VEP Test of the Blue-Sensitive Pathway in Glaucoma

Matthias Korth,* Nhung X. Nguyen,* Anselm Jünemann,* Peter Martus,† and Jost B. Jonas*

Purpose. The blue-sensitive pathway in normal subjects and in patients with primary open-angle glaucoma (POAG) was tested with the pattern visual evoked potential (VEP) method under selective adaptation.

Methods. Recording of pattern-onset VEP in response to blue (460-nm) stripes (0.88 c/deg) presented either without or with a bright yellow (570-nm) adaptation light (Maxwellian view, 33° diameter). Amplitude and peak times were evaluated, and the mean tritan score of the Farnsworth 100-hue test was determined. Age-matched normal subjects (n = 34) and (n = 32) patients with POAG were examined.

Results. The amplitude and peak time of the VEP without selective adaptation did not discriminate normal subjects from the POAG group. With selective adaptation, the amplitude was reduced (P = 0.002) and its peak time delayed (P < 0.0001) in POAG, yielding a sensitivity of 75% and a specificity of 94%. The VEP measures only under selective adaptation correlated significantly in patients with POAG with the mean perimetric defect, with the optic disc damage, and with the 100-hue test.


As is well known, glaucoma and ocular hypertension (OHT) can typically be associated with blue-color vision disturbances.1,2 Sensitive tests for detecting tritanomal vision in glaucomatous diseases are the Pickford-Nicolson anomaloscope, the Farnsworth 100-hue test (total error score),3-5 and the desaturated panel D-15 test.6,7 Tritanomal vision seems to correlate with visual field losses4,6-10 and has been found to predict field defects in patients with OHT.4,11 The latter conclusion has been challenged12 because several factors producing increased error scores were not taken into account. By controlling for age, lens density, pupil size, refraction, visual acuity, and medication it has been suggested12 that color-vision disturbances in glaucoma (100-hue test) are primarily the result of increased intraocular pressure. In agreement with this a temporary disturbance of yellow–blue discrimination in the 100-hue test could be evoked13 in normal subjects when the intraocular pressure was artificially raised.

Furthermore, correlations of blue-color vision disturbances (100-hue test, Pickford-Nicolson anomaloscope) with structural optic disc damages9,14 or with diffuse nerve fiber layer defects10,15,16 have been demonstrated. On the other hand, a missing correlation has been described also.5

More recent investigations into color-vision disturbances in glaucoma use colored luminance-increment stimuli or color-contrast stimuli. Increment threshold examinations can be carried out with suppression of the medium- and long-wavelength-sensitive receptors by an intensive yellow background light (selective or chromatic adaptation), which increases the relative sensitivity of the short-wavelength-sensitive cones, or by a white background, revealing the sensitivity of all three color mechanisms. Foveal colored increment stimuli showed that the sensitivity was reduced in the blue both in patients with glaucoma and in those thought to have glaucoma5 and that the patients with high-tension glaucoma had higher thresholds in the blue than did those with low-tension glaucoma.17 Blue test stimuli have been used also in a con-
ventional static projection perimeter, however with no avail.18 With blue perimetric stimuli on a yellow background light, it can be shown that this method is more sensitive in detecting incipient glaucoma, discloses field defects not present with conventional perimetric testing in patients with OHT, and exaggerates field losses in patients with glaucoma.19-24

Recently, a true color perimetry free of conventional luminance increments was introduced.25,26 By presenting blue targets on a television screen embedded in an equiluminant white surround field, defects were described in glaucoma that were of greater extent than in conventional perimetry.25 Finally, color-contrast sensitivity tests using a color-television monitor indicated reduced sensitivity in OHT and glaucoma especially along the tritan color confusion line.19-29

Visual evoked potentials (VEP) have been studied in glaucoma both with patterned and unpatterned stimuli and amplitude reductions as well as peak time delays have been described,30-43 but in general, prolongations in peak time seem to occur more frequently. Earlier studies were interested in correlating VEP findings with perimetric defects. However, because the VEP reflecting mainly macular function was altered only when the central visual field was disturbed it was regarded by some authors30,32,33,44 not useful in detecting early glaucoma. On the other hand, VEP corresponding to quadrants with small field defects showed a phase shift compared with responses from normal homonymous quadrants.45 A recent evaluation of the pattern-VEP and computerized static perimetry45 regarded perimetry as superior to the VEP in early glaucoma considering the latter only as an adjunct.

