The Effect of Lens-Induced Anisometropia on Accommodation and Vergence during Human Visual Development

Shrikant R. Bharadwaj¹ and T. Rowan Candy²

PURPOSE. Clear and single binocular vision, a prerequisite for normal human visual development, is achieved through accommodation and vergence. Anisometropia is associated with abnormal visual development, but its impact on accommodation and vergence, and therefore on the individual's visual experience, is not known. This study determined the impact of transiently induced anisometropia on accommodative and vergence performance of the typically developing human visual system.

METHODS. One hundred eighteen subjects (age range, 2.9 months to 41.1 years) watched a cartoon movie that moved between 80 and 33 cm under six different viewing conditions: binocular and monocular, and with ± 2 diopters (D) and ± 4 D of lens-induced anisometropia. Twenty-one subjects (age range, 3.1 months to 12.1 years) also watched the movie with 11% induced aniseikonia. Accommodation and vergence were recorded in both eyes using a videoretinoscope (25 Hz).

RESULTS. The main effect of viewing condition was statistically significant for both accommodation and vergence (both $P < 0.001$), with monocular accommodative and vergence gains statistically significantly smaller than the binocular and four induced anisometropia conditions ($P < 0.001$ for both accommodation and vergence). The main effect of age approached significance for accommodation ($P = 0.06$) and was not significant for vergence ($P = 0.32$). Accommodative and vergence gains with induced aniseikonia were not statistically significantly different from the binocular condition (both $P > 0.5$).

CONCLUSIONS. Accommodative and vergence gains of the typically developing visual system deteriorated marginally (accommodation more than vergence) with transiently induced anisometropia (up to ± 4 D) and did not deteriorate significantly with induced aniseikonia of 11%. Some binocular cues remained with ± 4 D of induced anisometropia and 11% induced aniseikonia, as indicated by the accommodative and vergence gains being higher than in monocular viewing. (*Invest Ophthalmol Vis Sci.* 2011;52:3595-3603) DOI:10.1167/iov.10-6214

From the ¹Champalimaud Translational Centre for Eye Research, Bausch and Lomb School of Optometry, L.V. Prasad Eye Institute, Hyderabad, India; and the ²Indiana University School of Optometry, Bloomington, Indiana.

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Corresponding author: Shrikant R. Bharadwaj, Champalimaud Translational Centre for Eye Research, Bausch and Lomb School of Optometry, L.V. Prasad Eye Institute, L.V. Prasad Marg, No. 2, Banjara Hills, Hyderabad, 500034 Andhra Pradesh, India; bharadwaj@lvpei.org.

Infants are commonly born with similar amounts of hyperopia in the two eyes (mean $\pm$ SD, approximately $+2$ diopters [D] ± 2 D).^{1,2} However, up to 25% of infants and approximately 2% to 8% of toddlers—depending on the population studied and the criterion used (typically ≥ 1 D³)—show a significant difference in refractive error between the two eyes (anisometropia).⁴⁻⁹ The amount of anisometropia fluctuates significantly during the initial years after birth, with a prevalence of 0% of persistent anisometropia from infancy noted in a cohort of 293 subjects.⁵ It is well established that chronic anisometropia is associated with abnormal cortical development (e.g., reduction in contrast sensitivity,¹⁰ stereopsis,¹¹ and a reduction in the number of binocularly tuned neurons in primary visual cortex^{10,12}), albeit with a complex cause-effect relationship.^{13,14} Anisometropia of only 1 D to 2 D is associated with amblyopia in children^{15,16}; the two factors become more strongly associated for anisometropia of greater than 3.5 D.¹⁵

Despite this well-established association, the visual experience of humans with anisometropia and the role of anisometropia in developmental disorders remain poorly understood.¹⁵ This is partly because anisometropia is rarely detected during infancy and early childhood given the absence of any obvious signs or symptoms; by the time it is detected in school screenings, the associated abnormalities are established.¹⁷⁻¹⁹ If anisometropia is indeed not present continuously throughout infancy and early childhood, the definition of chronic anisometropia that might lead to abnormal visual development must be determined. How much anisometropia might be needed (and at what age and for how long) to result in developmental abnormalities? How might abnormal visual experience resulting from anisometropia lead to abnormal visual development in humans, and how should clinicians manage it? Management strategies (e.g., preventative prescription of refractive correction) for anisometropia vary significantly among clinicians and are largely based on clinical consensus rather than objective evidence. For instance, in a survey of 59 pediatric ophthalmologists and 161 pediatric optometrists, Lyons et al.²⁰ noted that 47.3% of ophthalmologists and 28.5% of optometrists are likely to prescribe refractive correction for hyperopic anisometropia >1 D in 6-month-old infants. These percentages change for a higher magnitude of anisometropia, with 38.6% of ophthalmologists and 56.9% of optometrists waiting until hyperopic anisometropia reaches >3 D to prescribe in the same age group. Prescribing criteria for hyperopic anisometropia tended to become similar across the two professions for children aged 2 years and older.²⁰

