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Amblyopia in Astigmatic Children: Patterns of Deficits

Erin M. Harvey $^{\ast,1,2},$ Velma Dobson $^{1,3},$ Joseph M. Miller $^{1,2,4},$ and Candice E. Clifford-Donaldson 1

1 Department of Ophthalmology and Vision Science, The University of Arizona, Tucson, AZ

2College of Public Health, The University of Arizona, Tucson, AZ

3Department of Psychology, The University of Arizona, Tucson, AZ

4The Optical Sciences Center, The University of Arizona, Tucson, AZ

Abstract

Neural changes that result from disruption of normal visual experience during development are termed amblyopia. To characterize visual deficits specific to astigmatism-related amblyopia, we compared best-corrected visual performance in 330 astigmatic and 475 non-astigmatic kindergarten through 6th grade children. Astigmatism was associated with deficits in letter, grating and vernier acuity, high and middle spatial frequency contrast sensitivity, and stereoacuity. Although grating acuity, vernier acuity, and contrast sensitivity were reduced across stimulus orientation, astigmats demonstrated orientation-dependent deficits (meridional amblyopia) only for grating acuity. Astigmatic children are at risk for deficits across a range of visual functions.

Over the past several decades, clinical research has provided valuable insights into the role of visual experience in the development and organization of the visual system. Clinically, although specific diagnostic criteria vary, visual deficits that are present in the absence of any ocular causes are termed *amblyopia*, and are attributed to neural changes related to disruption of normal visual experience during early development. The relation between the cause of the deficits (i.e., amblyogenic factors), the patterns of the observed deficits, and the treatability of these deficits at various stages of development has provided researchers and clinicians with information on how and when development of the visual system is susceptible to the effects of abnormal visual input, and by implication, what types of visual experience are essential for normal development.

The goal of the present study is to characterize the patterns of visual deficits that result from uncorrected astigmatism in early childhood. This form of amblyopia differs from the forms of amblyopia most commonly studied in the literature (anisometropic and strabismic amblyopia) in that it is (a) often bilateral, reducing or eliminating potential effects of suppression, and (b) occurs as a result of orientation-specific blur and often results in stimulus orientation-dependent visual deficits.

^{*}Corresponding author Mailing Address: The University of Arizona, Department of Ophthalmology and Vision Science, 655 N. Alvernon Way, Suite 108, Tucson, AZ 85711-1824. Tel: 520-324-3162, fax:520-324-3161 E-mail address: emharvey@u.arizona.edu

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In astigmatism, refractive error varies across meridia. As a result, individuals with uncorrected astigmatism experience orientation-dependent defocus. The graphic in Figure 1 (Harvey, 2002, Harvey, Dobson, Miller, & Sherrill, 2004b, revised from Gwiazda, Mohindra, Brill, & Held, 1985) illustrates how the optical properties of astigmatism influence the quality of visual input. The examples illustrate the effects of with-the-rule astigmatism (i.e., plus cylinder axis near 90 deg), as all astigmatic subjects included in the present study had with-the-rule astigmatism. Patterns of blur that result from uncorrected astigmatism are dependent upon the orientation (in this case, with-the-rule) and type (e.g., hyperopic/myopic) of astigmatism present. Individuals with hyperopic astigmatism (sphere (plus cyl) ≥ 0 , Figure 1G and 1H) might be expected to experience greater blur for vertical than for horizontal stimuli, while individuals with myopic or mixed with-the-rule astigmatism (sphere (plus cyl) < 0, Figure 1D, 1E, and 1F) would be expected to experience greater blur for horizontal than for vertical stimuli. However, the predictions regarding the effects of astigmatism are somewhat complicated due to the fact that hyperopic astigmats can accommodate to bring either stimulus orientation into focus, can accommodate between the two focal points, or can fluctuate accommodation between the two focal points (Mitchell, Freeman, Millodot, & Haegerstrom, 1973), and due to the fact that, when viewing near targets, myopic and mixed astigmats may experience greater blur for vertical than for horizontal stimuli.

Previous research has demonstrated that astigmatic subjects will often have poor best-corrected acuity for stimulus orientations for which they experienced greatest optical blur during early development. This effect, termed meridional amblyopia (MA) (Mitchell et al., 1973), has been documented in measurements of grating acuity in both humans (Atkinson, Braddick, Bobier, Anker, Ehrlich, King, Watson, & Moore, 1996; Cobb & MacDonald, 1978; Dobson, Miller, Harvey, & Mohan, 2003A; Freeman, 1975a; Freeman, Mitchell, & Millodot, 1972; Gwiazda, Scheiman, & Held, 1984; Mitchell et al., 1973; Mitchell & Wilkinson, 1974; Mohindra, Jacobson, & Held 1983) and monkeys (Boothe & Teller, 1982), vernier acuity (Gwiazda, Bauer, Thorn, & Held 1986; Mitchell et al., 1973), contrast sensitivity in both humans (Freeman, 1975b; Freeman & Thibos, 1975; Mitchell & Wilkinson, 1974) and monkeys (Boothe & Teller, 1982, Harwerth, Smith, & Boltz, 1980, Harwerth, Smith & Okundaye, 1983), and stereoacuity (Mitchell et al, 1973). In addition to these orientation-dependent differences in visual function, previous studies have documented reduced best-corrected vision associated with astigmatism relative to normal in measures of recognition acuity (letters or shapes) (Atkinson et al., 1996; Dobson et al., 2003a; Dobson, Tyszko, Miller, & Harvey, 1996; Harvey, 2002; Kershner & Brick, 1984).

