Eye Movement Abnormalities in Carriers of Blue-Cones Monochromatism

Irene Gottlob

Purpose. Although impaired color vision and ERG changes have been detected in carriers of blue-cone monochromatism (BCM), no eye movement abnormalities have been identified. Quantitative eye movements of three obligate carriers of BCM were analyzed.

Methods. Horizontal and vertical eye movements of three obligate carriers of two families with BCM with visual acuity of 20/20 or better were recorded using the magnetic search coil technique. Subjects were examined fixing in primary and eccentric gaze and during horizontal and vertical smooth pursuit at 20°, 40°, and 80° per second.

Results. All carriers displayed fixation instability. In two subjects, fine-amplitude upbeat, jerk-type nystagmus was detected. Reduced pursuit gain was found in the carriers. The third subject had small downbeat nystagmus.

Conclusion. Abnormal eye movements are described for the first time in carriers of BCM. The nystagmus is clearly distinct from congenital or latent nystagmus and is similar to the nystagmus reported in BCM. Because all carriers had excellent visual acuity, in BCM, nystagmus is intrinsic to the disease and can appear independently of the visual defect. Invest Ophthalmol Vis Sci. 1994;35:3556-3560.

Blue-cone monochromatism (BCM) is a rare congenital color blindness in which normally functioning blue cones are believed to be present. Affected males have decreased visual acuity and nystagmus. Yee et al found that patients with BCM have continuous or intermittent pendular or jerk-type nystagmus that can be horizontal, vertical, or oblique. Photophobia and myopia are often present. An X-linked recessive pattern of inheritance in the absence of cone function is a reliable indicator of this disease. Most carriers are clinically normal but, on careful testing, demonstrate abnormalities in color vision, delays in dark adaptation, abnormal ERG flicker, and dark-adapted red flash responses or minor macula changes on fluorescein angiography.

Nystagmus and abnormal eye movements have been found in female carriers of X-linked congenital nystagmus. However, in the investigated female carriers of BCM, no pathologic nystagmus or abnormal eye movements have been detected. It is unclear whether in BCM nystagmus is intrinsic to the disease and if it can appear independently of the visual defect.

We describe three female carriers from two different families with BCM who displayed abnormalities on quantitative eye movement recordings.

PATIENTS AND METHODS. The research followed the tenets of the Declaration of Helsinki. All subjects gave informed consent, and the study was approved by the Institutional Review Board Committee of Wills Eye Hospital. Three patients and three obligate carriers of two families with X-linked inheritance pattern of color blindness, reduced visual acuity, and nystagmus were included in this study. In family A, examined carriers included the grandmother (47 years of age) (subject A1) and mother (28 years of age) (subject A2) of a 10-year-old boy with BCM. The carrier examined in family B (44 years of age) (subject B) was the mother of two boys (14 and 9 years of age) with BCM. Clinical examinations, electroretinograms, and color tests (Berson color plates, 100 Hue test, and Panel D 15 test) of patients were consistent with BCM. Both boys in family B had esotropia. Affected subjects had predominantly oblique intermittent pendular nystagmus on clinical examination and eye movement recordings (electrooculograms). Small fixation insta-
bility was observed on all carriers during direct funduscopy with a fixation mark. However, eye movements were too small to identify whether they were nystagmus or square wave jerks. All carriers were examined by electroretinograms and color vision tests. Subject B showed changes in the electroretinogram (60% reduced photopic ERG and no X-wave with a red stimulus in the scotopic ERG) and deutan defect on the 100 Hue test. Subject B also had 12 prism diopters of right esotropia. Otherwise, the ophthalmologic examinations, electroretinograms, and color vision tests of the carriers were normal. Visual acuities of subjects A1 and B were 20/20 OU, and those of subject A2 were 20/15 OU.

Normal data were obtained from 12 age-matched (mean 34 years, SD 6.7 years) subjects whose ophthalmologic examination results were completely normal. None of the control subjects had a history of nystagmus or vestibular disturbance, either personally or in the immediate or extended family. None of the control subjects or carriers was on any kind of medication, including sedatives or other psychoactive drugs. One control subject smoked fewer than five cigarettes a day. The other control subjects and the carriers were nonsmokers. None of the subjects smoked within 4 hours before eye movement recordings. In addition, subject A3, the 27-year-old healthy brother of subject A2, was examined; results were normal, and his visual

---

**FIGURE 1.** Vertical (*upper tracings*) and horizontal (*lower tracings*) eye movement recordings of position in primary gaze of the three carriers (subjects A1, A2, and B) and of subject A3, the healthy brother of subject A2, (subjects A1, A2, and A3 recordings with OD fixing and OS covered, subject B with OS fixing and OD covered). Upward directions on tracings indicate upward or right eye movements. Downward directions on tracings indicate downward or left eye movements.
acuity was 20/15 in each eye. After the procedure was fully explained, informed consent was obtained from all carriers and normal subjects.