An understanding of any abnormal visual experience resulting from anisometropia also depends on accommodative and vergence performance in the presence of the anisometropia because retinal image quality and retinal image correspondence are critically dependent on these motor responses. How might anisometropia lead to abnormal visual experience, and how much anisometropia might be required to disrupt oculo-

motor performance? In primates, accommodative and vergence responses are driven primarily by cortical (e.g., frontal eye fields²¹) and subcortical (e.g., supraoculomotor area²²) processing of retinal blur and disparity through negative feedback control.²³ The spatial content of the retinal images is typically similar in the two eyes under naturalistic binocular viewing conditions²⁴; under such conditions, accommodative and vergence performance become relatively accurate by around 3 months of age.^{25,26} However, the spatial content of the retinal images is dissimilar in anisometropia, and the performance of the developing accommodative and vergence motor systems under such viewing conditions remains unknown.

In the presence of anisometropia, dissimilar accommodative responses could be generated (aniso-accommodation^{27,28}), but accommodative responses of adults^{29–31} and infants³² are typically consensual, with accommodative performance deteriorating in the presence of significantly dissimilar interocular retinal image qualities (e.g., when optical blur changes in counterphase in the eyes of an adult³³ or when a +20 D lens is placed before one eye of an infant³²). Alternatively, the accommodative response in one eye could maintain focus on targets at different distances, while accommodation in the fellow eye consensually follows the tracking eye, resulting in chronic retinal defocus.^{28,34} In addition, a monovision type strategy could be used—that is, one eye is used for near viewing while the fellow eye is used for distance viewing.^{28,34,35} In this case, minimal modulation of accommodation might be expected in the two eyes in response to a change in target position.³⁴

The adult vergence system appears better suited to handle interocular differences in retinal image quality. For instance, horizontal fixation disparity and the ability to maintain single and clear binocular vision at near viewing distances are minimally affected in the presence of up to 3 D difference in “monovision” prescription for presbyopes.^{36,37} Similarly, subjective fusion of low-frequency global contours prevails for up to 1.5 D of induced anisometropia, even though local suppression scotomas of 1° to 2° occurred in most subjects.³⁸ Experienced adults also continue to fuse low-frequency (0.8 and 1.6 cpd) vertically oriented sinusoidal gratings in a haploscope even when the two monocular gratings differ in contrast by up to 30%.^{39,40}

There were two goals to this study. The first was to assess the impact of transiently induced anisometropia on the accommodative and vergence motor performance of infants and children and to determine the strategies that the accommodative and vergence systems might adopt under such viewing conditions. These data will help define the visual experience of young children who are at risk for conditions associated with anisometropia. The second was to compare accommodative and vergence performance of infants and children with that of

adults to determine whether the impact of induced anisometropia on accommodation and vergence changes with the maturity of the visual system. These data will help determine the relative vulnerability of the typically developing visual system to anisometropic visual experience.

SUBJECTS AND METHODS

Subjects

A total of 118 subjects (age range, 2.9 months–41.1 years), with no reported ocular or medical conditions were recruited (Table 1). The infants and children were recruited from local birth records and were born within 3 weeks of their due date. Adults were pre-presbyopic and near-emmetropic (low amounts of hyperopia or up to 1 D of myopia), had no reported accommodative, vergence, or ocular abnormalities, and were recruited from the local academic department. Some of the adult subjects had participated in our previous experiments and were not naive to our studies. However, all were naive to the goals of the current experiment. The infants and children were expected to be typically hyperopic,² and they did not wear any refractive correction during the experiment to retain their daily natural viewing conditions. Subjects with manifest anisometropia of >0.5 D in the vertical meridian, assessed before the start of data collection (using the PowerRefractor; Multi Channel Systems Reutlingen, Germany), were excluded from the study. Adults wore any habitual correction during the experiment (soft contact lenses only). The parents and adult subjects provided informed consent after the study had been approved by Indiana University's local institutional review board. The study adhered to the tenets of the Declaration of Helsinki.

Procedure

Accommodative and gaze responses of each eye were measured simultaneously using video-based (25-Hz) near-infrared eccentric photorefraction (PowerRefractor; Multi Channel Systems; Fig 1).^{41–44} Subjects were aligned at 1 m from a set of light-emitting diodes (LEDs) immediately beneath a camera aperture. Light from the LEDs passed into the eye and was reflected back from the retina through the pupil. The dioptric focus of the eye in the vertical meridian was derived from the slope of a linear regression fit to the distribution of this reflected light across the pupil. The horizontal and vertical gaze positions were determined from the relative displacement of the first Purkinje image with respect to the center of the pupil image,⁴⁵ and vergence was calculated as the difference in horizontal gaze position between the two pupillary axes. Vergence and gaze position recorded by the PR in angular units of prism diopters (pd) and degrees, respectively, were converted and scaled into meter angles (m^{-1}) using the subject's individual interpupillary distance (IPD).