In the present study, the effects of astigmatic defocus on the development of visual function are evaluated through use of a comparison of the effects of astigmatism across a variety of visual functions (letter acuity, grating acuity, vernier acuity, contrast sensitivity, and stereoacuity) relative to a normal (non-astigmatic) age-matched control group from the same population tested in exactly the same manner.

Early data from a relatively small number of subjects suggest that optical correction of astigmatism prior to age seven years can prevent the development of MA (Cobb & MacDonald, 1978; Mitchell et al., 1973; Mohindra et al., 1983), and data from two more recent studies indicate that the sensitive period for correction of astigmatism may be as young as two years (Gwiazda et al., 1986; Harvey et al., 2004b). Because results of previous studies suggest that early eyeglass correction may reduce or eliminate the negative effects of astigmatism on visual development, history of previous eyeglass wear was included in data analyses.

The present study is unique in that it includes a large sample of astigmatic subjects all tested on a variety of visual functions, allowing for detailed analysis of the effects of different patterns

of astigmatic blur (i.e., hyperopic vs. myopic astigmatism) and varying amounts of astigmatism on visual development.

METHODS

Subjects

The present study was conducted on the Tohono O'odham reservation, located in southern Arizona. This location was chosen because previous research has indicated that Tohono O'odham children and adults have an unusually high prevalence of astigmatism (Dobson, Miller, & Harvey, 1999a, Dobson, Miller, Harvey, & Sherrill, 1999b; Harvey, Dobson, & Miller, in press), and that many have developed non-optical visual deficits consistent with a history of uncorrected astigmatism (Dobson et al., 1996; Dobson et al., 2003a; Harvey et al., 2004b).

Subjects included in the present study were children in grades K-2 (recruited during the 2003/04 school year) and children in grades 4-6 (recruited during the 2001/02 school year) who attended one of five elementary schools located on the Tohono O'odham Reservation. Recruitment dates for the two cohorts were designed to minimize the possibility of recruiting children who had participated in a previous eyeglass treatment study of preschool children from the same population conducted from 1997-2001 (Dobson et al., 2003a, Harvey et al., 2004b; Miller, Dobson, Harvey, & Sherrill, 2000, 2001).

Children from a sixth elementary school on the reservation participated in a preliminary study during the 2000/01 and 2001/02 school year (Harvey, 2002). This study was conducted to collect preliminary data, and to finalize testing materials and procedures so that no differences between younger and older cohort data could reasonably be attributed to changes that were implemented between testing dates for the older and younger cohorts (2001/02 vs. 2003/04). Since no changes were made to the study protocol based on the results of the preliminary study, data from K-2nd and 4th- 6th grade children tested in 2000/01 or 2001/02 as part of the preliminary study were included in the present analysis.

The research was approved by the Institutional Review Board of the University of Arizona. Written informed consent was obtained from a parent or guardian prior to a child's participation and written assent was obtained from children in grades 4 through 6.

Procedures

Each child was scheduled to participate in an eye examination, followed by a baseline bestcorrected vision testing session. The eye examination, which was conducted by a pediatric ophthalmologist (JMM), included cycloplegic refraction at least 40 min after instillation of one drop of proparacaine (0.5%) and two drops of cyclopentolate (1%) separated by an interval of 5 min. Children were prescribed eyeglasses if they had \geq 2.00 diopters (D) of astigmatism in either eye, or if they had uncorrected letter acuity worse than 20/20 and met one or more of the following criteria: myopia \geq 0.75 D in either meridian, hyperopia \geq 2.50 D in either meridian, astigmatism \geq 1.00 D in either eye, anisometropia \geq 1.50 D spherical equivalent.

Prescriptions were determined by cycloplegic autorefraction (Nikon Retinomax K+, Nikon Inc, Tokyo, now manufactured by Righton Ophthalmic Instruments., Tokyo), confirmed by retinoscopy and subjective refinement (when possible). Correction of hyperopic refractive error was reduced by one-third or by 1.00 D, whichever was greater (Guyton, Miller, & West, 2003).

