuse loss of cone and rod function. It is possible that with small field

stimulation, restricted to the foveal region, the FVEP can become a better indicator for macular disorders [15].

In subjects with normal functioning visual system, the VECP elicited by a pattern stimulus is strongly dependent upon the size of the checks used to elicit it and upon the quality of the visual image formed on the retina (Figure 3). When the visual image is sharp, the implicit time is minimal and the amplitude is maximal for check size around 15′. Reduction of the check size to 7.5′ causes a slight prolongation of the implicit time and a slight reduction in amplitude. Similar observations have been reported before in numerous studies [1–4]. When the visual image is blurred due to a refractive error, the PVECP is of normal amplitude and implicit time when stimuli composed of medium to large checks (larger than about 45′) are used. However, with small checks (<15′), the implicit time is significantly prolonged and the amplitude is significantly reduced in size (Figure 3). These observations are similar, to those reported before [10,16–18]. In other studies, a gradual decrease in the amplitude of the PVECP was found as the major effect of blurring the image while no effect on implicit time was discussed [12,19].

The PVECPs were severely affected in cases of macular malfunction even when relatively large checks were used. In most cases of ARMD and Stargardt's disease that were tested here, the PVECP was considerably delayed and of subnormal amplitude even in eyes suffering from a mild form of the disorder that was expressed in only a slight reduction in visual acuity (Figure 9). Previous reports on VECP measurements in patients with different types of maculopathy also found that the PVECP was delayed and of subnormal amplitude even in eyes with normal or near normal visual acuity [13,20,21].

Comparing the PVECP to visual acuity in the three groups of subjects, each suffering from a different visual disorder, indicates that the VECP reflects the reduction in visual acuity but also depends upon the pathological mechanism causing it. For a given visual acuity, the PVECP elicited by checks of medium size (60′) is considerably more affected in ARMD and Stargardt's disease than in uncorrected refractive error. For checks of small size (30′ and 15′), the PVECP was non-recordable in most patients suffering from macular disorder and was only slightly affected in uncorrected refractive error (Figure 9). Similar conclusions were reported before for pattern VECP [19] and also when small field (2.5°) flash stimuli were used to elicit the VECP [15]. These observations indicate that the pattern reversal VECP can not be regarded as a test for visual acuity. It is more an indicator for foveal function than for visual acuity.

The data presented here and elsewhere, indicate that the VECP can be used to differentiate between uncorrected refractive error and a macular disease as causing a reduction in visual acuity. Pattern stimuli consisting of medium to

large checks (60′–90′) should be first used to elicit VECPs. If these responses are of normal amplitudes and normal implicit times, the check size should be reduced to 15′ and 7.5′. With these checks, PVECP of normal amplitude and slightly prolonged implicit time (only with 7.5′) indicates relatively good visual acuity. In contrast, a PVECP of subnormal amplitude and substantial prolongation of the implicit time is more consistent with an uncorrected refractive error. If the PVECPs recorded with medium to large checks (60′–90′) are of small amplitudes and prolonged implicit times and are considerably abnormal compared to the visual acuity, a macular disease should be considered. Such a procedure can be helpful when testing patients complaining of reduction in visual acuity but forget to bring their own prescription glasses or claim that their glasses do not improve visual performance.

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