The PR uses a population-average defocus calibration from adults to compute focus^{41,42} and a population-average Hirschberg ratio to calculate gaze position and vergence.^{42,45} Although individual defocus

TABLE 1. Subject Participation in the Binocular, Monocular, Four Induced Anisometropia, and the Defocus and Eye Position Calibration Conditions Used in This Study

Age Group (y)	Viewing Condition						Calibration
	−4 D Aniso	−2 D Aniso	Binocular	+2 D Aniso	+4 D Aniso	Monocular	
<1	12/17	19/21	25/31	21/28	13/20	05/14	04/07
1.1–4	11/14	14/17	21/27	21/25	20/25	17/21	18/18
4.1–8	08/09	09/09	15/15	15/15	15/15	15/15	13/13
8.1–13	12/13	14/15	14/16	14/16	14/16	13/14	16/16
Adult ≥20	14/14	15/15	19/19	18/19	19/19	19/19	19/19

For all columns, the denominator indicates the total number of subjects in each age group who were recruited for that viewing condition, and the numerator indicates the number of subjects from whom data collection was successful. Aniso, anisometropia.

FIGURE 1. The experimental set-up with its key elements highlighted. The visual target was displayed on the LCD screen and reflected from a beamsplitter to reach the subject. Both the screen and the beamsplitter were mounted on a motorized track that moved them in real space, while the subject was carefully aligned so that the target movement was centered on the midline between their eyes. Accommodative and vergence responses were recorded using the camera placed 1 m from the subject.

and eye position calibrations could not be performed on all subjects because of lack of cooperation, they were performed on 70 of 103 subjects (3.1 months–41.1 years) who gave usable data in all conditions (Table 1). The defocus and gaze position calibration procedures have been described in detail previously.^{32,41,46} Briefly, the defocus calibration factor was determined by placing trial lenses (+1 D to +4 D in steps of 1D) in front of the right eye, which was occluded using an IR filter, while the unoccluded left eye of the subject fixated on a target placed at 50 cm. Similarly, the gaze position calibration function was determined by optically shifting the Purkinje image of the occluded eye using base-out prisms (4 pd to 16 pd in steps of 4 pd) placed in front of the filter while the subject continued to fixate at 50 cm. The induced anisometropia and induced vergence were plotted as a function of lens power and prism power, respectively. The slopes of the functions were determined using linear regression, and these slopes were used to scale each participant's raw data.^{32,43,47} The default PR calibration was used for subjects who did not complete that part of the data collection. Calibration slopes of individual subjects are approximately evenly distributed about the default PR calibration slope values,⁴⁶ with no strong age-related trends.^{32,46} It was, therefore, assumed that the errors introduced by using the default PR calibration summed to zero in the calculation of mean population responses.

Subjects watched a high-contrast cartoon movie on the LCD display during all conditions (as shown in Fig. 1). The images subtended $2.3^\circ \times 2.3^\circ$ at 50 cm, and the mean slope of their spatial amplitude spectra was $-1.47 \pm \text{SD } 0.03$ in log-log coordinates for 100 randomly selected frames. Accommodative and vergence performance was assessed by moving the target eight times between 80 and 33 cm at one of three different speeds (0.25, 0.50, or 0.75 D/s or MA/s), with a stable period of 4 seconds at each viewing distance (see Fig. 3 for stimulus trace). Accommodative and vergence demands, therefore, changed by 1.75 D or MA. Multiple speeds were used to minimize the potential for predictive responses,^{48,49} and all three speeds have been shown to elicit only ramp tracking accommodative⁵⁰ and vergence⁵¹ responses in adults. No systematic difference in performance was noted across different speeds; therefore, the three sets of responses were pooled in analyses.

Subjects participated in six viewing conditions: typical binocular viewing, monocular viewing with one eye occluded, and binocular viewing with +2 D, −2 D, +4 D, and −4 D of induced anisometropia. In the typical binocular viewing condition, they watched the movie with both eyes open, and all cues available to accommodation and vergence were consistent with each other. In the monocular condi-

tion, the subject's right eye was occluded using an infrared transmitting filter (Wratten 87; Eastman Kodak, Rochester, NY) that enabled PR images to be collected from both eyes even though viewing was monocular. The IR filter measured 75 mm $\times$ 75 mm and covered the subject's right eye entirely, preventing the possibility of peeking. Positive and negative trial lenses were placed in front of the right eye to induce +2 D and +4 D of myopic anisometropia and −2 D and −4 D of hyperopic anisometropia, respectively. Ocular dominance appears to influence the effect of induced anisometropia on sensory and motor visual functions in adults.³⁵ Because it was not possible to assess ocular dominance objectively in infants and children, it was assumed that any effect would be averaged across subjects if the right eye was used consistently in this study⁵² and if ocular dominance was balanced equally between the eyes across the population. The trial lenses were hand-held at approximately 14 to 16 mm in front of the eye, with the optical centers aligned with the subjects' pupillary axes. Accommodative and vergence responses in the four anisometropia conditions were compared with those in the other two, binocular and monocular, conditions to determine the level of anisometropia at which performance significantly departed from habitual binocular performance and the level of anisometropia at which performance might reach monocular levels. The latter level would indicate the amount of transiently induced anisometropia required to apparently fully compromise binocularity.

