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Astigmatism in Monkeys with Experimentally Induced Myopia or Hyperopia

CHEA-SU KEE, BS(Optom), MA(Bio), PhD, LI-FANG HUNG, OD, PhD, YING QIAO-GRIDER, MD, RAMKUMAR RAMAMIRTHAM, BS(Optom), and EARL L. SMITH III, OD, PhD, FAAO
College of Optometry, University of Houston, Houston, Texas; and Vision CRC, University of New South Wales, Sydney, Australia

Abstract

Purpose—Astigmatism is the most common ametropia found in humans and is often associated with large spherical ametropias. However, little is known about the etiology of astigmatism or the reason(s) for the association between spherical and astigmatic refractive errors. This study examines the frequency and characteristics of astigmatism in infant monkeys that developed axial ametropias as a result of altered early visual experience.

Methods—Data were obtained from 112 rhesus monkeys that experienced a variety of lens-rearing regimens that were intended to alter the normal course of emmetropization. These visual manipulations included form deprivation ($n = 13$); optically imposed defocus ($n = 48$); and continuous ambient lighting with ($n = 6$) or without optically imposed defocus ($n = 6$). In addition, data from 19 control monkeys and 39 infants reared with an optically imposed astigmatism were used for comparison purposes. The lens-rearing period started at approximately 3 weeks of age and ended by 4 to 5 months of age. Refractive development for all monkeys was assessed periodically throughout the treatment and subsequent recovery periods by retinoscopy, keratometry, and A-scan ultrasonography.

Results—In contrast to control monkeys, the monkeys that had experimentally induced axial ametropias frequently developed significant amounts of astigmatism (mean refractive astigmatism = 0.37 ± 0.33 D [control] vs. 1.24 ± 0.81 D [treated]; two-sample t -test, $p < 0.0001$), especially when their eyes exhibited relative hyperopic shifts in refractive error. The astigmatism was corneal in origin (Pearson's r ; $p < 0.001$ for total astigmatism and the JO and J45 components), and the axes of the astigmatism were typically oblique and bilaterally mirror symmetric. Interestingly, the astigmatism was not permanent; the majority of the monkeys exhibited substantial reductions in the amount of astigmatism at or near the end of the lens-rearing procedures.

Conclusions—In infant monkeys, visual conditions that alter axial growth can also alter corneal shape. Similarities between the astigmatic errors in our monkeys and some astigmatic errors in humans suggest that vision-dependent changes in eye growth may contribute to astigmatism in humans.

Keywords

astigmatism; ametropia; refractive error; primate; emmetropization

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Astigmatism is the most common refractive error, occurring frequently in both healthy (for a review, see reference 1) and diseased eyes.^{2–4} For instance, in a recent multicentered, school-based study (ages 5–17 years), significant amounts of astigmatism were more prevalent (≥ 1.0

D, 28.4%) than myopia (≥ -0.75 D, 9.2%) or hyperopia ($\geq +1.25$ D, 12.8%).⁵ However, astigmatic errors, particularly large astigmatic errors, are frequently associated with significant spherical ametropias. Although emmetropes or subjects who have low degrees of spherical ametropia usually also exhibit small amounts of astigmatism, subjects who have high amounts of myopia or hyperopia frequently exhibit high amounts of astigmatism.^{6–11} In fact, it has been reported that the magnitudes of astigmatism and myopia are linearly correlated in children¹² and young adults.^{7,13}

Why is astigmatism associated with spherical ametropias? Although mechanical factors such as eyelid tension^{2,3,14} and ocular rigidity¹⁵ have been implicated in the genesis of astigmatism, little is known about the etiology of astigmatism or the mechanism(s) underlying the association between astigmatism and spherical ametropia. However, our recent studies in monkeys^{16,17} indicate that visual experience can alter corneal shape resulting in astigmatism. Specifically, when we reared infant monkeys with cylinder lenses in front of their eyes, we found that the optically imposed astigmatism not only altered emmetropization resulting in axial ametropias,¹⁷ but it also promoted the development of significant amounts of astigmatism.¹⁶ However, the fact that the axis of the ocular astigmatism was not in the appropriate direction to neutralize the astigmatic errors imposed by the treatment lenses suggested that the eye does not have an active vision-dependent “sphericalization” process analogous to emmetropization.¹⁸ Instead, the ocular astigmatism found in the cylinder lens-reared monkeys, which was associated with both axial myopia and hyperopia,¹⁷ seemed to be a byproduct of the vision-dependent mechanisms that regulate axial elongation and the emmetropization process. If this is true, then eyes that experienced altered refractive-error development as a result of other visual manipulations should also show a high frequency of astigmatism.

A variety of rearing strategies have been shown to predictably alter refractive development. For example, in many different animal species, including humans, form deprivation consistently produces axial myopia (e.g., humans,¹⁹ rhesus monkeys,²⁰ marmosets,²¹ tree shrews,²² and chickens²³). Moreover, optically imposing either myopia or hyperopia in young animals with spherical lenses results in compensating axial ametropias that are dependent on the sign and power of the treatment lenses (e.g., rhesus monkeys,²⁴ marmosets,²⁵ tree shrews,²⁶ and chickens²⁷). However, in part because experimentally induced refractive errors have traditionally been expressed in a spherical-equivalent format (i.e., the averaged correction for the two principal astigmatic meridians), only a few studies in chickens have previously noted an association between astigmatism and either axial hyperopia or myopia.^{28,29} The purpose of this study was to determine if vision-dependent alterations in axial growth also lead to the development of astigmatism in primates. Specifically, we examined the frequency and characteristics of astigmatism in infant monkeys that developed axial ametropias in response to a variety of different types of altered visual experience.

METHODS

Subjects

Data were obtained from 112 experimental monkeys (*Macaca mulatta*) that were each subjected to one of a variety of lens-rearing regimens early in life. An advantage of including monkeys reared under a variety of conditions was that, as a group, the experimental monkeys exhibited a wide range of spherical-equivalent refractive errors (-7.50 D to $+8.50$ D) that were primarily axial in nature.

All of the monkeys were obtained at 2 to 3 weeks of age and were housed in our primate nursery that was maintained on a 12-hour light/12-hour dark lighting cycle. After the initial biometry measurements that were performed at approximately 3 weeks of age, the monkeys were

randomly assigned to either the control group (normal unrestricted vision, $n = 16$; bilateral plano lenses, $n = 3$)^{16,17,30–32} or one of the experimental groups. The details of the individual rearing regimens and our methods for assessing refractive development have been described in detail in previous studies^{16,24,32–35} and are therefore outlined briefly here. All of the rearing and experimental procedures were reviewed and approved by the University of Houston's Institutional Animal Care and Use Committee and were in compliance with the Association for Research in Vision and Ophthalmology Statement on the Use of Animals in Ophthalmic and Vision Research.

Visual Manipulations

To control an animal's visual experience, we used lightweight helmets to hold diffuser lenses or spherical- or cylindrical-powered spectacle lenses in front of one or both eyes of infant monkeys. The lens-rearing regimens were started at approximately 3 weeks of age (mean = 23.4 days; range = 16–35 days), and the monkeys wore the helmets and treatment lenses continuously for an average of 109 ± 15 days. After the lens-rearing period, the helmets were removed and the monkeys resumed unrestricted vision.