Recent studies using rapidly alternating coarse patterns44 or unpatterned flickering stimuli39,40 showed that amplitude reductions or peak-time delays in glaucoma occurred mainly in the high-frequency range. This led to the conclusion that transient channels are probably more susceptible to glaucoma damage than sustained channels.

VEP changes in OHT have been previously described in various VEP tests,34,35,41,43,46,47 although other authors found none.31,37,39,40 Recent investigations evaluating the contrast sensitivity using pattern onset-offset stimulation43 or studying the recovery of the pattern VEP after exposure to a dazzling light stimulus47 also revealed response alterations in patients with glaucoma and OHT.

In the current study a first attempt was made to combine in glaucoma research the isolation of the blue-sensitive pathway with the recording of pattern-VEP. Onset VEP in response to a pattern of blue and black stripes (BB) were compared with responses to the same pattern presented on an intensive yellow adaption field (BY). In addition, the responses were correlated with visual field defects, with papillometric data, and with results obtained from the 100-hue test. In the literature mentioned above only the total error score of the 100-hue test was evaluated. Because in the current investigation the emphasis is on the function of the blue-sensitive pathway, only the tritan score of the 100-hue test was correlated with the VEP data.

**METHODS**

**VEP Stimuli**

The apparatus used to stimulate the retina has been described previously.46 In short, a two-channel Maxwellian view system was used to present the stimuli with a 900 Watt Xe high-pressure arc lamp as the light source. One channel (I) provided a square-wave stripe pattern with a spatial frequency of 0.88 c/deg, the other channel (II) provided the adaptation light. Grating monochromators (Polytech GM100) were used to produce a blue (460-nm) light in channel I and a yellow (570-nm) light in channel II. A slide having vertical transparent and opaque stripes was in channel I, producing a blue-"black"-looking stripe pattern (the BB pattern) with channel II closed. When in addition channel II was open a homogeneous yellow light was added to the stimulus, producing a pattern seen as alternate yellow-white stripes (the BY pattern). The luminance of channel I as determined with a digital photometer (Tektronix J 16) was 3.3 X 10^2 photopic Trobland (Td), and that of channel II was 1.3 X 10^4 Td.

The method of the vibrating scanner49 was used to stimulate the retina with the onset-offset procedure. The combined light paths of both channels were focussed on and reflected from a small mirror of an optical scanner (general scanning G100PD) that moved the stimulus horizontally in a triangular wave form back and forth across the retina at a frequency of 800 Hz. This produced a homogeneous unpatterned mixture of the lights of both channels. A digital function generator (HP 8116A) was used to control the scanner movement by providing bursts of oscillations at certain intervals. When the scanner vibrated the pattern disappeared and a homogeneous field was seen (offset, 500 ms), when the vibration stopped the pattern appeared (onset, 200 ms). A diaphragm in front of the final lens of the viewing system provided a steady circular edge of diameter of 35° around the stimulus field of both channels. Cross hairs provided a central fixation mark.

Psychophysical determinations of the spectral sensitivity of the onset and offset responses with this stimulus set up as described previously for three normal subjects48 ensured that the sensitivity curve had only one maximum in the blue (at 460 nm) providing evi-
dence that in fact the responses were dominated by the activity of the blue-cone pathway. There was a shoulder in the sensitivity curves at 550 nm and above indicating a residual contribution from the red- and green-sensitive pathway at these wavelengths.

**Recording**

The VEP was recorded monopolarly from the inion referenced to the left ear lobe, the right ear lobe was grounded. A positivity at the inion electrode resulted in an upward deflection in the records. After amplification (Gruber EEP402, 3-dB points at 0.5 and 30 Hz plus notch filter at 50 Hz) the EEG was averaged in a digital computer (IBM/AT personal computer) equipped with an analog-to-digital converter (Meilhaus ME26) controlled by a Pascal-written data acquisition program. The sampling rate was 500 Hz, the sweep length was 400 ms, and 150 sweeps were averaged per trial. Amplitude and peak-time measurements of the response waveforms were graphic-oriented, hard copies of the responses were obtained with a laser jet printer (Kyocera).