Baseline vision testing session was conducted approximately 2-3 weeks after the eye examination. Although not all children were prescribed eyeglasses, all wore eyeglasses

containing their refractive correction during vision testing. This was done so that measurements of all children would reflect their best possible vision, to minimize the variability of accommodative demand, and to mask the testers as to which children had been prescribed eyeglasses. For children who did not meet the prescribing criteria, the eyeglasses used during testing were selected from a set of "placebo" eyeglasses, with the restriction that right and left lenses were no more than 0.50 vector dioptric difference from the child's refractive error (calculation method described by Long, 1976, and modified by Harris, 1990).

A team of trained testers conducted five vision tests on each child: monocular distance logMAR letter acuity, monocular grating acuity for vertical, horizontal, and oblique stimuli, monocular vernier acuity for vertical, horizontal, and oblique stimuli, monocular contrast sensitivity for low, middle, and high spatial frequency vertical and horizontal sinewave grating stimuli, and stereoacuity. Due to time constraints and the limited attention span of young children, monocular assessments were limited to the right eye (RE), except that, for clinical reasons, monocular letter acuity was tested for both eyes. During monocular testing, the fellow eye was occluded with 5-cm wide adhesive paper tape (3M Micropore, Minneapolis, MN). Test order was counterbalanced across subjects.

Letter (Recognition) Acuity

Letter acuity was tested at a distance of 4 m using the 62- by 65-cm Early Treatment Diabetic Retinopathy Study (ETDRS) logMAR letter acuity charts (Ferris, Kassoff, Bresnick, & Bailey, 1982) mounted in an illuminator cabinet (Precision Vision, Inc., LaSalle, IL). Chart 1 was used for testing the RE, which was always tested first, and chart 2 was used for testing the left eye (LE). Beginning with the top line (20/200), the subject was asked to identify all five letters on each line, until he or she could no longer identify *any* letter on a line. Children who were unsure of their letters were given a lap card that contained the ten letters that appear on the chart, and were asked to respond by matching the letters on the chart to the letters on the card. Acuity was scored as the smallest letter size on which subjects identified at least three out of the five letters on the line. Threshold acuity scores were transformed to log values for data analyses.

Grating (Resolution) Acuity

Grating acuity stimuli were constructed using unmounted Teller Acuity Cards (Vistech Consultants, Inc., Dayton, OH) (Teller, McDonald, Preston, Sebris, & Dobson, 1986). Each Teller Acuity Card contains a 12.5-by 12.5-cm patch of grating surrounded by a luminance-matched gray background. The cards are constructed so that when an individual is unable to resolve the grating, the grating patch appears a uniform gray that matches the rest of the card.

The Teller Acuity Cards could not be used as manufactured because they included only vertical stimuli. Several sets of unmounted cards were purchased, and vertical, horizontal, and oblique grating stimuli were constructed by mounting the grating and a piece of matching gray area from the same card behind 5.6-cm diameter circular apertures to produce stimuli that could be used in a 3-alternative-forced-choice (3AFC) task. The subject's task was to identify which one of the circles (number 1, 2, or 3) contained the grating. Stimuli for four 3AFC trials were constructed for each of 12 grating spatial frequencies for each of the three stimulus orientations.

The stimuli were assembled into a test book that included grating spatial frequencies from 38 to 0.86 cy/cm, in approximately half-octave steps. At the test distance of 1.5 m, the spatial frequencies ranged from 99.5 to 2.3 cy/deg and the circular apertures that contained the gratings were 2.1° in diameter. The book was organized from lowest to highest spatial frequency grating. At each spatial frequency, vertical, horizontal, and oblique gratings were presented sequentially, with order of presentation constant across spatial frequencies for all children tested at a school, and order of orientation counterbalanced across schools. This procedure was

designed to reduce the chance that differences in measurements across orientations might be due to subject fatigue or boredom.

In order to further reduce testing time and subject fatigue, the tester started with the 6.5 cy/cm (17 cy/deg) grating and asked subjects to complete only the first trial at each orientation at each spatial frequency until he or she incorrectly identified the location of the grating on a trial (any orientation). The tester then went back two spatial frequencies (lower spatial frequencies) for all three orientations and required the subject to correctly identify the location of the grating on three of three or three of four trials for each orientation/spatial frequency before continuing to the next finer spatial frequency for that orientation of a particular spatial frequency but correctly identified the grating location on three out of four trials for one orientation of a particular spatial frequency but correctly identified the grating location on three out of the other spatial frequencies only for those orientations on which the child continued to correctly identify the grating location. Grating acuity for each stimulus orientation was scored as the highest spatial frequency at which a subject could correctly locate the grating on at least three of four trials. Using this method, the chance of correctly guessing the location of the grating on three of four trials was 11%.

Threshold grating acuity scores (cy/deg) were transformed to log values for data analyses. For subjects who were judged unable to resolve the largest grating available (0.86 cy/cm, 2.3 cy/deg), a grating acuity corresponding to the next lower spatial frequency in the Teller Acuity Card set (0.64 cy/cm, 1.7 cy/deg) was assigned.