Form Deprivation by Diffusers ($n = 13$)—A wide range of predominantly axial myopia was produced by rearing individual monkeys with one of three different diffuser lenses (weakest, $n = 3$; intermediate, $n = 4$; strongest, $n = 6$) over one eye while the fellow eyes viewed through plano lenses.³³ The different diffusers produced varying degrees of image degradation. The strongest diffusers reduced the spatial contrast sensitivity for normal human observers by more than 1 log unit at 0.125 cycles/degree (c/deg) with a resulting cutoff spatial frequency below 1 c/deg, whereas the weakest diffusers decreased contrast sensitivity by only 0.1 log units at 0.125 c/deg and by 0.75 log units at 8 c/deg.

Optically Imposed Defocus by Spherical Lenses ($n = 48$)—The effective refractive errors of these infant monkeys were altered by securing spherical spectacle lenses (+12 to –6 D) in front of one ($n = 4$) or both eyes ($n = 44$). Although most of the treated monkeys wore constant and equal-powered lenses in front of both eyes throughout the treatment period (positive, $n = 10$; negative, $n = 14$), two rearing strategies were used to increase the magnitude of the compensating ametropias. In one case, the treatment-lens powers were increased systematically in either the negative or positive directions for both eyes during the treatment period (sequential positive increments, $n = 6$; sequential negative increments, $n = 4$). The goal was to maintain a relatively constant degree of imposed hyperopia or myopia throughout the treatment period. In a second group of monkeys that wore positive lenses in front of one eye and negative lenses in front of the other eye, the degree of imposed anisometropia was increased systematically during the treatment period by increasing the power of the lenses in front of each eye. To ensure that the animals in this group actively fixated with both eyes, each eye was occluded for half the daily lighting cycle with the occluder being switched between the eyes halfway through the lighting cycle (alternating occlusion group, $n = 10$).

Continuous Ambient Lighting ($n = 12$)—Twelve infants were reared under continuous ambient lighting beginning at approximately 1 month of age.^{34,35} Half of these monkeys were reared with unrestricted vision (the “control” group for continuous light, $n = 6$), whereas the other half were reared with either +3.0 D ($n = 3$) or –3.0 D lenses ($n = 3$) in front of one eye and plano lenses in front of the fellow eye from the onset of continuous light until 4 months of age. All the animals were returned to a normal diurnal lighting cycle at an average age of 207.1 ± 15.7 days.

Optically Imposed Astigmatism ($n = 39$)—This group of monkeys was included for comparison purposes because we had previously shown that these animals developed *both*

axial myopia or hyperopia¹⁷ and significant amounts of astigmatism.¹⁶ During the rearing period, with-the-rule (WTR), against-the-rule (ATR), and oblique astigmatism were optically imposed by appropriately orienting the principal meridians of the spherocylindrical treatment lenses (+1.50–3.00 × 90, 180, 45, or 135). Six animals wore cylindrical lenses over one eye that optically imposed WTR astigmatism, whereas six others experienced monocular ATR astigmatism; the fellow eyes of these animals viewed through plano lenses. Twenty-seven animals wore cylindrical lenses in front of both eyes. For 19 of these binocularly treated animals, the direction of imposed astigmatism was the same in each eye (WTR, $n = 7$; ATR, $n = 6$; or oblique astigmatism, $n = 6$). Eight animals experienced ATR astigmatism with their right eyes and WTR astigmatism with their left eyes.^{16,17}

Biometry Measurements

Beginning at the onset of the treatment period and typically every 2 to 3 weeks thereafter, refractive error, corneal curvature, and the eye's axial dimensions were measured by retinoscopy, keratometry, and A-scan ultrasonography, respectively. To perform these measurements, the monkeys were anesthetized (intramuscular injection of 15–20 mg/kg ketamine hydrochloride and 0.15–0.2 mg/kg acepromazine maleate; topically 1–2 drops of 0.5% tetracaine hydrochloride) and cyclopleged (multiple drops of 1% tropicamide topically 20–30 minutes before retinoscopy). Spectacle-plane refractive corrections along the eye's pupillary axis were determined independently by two investigators using a streak retinoscope and handheld trial lenses. The mean spherocylindrical corrections were calculated³⁶ and specified in minus cylinder notation. The retinoscopy measurements were reasonably repeatable with 95% limits of agreement of ± 0.60 and ± 0.45 D for spherical-equivalent¹⁷ and astigmatic errors, respectively. Corneal curvature was measured with a handheld keratometer (Alcon Auto-keratometer; Alcon Systems Inc., St. Louis, MO) and/or a videotopographer (EyeSys 2000; EyeSys technologies Inc., Houston, TX). We have previously shown that both instruments provide repeatable and comparable measures of corneal curvature in infant monkeys.³² Ocular axial dimensions were measured by A-scan ultrasonography implemented with a 7-MHz transducer (Image 2000; Mentor, Norwell, MA). Intraocular distances were calculated from the average of 10 separate measurements using a weighted average velocity of 1550 m/sec.

Data Analysis

Minitab (release 12.21; Minitab Inc., State College, PA) or JMP Statistics (version 4, SAS Institute, Cary, NC) software were used for statistical analyses. Comparisons between the two eyes of a given monkey were made using paired t-tests. Comparisons across groups were performed using one-way analyses of variance (ANOVAs). If the one-way ANOVA revealed a significant effect, Tukey's pairwise comparisons were used to determine which groups were significantly different. Rayleigh's test³⁷ was used to determine whether the axis of astigmatism was randomly distributed in our subject populations. To determine the relationship between two dependent variables (e.g., corneal astigmatism and refractive astigmatism), a regression line was generated using orthogonal regression analysis.³⁸

RESULTS

Refractive Characteristics: Onset and End of the Treatment Period

At the onset of our experiment, the infant monkeys exhibited very similar refractive properties in their two eyes. As a group, there were no significant interocular differences in spherical-equivalent refractive error, corneal curvature, or the magnitude of refractive (i.e., as measured by retinoscopy) or corneal astigmatism (paired t-test, $p = 0.07$ – 0.64). Moreover, at the end of the lens-rearing period, there were no significant interocular differences between the left and right eyes of control and binocularly treated animals (paired t-test, $p = 0.13$ – 0.69).

Consequently, for the following statistical analyses, we used the right-eye data from the control and binocularly treated animals, data for both eyes from the alternating-occlusion group, and the treated-eye data from animals subjected to the monocular rearing regimens. As shown in Table 1 and Figure 1 (open symbols), there were no significant differences in either the spherical-equivalent refractive error or the magnitude of refractive or corneal astigmatism between the control animals and any experimental group at the onset of the experiment (open symbols, one-way ANOVA, all $p > 0.28$). In general, the infant monkeys' eyes were moderately hyperopic (median = +4.13 D) with only small amounts of refractive (median = 0.13 D) or corneal astigmatism (median = 0.55 D).

