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Eye-Movement Responses to Disparity Vergence Stimuli with Artificial Monocular Scotomas

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ABSTRACT The effects of artificial monocular scotomas on eye-movement responses to horizontal disparity vergence stimuli were studied in six subjects with normal binocular vision. Subjects viewed stereoscopic 1.5° horizontal step disparity vergence stimuli through liquid crystal shutter glasses. The central portion of the stimulus presented to the right eye was removed to simulate monocular artificial scotomas of variable diameters (2° to 10°). Eye movements were recorded with a binocular head-mounted eye tracker. Responses included pure vergence, vergence followed by saccades, and pure saccadic eye movements. The rate of responses with saccadic eye movements increased with the diameter of the artificial scotoma ($p < 0.0001$); there was an increase in the rate of responses starting with saccades ($p < 0.0001$), as well as an increase in the rate of saccades after initial vergence responses ($p < 0.01$). The probability of saccades after initial vergence responses was affected by the open-loop gain of the vergence response ($p < 0.001$). The open-loop gain decreased with increased diameters of the artificial scotomas ($p < 0.0001$). As the diameter of the artificial scotomas increased, the amplitude of the initial vergence eye-movement responses decreased, and the prevalence of saccadic eye movements and asymmetric vergence increased. The effects of the diameter of artificial monocular scotomas on eye-movement responses in subjects with normal binocular vision are consistent with the effects of diameter of suppression scotomas on eye-movement responses to disparity vergence stimuli in patients with infantile esotropia.

KEYWORDS disparity; eye movements; saccade; scotoma; vergence

INTRODUCTION

The presence of fusional vergence eye movements in patients with strabismus and more specifically in patients with infantile esotropia has long been a matter of debate. Kenyon et al. maintained that vergence eye movements in strabismic patients were limited to accommodative vergence.[1,2] Using subjective measurements, Burian et al.[3] demonstrated vergence eye-movements in children with infantile esotropia when the peripheral visual field was stimulated. In a later study, Boman and Kertesz[4] also demonstrated suboptimal vergence responses to fusional disparity stimuli in patients with infantile esotropia. We found that our own patients with infantile esotropia were capable of generating compensatory disconjugate eye movements to full-field fusional disparity vergence stimuli.[5–7] These eye movements, however, were often asymmetric, resulted in partial compensation for the vergence demand, and had a high prevalence of saccades when compared with eye-movement responses of children with normal binocular vision.

Preliminary data from our patients suggest the importance of the diameter of naturally occurring central suppression scotomas in determining the eye-movement responses to disparity vergence stimuli. In children with infantile esotropia, a central suppression scotoma develops in the deviating eye in an attempt to eliminate diplopia. Typical eye-movement responses to 1.5° disparity vergence stimuli in three patients with a history of infantile esotropia and consecutive micro-strabismus are presented in Figure 1. Figure 1A shows a pure vergence response in a patient with a 3° central suppression scotoma; Figure 1B shows a vergence response followed by a saccade and a consecutive monocular drift in a patient with a 5° suppression scotoma; and Figure 1C presents a pure saccadic response in a patient with a 8° suppression scotoma.

In subjects with central suppression scotomas, full field fusional disparity vergence stimuli are perceived as having two components: a central portion seen only by the nondeviating eye, which acts as a stimulus for saccadic eye movements, and a more peripheral portion of the stimulus that is seen by both eyes, which acts as a stimulus for vergence eye movements. For children with infantile esotropia, disparity vergence stimuli provide simultaneous stimuli to the saccadic and vergence eye movement control systems. The purpose of this paper is to study how fusional vergence eye movements in subjects with normal binocular vision are affected by artificial monocular scotomas when viewing disparity vergence stimuli. The mechanisms by which artificial monocular scotomas affect vergence responses in subjects with normal binocular vision may provide insights into the mechanisms that affect eye-movement responses to disparity vergence stimuli in patients with infantile esotropia.

MATERIALS AND METHODS

Visual Stimuli

Subjects viewed the visual stimuli through a stereoscopic display that included a pair of liquid crystal shutter glasses (StereoEyes: StereoGraphics Corporation, San Rafael, CA, USA) and a single display monitor. The shutter glasses were synchronized with the image presentation on the monitor. The images to the left and right eyes changed at a rate of 60 Hz.[7,8]