**Color Vision Test**

In addition to pattern-VEP recordings all subjects underwent the Farnsworth 100-hue test, which was carried out on a color-neutral gray surface under a constant illumination of 2000 lux provided by two fluorescent lamps (Osram biolux L 18W/72, color temperature 6500° K) approximating the CIE standard illuminant C for daylight illumination. The results of the 100-hue test were evaluated by a commercially available computer software (Loma Linda University Eye Medical Group), and the mean defect in the tritan range (color caps 2 to 6 and 46 to 52) was used for further evaluation. Presbyopic subjects were refracted at near-vision. In order to reduce a possible influence of diurnal variations on the measurements the color vision tests were made during approximately equal morning hours (9 AM), followed by the VEP recordings.

**Subjects, Patients, and Procedures**

All subjects gave their informed consent after the nature and the possible consequences of the test had been explained. The research followed the tenets of the Declaration of Helsinki and was approved by the institutional human experimentation committee. Both eyes were tested consecutively and one eye was chosen at random for evaluation. During VEP recording the subject rested the head on a chin rest with the forehead against a head band both mounted on a three-dimensional remote-controlled machine movement. Fixation by the subject was constantly monitored by a television camera. Whenever the subject moved the head a bright reflex appeared on the iris. In this case recording was stopped, the head realigned, and recording was continued. Before recording, the subjects adapted to the stimulus luminance for 1 minute. Both the BB and the BY conditions were tested at least twice in succession in all subjects in order to check for reproducibility of the records. Amplitude and peak time measurements were averaged from both recordings.

All subjects underwent a thorough ophthalmologic examination including slit lamp inspection, Goldmann-applanation tonometry, chamber-angle inspection, computerized static projection perimetry (Octopus, program G1, two phases), and fundoscopy. For optic disc morphometry\(^{30}\) 15° color stereo optic disc transparencies were taken for all eyes using a telecentric fundus camera equipped with an Allen stereo separator. The disc slides were projected in a scale of 1:15. The outlines of the optic disc and cup were plotted on paper and morphometrically analyzed. To obtain values in absolute size units, ie, in millimeters or squared millimeters, the ocular and the photographic magnification were accounted for. The photographs were evaluated in a masked fashion without knowledge of the clinical diagnosis and the visual field data. The optic cup was defined on the basis of contour and not of pallor. The border of the optic disc was identical with the inner side of the peripapillary scellar ring. The latter was a thin white band encircling the optic disc. On the temporal disc side it could be more easily detected than on the nasal side. Subjects with severe systemic diseases (eg, diabetes) or eye diseases other than primary open-angle glaucoma (POAG) or OHT (eg, cataract, retinal, or vascular disease) were excluded from the study.

**Normal Subjects.** Fifty-eight normal subjects of age 43.8 ± 11 years (mean ± SD) participated in the study; 23 were women, and 36 were men. They were recruited from the staff of the hospital and of the university administration. They had visual acuities of 0.8 or better; their intraocular pressures were below 21 mmHg; their mean defects in perimetry were below 3.7 dB; slit lamp examination and fundoscopy revealed no pathologies; and the optic discs did not show glaucomatous damage.

**Patients.** Forty patients with POAG of age 56.5 ± 12.2 years (mean ± SD) took part in the study; 29 were women, and 13 were men. Their visual acuities were not below 0.7, the intraocular pressures were above 21 mmHg upon repeated measurements, and their perimetric mean defect values were above 3.7 dB on at least two occasions. Morphometry of the optic disc revealed optic disc damages such as an unusually small neuroretinal rim area in relation to the optic disc size, an abnormal form of the neuroretinal rim, cup/disc ratios being vertically higher than horizontally. In addition, localized or diffuse retinal nerve-fiber layer de-
fects were observed. No other ocular abnormalities were present.

Because the normal subjects and patients with POAG were of different mean age, two age-matched groups (between 40 and 65 years) were formed that did not differ significantly from each other ($P > 0.05$). Thus, 34 normal subjects (mean age 50.3 years ± 6.79 SD; 13 women and 21 men) and 32 patients with POAG (mean age 53.5 years ± 6.75 SD; 22 women, 10 men) were further evaluated. The following therapeutic measures were taken in the patients with POAG: 4 patients had a laser trabeculoplasty and 2 a filtering surgery. In 1 patient only pilocarpine eye drops were administered; in 5, pilocarpine was combined with β-blocking agents. In 10 patients, only β-blocking agents were prescribed; in 2, β-blocking agents and Clonidine; and in 2, β-blocking agents and epinephrine. Six patients were treated only with Clonidine. Patients taking pilocarpine eye drops discontinued their medication the day before examination.