By approximately 4 months of age (Fig. 1, filled symbols), i.e., at or near the end of the treatment period, both the control animals reared under diurnal lighting conditions and those that were reared under continuous ambient lighting conditions had become less hyperopic (i.e., emmetropization occurred) and showed similar refractive errors (diurnal light: median = +2.4 D, range = +0.88 to +5.38 D; constant light: median = +2.8 D, range = +1.69 to +3.50 D; see also Table 1). All of the lens-rearing regimens significantly altered the normal course of emmetropization and led to either relative myopic or hyperopic refractive errors (one-way ANOVA, all $p \leq 0.001$). The direction of the refractive-error changes was typically consistent within a given experimental group.^{16,24,32–35} Compared with control monkeys, relative myopia was found in monkeys reared with diffusers or negative spectacle lenses, whereas relative hyperopia was found in the monkeys that were treated with positive lenses (range = -7.5 to +7.0 D). The cylinder lens-reared animals also showed a wider range of spherical-equivalent refractive errors (range = -4.6 to +8.5 D) than the control animals at the end of the treatment period. The spherical-equivalent refractive errors observed in the experimental subjects were significantly correlated with vitreous chamber depth (Pearson's $r = -0.82$, $p < 0.001$). In addition to the expected alterations in spherical ametropia, the lens-rearing regimens also resulted in significantly higher amounts of refractive (Table 1; Fig. 1B) and corneal astigmatism (Table 1; Fig. 1C) (one-way ANOVAs, $p < 0.01$). However, there were no significant differences in the average corneal curvatures (i.e., average of the steeper and flatter corneal meridians) between the control and experimental animals (one-way ANOVA, $p = 0.34$).

Frequency of Ocular Astigmatism

Figures 2–4 illustrate the longitudinal changes in the magnitude of refractive (filled symbols) and corneal astigmatism (open symbols) that occurred during the treatment period for representative monkeys reared with diffusers, negative lenses, and positive lenses, respectively. The experimental monkeys in each figure were chosen because, as a group, they exhibited the range of astigmatic errors found in each treatment group. As shown in Figures 2–4, in all treatment groups, the magnitudes of refractive and corneal astigmatism typically increased systematically over time but tended to level off after approximately 3 months of age. Although higher magnitudes of astigmatism were typically found near the end of the lens-rearing period, the highest amounts of astigmatism for individual monkeys were often achieved before the end of the treatment period (Fig. 2: KIT, IRA, BEN; Fig. 3: ZEB, FAI; Fig. 4: KYL, WIN, SAM, CHU). However, in all animals, both the increases and the decreases in the magnitudes of refractive and corneal astigmatism were closely synchronized in time.

Figure 5 compares the frequency of refractive (left column) and corneal astigmatism (right column) in the control animals and the different groups of experimental monkeys at 4 months of age. Because there were no significant differences in the magnitudes of refractive (two-sampled t-test, $T = 0.18$, $p = 0.86$) or corneal astigmatism (two-sampled t-test, $T = -0.34$, $p = 0.74$) between the control group reared under normal diurnal lighting conditions and the control animals that were reared under constant light, their data were combined for the following

analyses. Overall, the frequency of significant astigmatism (defined as >1.0 D) in the treated groups was much higher than that in the control groups. Although none of the control monkeys had more than 1.0 D of refractive astigmatism, the percentage of treated monkeys that showed >1.0 D of refractive astigmatism varied from 21.4–66.7% for the four experimental groups (chi-squared test, $df = 4$, $p < 0.001$). Similarly, although only 20% of the control monkeys showed >1.0 D of corneal astigmatism, 53.8–83.3% of the experimental monkeys had corneal astigmatic errors that were >1.0 D (chi-squared test, $df = 4$, $p < 0.001$). One-way ANOVAs showed that at 4 months of age, all of the experimental groups had significantly higher magnitudes of refractive and corneal astigmatism (mean value marked by the arrows in Fig. 5) than the control monkeys ($df = 4$, both $p < 0.001$; Tukey's pairwise comparisons).

Properties of the Astigmatism

Axis of Astigmatism—The axes of the refractive and corneal astigmatism were similar for all of the experimental regimens and were typically oblique and mirror-symmetric in the two eyes. To illustrate the characteristics of the ocular astigmatism, the polar plots in Figure 6A show the distributions of astigmatism for the right (filled symbols) and left eyes (open symbols) of individual experimental monkeys at 4 months of age. The magnitude and axis of astigmatism for individual monkeys are represented by the distance from the origin of the polar plots and the vector angle, respectively. It is obvious from the plots that the axes for both refractive and corneal astigmatism were clustered along the oblique meridians. Because there were no apparent differences in the direction of the astigmatism between the different treatment groups (Fig. 6A), the data from all of the experimental groups were pooled. Rayleigh's test³⁷ showed that the axes for both refractive and corneal astigmatism were not randomly distributed in either eye (all $r_2 > 0.63$, $p < 0.001$). For the right eyes, the axes for refractive and corneal astigmatism were clustered about means of 145.5° and 145.0° , respectively. The axes for refractive and corneal astigmatism for the left eyes were clustered about means of 30.7° and 22.1° , respectively. These mean values were very similar to the average astigmatic axes observed previously in cylinder lens-reared monkeys (right: refractive = 135.1° , corneal = 139.9° ; left: refractive = 38.9° , corneal = 31.6°).¹⁶ Furthermore, like in the cylinder lens-reared monkeys, the axis of astigmatism was fairly stable during development. For instance, the average standard deviation of the astigmatic axes during the emergence of astigmatism for the 49 treated eyes that developed at least 1.0 D of refractive astigmatism was 11.2° (median = 9.0° ; the standard deviation for individual monkeys was calculated by analyzing all the data from the time the magnitude of astigmatism first exceeded 0.50 D until the time when the highest amount of astigmatism was detected).

To quantify the symmetry of the astigmatic axes in the two eyes, we calculated for individual monkeys the angular difference between the normal astigmatic axis for the right eye and the "reflected" astigmatic axis for the fellow left eye (referred to subsequently as the "reflected difference"). The reflected axes for the left eyes were calculated by subtracting the left eyes' axes from 180° . For example, the reflected axis for an axis of 30° is 150° . Figure 6B shows the distributions of the "reflected differences" for the experimental monkeys that wore diffusers or spherical lenses. The reflected differences for refractive and corneal astigmatism were less than $\pm 30^\circ$ in 77.6% and 62.7% of the treated monkeys, respectively. Furthermore, Rayleigh's test revealed that the reflected differences between the two eyes were not randomly distributed, but instead were clustered near 0° for both refractive and corneal astigmatism (refractive: mean = -4.3° ; $r_2 = 0.64$; corneal: mean = -11.5° , $r_2 = 0.59$; $n = 67$, $p < 0.001$), indicating that the axes of astigmatism in the two eyes were mirror-symmetric.

Refractive vs. Corneal Astigmatism—Figure 7 compares the three astigmatic components for refractive and corneal astigmatism at 4 months of age for individual animals, i.e., the total amount of astigmatism, the J0 component, which primarily represents with- or

against-the-rule astigmatism, and the J45 component, which primarily represents oblique astigmatism. The J0 and J45 astigmatic components were decomposed from the spherocylindrical correction by Fourier analysis.³⁹ Because there were no differences in the magnitudes of refractive or corneal astigmatic components between the treatment groups (one-way ANOVA, all $p > 0.56$), data from the different treatment groups were pooled for statistical analysis. Pearson's correlational analysis indicated that the corneal and refractive astigmatic errors were significantly correlated for all three components ($r = 0.83, 0.55$ and 0.84 for total astigmatism, the J0, and the J45 components, respectively; all $p < 0.001$). Presumably, the correlation was higher for the J45 versus the J0 component because the astigmatic errors were typically oblique. The slopes of the best-fitting lines obtained using orthogonal regression analysis (short-dashed lines in Fig. 6) were 0.82 for total astigmatism, 0.60 for the J0 components, and 1.14 for the J45 components, in agreement with the values that we previously observed in cylinder lens-reared monkeys (0.86 for total astigmatism, 0.38 for J0, and 0.76 for J45).¹⁶

Reversibility of the Astigmatic Errors—The astigmatism that developed during the treatment period was reversible. Figure 8A illustrates the longitudinal changes in refractive and corneal astigmatism that occurred during and after the lens-rearing period for four representative monkeys. These four monkeys were among those monkeys in each treatment group that developed high amounts of astigmatism. As shown in Figure 8A, these monkeys showed systematic increases and decreases in the magnitudes of refractive and corneal astigmatism during the observation period. The recovery from the highest magnitudes of astigmatism frequently occurred before the end of the treatment period (see also Figs. 2–4).