Vernier Acuity

Vernier acuity for horizontal, vertical and oblique stimuli were generated using a computer program (Miller, Harvey, & Dobson, 2002) and printed on a laser printer with a resolution of 600 dpi. Stimulus orientation refers to the orientation of the carrier (rather than the offset). Ten vernier offset sizes were used. At the test distance of 1.75 m, the offsets range from 80 arc sec to 5 arc sec. The stimuli were printed, mounted, and organized into a test book. As in the grating acuity test book, vertical, horizontal, and oblique stimuli were interleaved throughout the book, with stimulus orientation order counterbalanced across schools.

The test procedure was essentially the same as the 3AFC procedure described for grating acuity, except here the subject's task was to identify which of the three circles contained the "wiggly" line, and the tester began with the largest offset size. Vernier acuity for each stimulus orientation was scored as the smallest vernier offset at which the child could correctly identify the vernier stimulus on at least three of four trials.

Threshold vernier acuity scores (arc sec) were transformed to log values for data analyses. Subjects who were judged unable to detect the largest offset (80 arc sec) were assigned a vernier acuity 100 arc sec, i.e., 0.1 log unit larger than the largest offset included in the test book.

Contrast Sensitivity

Contrast sensitivity for horizontal and vertical grating stimuli was determined for three grating spatial frequencies: 1.5, 6, and 18 cy/deg at a test distance of 3 m. Contrast sensitivity stimuli were constructed from VCTS6500 Contrast Sensitivity Charts (Vistech Consultants, Inc., Dayton, OH). For each spatial frequency, the test included eight levels of contrast (max-min/max+min) ranging from 0.33 to 0.006 for 1.5 cy/deg, 0.20 to 0.004 for 6 cy/deg, and 0.25 to 0.011 for 18 cy/deg. When the chart is used clinically, subjects must identify whether the grating stimulus is oriented vertically, or rotated 15 degrees clockwise or counter-clockwise from vertical. However, because the original configuration of the test includes only vertical stimuli and only one trial for each level of contrast/spatial frequency, we used several charts

to construct three test books (one book for each of the three spatial frequencies, with four trials at each contrast level/orientation (horizontal/vertical)). The test procedure was similar to that used to test grating acuity and vernier acuity: each trial was a 3AFC task (horizontal, tilted clockwise, or tilted counter-clockwise, or vertical, tilted clockwise, or tilted counter-clockwise), and the subject had to correctly identify the grating orientation, by holding a pen in front of him/herself, and matching the orientation of the pen to the orientation of the grating, on at least three of four trials before continuing on to the next contrast level for that orientation. Vertical and horizontal stimuli were interleaved within the test book, with order (vertical first or horizontal first) counterbalanced across schools.

Contrast sensitivity for each grating orientation for each spatial frequency was scored as the lowest contrast level on which the child was able to correctly identify the orientation of the grating on at least three of four trials. Order of testing across the three spatial frequencies was always the same for an individual child, was counterbalanced across subjects, and was randomly selected by the tester prior to the child's first testing session.

Threshold contrast sensitivity results were transformed to log values for data analyses. For subjects who were judged unable to resolve the highest contrast stimulus, a contrast sensitivity threshold one step higher than the highest contrast level included in the test book (average step size was 0.2 log unit) was assigned. This resulted in contrast threshold values of 0.52, 0.32 and 0.39 for 1.5, 6.0, and 18.0 cy/deg stimuli, respectively.

Stereoacuity

Stereoacuity was assessed using the Randot Preschool Stereoacuity Test (Stereo Optical Co., Chicago, IL) (Birch, Williams, Hunter, & Lapa, 1997), a commercially available clinical test that utilizes random dot stimuli to assess stereoacuity in the absence of monocular depth cues and can be used with young children. The test includes six levels of disparity, ranging from 800 to 40 arc sec at the test distance of 40 cm, presented in three test books, and was administered with subjects wearing test-specific polarized glasses over their eyeglasses.

Beginning with the largest disparity level, subjects were asked to identify shapes (e.g., star, house, duck) that appear in random dot displays on the right side of the book. Because the possible shapes that can appear are shown in silhouette form on the left side of the book, subjects could respond either verbally or could point to the silhouette form. If a subject correctly identified at least two of three shapes at a given disparity level, the tester proceeded to the next finer disparity level, until subject was unable to correctly identify at least two shapes or until the subject correctly identified at least two shapes at the finest disparity level. Stereoacuity was recorded as the smallest disparity at which the subject could correctly identify two of three shapes in the random dot display.

Threshold stereoacuity scores (arc sec) were transformed to log values for data analyses. For subjects who were judged unable to resolve the largest (800 arc sec) disparity level, a stereoacuity of 1600 arc sec was assigned. This value is 0.3 log unit (the interval between levels at the poorer range of the stereoacuity test) larger than the largest disparity included on the test.