Visual stimuli alternated between a reference stimulus and test stimuli. The reference stimulus was a red cross (45° horizontal × 32° vertical at a viewing distance of 50 cm) on a black background (see Fig. 2A). The vertical line of the cross was presented to each eye in the same physical location on the computer monitor, so when the two vertical lines were fused, the vertical line appeared at the surface of the monitor. The test stimuli were a set of 1.5° horizontal step disparity vergence stimuli with monocular artificial scotomas to the right eye. A horizontal disparity of 1.5° was selected for the disparity vergence stimuli as this has been shown to be the easiest to perceive stereoscopically.[9] A detailed explanation of the design of the test stimuli (Fig. 2D) is provided in Figure 2B and 2C. To achieve 1.5° horizontal disparity, the vertical line presented to the left eye was displaced 0.75° to the right, and the vertical line presented to the right eye was displaced 0.75° to the left (see Fig. 2B). To simulate a monocular scotoma, the central portion of the disparity vergence stimulus to the right eye was removed (see Fig. 2C). Each subject viewed visual stimuli with simulated monocular scotomas ranging from 2° to 10° in steps of 2°. In the test stimulus (Fig. 2D), two 10° vertical lines (at a viewing distance of 50 cm) of the crossed-disparity stimulus, shown in Figure 2B, were presented to both eyes. The vertical distance of the upper and lower 10° vertical lines from the center of the screen (the subject's fixation point) was determined by the size of the artificial scotoma. Because the distance of the disparity stimuli from the subject's fixation point has been shown to affect the amplitude of the vergence response,[4,10–12] the input to the vergence control system was modified with the diameter of the artificial scotoma. The test stimulus that was presented to the left eye also included the central 1° segment (at a viewing distance of 50 cm) of the stimulus in Figure 2B. Whereas the portion of the stimulus that was seen by both eyes varied with the size of the scotoma, the central portion that was seen only by the left eye remained fixed; thus keeping the stimulus to the saccadic control system constant. By using a variable input to the vergence control system and a fixed input to the saccadic control system, the effects of changes in the input to the vergence control system on the rate