Almost all of the experimental monkeys that developed significant amounts of astigmatism showed complete recovery from astigmatism. Figure 8B shows the magnitudes of refractive and corneal astigmatism for individual monkeys at three time points, i.e., at the onset of the rearing period, at the time when the highest magnitude of astigmatism was observed, and at approximately 9 months of age. One-way ANOVAs and Tukey's pairwise comparisons showed that the magnitudes of the peak refractive (1.74 ± 0.93 D) and corneal astigmatism (2.13 ± 0.84 D) were significantly higher than those at the onset of the experiment or at 9 months of age (both $p < 0.001$). In contrast, there were no significant differences in the magnitudes of refractive (0.17 ± 0.19 vs. 0.40 ± 0.38 D) or corneal astigmatism (0.66 ± 0.37 vs. 0.58 ± 0.40 D) at 1 and 9 month of age, indicating that the monkeys had recovered fully by 9 months of age.

Association of Astigmatism with Spherical Ametropias

If the experimental monkeys had spherical ametropias that fell outside the range for control monkeys, they were more likely to exhibit higher than normal amounts of ocular astigmatism. Figure 9A shows the magnitude of refractive astigmatism at 4 months of age as a function of the refractive error for the most hyperopic meridian for control monkeys (open circles) and monkeys that wore spherical lenses in front of both eyes (filled diamonds). Although none of the control monkeys exhibited more than 1.0 D of refractive astigmatism, as a group, the experimental monkeys showed a wide range of astigmatic errors. The experimental monkeys that had spherical ametropias that were similar to those of control monkeys usually exhibited smaller amounts of refractive astigmatism. In contrast, the experimental animals that had larger spherical ametropias typically also had high amounts of refractive astigmatism. Figure 9B illustrates the frequency distributions of spherical ametropia for the same control and experimental monkeys. The data for the lens-reared monkeys were subdivided into groups according to the degree of astigmatism. As shown in Figure 9B, the range of spherical ametropias in lens-reared monkeys was much larger than in control monkeys. In particular, the distributions of spherical ametropia in the experimental monkeys that exhibited the higher

amounts of astigmatism were broader and shifted in the hyperopic direction relative to the mode of control monkeys. Indeed, all of the monkeys that exhibited more than 2.0 D of astigmatism had hyperopic refractive errors that were greater than +3.8 D.

The association between high amounts of spherical ametropia and high amounts of astigmatism was also observed in experimental monkeys from the other treatment groups. Figure 10 shows data at 4 months of age for monkeys that were treated with monocular or binocular cylindrical lenses (A), monocular spherical lenses (B), and monocular diffusers (C). In general, the more the spherical ametropia deviated from the control values, the more likely it was that the monkey would have high amounts of refractive astigmatism. To quantify the relationship between the magnitude of spherical ametropia and the magnitude of refractive astigmatism, we pooled the data obtained at 4 months of age from control monkeys and all of the experimental monkeys. Because the slopes of the functions on either side of the median value for the control animals (i.e., +2.4 D) had opposite signs (see Figs. 9A and 10), we specified ametropia as the absolute difference from the median value for control animals. For example, the “absolute difference” for a spherical myopia of -1.0 D was 3.4 D. Pearson’s correlational analysis showed that the magnitude of refractive astigmatism was significantly correlated with the absolute difference in spherical ametropia from the median value for control monkeys (Pearson’s $r = 0.26$; $p = 0.002$). Analyzing the data for experimental animals with relative hyperopic and myopic errors separately revealed that the degree of correlation between spherical ametropia and the magnitude of astigmatism was stronger for hyperopes (Pearson’s $r = 0.39$; $p < 0.001$) than for myopes (Pearson’s $r = 0.13$; $p = 0.33$).

DISCUSSION

The main findings of this study were that 1) in contrast to control monkeys, experimental monkeys that developed axial ametropias also showed a high frequency of significant astigmatism; 2) high amounts of astigmatism were more frequently associated with large spherical ametropias, especially high hyperopia; 3) the characteristics of the experimentally induced astigmatic errors were similar for all of the experimental lens-rearing regimens; and 4) the astigmatic errors observed in the experimental monkeys were corneal in nature, oblique in axis, bilaterally mirror-symmetric, and reversible.

In addition to the well-known effects of visual experience on spherical refractive development and axial growth,^{17, 20,24,33,35,40,41} the results of the present study show that a wide range of visual experiences can also alter corneal development resulting in astigmatic errors. In particular, both open-loop viewing conditions that result in unregulated axial elongation (e.g., form-deprivation) and closed-loop viewing conditions that either increase (negative lenses) or decrease axial growth (positive lenses) alter corneal shape and produce qualitatively very similar astigmatic errors. The close similarity in the properties of these astigmatic errors reinforces the conclusion reached in our previous study of cylinder lens-reared monkeys,¹⁶ specifically that the observed astigmatism is a secondary outcome or side effect of vision-dependent alterations in axial growth associated with the emmetropization process. Although in our experiments, visual experience provided the stimulus for altered axial growth, it is possible that any condition that perturbs axial growth would produce similar astigmatic changes. In this respect, the presence of significant amounts of corneal astigmatism, and specifically oblique astigmatism in monkeys, can be taken as an indicator that the normal axial growth of the eye has been or is being altered. On the other hand, the recovery from the induced astigmatic errors, which could be an age-dependent phenomenon, may be taken as an indication that the stimulus for altered axial growth has been reduced or eliminated (for example, after an eye has compensated for an optically induced ametropia) or that axial growth rates have returned to normal.

A variety of visual manipulations have also been shown to alter corneal development in chickens.^{28,29,42–47} For example, rearing chickens with cylinder lenses results in greater than normal amounts of astigmatism,^{28,29} and rearing chickens with form deprivation results in astigmatic errors that are significantly different from those in their fellow control eyes.²⁸ Moreover, as observed in our experimental monkeys, the astigmatic errors produced in chickens by these viewing conditions were largely corneal in nature and associated with altered axial growth.^{28,29} It has previously been argued that the many similarities between chickens and monkeys in the emmetropization process and in the effects of visual experience on spherical refractive development (see, for example, reference 48) indicate that the vision-dependent mechanisms that regulate ocular growth have generally been conserved across species. The fact that the effects of visual experience on the eye's astigmatic error are also comparable in monkeys and chickens reinforces this idea and suggests that visual experience may promote astigmatic errors in other species, including humans.