Each viewing condition took approximately 2 to 3 minutes to complete, and the order of the viewing conditions was randomized across subjects. Infants tend to become uncooperative with monocular occlusion.^{32,53} Therefore, monocular viewing was performed as the last condition in all infants younger than 1 year. Subjects who were unable to complete all the viewing conditions in one visit were scheduled for a second visit to complete the remaining conditions. In a subset of participants ($n = 5$; four 3-month-olds and one 3.8-year-old), the binocular viewing condition was repeated on the second visit to assess repeatability. Accommodative and vergence gains (gain = response amplitude/stimulus amplitude) in the repeated binocular conditions were all within 0.2 of each other. If repeated binocular data were available, only the first measurement was included in the other data analyses. An experimenter gently supported each infant or young child's chin during all the conditions, to keep them aligned and to minimize head movements. Older children and adults were instructed to hold their heads as stable as possible. No specific instructions were given to the older children and adults regarding the task; they were merely asked to watch the target.^{54,55}

Effect of Aniseikonia on Accommodative and Vergence Performance

In addition to defocus, the trial lenses used in the main experiment induced a change in the size of the retinal image. For instance, a +4 D trial lens induces a magnification of approximately 7% to 9% when placed at a vertex distance of 14 to 16 mm.⁵⁶ Subjects who participated in the main experiment, therefore, experienced a combination of anisometropia (difference in retinal image defocus in the two eyes) and aniseikonia (difference in retinal image size in the two eyes). The presence of aniseikonia affects binocular sensory processes such as fusion,³⁹ stereopsis,⁵⁷ binocular summation, and contrast sensitivity⁵⁸ in adults, whereas its effect on accommodative performance has not been assessed thus far. To assess whether transiently induced aniseikonia can influence accommodative and vergence performance in infants and children, a second experiment was performed on a subset of 21 subjects (3.1 months–12.1 years; five infants, ten 2- to 4-year-olds, and six 5- to 13-year-olds). An 11% afocal magnifier was placed in front of the right eye of the subjects while they watched the cartoon movie binocularly. The front and back surface optical powers of this thick lens were designed to cancel each other, thereby inducing no change in defocus but magnifying the image solely because of lens thickness.⁵⁶ All other experimental conditions remained the same as the main experiment.

The trial lenses used in the experiment also changed the apparent size of the pupil in the PR image. It is feasible that the measured accommodative responses in the right eye (the eye with the trial lenses in front of it) were underestimated and the gaze position responses (and therefore vergence) were overestimated because of positive lens-induced magnification of the PR image. Similarly, the accommodative responses might be overestimated and the gaze position responses might be underestimated because of negative lens-induced minification of the PR image. A control experiment was performed on five cooperative adults. They watched a cartoon movie monocularly (right eye occluded with the IR filter) at 80 cm while the 11% afocal magnifier was placed in front of the occluded eye for 10 seconds. This procedure was repeated at least five times on each subject, and their defocus and gaze position data were recorded using the PR. Because the magnifier was placed over the occluded eye, the subject did not experience aniseikonia; hence, any systematic change in accommodation and vergence after placement of the magnifier was attributed to the optical effect of the magnifier in the image alone. There were no changes in the PR data that were synchronized with the placement of the magnifier in this condition, and it was concluded that any direct lens-induced change in PR image size had only a negligible effect on the data reported here.

Data Analysis

Data collection was considered successful only if the subject cooperated in the binocular condition and in 2 of the 4 anisometropia conditions. The raw stimulus and accommodation, vergence, and gaze position data were all smoothed using a 200-ms averaging window, thereby maintaining the temporal relationship between them. The stimulus profile was then divided into epochs, each containing a 4-second stable stimulus period plus the change in stimulus before and after this period (see Fig. 3). The responses in each epoch were included in the analyses only if they met all the criteria described here³²:

First, accommodation data were within the linear operating range of the instrument (+4 D to −6 D) and pupil diameters were between 3 and 8 mm (required for the instrument to collect data).^{41,42}

Second, data were collected from a gaze eccentricity of <15° from the pupillary axis to minimize the chances of peripheral refraction influencing the accommodation data.^{59,60} This threshold criterion was based on adult data because there are no comparable data from infants. The infants and adults typically maintained stable gaze on the target, and <1% of the data were excluded as a result of this criterion. Furthermore, eye movement responses were qualitatively similar across all viewing conditions (data not shown), and so any effect of peripheral refraction would be similar across conditions.

Third, the subject generated an eye movement to track the stimulus; therefore, the accommodation and vergence responses represented a valid attempt to follow the target along the midline between the eyes.³² This criterion was applied to the data from the left eye in all viewing conditions, irrespective of the viewing condition for the right eye. All response epochs with a correlation of ≥ 0.7 between left eye position and stimulus position were automatically included in the analyses. Response epochs with correlations between 0.6 and 0.7 were visually inspected and included in the analyses only if the left gaze position appeared to systematically track the movement of the stimulus.³²

The final accommodative and vergence responses were then obtained by averaging 2 seconds (50 data points) of the most stable portion of each usable epoch (typically found in the middle of the 4-second stable portion of the stimulus epoch). This stable 2-second period was identified using visual inspection of the raw data. Gains were calculated as the ratio of the difference in response to the difference in stimulus (i.e., 1.75 D) between the two viewing distances. To estimate the change in accommodative gain with induced anisometropia, only data from the left eye (with no lens before it) were used. To determine whether accommodation was consensual across

different viewing conditions, gains were calculated for both eyes. A gain of unity indicates a perfect response to the change in stimulus. If a subject provided multiple responses in each condition (typically five or six responses), the responses were averaged to obtain the overall mean accommodation and vergence gains.