Data Analysis

Subjects were assigned to the control group or the astigmatic group based on the results of the eye examination (Table 1). Subjects with low or no astigmatism were included in the non-astigmatic control (NonA) group, and subjects with high RE astigmatism (° 1.00 D) were assigned to the astigmatic group. Because the pattern of deficits in astigmatism-related amblyopia is likely to differ based on the type of astigmatism present, subjects in the astigmatic group were further divided into two subgroups: (a) subjects with hyperopic astigmatism (HA)

(Figure 1G and 1H), and (b) subjects with myopic or mixed astigmatism (M/MA) (Figure 1D, 1E, and 1F).

Analyses of covariance (ANCOVAs) were used to compare best-corrected visual performance in the astigmatic groups (HA vs. M/MA) to the control group (NonA). Previous treatment (previous eyeglass wear – per parent report on an eye care history questionnaire completed prior to the study eye examination) was also entered into the model (to control for the effects of previous treatment on best-corrected vision). Covariates entered were: age in years (to control for any differences in mean age across astigmatism groups), and amount of astigmatic anisometropia (to control for reduced acuity due to potential differences in presence and amount of astigmatic anisometropia across astigmatic groups). Astigmatic anisometropia was calculated as RE cylinder-LE cylinder, with positive numbers representing greater RE astigmatism, negative numbers representing greater LE astigmatism. Amount of anisometropia defined by sphere or spherical equivalent was not included in analyses, as children with spherical equivalent anisometropia (> 1.50 D) were excluded from analyses.

RESULTS

A total of 1,048 K-2nd and 4th-6th grade children were enrolled in the study and completed the eye examination. Of these children, 243 were excluded from analyses for the following reasons: did not meet the criteria for the non-astigmatic group or for either of the astigmatic groups (n=157), lost to follow-up after the eye exam (no best-corrected visual acuity data collected, n=39), anisometropia (n=18), strabismus (n=11), ocular abnormality other than strabismus (n=11), anisometropia and strabismus (n=2), undilated at exam (n=2, 1 refused, 1 poorly dilated), history of patching (n=1), anisometropia and ocular abnormality (n=1), strabismus and ocular abnormality (n=1). Overall, children ranged in age from 4.75 to 13.81 years (mean = 8.49, SD=2.38).

Of the 805 children, 475 met the criteria for the NonA group, 158 met the criteria for the HA group, and 172 met the criteria for the M/MA group. Comparison of mean age across astigmatic groups yielded a significant effect (F(2,802)=20.30, p < 0.001). Post-hoc comparison indicated that, on average, children in the HA group (7.44 years, SD=2.12) were significantly younger than children in the NonA (8.72 years, SD=2.35) and M/MA groups (8.83 years, SD=2.44) (all ps < 0.001).

Information on previous eyeglass wear was available for 793 of the 805 children. Percentage of children with positive history of previous eyeglass wear (per parent report) was significantly different across astigmatism groups (X^2 (2)=300.98, p < 0.001). Post-hoc analyses indicated that a significantly smaller percentage of children in the NonA group (51/470 (10.9%)) had a previous history of eyeglass wear compared to children in the HA group (95/155 (61.3%)) and the M/MA group (130/168 (77.4%)), and that children in the HA group were less likely than children in the M/MA group to have a history of eyeglass wear (ps < 0.01).

Letter (Recognition) Acuity (Figure 2)

The sample size for letter acuity analyses was 790. Letter acuity data were missing for 15 children: 1 because the tester judged that the child was unable to perform the task, 1 because of a shortage of time, 1 due to experimenter error (child wearing the wrong eyeglasses), and 12 because history of eyeglass wear information was missing. ANCOVA on best-corrected letter acuity results yielded a significant main effect of astigmatism group (F(2,782)=77.82, p < 0.001). The main effect of previous eyeglass wear was not significant, although the interaction between eyeglass wear and astigmatism group was significant ((F(2,782)=3.61, p < 0.03). The effect of subject age was significant (F(1,782)=104.65, p < 0.001), but the effect of amount of anisometropic astigmatism was not.

Post hoc analyses on the interaction between astigmatism group and history of previous eyeglass wear indicated that, when age and astigmatic anisometropia are controlled for, children in the NonA group with no history of previous eyeglass wear had better acuity than children with a history of eyeglass wear (p < 0.01). There were no differences in acuity between children with or without history of eyeglass wear for either the HA or M/MA group. However, an analysis comparing astigmatic children with no history of eyeglass wear (n=98) to astigmatic children with a positive history of eyeglass wear *who were wearing glasses* upon arrival at the initial eye examination (i.e., compliant children, n=60) showed a statistically significant main effect of previous wear (F(1,152)=5.28, p < 0.03): Astigmatic children who were compliant with wearing their glasses had significantly better best-corrected acuity than astigmatic children with no history of optical treatment.