**Statistical Analysis**

Comparisons between groups or variables were performed using distribution free tests (Mann-Whitney $U$ test, Wilcoxon test for dependent samples). Correlation analysis used Pearson's product moment correlation coefficient. Optimal cutpoints for discrimination were obtained by logistic regression analysis. For statistical analysis, SPSS/PC 4.01 was used.

**RESULTS**

**Normal Subjects**

The onset-offset VEP of the 34 normal 40–65 years old subjects in response to a BB and BY stimulus are reproduced in Figure 1. Although a large variability in response amplitudes and wave forms exists, there is a rather consistent difference between the responses obtained under the two stimulus conditions. These differences become more evident when the responses of all subjects are averaged. This is shown for the normal subjects and for the age-matched POAG group in Figure 2. The BB onset response under the current stimulus conditions is a prominent positive wave (P) with a peak time of about 100 ms, whereas the BY response is mainly a negative potential (N) of larger amplitude and longer peak time. The offset response is more pronounced with the BB stimulus but less conspicuous with the BY pattern. Thus, only the onset response amplitudes and peak times were evaluated as indicated by the arrows in Figure 2. From these averaged recordings it can also be seen that the BY onset response in POAG seems to be smaller and of longer peak time than the corresponding normal response.

The reproducibility and intersession variability was tested in control measurements in five normal subjects with both stimuli on 5 different days at different times of day in five repetitions for each day and subject. The results for the BY condition are shown for both the amplitudes (Fig. 3A) and peak times (Fig. 3B). The high stability of the response measures is par-
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FIGURE 2. Pattern onset-offset VEP averaged from the 34 normal subjects taken from Figure 1 and from 32 patients with POAG for both the BB and the BY conditions. Arrows indicate the methods of amplitude and peak-time measurement. Only under the BY condition is the N component significantly reduced and delayed. Onset at 0 ms; offset at 200 ms.

particularly evident for the peak times. Similar results were obtained with the BB condition.

The analysis of the effects of increasing age (Fig. 4) exhibited no significant relations with any of the different variables tested. (The correlation coefficients and their significances were for the BB amplitude: $r = -0.04$, $P = 0.77$, for the BY amplitude: $r = -0.19$, $P = 0.16$, for the BB peak time: $r = 0.006$, $P = 0.96$, for the BY peak time: $r = 0.2$, $P = 0.13$.) As will be shown below, the peak times of the BY onset responses yielded the best separation between normal subjects and patients with POAG.

Patients

Figure 4 shows a scatterplot of the BY peak times of all subjects examined as a function of age. It can be seen that most patients with POAG have consistently longer peak times than the normal subjects. It is also evident that the normal subjects are of considerably younger age and the patients with POAG of somewhat higher ages. In order to minimize this imbalance an age group between 40 and 65 years was selected. This age-matched group lies within the two vertical dashed lines of Figure 4. The two groups within these boundaries are not of significantly different age any more (see methods) and comprise 34 normal subjects and 32 patients with POAG. The records of these 34 normal subjects are shown in Figure 1.

Tables 1 and 2 show the amplitudes and peak times respectively under the two stimulus conditions obtained from the two age-matched groups. Figures 5 and 6 show respectively the amplitude and peak-time histograms. Table 1 and Figure 5A indicate that in the normal subjects the BY amplitudes are larger than the BB amplitudes (by a factor of 1.56). This difference is statistically significant ($P = 0.001$). Furthermore, Table 1 and Figure 5A show that the BB amplitudes are not significantly different from each other ($P > 0.05$) in the two age-matched subject groups. Thus, POAG has no significant effect on the BB response amplitude. However, the BY amplitudes are significantly larger in the control group than in the patients with POAG (Table 1 and Fig. 5B). The difference between BB and BY amplitudes present in the normal subjects is not present any more in POAG.

Furthermore, the response amplitudes that show a large intersubject variability (Table 1) were compared with each other for both stimulus conditions in both subject groups. A correlation analysis revealed that in the normal subjects a large BB response was generally associated with a large BY response and vice versa ($r = 0.49$, $P = 0.004$), whereas this relation was somewhat less pronounced in the POAG group ($r = 0.35$, $P = 0.05$). The peak-time data that show a much weaker variability (Table 2) did not exhibit a significant relationship between BB and BY conditions.