The subjects were divided into five age groups: (≤ 1 year, 1 to ≤ 4 years, 4 to ≤ 8 years, 8 to ≤ 13 years, and adults ≥ 20 years) to keep the number of subjects approximately constant in each group. The effects of age and viewing condition on the response frequency (i.e., the percentage of the total number of epochs collected in each viewing condition that could be included in the analyses) and gain of accommodation and vergence were examined using two-factor ANOVA. Results of multiple-regression analyses of the effect of viewing condition on accommodative and vergence gains, with age as a continuous variable, were very similar to those of two-factor ANOVA, with no qualitative difference.

RESULTS

Data were successfully collected from 103 of the 118 subjects who participated in the study (Table 1). Data from 15 subjects were excluded because they had anisometropia >0.5 D in the vertical meridian or they failed to provide usable data in at least two anisometropia conditions. Of the remaining three criteria, individual responses were typically rejected because they failed to meet the criterion of correlation between gaze and stimulus position.

Two-factor ANOVA (viewing condition $\times$ age) of response frequency showed significant main effects of both viewing condition ($F_{(5,448)} = 11.13$; $P < 0.001$) and age ($F_{(4,448)} = 37.53$; $P < 0.001$) but no interaction ($F_{(20,448)} = 1.19$; $P = 0.26$; Fig. 2). A post hoc Games Howell test (with no assumption about equal variance in each group) for viewing condition showed that the response frequency for the binocular condi-

FIGURE 2. Mean ($\pm$ SE) response frequency (percentage of the total number of epochs collected that could be included in the analyses) plotted as a function of the level of induced anisometropia for the (a) <1-year-olds, (b) 2- to 4-year-olds, (c) 4- to 8-year-olds, (d) 8- to 13-year-olds, and (e) adults. A response frequency of 100% indicates that all the epochs that were collected were included in the analyses, and 0% indicates that none of the epochs that were collected were included. Zero on the abscissa is the binocular viewing condition.

tion was statistically significantly larger than the -4 D anisometropia condition only ($P < 0.001$). The four anisometropia conditions were not statistically significantly different from each other ($P > 0.7$ for all conditions), indicating that a similar proportion of usable epochs was included in all anisometropia conditions. The monocular condition was statistically significantly different from the binocular, -2 D, and $+4$ D anisometropia conditions ($P < 0.01$ for all conditions). A post hoc test for age indicated that the proportion of usable epochs included in the analyses gradually increased with age, with the response frequency in each age group significantly larger than all the preceding ones ($P < 0.005$ for all comparisons).

Raw accommodative and vergence data from a representative 2.3-year-old subject for different viewing conditions is shown in Figure 3. These raw data are representative of accommodative and vergence performance across all age groups. Visual inspection shows that the monocular accommodative and vergence responses were more attenuated than their binocular counterparts. When compared with the binocular condition, the accommodative and vergence responses reduced only marginally with different levels of induced anisometropia, with the size of the accommodative responses changing slightly more than those of the vergence responses. Typically, the eye without the lens (i.e., the effectively less ametropic eye) was more closely focused on the stimulus at all times, and the accommodative response in this eye appeared to track the stimulus. The fellow eye typically generated a consensual, accommodative response, resulting in chronic defocus of that eye's retinal image throughout the period of the experiment. Accommodative responses obtained using the PR were not calibrated for absolute accuracy in this study (they were calibrated only for their gain or slope as described earlier); therefore, quantitative analyses of the absolute states of accommodation in the two eyes were not performed.

The accommodative gain of the left eye (no lens) did not change dramatically as a function of the subjects' age or level of induced anisometropia (Fig. 4). The main effect of viewing

condition on the accommodative gain was statistically significant ($F_{(5,466)} = 14.7$; $P < 0.001$), the main effect of age approached statistical significance ($F_{(4,466)} = 2.3$; $P = 0.06$), and their interaction was not significant ($F_{(20,466)} = 1.5$; $P = 0.09$). A post hoc Games Howell test for viewing condition indicated that the binocular accommodative gain was statistically significantly larger than the gains under -4 D ($P = 0.006$), $+2$ D ($P = 0.001$), and $+4$ D ($P = 0.02$) anisometropia conditions. The four anisometropia conditions were not statistically significantly different from each other ($P > 0.14$ for all conditions). The monocular accommodative gain was statistically significantly smaller than the gains under all other viewing conditions ($P < 0.001$ for all conditions). These results indicate that the presence of induced anisometropia (2 D or more for myopic and 4 D for hyperopic anisometropia) significantly decreased the gain of accommodation from binocular conditions, but they all remained greater than the gains under monocular conditions.