Although oblique astigmatism is not common in humans, the properties of the astigmatism observed in our experimental monkeys are comparable to those reported in humans in many respects. First, as numerous human studies have shown,^{1,49–53} the induced astigmatism in our experimental monkeys was primarily corneal in nature. Second, as observed in our monkeys, bilateral mirror symmetry in the axes of astigmatism (Fig. 6) has been commonly observed in clinical practice⁵⁴ and has been found in large-scale clinical studies^{55,56} (however, see also reference 57). Third, the magnitude of astigmatism in monkeys and humans is correlated with the amount of spherical ametropia.^{7,8,11–13} In particular, the correlation coefficient ($r = 0.26$) between the magnitude of astigmatism and spherical ametropia found in our experimental monkeys is very similar to the degree of correlation observed in humans (e.g., astigmatism and myopia, $r = 0.38$,⁷ 0.12 ,¹² 0.20 ,¹³ and 0.15 ¹¹; astigmatism and hyperopia, $r = 0.28$ ¹¹). Moreover, as observed in our experimental monkeys (Fig. 9), high amounts of astigmatism have been more frequently associated with high hyperopia than high myopia in humans.^{8,58} Fourth, astigmatism is frequently transient and reversible during early childhood in humans when axial growth rates are high.^{59–66} The similarities in the properties of astigmatic errors between humans and our experimental monkeys suggest that visual experience may contribute to common astigmatic errors found in humans.

What is the etiology of the corneal astigmatism observed in the experimental monkeys? We have previously shown that the development of astigmatism in cylinder lens-reared monkeys appears to be caused by altered corneal flattening rates in the two oblique meridians, i.e., the steeper principal meridian flattens at a slower-than-normal rate, whereas the flatter principal meridian flattens at a faster-than-normal rate. The resulting alterations in corneal curvature are associated with changes in corneal diameter. Specifically, the steeper principal meridian, which is in the superior–nasal to inferior–temporal direction, also has a smaller corneal diameter than the flatter principal meridian.¹⁶ The consistent and characteristic direction of the induced astigmatic errors suggests that vision-dependent alterations in astigmatism are a consequence of some normal and consistent anisotropy in ocular physiology or anatomy. For example, it is possible that the induced astigmatism reflects regional variations in the cornea's biomechanical properties that are impacted by the development of axial ametropias. In this respect, the collagen fibrils in the center of the human cornea^{67–69} are not randomly oriented, but are predominantly oriented in the superior–inferior or nasal–temporal directions. It is likely that this anisotropy contributes to the predominance of WTR and ATR astigmatism in humans and presumably the low prevalence of oblique astigmatic errors.^{1,9,70,71} Interestingly, the corneal collagen fibrils in the marmoset are predominantly oriented in only the superior–inferior direction.⁷² Although the distribution of collagen fibril orientations in the macaque monkey is not known, measures of corneal polarization suggest that the predominate fibril orientation in macaques is different from those in humans,⁷² which could explain why ametropic monkeys

typically manifest oblique astigmatism, whereas humans typically have WTR or ATR astigmatism.

WTR corneal astigmatism has been observed in humans during convergence, which suggests that mechanical forces exerted by extraocular muscles could potentially alter corneal shape.^{73,74} Because the insertions of the oblique muscles are somewhat aligned with the flatter principal meridians in our experimental monkeys, one could imagine that when the eyes were undergoing axial ametropic changes, the actions of the oblique muscles on the posterior globe could somehow produce astigmatism. For example, the normal tension exerted by the oblique muscles on the posterior globe may be influenced by the altered mechanical properties of the sclera during the development of refractive errors⁷⁵ and indirectly alter corneal shape. If this is the case, we would expect that eyes that developed axial hyperopia would exhibit different directions of astigmatism than axially myopic eyes. Obviously, our results are not consistent with this prediction.

The observed alterations in corneal diameter and corneal curvature could reflect asymmetries in the growth and/or the biomechanical properties of the sclera. It has been reported that in human myopes, the shape of the posterior pole is different in the vertical and horizontal meridians; specifically, the horizontal meridian is more prolate in shape.⁷⁶ It is not clear how this would affect corneal diameter and/or curvature, but the direction of this anisotropy corresponds to the most common directions of astigmatism in humans.^{1,9,70,71} It is possible that vision-induced alterations in axial growth in monkeys produce similar asymmetries in the shape of the posterior globe in the oblique meridians. A longitudinal investigation of eyeball shape (particularly the posterior segment) in animals that are subjected to altered early visual experience could shed light on the etiology of astigmatism.

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APPENDIX

Tables A1, A2, and A3 with data to Figures 6A, 6B, and 7A–C are available online only at www.optvissci.com.

FIGURE 1.

The average magnitudes of spherical-equivalent refractive error (A), refractive astigmatism (B), and corneal astigmatism (C) at the onset of the experiment (open symbols) and at 4 months of age (filled symbols) for the control and experimental groups. Control, control monkeys reared under normal diurnal lighting conditions; CL "control," control group reared under continuous light; Sph, spherical lenses; CL, monkeys reared under continuous light. In contrast to the control groups, all of the experimental lens-rearing regimens resulted in significant spherical ametropias and significant amounts of refractive and corneal astigmatism.

FIGURE 2.

Refractive (filled symbols) and corneal astigmatism (open symbols) as a function of age for the treated eyes of eight representative monkeys that were reared with diffusers in front of one eye. The figures are arranged in order according to the maximum magnitude of refractive astigmatism observed during the treatment period (range = 0.5–5.6 D). The strength of the diffusers is indicated in the parentheses after the three-letter name code (“W,” weakest; “I,” intermediate; “S,” strongest).

Negative Lenses

FIGURE 3.

Refractive (filled symbols) and corneal astigmatism (open symbols) as a function of age for the right eyes for eight representative monkeys that wore negative spherical lenses in front of both eyes. The exact lens-rearing strategy, either involving fixed lens powers or sequential increases in power (“Seq”), is indicated in the parentheses after the three-letter name code. The peak refractive astigmatism for individual monkeys ranged from 0.98 to 3.25 D. See Figure 2 for details.

Positive Lenses **FIGURE 4.**

Refractive (filled symbols) and corneal astigmatism (open symbols) as a function of age for the right eyes for eight representative monkeys that wore positive spherical lenses in front of both eyes. The peak refractive astigmatism for individual monkeys ranged from 0.25 to 3.49 D. See Figures 2 and 3 for details.

FIGURE 5.

Frequency distributions of refractive (left column) and corneal astigmatism (right column) for control monkeys and experimental monkeys that were subjected to the different lens-rearing regimens. The number of subjects within each group and the percentage of subjects with astigmatism > 1.0 D are indicated in each plot. The arrow along the abscissa in each plot marks the mean astigmatic error for each group. Tukey's pairwise comparisons indicate that all experimental groups had significantly higher magnitudes of refractive and corneal astigmatism than the control animals.

FIGURE 6.

A: The distributions of refractive and corneal astigmatism in the right (filled symbols) and the left eyes (open symbols) for all the experimental monkeys at approximately 4 months of age, i.e., near the end of the treatment period. The magnitude and axis of astigmatism for an individual monkey are represented by the radius and the angular direction in the polar plots, respectively. The different lens-rearing regimens are represented by different symbols. B: Frequency distributions of the reflected differences between the cylinder axes in the two eyes for all treated monkeys. The reflected difference between the correcting cylinder axis in the two eyes is equal to the right eye's cylinder axis minus the left eye's reflected cylinder axis (i.e., $180 - \text{axis of astigmatism}$). The different lens-rearing regimens are represented by the different fill patterns. The data for Figure 6A and 6B are available online at www.optvissci.com.