In the normal subjects the peak times obtained with the BB stimulus (Table 2 and Fig. 6) are significantly ($P = 0.001$) shorter than those obtained with the BY stimulus. The peak times of the BB response are not significantly altered in the patient group as compared to the normal subjects (Table 2 and Fig. 6A). Thus, POAG has no significant effect on the BB peak time either. However, in the POAG group the prolongation of the BY peak time is highly significant (Table 2 and Fig. 6B). Furthermore, Figure 6B and the standard deviations of Table 2 indicate a much larger scatter of peak-time values in the patient group as compared to the normal subjects. The horizontal dashed line in Figure 4 is the result of a logistic regression analysis providing the "best" separation between the age-matched normal subjects and patients with POAG using the BY peak-time criterion. The cutpoint of 125 ms also maximizes the product of sensitivity (75%) and specificity (94%).

As can be seen from Tables 1 and 2 and Figure 4, the intersubject variability of the BY amplitudes and
peak times is larger in the patients than in the normal subjects probably because of a wide variety of glaucoma stages leading to a large scatter of response measures. For the BY measurements small response amplitudes are associated with long peak times ($r = -0.58, P = 0.0007$) in the patients. For the normal subjects such a relationship could not be found.

The data of the age-matched patients with POAG of the current study were correlated also with the mean defect of the visual field within the central 33°, with the neuroretinal rim area of the optic disc, and with the results of the color-vision test.

**Perimetry**

Figure 7 shows a scatterplot of the BY amplitude of the age-matched patients with POAG with the perimetric mean defect (logarithmic scale). Only those cases in whom the sum of the false positive and false negative perimetric responses was below 8% are included in this analysis. This reduced the number of cases from 32 to 28. There is a large variability of the amplitude even with small visual field defects because very large and small responses can be observed. However, the diagram suggests that only small amplitudes together with

| TABLE I. BY and BB Amplitudes in Normals and POAG Patients and Their Significances |
|----------------|----------------|
|                | **BY** | **BB** |
| N              | Amplitude ($\mu$V) | Amplitude ($\mu$V) | P     | P     |
| Normal         | 34     | 6.09 ± 2.0 | 3.84 ± 1.7 | 0.001 | 0.2   |
| POAG           | 32     | 4.09 ± 2.6 |               |       |       |

Values are mean ± SD.
a reduction in scatter occur with strong visual field defects. Table 3 indicates that the correlation between (log) mean field defect and BY peak time is also significant. However, with the BB stimulus the correlations with either the amplitude or the peak time do not reach the significance level of $P = 0.05$.

**Optic Disc Morphometry**

A significant correlation can be observed also between the peak time of the BY response and the neuroretinal rim area in the POAG group. Figure 8 indicates still a high degree of scatter, but a gradual increase in peak time can be observed as the neuroretinal rim area decreases. Table 4 shows that again the correlations with the BB stimulus were weaker than those with the yellow background. Because in one patient the optic disc photograph could not be evaluated because of poor quality the number of cases reduced from 32 to 31.

**Color Vision**

The 100-hue tritan scores in the age-matched groups were $2.66 ± 0.61$ (mean ± SD) for the normal subjects and $3.48 ± 1.6$ for the patients with POAG. The POAG scores were significantly different from the normal subjects at the $P = 0.006$ level. Figure 9 plots the BY peak times as a function of the logarithm of the tritan score of the 100-hue test. In addition, the tritan scores of the normal subjects have been included in the figure (filled squares). One of the 32 patients failed to perform the test. The linear regression line was fitted to the POAG data only. There is a large overlap between the normal subjects and the patients suggesting that many patients with POAG had normal color vision in the blue. Although the patient data show a large scatter the peak times appear to increase significantly with the increase of the tritan defect. As can be seen from Table 5 correlations are again not significant with the BB stimulus but become significant with the yellow background light.