Consensuality of accommodative gain in the right and left eyes was quantified in the binocular, $+2$ D, and -2 D anisometropia and monocular conditions. The $+4$ D and -4 D anisometropia conditions were not included in this analysis because the lens-induced shift in the raw accommodative data reached the limits of the PR's linear operating range in a number of subjects. Since the difference between left and right eye accommodative gain did not show any strong age-related trends, data from all ages were pooled for this analysis. Two-factor ANOVA (viewing condition $\times$ eye) of the accommodative gain showed a significant main effect of viewing condition ($F_{(3,634)} = 31.3$; $P < 0.001$) but not of eye ($F_{(1,634)} = 2.26$; $P = 0.13$). The interaction between viewing condition and eye was significant ($F_{(3,634)} = 3.88$; $P = 0.009$), indicating that the difference between left and right eye accommodative gain was not uniform across the four viewing conditions. However, the mean ($\pm 95\%$ confidence interval [CI]) difference in accommodative gain in the binocular, $+2$ D, and -2 D anisometropia and monocular conditions were -0.09 ± 0.35 , 0.08 ± 0.41 ,

FIGURE 3. Raw stimulus, right and left eye accommodation, and vergence data plotted as a function of time for a representative 2.3-year-old subject in all viewing conditions. The stimulus and response traces have been shifted vertically for the sake of clarity. The horizontal relationship between the two traces has not been altered. The abscissa and ordinate scales are shown in the bottom right. Dashed box, bottom middle: representative epoch used for calculating the correlation between gaze and stimulus position (third inclusion criterion). Bino, binocular; LE, left eye; mono, monocular; RE, right eye.

FIGURE 4. (a) Scatter plot of accommodative gain in the left eye as a function of the subject's age under binocular, monocular, and the four induced anisometropia conditions. Mean ($\pm$ SE) accommodative gain of the left eye plotted as a function of the level of induced anisometropia for the (b) <1-year-olds, (c) 2- to 4-year-olds, (d) 4- to 8-year-olds, (e) 8- to 13-year-olds, and (f) adults. All other details are the same as for Figure 2. Dashed lines: unity gain.

-0.11 ± 0.42 , and 0.08 ± 0.48 , respectively, indicating that there was minimal bias in the data and that the difference across viewing conditions should have little clinical significance. Overall, these results indicate that accommodative changes in the right and left eyes were consensual under the binocular, monocular, and +2 D and -2 D anisometropia conditions. Visual inspection of the raw data indicated that the accommodative responses were also consensual in the +4 D and -4 D anisometropia conditions.

Like accommodation, the vergence gain also did not change dramatically as a function of the subject's age and the level of induced anisometropia (Fig. 5). The main effect of viewing condition on the vergence gain was statistically significant ($F_{(5,466)} = 51.9$; $P < 0.001$), whereas the main effect of age was not ($F_{(4,466)} = 1.19$; $P = 0.32$). The interaction between viewing condition and age was only marginally significant ($F_{(20,466)} = 1.66$; $P = 0.04$). A post hoc Games Howell test for viewing condition indicated that the binocular vergence gain was not statistically significantly different from the gains in any anisometropia condition ($P > 0.39$ for all conditions) except for -4 D of anisometropia ($P < 0.001$). The vergence gain in the -4 D anisometropia condition was statistically significantly smaller than the gain in the +2 D ($P = 0.004$) and +4 D ($P = 0.05$) anisometropia conditions but only approached signifi-

cance in the -2 D anisometropia condition ($P = 0.07$). The gains across the remaining three anisometropia conditions (-2 D, +2 D, and +4 D) were not statistically significantly different from each other ($P > 0.8$ for all conditions). The monocular vergence gain was statistically significantly smaller than the vergence gains under all other viewing conditions ($P < 0.001$ for all conditions). Some level of binocular fusion, therefore, appears to remain even with ± 4 D of induced anisometropia, as indicated by the gains being statistically significantly higher than under monocular conditions.

Figure 6 plots the difference in accommodative and vergence gains between binocular and 11% induced aniseikonia conditions as function of the mean gain under the two viewing conditions for the 23 subjects (3.0 months-24.9 years) who participated in this condition (viewing was binocular; the 11% afocal magnifier was placed in front of the right eye). Mean ($\pm$ SE) accommodative (binocular, 0.77 ± 0.03 ; aniseikonia, 0.80 ± 0.06) and vergence (binocular, 0.87 ± 0.04 ; aniseikonia, 0.85 ± 0.04) gains in the two viewing conditions were not statistically significantly different (accommodation, $P = 0.63$; vergence, $P = 0.77$). The difference in gains between the two viewing conditions was distributed around zero, with the mean difference in accommodative gain -0.03 (95% CI, ± 0.24) and the mean difference in vergence gain 0.02 (95% CI, ± 0.25).