FIGURE 7.

The correlations between corneal and refractive astigmatism at 4 months of age. Although the total astigmatism (A), the cosine JCC component (J0) (B), and the sine JCC component (J45) (C) were all significantly correlated at the end of the treatment period, the correlation for the J0 component was weaker than those for the other two components. Diamond = spherical lenses; up triangle = diffusers; down triangle = constant light with spherical lenses. The data for Figure 7A–C are available online at www.optvissci.com.

FIGURE 8.

A: Refractive and corneal astigmatism as a function of age for the right eyes of four representative experimental monkeys that developed relatively large amounts of astigmatism. The lens-rearing regimens are indicated in the parentheses after the three-letter name codes (Sph, spherical lens; Cyl, cylindrical lens; Dif, diffuser; CL, constant light with spherical lenses). The black bar in each plot indicates the lens-rearing period. B: Magnitudes of refractive and corneal astigmatism for individual experimental monkeys at three time points, specifically, at the onset of the experiment (“initial”), when the peak astigmatism occurred during the treatment period (“peak”), and approximately 5 months after lens removal (“recovery”).

FIGURE 9.

A: The magnitude of refractive astigmatism measured at 4 months of age is plotted as a function of the ametropia for the most hyperopic meridian for control (open symbol) and experimental monkeys that were reared with binocular spherical lenses (filled symbol). B: Frequency distributions of the ametropias for the most hyperopic meridian in control (open bars) and spherical lens-reared monkeys (filled bars). Data from the experimental monkeys were divided into subgroups according to the magnitude of refractive astigmatism as indicated in each histogram.

FIGURE 10.

The magnitude of refractive astigmatism is plotted as a function of the ametropia for the most hyperopic meridian for monkeys reared with binocular or monocular spherocylindrical lenses (A), monocular spherical lenses (B), and monocular diffusers (C). For comparison purposes, data for the 19 control monkeys (open symbols) are included in each plot.

TABLE 1
Refractive characteristics (mean $\pm$ standard deviation) at the onset and end of the treatment period.

Group	Spherical equivalent refractive error (D)			Refractive astigmatism (D)			Corneal astigmatism (D)		
	Start	End	Difference	Start	End	Difference	Start	End	Difference
Control	3.65 $\pm$ 1.87	2.48 $\pm$ 0.97	-1.17 $\pm$ 1.94	0.18 $\pm$ 0.28	0.38 $\pm$ 0.33	0.20 $\pm$ 0.42	0.74 $\pm$ 0.66	0.63 $\pm$ 0.36	-0.11 $\pm$ 0.69
Diffusers	4.03 $\pm$ 1.40	-1.59 $\pm$ 3.69	-5.62 $\pm$ 3.26	0.19 $\pm$ 0.23	1.26 $\pm$ 1.03	1.07 $\pm$ 0.99	0.62 $\pm$ 0.36	1.53 $\pm$ 1.18	1.08 $\pm$ 1.35
Cylindrical lenses	4.36 $\pm$ 1.45	2.82 $\pm$ 2.64	-1.54 $\pm$ 2.49	0.16 $\pm$ 0.15	1.31 $\pm$ 0.81	1.15 $\pm$ 0.80	0.50 $\pm$ 0.41	1.68 $\pm$ 0.95	1.17 $\pm$ 1.05
Spherical lenses									
Plus	4.30 $\pm$ 1.22	4.17 $\pm$ 1.92	-0.13 $\pm$ 1.68	0.15 $\pm$ 0.21	1.34 $\pm$ 0.97	1.20 $\pm$ 1.05	0.62 $\pm$ 0.43	1.60 $\pm$ 0.97	1.02 $\pm$ 1.23
Minus	4.18 $\pm$ 1.33	0.88 $\pm$ 2.58	-3.30 $\pm$ 2.40	0.22 $\pm$ 0.23	1.05 $\pm$ 0.57	0.83 $\pm$ 0.59	0.68 $\pm$ 0.36	1.25 $\pm$ 0.86	0.52 $\pm$ 0.95
Constant light									
No lens	3.79 $\pm$ 1.28	2.73 $\pm$ 0.68	-1.06 $\pm$ 0.80	0.15 $\pm$ 0.15	0.35 $\pm$ 0.34	0.20 $\pm$ 0.35	0.81 $\pm$ 0.61	0.70 $\pm$ 0.43	-0.12 $\pm$ 0.62
Plus	5.38 $\pm$ 0.72	5.35 $\pm$ 1.10	-0.02 $\pm$ 0.67	0.12 $\pm$ 0.12	1.42 $\pm$ 0.52	1.01 $\pm$ 0.31	0.58 $\pm$ 0.28	1.77 $\pm$ 0.42	1.17 $\pm$ 0.59
Minus	3.08 $\pm$ 0.51	1.79 $\pm$ 1.48	-1.29 $\pm$ 1.39	0.21 $\pm$ 0.08	1.22 $\pm$ 0.24	1.30 $\pm$ 0.60	0.62 $\pm$ 0.00	1.84 $\pm$ 0.89	1.68 $\pm$ 0.57

TABLE A1

Figure 6A data. The magnitude and axis of astigmatism for a data point are given in adjacent columns within a row. The data are divided into subgroups according to the lens-rearing regimens. For example, the numbers in the first two cells under the headings "Sph-OD-Rast" and "Sph-OD-Rxis" represent a monkey from the "spherical lenses" group that has 1.00 D of astigmatism with 150-degree axis in its right eye.

Sph-OD-Rast	Sph-OD-Rxis	Sph-OS-Rast	Sph-OS-Rxis	CL-OD-Rast	CL-OD-Rxis	CL-OS-Rast	CL-OS-Rxis	Dif-OD-Rast	Dif-OD-Rxis	Dif-OS-Rast	Dif-OS-Rxis
1.0000	150.0000	1.5000	30.0000	0.9659	127.5000	0.4986	46.2476	0.5000	180.0000	0.0000	0.0000
1.5000	130.0000	0.5966	62.1869	1.2500	160.0005	1.2500	40.0006	3.2500	135.0000	2.2196	46.6819
0.2500	0.0000	0.1243	0.0010	1.4489	142.5000	1.6250	60.0000	2.4905	117.5000	2.7086	64.5408
0.8233	168.5118	1.1098	6.6819	0.9436	137.4004	0.4130	151.7032	0.6879	126.9176	0.5590	58.2825
1.0000	0.0000	1.0000	0.0000	1.9696	155.0000	1.4772	155.0000	0.2500	0.0010	0.7099	6.5412
0.5000	160.0000	0.6250	0.0000	1.3543	144.5408	0.9848	45.0000	0.5000	0.0000	0.6250	0.0004
1.0649	156.5412	0.1250	0.0000					0.8233	171.4882	1.0580	168.8421
0.9848	165.0000	0.7048	10.0000					0.9886	122.4808	0.9397	30.0000
0.6250	160.0000	0.6159	13.9901					1.0000	160.0000	1.0000	45.0000
0.3953	125.7825	0.2500	0.0000					0.9848	145.0000	2.2162	24.4388
1.2928	120.9476	1.1777	32.9183					0.6250	0.0000	0.0005	90.0010
0.7603	147.6425	0.8458	38.5961					1.0000	180.0000	0.5000	180.0000
1.0000	0.0000	2.0000	45.0000					3.2614	138.3527	1.6189	37.3072
0.6159	173.9901	0.9397	10.0000								
1.4095	100.0000	0.8750	40.0000								
0.2495	0.0010	0.0011	90.0027								
0.3750	150.0000	0.2500	0.0000								
1.8679	142.6671	0.7806	178.0511								
0.7471	137.5000	0.3750	80.0000								
1.8750	140.0000	0.9763	16.8352								
1.7240	125.7215	1.1208	42.2215								
0.7475	138.3352	0.0872	87.5000								
0.9848	145.0000	0.6159	53.9901								
1.0000	135.0000	1.0000	35.0000								
1.2318	143.9901	0.8233	11.4882								
2.4905	132.5000	2.2500	40.0000								
0.5000	0.0005	0.5000	0.0030								
1.7422	141.3207	0.4698	35.0000								
2.2415	137.2215	0.4698	50.0000								
4.6780	145.2659	0.9848	25.0000								
0.4698	120.0000	0.7273	55.0520								
2.0804	139.3196	1.6467	28.5118								
0.4507	96.9489	1.3750	110.0000								
1.3285	126.8023	0.7386	25.0000								
1.1250	140.0000	1.0871	38.3527								
1.8466	134.6633	2.2415	42.2215								
1.5000	135.0000	0.2462	95.0000								
1.3681	159.1046	1.2473	31.2863								
0.6614	39.5533	1.2318	16.0099								
0.7399	133.3181	0.7500	30.0000								
1.1250	100.0000	0.7500	45.0000								
0.9962	132.5000	1.1208	47.7785								
0.2500	80.0000	0.2496	20.0369								
1.7500	130.0000	1.8750	30.0000								
3.4867	132.5000	1.6016	33.8349								
1.4943	132.5000	1.6250	50.0000								
1.8750	135.0000	1.9329	36.5408								
0.7399	163.3181	1.6191	46.9217								