Eye movements of the carriers and control subjects were recorded using the magnetic search coil technique. An induction coil, mounted in a scleral contact lens, was placed on the patient's eyes. Subjects wore the contact annuli simultaneously on both eyes. Subjects sat within a magnetic frame, their heads comfortably stabilized with adjustable plastic restraints placed around the skull and under the chin. A microcomputer (DEC 11/73; Digital Equipment Corp., Maynard, MA) recorded the eye movements, and data were sampled and stored every 2 msec. By averaging two consecutive samples of eye position, the signal noise was reduced to about 0.1°. Eye velocity tracings were calculated using a two-point central difference algorithm selected to reject noise optimally.

A green laser target (size 0.2 mm, brightness 35 cd/m²) was back-projected on a diffusely illuminated screen (1 cd/m²) at 1 m and used for central fixation and smooth pursuit. All recordings were obtained with the room lights turned off. For calibration, eye position and gain were adjusted while subjects attended to the laser target placed over a ±20° range horizontally and vertically on the screen. Central fixation was recorded during three 10-second periods with binocular viewing and monocular viewing. Fixation was also recorded for a period of 5 seconds at 10° and 20° above, below, right, and left of primary position. Amplitudes and frequencies of all square wave jerks (SWJ) over 0.2° amplitude (clearly distinguishable from

FIGURE 2. Horizontal smooth pursuit of subject A2 at 20°/sec (A) and 40°/sec (B) and her healthy brother, subject A3 at 20°/sec (C) and 40°/sec (D). 1 = Target velocity in degrees per second; 0 = right eye velocity in degrees per second; e = target position in degrees; a = right eye position in degrees. Upward directions on tracings indicate eye movements to the right. Downward directions on tracings indicate eye movements to the left. Time scale at the bottom is shown in milliseconds.
Reports 3559

noise) were evaluated during central fixation with the right eye while the left eye was covered. Because subject B’s left eye is dominant, her right eye was covered for quantitative measurements. Smooth pursuit was elicited with a constant velocity trapezoid target at 20°, 40°, and 80° second horizontally (between 10° right and 10° left) and vertically (between 10° above and 10° below). In carriers and control subjects, pursuit of the right eye was evaluated while the left eye was covered. Because subject B had strabismus, her smooth pursuit data were not used in the evaluations. Smooth pursuit was recorded for at least eight cycles under each condition. Velocity of smooth pursuit was evaluated on eye position tracings measuring a slope of constant velocity portion of at least 200 msec for each cycle, and the mean was calculated for each velocity. Smooth pursuit gain was calculated as the ratio between the mean eye velocity and the target velocity.

RESULTS. Fixation. Figure 1 shows recordings during central fixation of the right eyes of two carriers, and the left eye of one carrier. Eye movements of the right and left eyes of the three carriers and of all normal subjects were always symmetrical in phase and equal in amplitude. Fine vertical upbeat nystagmus was found in subjects A2 and B. The upbeat nystagmus amplitude was between 0.3° and 0.6° with a frequency between 0.5 and 2 Hz in both subjects. The slow component of the nystagmus usually appeared to have a constant velocity trajectory. However, because of the small nystagmus amplitude, it was difficult to assess the trajectory. Upon covering each eye, no change in nystagmus amplitude or direction occurred. The nystagmus did not change in direction, amplitude, or frequency with different positions of gaze. The vertical recordings of subject A1 show a fixation instability and a small downbeat nystagmus, with an amplitude between 0.1° and 0.3° and a frequency of about 1 Hz. None of the control subjects displayed vertical nystagmus. On the vertical eye movement recordings, few SWJ were found in normals (mean frequency 2.4/min, mean amplitude 0.47°) or in carriers (mean frequency 4.0/min, mean amplitude 0.54°).