FIGURE 5. (a) Scatter plot of vergence gain as a function of the subject's age under binocular, monocular, and the four induced anisometropia conditions. Mean ($\pm$ SE) vergence gain of the left eye plotted as a function of the level of induced anisometropia for the (b) <1-year-olds, (c) 2- to 4-year-olds, (d) 4- to 8-year-olds, (e) 8- to 13-year-olds, and (f) adults. All other details are the same as for Figure 2. Dashed lines: unity gain.

FIGURE 6. The difference in accommodative (*light diamonds*) and vergence (*dark diamonds*) gains between binocular and 11% induced aniseikonia conditions, plotted as a function of the mean gain in the two viewing conditions. 95% CIs about the mean accommodative (*light dashed line*) and vergence (*dark dashed line*) gains are also shown.

These results suggest that the aniseikonia induced by the 11% afocal magnifier did not significantly influence the gain of accommodation and vergence in typically developing infants and children.

DISCUSSION

The impact of briefly introduced myopic and hyperopic anisometropia was assessed in this study. The accommodative and vergence responses were compared with those obtained under full binocular and monocular viewing conditions to determine the level of anisometropia at which performance might depart from habitual binocular levels and reach monocular levels. Binocular accommodative and vergence gains were close to unity for all ages tested, but their monocular counterparts were smaller in infants and there was a trend for the monocular gains to gradually increase with age to reach adult-like levels (Figs. 4, 5). These results are similar to those observed previously and reinforce the importance of binocular cues in driving both accommodation and vergence during typical visual development.^{32,61} The mean ($\pm$ SE) gains of adult accommodation (0.85 ± 0.06) and vergence (0.82 ± 0.04) obtained here are comparable to those obtained by Horwood et al.⁵⁴ (accommodation, 0.77; vergence, 0.71) for naive uninstructed adults using the PR. Most older children and adults who participated in the present study were largely naive to vision experiments (some adults had participated in previous experiments in the laboratory, but they were naive to the aims of the current experiment) and no specific instructions were provided to them. The resulting steady state errors in accommodation and vergence are larger than expected from experienced adults using strictly controlled psychophysical techniques. Mean vergence error in this study was approximately 0.8° (1.4 pd) for a 1.75-MA vergence demand for an adult with 6.1 cm IPD, as opposed to approximately 0.3° (0.5 pd) for the same vergence demand and IPD noted by Ogle and Mussey,⁶² suggesting that some subjects might have experienced residual blur and/or diplopia even under binocular viewing, although none of them described these symptoms.

Across all ages tested, accommodative and vergence gains reduced only marginally relative to full binocular conditions (accommodation slightly more than vergence) with up to ± 4 D of induced anisometropia (Figs. 4–6) and did not change significantly with 11% induced aniseikonia (Fig. 6). The gains with ± 4 D of induced anisometropia were still significantly larger than those obtained under monocular conditions (Figs. 4–6), suggesting that the typically developing visual system is

capable of accommodating and converging in the presence of transiently induced interocular differences in retinal image quality and that some level of binocularity is retained up to ± 4 D of induced anisometropia and with 11% induced aniseikonia. These population-level trends for a given age group were also observed on an individual basis, but the small sample size prevented further analysis. Overall, these results were qualitatively similar to those observed in previous adult studies.^{27,28,33,34,38–40}

Adult accommodative performance deteriorates significantly when the two eyes experience greater than 1 D difference in optical blur^{28,33} while binocular fusion prevails up to 3D of difference^{36,37} and up to 30% difference in contrast between the two monocular images.^{39,40} This study showed that the reduction in accommodative gain with induced anisometropia was larger than the reduction in vergence gain for all ages (Figs. 4, 5), suggesting that accommodation is more vulnerable to interocular differences in retinal image quality than vergence, although their relative impact on normal development is not known. The reduction in accommodative gain with induced change in anisometropia might be due to the combination of dissimilar monocular blur inputs from the two eyes,³³ whereas the reduction in vergence gain with induced anisometropia might be related to the spatial characteristics of Panum's fusional area (i.e., the sensory limit for perceiving diplopia). The primary effect of optical blur is to attenuate the high spatial frequency information in the image,^{63,64} leading to the loss of fine detail. With anisometropia, therefore, only the low spatial frequency content is common to the two eyes for fusion. In adults, the size of Panum's fusional area tends to be larger for low spatial frequencies than for high spatial frequencies,^{65,66} reducing the need for accurate motor vergence in fusing the low spatial frequency content in the image. The size of Panum's fusional area and its change with spatial characteristics of the target must be determined in infants and children to determine whether the current results are consistent with any of these theoretical predictions.

The accommodative system could adopt various strategies to optimize unequal blur in the two eyes resulting from anisometropia. Aniso-accommodative responses could be generated to overcome the dissimilar accommodative demands and achieve simultaneous focus in the two eyes.²⁷ The accommodative gains in this study were, however, not significantly different in the two eyes with ± 2 D of induced anisometropia, and the raw traces also showed qualitatively that the accommodative responses modulated by similar amounts with ± 4 D of induced anisometropia (Fig. 3). These results indicate that the developing accommodative system does not appear to use aniso-accommodation to achieve simultaneous focus in transient anisometropia.