**DISCUSSION**

Previous VEP studies in normal subjects using onset-offset luminance-contrast stripe patterns$^{51,52}$ revealed similar onset responses of positive polarity as obtained in the current study with the BB pattern (P, Fig. 2). A potential waveform of mainly negative polarity and of prolonged peak time as observed with the BY stimulus (N, Fig. 2) has been described recently in greater detail.$^{53,54}$ In addition, under the current background

### TABLE 2. BY and BB Peak Times in Normals and POAG Patients and Their Significances

<table>
<thead>
<tr>
<th></th>
<th>BY Peak Time (msec)</th>
<th>BB Peak Time (msec)</th>
<th>P</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>34</td>
<td>117.8 ± 4.1</td>
<td>102.2 ± 14.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>POAG</td>
<td>32</td>
<td>135.9 ± 14.3</td>
<td>99.5 ± 9.9</td>
<td>0.6</td>
</tr>
</tbody>
</table>

Values are mean ± SD.
In the luminance condition it could be shown\(^5\) that the peak spectral sensitivity of the N component occurred in the blue. Furthermore, in single cases of congenital tritanomaly, anisometropic amblyopia, and diabetic retinopathy an alteration of the blue-sensitive pattern VEP could be demonstrated.\(^5\) This response also shows a spatial amplitude tuning\(^5\) that is the basis for the selection of a 0.88-cyc/° pattern in the current study. The reason why the BY responses are larger than the BB responses (Table 1) remains unclear. Studies of the scalp topography of these potentials that could clarify this point have not been carried out yet.

The results of this investigation indicate the usefulness of BY pattern-onset VEP in glaucoma research. No amplitude decreases or peak-time delays were observed with the BB pattern in patients with POAG (Tables 1, 2). BB square-wave stripe patterns presented in the onset-offset mode have not been used before in glaucoma research. However, pattern onset-offset stimuli presented as colorless checkerboards on a television screen have been previously employed. With this stimulus diminished VEP amplitudes\(^4\) and a reduced contrast sensitivity of the VEP\(^4\) was observed in glaucoma. Stripe patterns presented as reversal stimuli have been used in two glaucoma studies\(^3\) and resulted in peak-time prolongations. The most commonly employed pattern stimulus in glaucoma research is a checkerboard pattern presented in the re-

![FIGURE 6](image_url)  
**FIGURE 6.** Histograms of (A) the BB and (B) the BY peak times of the two groups tested. Note the different ordinate scale for the normal BY peak times.

![FIGURE 7](image_url)  
**FIGURE 7.** Scatterplot of the BY amplitude as a function of the mean visual field defect (logarithmic scale) in 28 patients with glaucoma. The regression line demonstrates a significant correlation between the two.

<table>
<thead>
<tr>
<th>VEP Amplitudes and Peak Times With the Log Mean Field Defect in POAG</th>
<th>(N)</th>
<th>(r)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BB amplitude</td>
<td>28</td>
<td>-0.15</td>
<td>0.46</td>
</tr>
<tr>
<td>BB peak time</td>
<td>28</td>
<td>0.33</td>
<td>0.06</td>
</tr>
<tr>
<td>BY amplitude</td>
<td>28</td>
<td>-0.65</td>
<td>0.0002</td>
</tr>
<tr>
<td>BY peak time</td>
<td>27</td>
<td>0.49</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Only with the BY stimuli are the correlations significant. One patient had a zero-amplitude BY response and, thus, a peak time could not be determined.
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FIGURE 8. Scatterplot of the BY peak time as a function of the NNR area in 31 patients with glaucoma. One optic disc could not be evaluated because of poor photographic quality. The regression line indicates a significant increase in peak time with decreasing neuroretinal rim area.

versal mode. In most cases peak-time or phase delays were observed\(^{31-37, 41-53}\) and amplitude reductions less frequently noted.\(^{30, 35, 55}\)

The current results, using for the first time a blue pattern on a yellow background, suggest that under the isolation of the blue-sensitive pathway the peak time delay seems to be the most important aspect of the VEP in differentiating between normal and POAG (Figs. 4, 6 and Table 2). Reasons for the high susceptibility of the BY VEP to glaucoma damage are probably the low number (6% of all ganglion cells in the primate)\(^{56}\) or a higher vulnerability of blue-yellow antagonistic retinal neurons. The latter has been ascribed to the narrow range of blue-sensitive responses.\(^{57}\) Recently, a loss of blue cones and a patchy damage to red and green cones has been demonstrated in eyes with chronic glaucoma,\(^{58}\) which could also explain the tritan-like color deficits in this disease.