Sph-OD- RAst	Sph-OD-RXIs	Sph-OS- RAst	Sph-OS-RXIs	CL- OD- RAst	CL-OD- RXIs	CL- OS- RAst	CL-OS- RXIs	Dif-OD- RAst	Dif-OD- RXIs	Dif-OS- RAst	Dif-OS- RXIs
1.6100	126.9288	0.9714	11.5000	0.9148	137.5291	0.5432	179.5000	0.6035	126.8814	0.7796	30.8532
0.6409	104.8666	0.6923	174.3350	1.8957	0.2385	1.6692	7.9367	3.4249	148.7012	2.7290	44.3469
0.2175	92.0000	0.2067	114.0000	2.7008	148.3537	2.4510	58.6102	2.2798	116.0000	2.4867	60.8505
0.7492	162.8223	3.1511	7.2473	1.2798	154.2286	1.2107	173.7514	1.4810	135.3856	1.0720	54.0742
1.9893	164.7431	2.6834	8.9758	2.0778	148.5603	1.3972	5.7226	0.7794	134.3360	0.4524	29.4392
1.1453	169.9116	1.0332	8.2410	1.9126	122.9564	1.4119	16.4131	0.2891	148.3920	0.3662	0.7959
1.8874	149.7943	0.0003	90.0010					1.6436	165.9040	1.1792	157.1684
0.2801	167.5828	2.4642	174.5952					1.0756	135.6757	1.1914	19.0941
1.1333	132.7751	0.3333	28.0000					0.7555	138.5264	1.4957	48.9988
1.0948	156.9028	0.8894	35.2752					0.9793	136.5693	2.7562	17.3511
1.1077	146.0723	1.3573	30.8520					0.6406	140.0811	1.2244	48.5011
1.1548	164.8999	0.3211	56.7154					1.5791	169.2704	0.3733	42.0000
2.3547	2.1297	0.0005	90.0020					4.3282	150.9908	2.0781	174.8592
0.6580	157.5557	1.9031	10.6807								
0.4720	25.0453	1.1900	36.8917								
0.1586	179.7187	0.6679	33.9055								
0.5238	136.0673	0.4107	168.4176								
2.5738	153.0970	2.2677	176.4638								
0.6615	146.9911	0.1233	84.0000								
2.3183	165.2139	1.6289	13.3546								
2.6922	130.2630	1.6614	40.3363								
2.0236	125.1691	0.8274	31.7437								
1.2191	131.3115	1.2891	63.0334								
0.4350	138.0000	0.9349	31.4652								
1.2284	151.6168	1.0768	2.5450								
2.9731	129.4378	2.7546	22.6349								
1.1822	173.3657	0.2384	10.9774								
2.2086	142.0597	0.1909	23.1517								
3.1511	140.0495	0.8726	13.7690								
4.5284	147.8255	1.2473	19.3821								
0.8756	109.3236	0.4190	147.0610								
2.8437	136.3095	2.4948	22.7237								
0.4523	114.3820	1.0419	98.1445								
1.4866	153.6469	1.4241	9.1912								
1.4684	140.2181	0.8058	27.0667								
2.2977	158.1168	2.2961	43.3761								
1.4141	136.3294	0.2016	49.7793								
2.2458	152.0742	1.6685	22.2165								
1.0999	158.5435	1.6219	1.2832								
1.3550	131.7666	1.2206	5.0268								
0.2098	144.5000	1.0672	3.6817								
0.5527	123.0000	0.7337	27.4404								
0.2875	37.7068	0.6220	9.3252								
2.0438	134.2288	2.3872	16.3146								
2.6137	122.3965	2.5525	23.3942								
2.5173	137.3587	1.8921	18.6541								
1.4583	127.2059	2.0544	29.8509								

Sph-OD- CAst	Sph-OD-CXis	Sph-OS- CAst	Sph-OS-CXis	CL- OD- CAst	CL- OD- CXis	CL- OS- CAst	CL- OS- CXis	Dif-OD- CAst	Dif-OD- CXis	Dif-OS- CAst	Dif-OS- CXis
0.4922	175.3924	2.4380	22.8180								

Sph, spherical lenses; CL, "CL" spherical lenses; Dif, diffusers; RAst, refractive astigmatism; CAst, corneal astigmatism; OD, right eye; OS, left eye.

TABLE A2

Figure 6B data. The frequency distributions for different lens-rearing groups are given in separate columns. For example, the column with heading “Sph-RAst-F” contains frequency distribution of refractive astigmatism for monkeys that were reared with spherical lenses.

Axis-Bin	Sph-RAst-F	CL-RAst-F	Dif-RAst-F	Sph-CAst-F	CL-CAst-F	Dif-CAst-F
-90.0000	1.0000	0.0000	0.0000	2.0000	1.0000	0.0000
-80.0000	1.0000	0.0000	1.0000	1.0000	0.0000	0.0000
-70.0000	1.0000	0.0000	0.0000	0.0000	0.0000	0.0000
-60.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
-50.0000	1.0000	0.0000	0.0000	0.0000	0.0000	0.0000
-40.0000	1.0000	0.0000	0.0000	2.0000	1.0000	0.0000
-30.0000	2.0000	0.0000	0.0000	2.0000	0.0000	1.0000
-20.0000	7.0000	0.0000	1.0000	10.0000	1.0000	3.0000
-10.0000	5.0000	0.0000	1.0000	7.0000	0.0000	1.0000
0.0000	14.0000	1.0000	4.0000	8.0000	0.0000	1.0000
10.0000	5.0000	1.0000	4.0000	2.0000	0.0000	3.0000
20.0000	3.0000	0.0000	0.0000	3.0000	0.0000	1.0000
30.0000	1.0000	2.0000	1.0000	1.0000	1.0000	0.0000
40.0000	2.0000	0.0000	0.0000	2.0000	0.0000	1.0000
50.0000	3.0000	0.0000	0.0000	1.0000	0.0000	0.0000
60.0000	0.0000	0.0000	0.0000	2.0000	0.0000	0.0000
70.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
80.0000	0.0000	0.0000	0.0000	1.0000	0.0000	0.0000
90.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
100.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
110.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
120.0000	1.0000	2.0000	1.0000	4.0000	2.0000	2.0000

Sph, spherical lenses; CL, “CL” spherical lenses; Dif, diffusers; RAst, refractive astigmatism; CAst, corneal astigmatism.