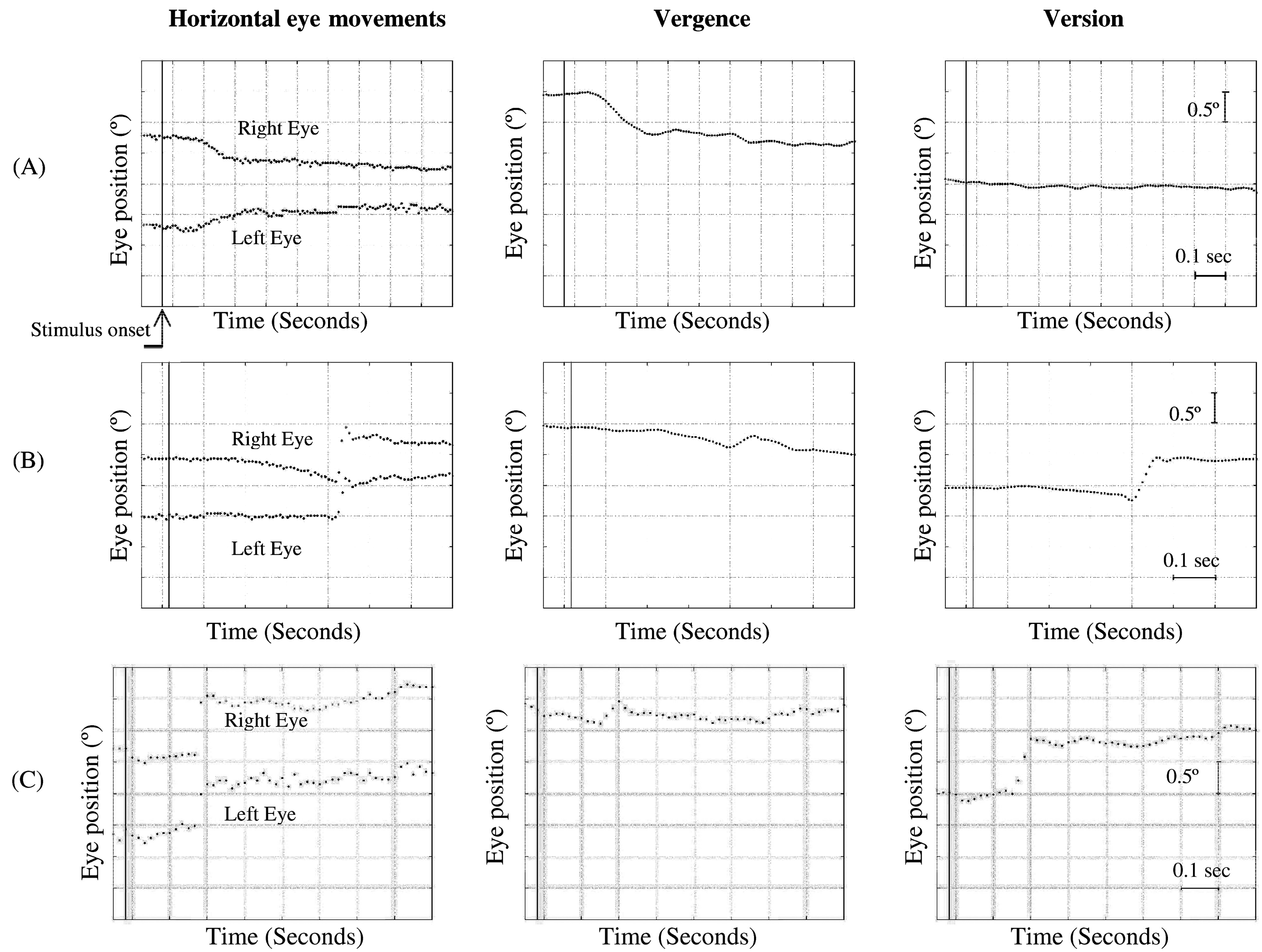

FIGURE 1 Eye-movement responses of patients with infantile esotropia to disparity vergence stimuli. Horizontal eye movements of the left and right eyes (left column, raw data) are shown. A positive change in eye position represents a movement to the right. In each image, the vertical line represents a transition from the reference stimulus to a test stimulus. Vergence eye movements (middle column): Negative changes in vergence represent convergence. Version eye movements (right column): A positive change in eye position represents a rightward conjugate movement. (A) Asymmetric vergence response in patient R.E.N. R.E.N. had a suppression scotoma with a diameter of 3°. (B) Asymmetric vergence response followed by a saccade and an asymmetric monocular drift in patient K.K. who had a 5° suppression scotoma. (C) Pure saccadic response in patient H.G. who had an 8° suppression scotoma.

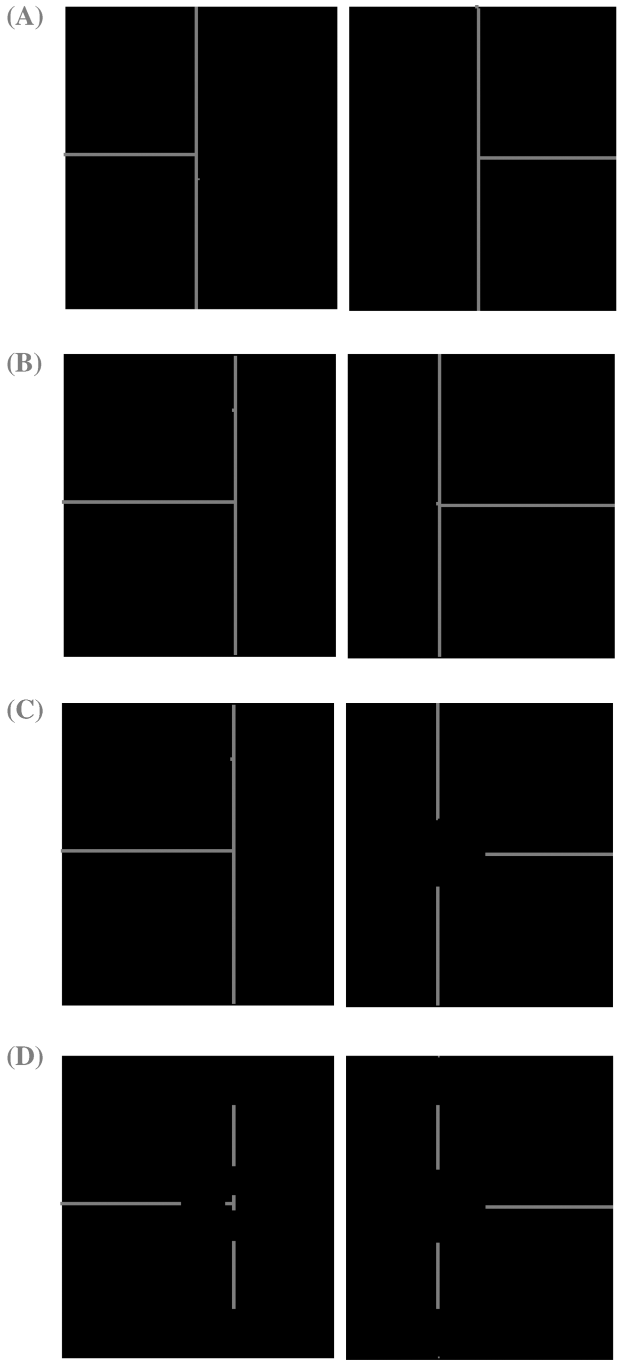

FIGURE 2 Stereoscopic stimuli. Images to the left and right eyes are presented on the left and right sides of the figure, respectively. (A) Reference stimulus. (B) 1.5° horizontal step crossed disparity stimulus. (C) 1.5° horizontal step crossed disparity stimulus with monocular artificial scotoma in the right eye. (D) Test stimulus. In Figure 2 D, the two 10° vertical lines that are presented to both eyes are segments of the crossed-disparity stimulus presented in Figure 2B. The distance of the 10° vertical lines from the center of the screen (the subject's fixation point) is determined by the diameter of artificial monocular scotoma. The central 1° stimulus to the left eye is also a segment of the stimulus presented to the left eye in Figure 2B. This central segment remains constant in all test stimuli.

of responses with saccadic eye movements could be studied.