Several previous psychophysical studies using blue-on-yellow stimuli recommended a correction of the blue light intensity depending on the individual density of the lens,\(^{21, 22, 59}\) which shows an increasing yellowness with increasing age thus reducing the intensity of the blue light within the eye. However, the influence of lens density is probably of less importance in the current evaluation for the following reasons. (1) A lens density correction is probably necessary in psychophysical studies using threshold intensities but it seems to be less important in VEP studies employing intensities that are usually far above psychophysical threshold levels. (2) Care was taken that patients with clear lenses were included in the study. (3) The VEP

TABLE 4. Correlations of VEP Amplitudes and Peak Times With the Area of the NRR in POAG

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>r</th>
<th>P</th>
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<tbody>
<tr>
<td>BB amplitude</td>
<td>31</td>
<td>-0.02</td>
<td>0.92</td>
</tr>
<tr>
<td>BB peak time</td>
<td>31</td>
<td>0.11</td>
<td>0.6</td>
</tr>
<tr>
<td>BY amplitude</td>
<td>31</td>
<td>0.52</td>
<td>0.002</td>
</tr>
<tr>
<td>BY peak time</td>
<td>30</td>
<td>-0.63</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

One patient had a zero-amplitude BY response and, thus, a peak time could not be determined.

TABLE 5. Correlations of VEP Amplitudes and Peak Times With the Log of the Tritan Score in POAG

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>r</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>BB amplitude</td>
<td>31</td>
<td>-0.29</td>
<td>0.12</td>
</tr>
<tr>
<td>BB peak time</td>
<td>31</td>
<td>0.24</td>
<td>0.2</td>
</tr>
<tr>
<td>BY amplitude</td>
<td>31</td>
<td>-0.51</td>
<td>0.003</td>
</tr>
<tr>
<td>BY peak time</td>
<td>30</td>
<td>0.65</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

One patient had a zero-amplitude BY response and, thus, a peak time could not be determined.
measures do not depend on age. If the yellowness of the lens increases with age in normal subjects, one would expect a decreasing amplitude or an increasing peak time, or both, in the BY response with increasing age. However, this was not the case (Fig. 4). (4) Possible effects of lens yellowness on the data are further reduced by studying age-matched groups. It has been shown that chromatic effects of the lens become increasingly important with subjects over 65 years of age. Based on these data subjects above this age were not included in the evaluation of the current study.

In the POAG group particularly the amplitudes of the BY responses and to a lesser degree their peak times show a larger relative scatter than in the normal subjects (Fig. 4 and Tables 1, 2). This could perhaps be due to the different individual severities of the glaucoma stage with advanced stages associated with longer peak times and smaller amplitudes than earlier stages. Such a relationship is particularly evident from the correlation between the BY peak time and the neuroretinal rim area (Fig. 8). Amplitude values show an even stronger scatter even with earlier stages involving mild field defects (Fig. 7).

If the BY pattern VEP is to become a useful test in glaucoma research it should be compared with other established tests revealing typical glaucoma deficits and describing its severity. Besides elevated intraocular pressures, visual field defects and optic disc damages form the basis of glaucoma diagnosis. Although the correlations shown in Figures 7 and 8 are significant, it must be kept in mind that they cannot reflect direct cause-effect relationships because the visual field defects (Fig. 7) were not obtained by blue-on-yellow perimetry and the decrease in NNR area (Fig. 8) is an even stronger scatter even with earlier stages involving mild field defects (Fig. 7).

In the current study the yellow background serves to isolate the blue-sensitive pathway by depressing the red- and green-sensitive one. Thus the question arises whether VEP abnormalities noted in the patients with POAG are associated with psychophysically determined color-vision losses. Blue-color vision disturbances are not part of the glaucoma diagnosis. However, as mentioned in the introduction, these deficits can occur in glaucoma. Figure 9 demonstrates that most of the patients with POAG evaluated had normal tritan scores. Although the correlation illustrated in Figure 9 is significant the analysis nevertheless suggests that because of the large overlap between normal subjects and patients with POAG the tritan score of the 100-hue test is not a very sensitive discriminator. On the other hand, the BY VEP test, which examines in the same patients the blue-sensitive mechanism in a different way, is a much more precise method for identifying POAG.

Key Words
blue-color vision, blue-sensitive pathway, glaucoma, selective adaptation, visual evoked potential

References
16. Lachenmayer BJ, Airaksinen PJ, Drance SM, Wijsman, K. Correlation of retinal nerve-fiber-layer loss,