TABLE A3

Figure 7A–C data. Figure 7A–C. Astigmatic components for a data point are represented in separate columns within a row. The data are divided into subgroups according to the lens-rearing regimens. For example, the three cells under the headings of “Sph-RCyl”, “Sph-RJ0” and “Sph-RJ45” contain the refractive astigmatism, refractive J0 and refractive J45, respectively, for a monkey reared with spherical lenses.

Sph-RCyl	Sph-RJ0	Sph-RJ45	Sph-CCyl	Sph-CJ0	Sph-CJ45	CL-RCyl	CL-RJ0	CL-RJ45	CL-CCyl	CL-CJ0	CL-CJ45	Dif-RCyl	Dif-RJ0	Dif-RJ45	Dif-CCyl	Dif-CJ0	Dif-CJ45
1.0000	0.2500	-0.4330	1.6100	-0.2238	-0.7733	0.9659	-0.1250	-0.4665	0.9148	0.0403	-0.4556	0.5000	0.2500	0.0000	0.6035	-0.0844	-0.2897
1.5000	-0.1302	-0.7386	0.6409	-0.2783	-0.1589	1.2500	0.4788	-0.4017	1.8957	0.9478	0.0079	3.2500	0.0000	-1.6250	3.4249	0.7881	-1.5203
0.2500	0.1250	0.0000	0.2175	-0.1085	-0.0076	1.4489	0.1875	-0.6998	2.7008	0.6069	-1.2063	2.4905	-0.7142	-1.0200	2.2798	-0.7018	-0.8983
0.8233	0.3790	-0.1607	0.7492	0.3092	-0.2114	0.9436	0.0395	-0.4701	1.2798	0.3980	-0.5011	0.6879	-0.0958	-0.3303	1.4810	0.0100	-0.7404
1.0000	0.5000	0.0000	1.9893	0.8569	-0.5050	1.9696	0.6330	-0.7544	2.0778	0.4736	-0.9247	0.2500	0.1250	0.0000	0.7794	-0.0090	-0.3896
0.5000	0.1915	-0.1607	1.1453	0.5375	-0.1975	1.3543	0.2214	-0.6399	1.9126	-0.3903	-0.8730	0.5000	0.2500	0.0000	0.2891	0.0651	-0.1290
1.0649	0.3637	-0.3889	1.8874	0.4660	-0.8206							0.8233	0.3936	-0.1205	1.6436	0.7243	-0.3883
0.9848	0.4264	-0.2462	0.2801	0.1271	-0.0588							0.9886	-0.2092	-0.4479	1.0756	0.0127	-0.5377
0.6250	0.2394	-0.2009	1.1333	-0.0440	-0.5649							1.0000	0.3830	-0.3214	0.7555	0.0464	-0.3749
0.3953	-0.0625	-0.1875	1.0948	0.3789	-0.3951							0.9848	0.1684	-0.4627	0.9793	0.0268	-0.4889
1.2928	-0.3045	-0.5702	1.1077	0.2088	-0.5130							0.6250	0.3125	0.0000	0.6406	0.0565	-0.3153
0.7603	0.1624	-0.3438	1.1548	0.4990	-0.2904							1.0000	0.5000	0.0000	1.5791	0.7348	-0.2888
1.0000	0.5000	0.0000	2.3547	1.1741	0.0874							3.2614	0.1904	-1.6196	4.3282	1.1462	-1.8357
0.6159	0.3012	-0.0641	0.6580	0.2331	-0.2322												
1.4095	-0.6623	-0.2410	0.4720	0.1514	0.1810												
0.2495	0.1247	0.0000	0.1586	0.0793	-0.0008												
0.3750	0.0938	-0.1624	0.5238	0.0098	-0.2617												
1.8679	0.2470	-0.9007	2.5738	0.7599	-1.0385												
0.7471	0.0326	-0.3722	0.6615	0.1344	-0.3022												
1.8750	0.1628	-0.9233	2.3183	1.0081	-0.5721												
1.7240	-0.2743	-0.8172	2.6922	-0.2216	-1.3278												
0.7475	0.0434	-0.3712	2.0236	-0.3404	-0.9528												
0.9848	0.1684	-0.4627	1.2191	-0.0783	-0.6045												
1.0000	0.0000	-0.5000	0.4350	0.0227	-0.2163												
1.2318	0.1901	-0.5858	1.2284	0.3366	-0.5138												
2.4905	-0.1085	-1.2405	2.9731	-0.2868	-0.14586												
0.5000	0.2500	0.0000	1.1822	0.5753	-0.1357												
1.7422	0.1906	-0.8500	2.2086	0.2694	-1.0709												
2.2415	0.0868	-1.1174	3.1511	0.2763	-1.5511												
4.6780	0.8204	-2.1904	4.5284	0.9801	-2.0410												
0.4698	-0.1175	-0.2034	0.8756	-0.3419	-0.2734												
2.0804	0.1562	-1.0284	2.8437	0.0650	-1.4204												
0.4507	-0.2188	-0.0541	0.4523	-0.1491	-0.1701												
1.3285	-0.1875	-0.6373	1.4866	0.4504	-0.5913												
1.1250	0.0977	-0.5540	1.4684	0.1330	-0.7220												
1.8466	-0.0109	-0.9233	2.2977	0.8297	-0.7947												
1.5000	0.0000	-0.7500	1.4141	0.0328	-0.7063												
1.3681	0.5100	-0.4559	2.2458	0.6303	-0.9293												
0.6614	0.0625	0.3248	1.0999	0.4028	-0.3745												
0.7399	-0.0217	-0.3693	1.3550	-0.0763	-0.6732												
1.1250	-0.5286	-0.1924	0.2098	0.0341	-0.0992												
0.9962	-0.0434	-0.4962	0.5527	-0.1124	-0.2525												
0.2500	-0.1175	0.0428	0.2875	0.0362	0.1391												
1.7500	-0.1519	-0.8617	2.0438	-0.0275	-1.0215												
3.4867	-0.1519	-1.7367	2.6137	-0.5566	-1.1824												
1.4943	-0.0651	-0.7443	2.5173	0.1035	-1.2544												
1.8750	0.0000	-0.9375	1.4583	-0.1959	-0.7023												
0.7399	0.3090	-0.2034	0.4922	0.2429	-0.0394												

Sph, spherical lenses; CL, “CL” spherical lenses; Dif, diffusers; RCyl, refractive astigmatism; R0, refractive J0; RJ45, refractive J45; CCyl, corneal astigmatism; C0, corneal J0; CJ45, corneal J45.