Sixteen test stimuli were presented for each size of artificial monocular scotoma. Two control stimuli were used: binocular disparity vergence stimuli (1.5° crossed disparity) without artificial scotomas and saccadic stimuli to the left eye (1° vertical segment displaced 0.75° to the right). In order to avoid anticipation, several uncrossed step disparity vergence stimuli were integrated into the presentation. The sequence of stimulus presentation was randomized, and each stimulus was presented for 1.5–2.5 s. Each sequence of stimuli lasted for approximately 130 s.

The stereoscopic display was integrated into a binocular head mounted eye-tracking system (Vision 2000; EL-MAR Inc., Toronto, Ontario, Canada).[7,8] Vertical and horizontal eye movements were recorded at a rate of 120 Hz with a resolution of ±0.1°.[13–16] A chin rest was used to minimize head movements. Subjects were instructed to fixate steadily on the center of the screen (which coincided with the center of the cross in the reference stimulus) to minimize changes in eye position.[17,18]

Subjects

Eight subjects with normal binocular vision between 16 and 33 years of age were recruited. Subjects with normal binocular vision vary in their ability to fuse crossed and uncrossed disparity stimuli.[19] To ensure that our subjects were capable of fusing horizontal 1.5° step crossed disparity visual stimuli, each subject participated in a screening test in which visual stimuli ranging from 0.5° to 4° of horizontal disparity (in disparity increments of 0.5°) were presented randomly on the computer screen. The fused visual stimuli were perceived as a red cross (45° horizontal × 32° vertical at a viewing distance of 50 cm) with the vertical axis presented at either crossed or uncrossed disparity. Subjects were instructed to report whether they could fuse the stimuli and to indicate the location of the cross in space (in front of or behind the plane of the computer screen). Only six of the subjects were capable of fusing the 1.5° crossed and uncrossed horizontal step disparity vergence stimuli and participated in the study. All six subjects had a visual acuity of at least 0.0 logMAR in each eye and a stereoacuity of 40″ using the Titmus stereotest. All subjects had normal sensory fusion based on the Worth 4 dot and Bagolini's striated glasses tests. The "tube test"[20] was used to determine ocular preference. Subjects 2 and 5 demonstrated a preference for the right eye.

The research followed the tenets of the Declaration of Helsinki. The subjects signed a consent form for their participation in the study, acknowledging that the research procedures had been described, questions had been answered, and harms and benefits of participating were explained. Approval for this study was obtained from the Research Ethics Board at The Hospital of Sick Children, Toronto, Canada.

Analysis

Data were analyzed off-line by semi-automated algorithms that classified and quantified the eye-movement responses. The instantaneous horizontal vergence angle was calculated by subtracting the horizontal position of the left eye from that of the right eye. Vergence velocity was calculated by using an 11-point parabolic differentiator.[7,8] The criterion for the detection of vergence eye movements was a peak velocity of horizontal vergence movements exceeding a threshold of 3 deg/s.[12] The beginning of vergence eye movements was determined as the point in time before reaching the threshold peak velocity in which the vergence velocity was equal to or lower than 0 deg/s. The conjugate response was calculated as the average of the horizontal positions of the right and left eyes. The detection of a saccadic response was based on the presence of a peak velocity of the conjugate response exceeding 12 deg/s.[20] The eye velocity was obtained by using a 5-point parabolic differentiator.[7,8] The initial 800-ms time intervals after the presentation of the test stimuli were analyzed.

Eye-movement responses to the test stimuli were divided into responses with and without saccadic eye movements. Responses with saccadic eye movements were divided further into two groups: (i) responses that started with vergence and were followed by saccades and (ii) responses that started with saccadic eye movements. The rate of responses in each group was calculated by dividing the number of responses in each group by the total number of responses. The latency, polarity, and amplitude of the saccades were also analyzed. For each response that started with vergence, an estimate of the vergence open-loop gain was derived from the ratio between the vergence amplitude, 150 ms after the onset of the vergence response, and the vergence demand of the visual stimuli (1.5° disparity).[21]

Vertical eye movements were monitored, and eye-movement responses with vertical saccades were rejected. Responses were rejected also if fixation prior to the onset of the stimulus was unstable (i.e., saccades occurred at a latency of <80 ms from the presentation of the test stimulus) and if blinks occurred within the 800-ms time interval after the presentation of the test stimulus.