Acuity × Amount and Type of Astigmatism—Figure 3 plots best-corrected letter acuity by amount of astigmatism present. Although there was considerable variability in acuity results at each level of astigmatism, regression analysis indicated that, for the overall sample, letter acuity was significantly related to amount of astigmatism (logMAR acuity = $0.04 + 0.08 \times$ astigmatism (D), p < 0.001). This was also true for the HA (logMAR acuity= $0.17 + 0.04 \times$ astigmatism (D), p < 0.001) and M/MA (logMAR acuity= $0.10 + 0.05 \times$ astigmatism (D), p < 0.001) groups.

Clinical Diagnosis of Astigmatism-related Amblyopia—Significantly more children in the HA group (46.2%, $X^2(1)=120.89$, p < 0.001) and the M/MA group (52.3%, $X^2(1)$ =157.59, p < 0.001) met the criterion for RE amblyopia (best-corrected letter acuity of 20/40 or worse), compared to the NonA group (7.8%). Figure 4 shows the percentage of children in each group who met the criterion. Data are presented by age because, as noted above, there is a significant relationship between age and visual acuity.

In order to explore possible reasons that some children in the NonA group had best-corrected visual acuity of 20/40 (0.30 logMAR) or worse, we examined data collected following their vision testing session (Table 2). Of the 37 NonA children who met the amblyopia criterion, 26 no longer met the criterion for amblyopia when acuity was retested approximately 1 month later. Since the majority of these 26 children received no treatment (only two had been prescribed eyeglasses (1 for myopia and 1 for hyperopia), it is likely that their poor performance on the initial test was not related to optical factors, nor was it likely that their improvement on acuity retesting was related to a reduction in amblyopia. Nine of the remaining 11 children were re-examined by the ophthalmologist, who confirmed that the refraction was accurate and that no ocular abnormalities were present in 8 children, and determined that 1 child (a hyperope) was over-corrected. Further information was not available on 2 children.

Grating (Resolution) Acuity (Figure 5)

The sample size for grating acuity analyses was 786. Grating acuity data were missing for 19 subjects: 5 because the tester judged that the child was unable to perform the task, 2 because of a shortage of time, and 1 due to experimenter error (child wearing the wrong eyeglasses), and 11 because history of eyeglass wear information was missing. History of eyeglass wear information was also missing for 1 subject who was missing grating acuity data for a reason listed above.

Repeated measures ANCOVAs on best-corrected grating acuity results yielded a significant main effect of group (F(2,778)=42.27, p < 0.001), a significant interaction between stimulus

orientation and group (F(4,1556)=9.39, p < 0.001), and significant effect of age (F(1, 778)= 34.98, p < 0.001). Effects of orientation, previous eyeglass wear and astigmatic anisometropia were not significant, although the main effect of orientation approached significance (p=0.08).

Post-hoc analyses indicated that, for all three stimulus orientations, mean acuity in the NonA group was significantly better than mean acuity in the HA and M/MA groups (ps < 0.001). In addition, for horizontal stimuli, mean acuity in the M/MA group was poorer than in the HA group (p = 0.003 after Bonferroni correction).

Presence of MA was evaluated by comparing, using ANCOVA, the mean difference between vertical and horizontal (V-H) grating acuity across astigmatism groups. Results yielded a significant main effect of astigmatism group (F(2,778)=15.45, p < 0.001), reflecting better acuity for horizontal than vertical gratings for the HA group (p=0.03) and better acuity for vertical than horizontal gratings for the M/MA group (p < 0.001), relative to the NonA group. The HA group had, on average, only slightly better acuity for horizontal than vertical stimuli. However, the effect was significant relative to the NonA group, who had slightly better acuity for vertical than for horizontal stimuli.

To determine the presence and extent of the "oblique effect" (reduction in acuity for oblique stimuli relative to vertical and horizontal stimuli) (Appelle, 1972), we compared the mean difference between vertical and oblique grating acuity (V-O) and between horizontal and oblique grating acuity (H-O) across groups using ANCOVA. For V-O grating acuity, there were no significant differences across groups. For H-O grating acuity, there was a significant main effect of group (F(2,778)=12.82, p < 0.001). Post hoc analyses indicated that all pairwise comparisons across groups were significant (ps < 0.05, after correction for multiple comparisons). The H-O oblique effect for HA was greater than for NonA, and the H-O oblique effect in the opposite direction, i.e., oblique acuity was better than horizontal acuity) (see Figure 5).