On horizontal eye movement recordings, the 12 normal subjects showed a mean of 9.6 SWJ/min (9.4 SD) with a mean amplitude of .36° (0.11° SD). The three carriers showed a mean of 29.3 horizontal SWJ/min (6.9 SD) with a mean amplitude of 0.47°. Subjects A1 and A2 displayed 30 SWJ/min and 32 SWJ/min, respectively, (above twofold standard deviation), and subject B displayed 24 SWJ/min (above onefold standard deviation). In addition, subject B showed fine horizontal nystagmus between 0.5 and 2 Hz and between 5° and 8° beating to the left with both eyes viewing or with the right eye covered, and beating to the right when the left eye was covered. Upon covering either eye, no change in amplitude was observed. Because subject B had a right esotropia, her horizontal nystagmus most likely represents small manifest latent nystagmus. Eye movement recordings of subject A3, the healthy brother of subject A2, appear on the bottom of Figure 1. They show stable vertical and horizontal central fixation with one vertical and one horizontal SWJ of 0.3° amplitude, respectively.

Smooth Pursuit. Figure 2 shows horizontal smooth pursuit at 20° and 40° per second of subject A2 (Figs. 2A, 2B) and of her healthy brother, subject A3, (Figs. 2C, 2D) with the right eye viewing. The carrier (subject A2) showed a higher frequency and amplitude of saccades at both velocities. The velocity of the smooth pursuit of subject A1 was clearly reduced compared to that of her brother. Her pursuit had a higher velocity from left to right than from right to left, where large saccades replaced the pursuit. In subject A1, asymmetry was not found. However, subject A1 displayed the same pattern of pursuit with decreased velocity and compensatory saccades. Figure 3 shows the horizontal (A) and vertical (B) smooth pursuit gain of the two carriers and the mean gain and standard deviation of the 12 normal subjects at

![Figure 3](http://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933407/)
the three examined velocities. Pursuit gain of the carriers was under onefold or twofold standard deviation for all measurements.

DISCUSSION. In this study, abnormal eye movements are described for the first time in carriers of BCM. Quantitative eye movement recordings showed an increased number of SWJ, fine vertical nystagmus, and decreased smooth pursuit.

None of our control subjects showed nystagmus. In agreement, examining more than 50 normal subjects, Shallo-Hoffmann et al found a small number of SWJ but no nystagmus with slow-phase instability.

Yee et al showed that patients with BCM have jerk-type or pendular nystagmus. The jerk nystagmus of his patients was horizontal, vertical, or oblique, of small amplitude (1° to 5°) and frequency (1 to 4 Hz), and it appeared to have a constant velocity trajectory. The nystagmus of our carriers was similar, small in amplitude and frequency, and it most likely had a constant velocity trajectory of the slow component. The three affected patients examined in our study had predominantly oblique pendular nystagmus. However, we observed in patients with rod monochromatism that nystagmus changes its waveform with the patient’s age. Most children had pendular nystagmus, whereas most adults had jerk-type nystagmus. In two patients, we observed in longitudinal studies that the nystagmus waveform changed over time from pendular to jerk type. We also observed jerk-type nystagmus in one patient with rod monochromatism and pendular nystagmus in his affected son. Therefore, it is also conceivable that carriers of BCM show different nystagmus waveforms than their offspring. Nystagmus of the carriers with BCM was clearly distinct from predominantly horizontal congenital and latent nystagmus. Similar to the findings in our carriers, patients with BCM displayed a reduced pursuit gain. However, Yee et al did not find any eye movement abnormalities in carriers of BCM. In his study, only horizontal eye movements were recorded and, therefore, fine vertical nystagmus may not have been detected. Although, Yee et al used a different stimulus for pursuit (sinusoidal with variable velocity), differences between the results are difficult to explain on that basis. However, the scleral search coil method used in our study is more sensitive to subtle changes than the electrooculography employed by Yee et al. In addition, as in other X-linked diseases, carriers of BCM may show a wide range of severity of manifestations. Normal to severely abnormal results were found by Farley et al testing color vision and electroretinograms in carriers of BCM.

Unaffected carriers in other nystagmus forms have also been found to have eye movement abnormalities. Overt and micromanifested nystagmus was detected in female carriers of X-linked congenital nystagmus. Shallo-Hoffmann et al found increased intensity of SWJ, small amplitude nystagmus, or both in family members of patients with dominant or X-linked recessive congenital nystagmus.

In conclusion, eye movement recordings of obligate carriers of BCM demonstrate that in addition to changes in the fundus appearance, ERG, color vision, and dark adaptation, pathologic eye movements are present. All our subjects had 20/20 or better visual acuity. Therefore, in BCM, nystagmus seems to be intrinsic to the disease and can appear independently of the visual defect.

Key Words
blue–cone monochromatism, fixation instability, nystagmus, smooth pursuit gain, square wave jerks

Acknowledgment

The author thanks Dr. L. A. Abel for helpful discussions and review of the manuscript.

References