A repeated measures Poisson regression for continuous data was used to assess whether the rate of responses containing a saccade or the rate of responses that started with saccades changed with the size of the artificial monocular scotoma. A repeated measures ANOVA was used to compare (i) the open-loop gain of responses that started with vergence and were not followed by saccades with the open-loop gain of vergence responses that were followed by saccades; and (ii) the open loop gain of responses that started with vergence eye movements and were followed by saccades versus the diameter of artificial monocular scotomas. Statistical significance was taken as $p < 0.05$.

RESULTS

Typical eye-movement responses to the step disparity visual stimuli (subject 4) are presented in Figure 3. Figure 3A shows a typical response to a disparity vergence stimulus without an artificial scotoma; the eye movement response does not have saccadic eye movements, and the vergence demand is compensated through symmetric vergence eye movements. Figure 3B shows a typical response that starts with a vergence eye movement that is followed by a saccade and asymmetric vergence. Figure 3C shows a typical response that starts with a saccade. Most of the responses to control disparity vergence stimuli were symmetric vergence eye movements without saccades. However, the addition of monocular artificial scotomas of different diameters to the disparity vergence stimuli resulted in an increased prevalence of asymmetric vergence and saccadic eye movements. For example, when disparity vergence stimuli with a monocular scotoma of 2° were presented, the average rate of responses containing a saccade was 34%. When disparity vergence stimuli with a monocular scotoma of 10° were presented, responses with saccadic eye movements constituted 78% of the total number of responses. Figure 4 shows a summary of the mean and