The current results also do not provide any strong evidence for the use of a monovision type of focusing strategy for these ramp stimuli.^{28,34,35} With myopic anisometropia, the less ametropic eye could be used for distant viewing and the more myopic fellow eye could be used for near viewing, thereby achieving retinal image focus, at least for part of the time, in each eye.^{28,34,35} With this strategy, minimal modulation of accommodation would be expected in either eye with a change in target distance.³⁴ This trend was not seen in the current results (Figs. 4, 5). Instead, the raw accommodative traces demonstrated that the eye with no lens in front of it (left eye) typically tracked the stimulus continuously (Fig. 3). Use of the monovision and continuous tracking strategies, however, may depend on the temporal characteristics of visual stimulation.³⁴ Abrupt step changes in optical blur in the presence of induced anisometropia might result in minimal modulation of accommodation in the two eyes—a pattern expected with the monovision strategy—while slow ramp changes in optical blur

in the presence of induced anisometropia might result in one eye tracking the target³⁴ continuously, with the more ametropic fellow eye following consensually. In this study, the visual stimulus ramped slowly between 80 and 33 cm in front of the subject (Fig. 3), with the stimulus profile always starting at 80 cm. This starting point was optically more conjugate to the left eye, and this might have driven an accommodative tracking response in the left eye that persisted for the entire period of stimulation.

The pattern of consensual accommodative responses observed with myopic and hyperopic anisometropia implies that the more ametropic right eye experienced blurred vision for the entire period of stimulation (2–3 minutes). For instance, the average accommodative gain under binocular conditions was approximately 0.85 across all ages, and it was reduced to approximately 0.65 with 4 D of induced myopic and hyperopic anisometropia (Fig. 4b). The change in accommodative lag between the binocular and 4 D conditions was much larger in the right eye (with the lens before it) than in the left eye. Increased levels of sustained retinal blur, if experienced on a chronic basis, are likely to be associated with developmental abnormalities such as amblyopia.^{15,16} Indeed, Phillips⁶⁷ observed that myopic children who were under-corrected in the non-dominant eye (resulting in myopic anisometropia) continued to accommodate with the dominant distance corrected eye even after several months of adaptation to this type of prescription. This suggests that the pattern of focusing responses observed with transiently induced anisometropia may well be observed on a long-term basis, too.

The changes in disparity-driven vergence demand, blur-driven accommodative demand, and target proximity were always consistent with each other in the four induced anisometropia conditions. Accommodative responses in the anisometropia conditions could have been driven by some combination of blur, proximity, and disparity cues.^{23,68} The accommodative gains in the four induced anisometropia conditions were larger than the gain in the monocular viewing condition where blur and proximity were the primary cues to accommodation (Fig. 4). This indicates that the accommodative responses with induced anisometropia were not driven solely by monocular cues. The relative contribution of the different binocular and monocular sensory cues with induced-anisometropia remains to be determined.

Anisometropia tends to fluctuate during the initial years after birth, and it poses a significant risk for developmental abnormalities such as amblyopia. Determining when its presence might lead to cortical abnormalities and the nature of the visual experience during that period are important. This study observed that induced-anisometropia, albeit transient, resulted in a marginal decline in accommodative and vergence performance compared with habitual binocular viewing and that this decline was actually similar across age groups (Figs. 4, 5). A limitation of this study was that the long-term impact of the relatively small initial decline in oculomotor performance was not determined. However, the present study does address the question of the immediate impact on visual experience and, therefore, the distinction between normal and abnormal visual experience that arises purely as a result of the optical effects—a situation that clinicians consider frequently. Even though the reduction in gains was marginal, this evidence demonstrates that oculomotor performance and its impact on visual experience may not be fully normal with these amounts of anisometropia. The abnormal experience may extend beyond just blur in one eye, to include poor image correspondence and even poor accommodative performance in the dominant eye.

A second limitation of the study was that the impact of any underlying hyperopia or anisometropia in participants was not fully determined. Noncycloplegic refraction was measured in

the vertical meridian only here, and though this approach provided crude screening for anisometropia, it is possible that some subjects who were included in the study had an underlying spherical equivalent or astigmatic anisometropia greater than 0.5D that was missed as a result of astigmatism. Although the aim was to test the subjects relative to their habitual refractive state, the impact of any underlying hyperopia or anisometropia in persons on accommodative and vergence performance remains to be determined.

In conclusion, this study assessed the impact of transient lens-induced anisometropia and aniseikonia on the accommodative and vergence performance of typically developing infants and children. Accommodative and vergence gains of the typically developing visual system deteriorated marginally (accommodation more than vergence) with transiently induced anisometropia (up to ± 4 D) and did not deteriorate significantly with induced aniseikonia of 11% for all ages tested. The accommodative and vergence gains with induced anisometropia were, however, significantly higher than those under monocular conditions, suggesting that binocular cues remain with ± 4 D of induced anisometropia and 11% induced aniseikonia. Although the reduction in gains was marginal, the impact of this anisometropia on young patients is likely to include disruptions of image correspondence and even poor accommodative performance in the dominant eye.

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