Vernier Acuity (Figure 6)

The final sample size for vernier acuity data was 782. Data were missing for 23 subjects: 9 because the tester judged that the child was unable to perform the task, 1 because of a shortage of time, 2 due to experimenter error (data not recorded, child wearing the wrong eyeglasses), and 11 because eyeglass wear data were missing. Eyeglass wear data were also missing for 1 subject who was missing vernier acuity data for a reason listed above. Repeated measures ANCOVA on best-corrected vernier acuity results yielded a significant main effect of astigmatism group (F(2,774)=15.61, p < 0.001) and a significant effect of age (F1, 774)=73.17, p < 0.001). No other effect reached or neared significance (ps > 0.10). Results of post hoc tests indicated that mean vernier acuity was significantly better for the NonA group than for the HA and M/MA groups (ps < 0.001). Mean vernier acuity yielded no significant effects, although the main effect of astigmatism group approached significance (p < 0.08).

Contrast Sensitivity (Figure 7)

The final sample size for contrast sensitivity data was 726. Data were missing for 79 subjects: 66 because the child was unable to perform the task, 2 because of a shortage of time, 1 due to experimenter error (child wearing the wrong eyeglasses), and 10 because eyeglass wear data were missing. Eyeglass wear data were also missing for 2 subjects whose contrast sensitivity data were missing for reasons noted above. Repeated measures ANCOVA yielded significant main effects of stimulus spatial frequency, stimulus orientation, astigmatism group and age, and interactions between spatial frequency and astigmatism group, and spatial frequency and

orientation. Overall, however, effects were qualified by a significant interaction between spatial frequency, orientation and astigmatism group.

Post-hoc analyses indicated that the NonA group had significantly better contrast sensitivity than the HA and M/MA groups for 6.0 and 18.0 cy/deg vertical and horizontal stimuli (all ps < 0.05 after Bonferroni correction), but contrast sensitivity in the astigmatic groups did not differ significantly from the NonA group for 1.5 cy/deg stimuli. The HA and M/MA groups did not differ significantly on any measure of contrast sensitivity.

The difference in contrast sensitivity for vertical and horizontal (V-H) 1.5, 6.0 and 18 cy/deg stimuli did not differ significantly for any of the astigmatism group pairwise comparisons, although the difference between the NonA and HA groups neared significance (after correction) for 18 cy/deg stimuli (p=0.07 after Bonferroni correction).

Stereoacuity (Figure 8)

The final sample size for stereoacuity data was 787. Stereoacuity data were not included for 18 subjects: 4 because the tester judged that the child was unable to perform the task, 2 because of a shortage of time, and 2 due to experimenter error (data not recorded, child wearing the wrong eyeglasses), and 10 for whom eyeglass wear data were missing. Eyeglass wear data were also missing for 2 subjects who were missing stereoacuity data for reasons listed above. ANCOVA on best-corrected stereoacuity results yielded a significant main effect of astigmatism group (F2,779)=35.75, p < 0.001). The effect of age approached but did not reach significance (p=0.07), and the effects of history of eyeglass wear and anisometropic astigmatism were not significant.

Post hoc analyses indicated that the NonA group had significantly better mean stereoacuity than the HA and M/MA groups (ps < 0.001), but the HA and M/MA groups did not differ significantly.

DISCUSSION

The results of the present study indicate that astigmatic elementary school children show deficits in best-corrected letter acuity, grating acuity, vernier acuity, contrast sensitivity, and stereoacuity.

Letter Acuity

Children with high astigmatism (\geq 1.00 D) have significantly poorer best-corrected letter acuity, on average, than children with little or no astigmatism. In addition, children with high astigmatism are more likely to meet the criterion for clinical amblyopia (defined here as right eye best-corrected visual acuity of 20/40 or worse) than are non-astigmatic children. These results are consistent with three previous studies that have reported reduced best-corrected letter acuity in astigmatic preschool (Dobson et al., 2003a), grade-school (Harvey, 2002; Harvey, Dobson, & Miller, 2004a; Kershner & Brick, 1984), and adult (Dobson et al., 1996) members of the Tohono O'odham Nation.

On average, letter acuity deficits are small, ranging from a one-line deficit reported for preschool children (Dobson et al., 2003a) to a deficit of approximately two lines reported in the present study for elementary-school children. The increase in the magnitude of the letter acuity deficit between preschool and elementary school suggests that astigmatism may continue to have detrimental effects on development of letter acuity beyond the preschool years. However, comparisons across studies should be made cautiously, as there were significant differences between the method used in the previous study of preschool children (acuity for Lea symbols (Hyvärinen, Näsänen, & Laurinen, 1980) measured while children were

cyclopleged and wearing trial frames) (Dobson et al., 2003a) and the method used in the present study to test elementary school children (acuity for ETDRS chart letters measured while the children were uncyclopleged and wearing eyeglasses).

There were a number of children in the NonA group who demonstrated poor best-corrected visual acuity, as can be seen in Figures 3 and 4. The reason for reduced visual performance in these children is not clear. However, we were able to rule out optical or other visual system abnormalities as the cause for poor visual performance in the majority of these NonA children, suggesting that poor performance was most likely due to cognitive factors, e.g., for younger children, poor task performance due to unfamiliarity with their letters, or other unknown factors. Regardless of the reason for reduced acuity in these children, the astigmatic groups still performed more poorly on average than the NonA group.