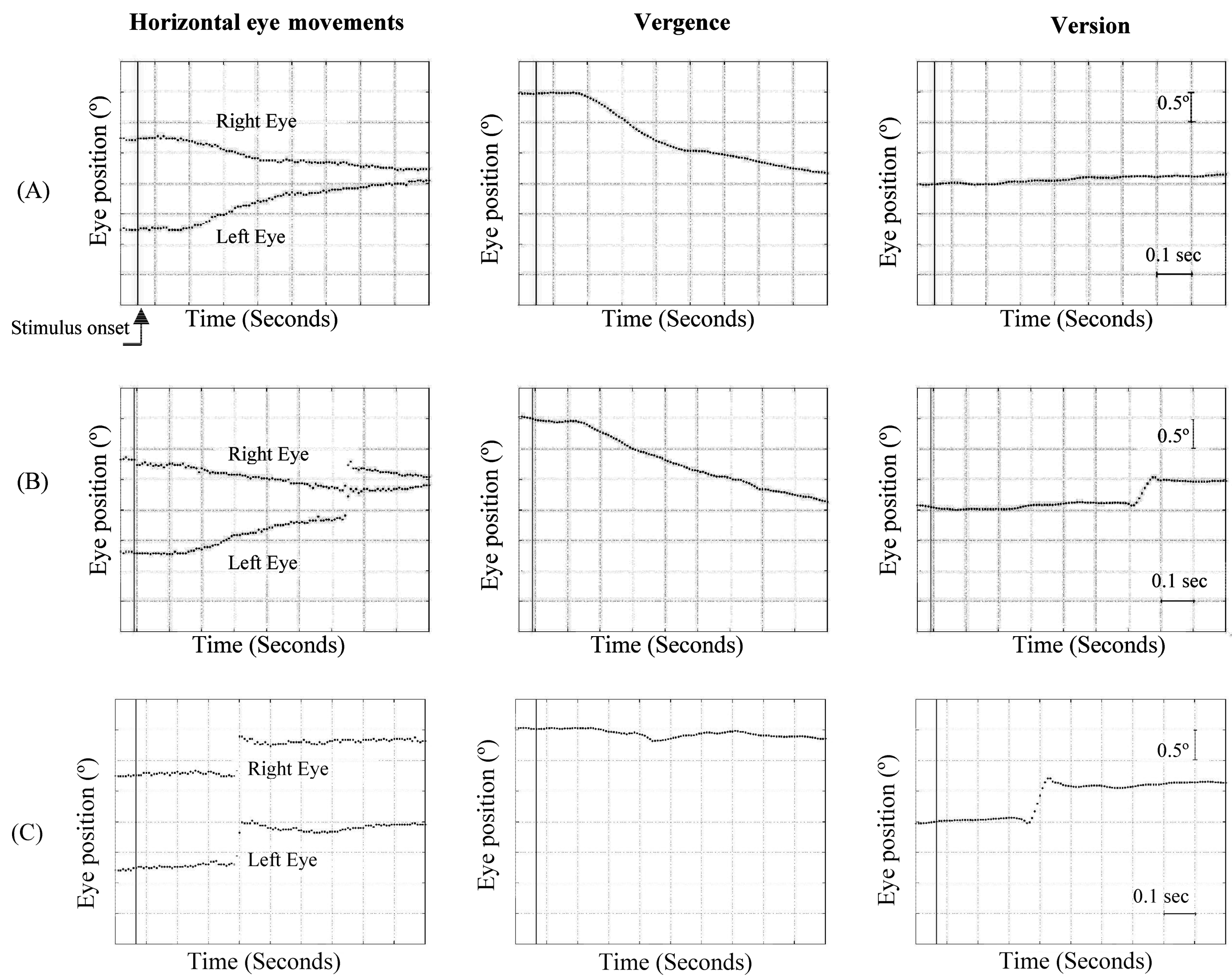

FIGURE 3 Eye-movement responses in subject 4 to 1.5° horizontal step crossed-disparity stimuli with and without artificial monocular scotomas. Horizontal eye movements of the left and right eyes (left column, raw data) are shown. A positive change in eye position represents a movement to the right. In each image, the vertical line represents a transition from the reference stimulus to a test stimulus. Vergence eye movements (middle column): Negative changes in vergence represent convergence. Version eye movements (right column): A positive change in eye position represents a rightward conjugate movement. (A) Symmetric vergence response. (B) Vergence response followed by a saccade and an asymmetric monocular drift. (C) Pure saccadic response. Note: Middle row and bottom row are examples of responses with saccadic eye movements.

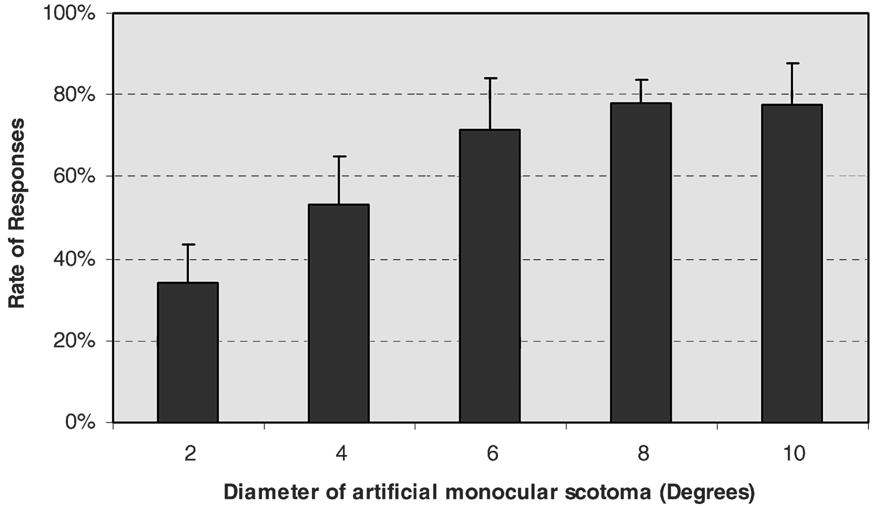

FIGURE 4 **Rates of responses with saccadic eye movements as a function of the diameter of artificial monocular scotoma. The mean and standard error of the rate of eye movement responses with saccadic eye movements in the six subjects are presented. Note the increase in the rate of responses with saccadic eye movements as a function of the diameter of the artificial monocular scotoma ($p < 0.0001$).**

standard error of the rates of responses with saccadic eye movements as a function of the diameter of artificial scotoma for all six subjects. A repeated measures Poisson regression demonstrated a significant increase in the rate of responses with saccadic eye movements as a function of the diameter of the artificial monocular scotoma ($p < 0.0001$).

Responses with saccadic eye movements included responses that started with vergence eye movements and were followed by saccades, as well as responses that started with saccades. In all six subjects, responses that started with saccades had a polarity that was consistent with the direction of movement of the monocular component of the test stimuli to the left eye (i.e., rightward saccades). These rightward saccades had a mean latency of 340 ± 108 ms and mean amplitude of 0.48° ± 0.14°. The saccades had lower amplitudes and longer latencies than saccadic eye movements to control saccadic stimuli (latency 277 ± 56 ms; amplitude 0.62° ± 0.2°). Both the latency and the amplitude of responses that started with saccadic eye movements were not dependent on the size of the artificial scotoma. Figure 5 presents the mean and standard error of the rate of responses that started with saccades as a function of the diameter of the artificial scotoma. Repeated measures Poisson regression for continuous

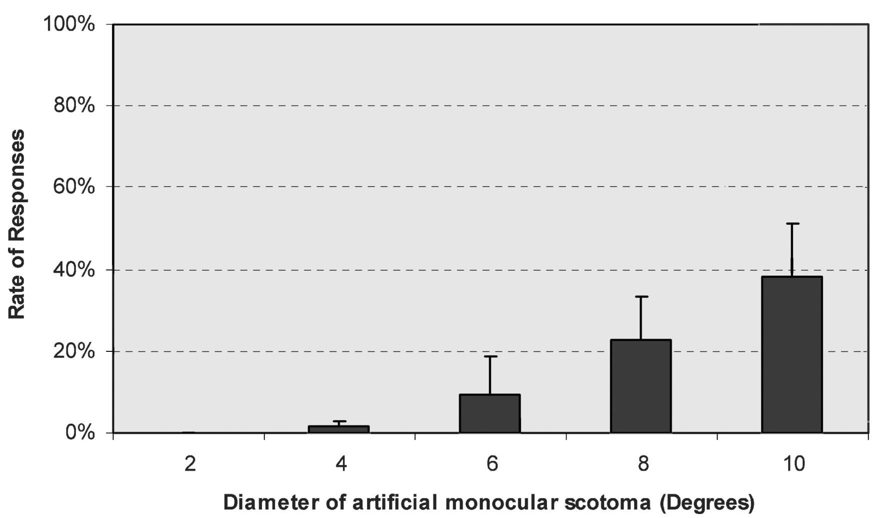

FIGURE 5 **Rates of responses starting with saccades as a function of the diameter of the artificial monocular scotoma. The mean and standard error of the rate of eye movement responses starting with a saccade in the six subjects are presented. Note the increase in the rate of responses starting with saccades with the diameter of the artificial monocular scotoma ($p < 0.0001$).**

data demonstrated an increase in the rate of responses starting with saccades as a function of the diameter of suppression scotoma ($p < 0.0001$).

For responses that started with vergence eye movements and were followed by saccades, the rate of saccades increased with the diameter of the artificial monocular scotoma ($p < 0.01$). In five of the six subjects (the only exception was subject 2, see the "Discussion" section for a possible explanation of these eye movements), the polarity of the saccades was consistent with the direction of movement of the monocular component of the test stimulus (i.e., rightward saccades). These saccades had a mean latency of 368 ± 107 ms and mean amplitude of 0.30° ± 0.03°. To explore the hypothesis that the probability of triggering saccadic eye movements after an initial vergence response is influenced by the open-loop gain of the vergence response, the open-loop gain of responses that started with vergence and were followed by saccades was compared with the open-loop gain of responses that were not followed by saccades. A repeated measures ANOVA demonstrated a significant difference ($F_{5,116} = 7.291$, $p < 0.001$) between the open-loop gain of responses that started with vergence and were not followed by saccades (0.34 ± 0.14) compared with vergence responses that were followed by saccades (0.29 ± 0.14). For responses that started with vergence eye movements and were followed by saccades, the open-loop gain to stimuli with 10° artificial monocular scotomas (0.27 ± 0.04) was significantly ($F_{1,14} = 6.802$, $p = 0.021$) lower than the open-loop gain to stimuli with 2° artificial monocular scotomas (0.43 ± 0.18).

An increase in the rate of responses containing a saccade as a function of the size of the artificial monocular scotoma was demonstrated in five of the six subjects. However, different subjects demonstrated different rates of responses for each diameter of artificial monocular scotoma. For example, subject 1 did not have saccadic eye movements in response to visual stimuli with monocular scotomas of 2°. However, for this subject, 57% of the total number of responses to visual stimuli with monocular scotomas of 6° and 88.9% of the total number of responses to visual stimuli with monocular scotomas of 10° had saccadic eye movements. For subject 4, 33.3% of the total number of responses had saccadic eye movements when the vergence stimuli were presented with a monocular scotoma of 2°. With either 6° or 10° monocular scotomas, almost all of the responses contained saccades. Subject 2 did not follow the general pattern that was observed in the other subjects. Subject 2 demonstrated a rather high rate (33.3%) of responses with vergence and disjunctive saccades (saccades with different amplitudes to the left and right eyes) even to control vergence stimuli (i.e., stimuli without a monocular scotoma). This rate was approximately three times higher than the average rate demonstrated by the other subjects (12%). Forty-three percent of the eye movement responses, in subject 2, to stimuli with an artificial monocular scotoma of 2° had saccadic eye movements. This rate of responses did not change significantly with the size of the monocular scotoma.

DISCUSSION

The main finding of this study was that the rate of responses with saccadic eye movements to disparity vergence stimuli increased with the diameter of the artificial monocular scotomas ($p < 0.0001$). For visual stimuli with small artificial scotomas (2°), the disparity vergence demand was mainly compensated by vergence eye movements and the rate of saccades was relatively low (33%). As the size of the scotomas increased, the disparity vergence error was compensated through a combination of vergence and saccadic eye movements and the rate of saccades increased (72% with 6° scotoma). For even larger artificial scotomas (10°), a larger percentage (78%) of the responses had saccadic eye movements. The diameter of artificial scotomas affected the rate of responses with saccadic eye movements through two processes: (i) a higher rate of responses that started with saccades and (ii) a higher rate of saccades, after initial vergence responses.

Saccades and vergence are distinct subclasses of eye movements with considerable differences in their control system characteristics; the vergence control system allows fixation in different depth planes by horizontal rotations of the eyes relative to each other, whereas the saccadic (version) control system allows directional shifts of gaze by moving both eyes in the same direction. Under normal viewing conditions, binocular tracking of a target that changes position in both depth and direction requires coordinated saccadic and vergence eye movements. When saccadic and vergence eye movements are performed simultaneously, vergence is facilitated by both horizontal and vertical saccades.[20,22,23] Zee et al.[23] proposed that the interactions between the saccadic and vergence control systems are governed by a shared structure of omnidirectional pause neurons (OPN) in the brain stem. The single cell recordings of Mays and Gamlin[24] lend support to the model proposed by Zee et al.

The coordination between the vergence and saccadic control systems is also facilitated by a common signal processing stage for target selection, amplitude computation, and triggering.[25,26] At the common signal processing stage, a process of "weighting" of the relative sensory inputs to the vergence and saccadic control systems takes place before triggering either vergence or saccadic eye movement responses. Through this "weighting" process, the sensory input to the vergence control system might affect the probability of triggering saccadic eye movements. In this study, the input to the saccadic control system remained constant while the input to the vergence control system decreased with the diameter of the artificial scotoma. Consequently, the relative "weight" of the input to the saccadic control system increased and therefore the probability of triggering responses that start with saccades increased (see Fig. 5). It is worth noting that the high intersubject variability with respect to the rate of the responses starting with saccades may be the result of different weighting processes for vergence and saccadic eye movements in different subjects.

Data from the study show that (i) the probability of saccades following initial vergence responses increased as the magnitude of the open-loop gain of the vergence response decreased and that (ii) the open-loop gain of the vergence response decreased with the diameter of the artificial monocular scotoma. Taken together, the higher probability of saccades after initial vergence responses could be explained by the decrease in the vergence open-loop gain in response to visual stimuli with larger artificial scotomas. The open-loop gain may act as a predictor for the ability of the vergence response to compensate for the disparity error presented by the visual stimulus. A low open-loop gain may act as an indicator that the magnitude of the vergence response would be inadequate to compensate for the disparity demand. This may subsequently result in the triggering of saccadic eye movements so that the image presented to at least one of the eyes is foveated.

For subject 2, the rate of responses with saccadic eye movements did not increase significantly with the diameter of the artificial scotoma. It is worth noting that in this subject, the rate of disjunctive saccades after a vergence response to disparity stimuli (without artificial scotomas), was three times higher than the rate observed in other subjects. Also, unlike all other subjects in which the direction of saccadic eye movements that followed initial vergence response was always in the direction of the saccadic component of the test stimulus (i.e., rightward saccades), subject 2 demonstrated both leftward and rightward saccades. Subject 2 demonstrated a strong preference for the right eye in the "tube test."[20] It is possible that in subject 2, the high prevalence of saccadic eye movements as well as the polarity of saccades after initial vergence response is part of an oculomotor strategy that is affected by monocular preferences.[20] Ocular preference, much like the presence of monocular scotomas, could result in an increased prevalence of responses with saccadic eye movements because of "unequal weighting" of the sensory inputs to the two eyes.

Looking at the three responses shown in Figure 1, the patient with the largest suppression scotoma (8°) had only pure saccadic responses to disparity vergence stimuli (Fig. 1C). The patient with a smaller suppression scotoma (5°) was capable of initiating vergence eye movements to disparity vergence stimuli. However, these vergence eye movements were generally followed by saccades and a consecutive asymmetric monocular drift (Fig. 1B). The patient with the smallest suppression scotoma (3°) were capable of compensating for 80% of the vergence demand by symmetric vergence eye movements without saccades (Fig. 1A). The effects of the diameter of suppression scotomas on eye movement responses to disparity vergence stimuli in patients with infantile esotropia are consistent with the effects of artificial monocular scotomas on eye movements in subjects with normal binocular vision. It is possible that suboptimal vergence eye movements in patients with infantile esotropia could be attributed to the effect of central suppression scotomas on the sensory input to the vergence control system rather than to a primary defect in the vergence control system.

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