Grating Acuity

In the present study, we found that significant MA was present in children with mixed/myopic astigmatism, which is consistent with findings of several previous studies of astigmatic children (Dobson et al., 2003a; Gwiazda et al., 1984) and adults (Freeman et al., 1972, 1975a; Mitchell et al., 1973). MA was also apparent in hyperopic astigmats, although the effect was small, and would not have been significant if it were not evaluated relative to the non-astigmatic group, which showed a trend in the opposite direction (see Figure 5). The finding of MA in the HA group is consistent with several studies that have found MA in adults with hyperopic astigmatism (Freeman et al., 1972, 1975a; Mitchell et al., 1973), but not with the results of children with hyperopic astigmatism who were tested in our previous study of Tohono O'odham preschoolers (Dobson et al., 2003a).

The reason for the lack of consistent results with regard to presence or absence of MA in hyperopic astigmats is unclear. One possibility is that, because the effect is small, it was masked by variability in the data collected from preschool children, who were tested following a cycloplegic refraction, while wearing trial frames. In contrast, the older children in the present study were tested while wearing eyeglasses, several weeks after the cycloplegic refraction.

The results of the present study indicated that, in addition to showing MA, subjects in the two astigmatism groups had reduced best-corrected acuity for the grating orientation (horizontal for the hyperopic astigmats and vertical for the myopic/mixed astigmats) that would have been in better focus at distance when subjects were uncorrected. A similar finding can be seen in best-corrected grating acuity results from adults tested in previous studies of astigmatism-related MA (Freeman et al., 1972; Mitchell et al., 1973).

It is well documented that non-astigmatic individuals show poorer acuity for oblique gratings than for horizontal and vertical gratings, which has been termed the "oblique effect" and has been attributed to the greater exposure of the developing visual system to vertical and horizontal lines, in comparison to oblique lines (Appelle, 1972). Previous results from astigmatic subjects have suggested that the "oblique effect" is larger in astigmatic individuals than in non-astigmatic individuals, perhaps due to the inability of the astigmatic eye to focus oblique lines (Freeman et al., 1972; Held, Thorn, McLellan, Grice, & Gwiazda, 2003; Mitchell et al., 1973). The results of the present study showed that there was no difference in the magnitude of the oblique effect in NonA, HA, and M/MA groups for comparisons of vertical and oblique grating acuity. However, in comparisons of horizontal and oblique grating acuity, only the NonA and HA groups showed the typical oblique effect; the M/MA group did not. The failure to observe a typical oblique effect for H-O grating acuity in the M/MA group appears to be due to the presence of MA in the M/MA group, which reduced horizontal grating acuity to the level of oblique acuity (see Figure 5).

Vernier Acuity

Results of the present study indicate that the HA and M/MA groups did not show meridional differences in vernier acuity, but did show reduced vernier acuity for all three stimulus orientations (vertical, horizontal, and oblique) relative to the NonA group. The failure to observe evidence of MA in vernier acuity is not consistent with previous studies that have documented meridional differences in vernier acuity in astigmatic subjects (Gwiazda et al., 1986; Mitchell et al., 1973). It is not clear why significant MA was not observed in the present study. However, there was a trend in the predicted direction, with subjects in the HA group showing better acuity for horizontal than for vertical gratings and subjects in the M/MA group showing better acuity for vertical than for horizontal gratings.

Contrast Sensitivity

The results of the present study did not yield evidence of MA in measurements of contrast sensitivity. However, there was significantly reduced contrast sensitivity for the HA and M/ MA groups, relative to the NonA group, for both vertical and horizontal middle (6 cy/deg) and high (18 cy/deg) spatial frequency stimuli, although contrast sensitivity for low spatial frequency stimuli (1.5 cy/deg) did not differ between the astigmatic and non-astigmatic groups.

The failure to find evidence of MA in measures of contrast sensitivity is not consistent with several previous studies that reported MA in human adult astigmats (Freeman, 1975b, Freeman & Thibos, 1975, Mitchell & Wilkinson, 1974; St. John, 1997) and in astigmatic monkeys (Boothe & Teller, 1982, Harwerth et al., 1980, 1983). However, the results are consistent with previous studies that reported that astigmatic subjects have reduced contrast sensitivity at all stimulus orientations, relative to non-astigmats (Mitchell & Wilkinson, 1974; St. John, 1997). It is possible that the failure to observe MA is due to the fact that some of the children were unable to see the highest level of contrast, and were therefore assigned a contrast value one step above the highest level stimulus available for both vertical and horizontal stimuli. We chose this method of scoring because it allowed us to include the data from these subjects and because it was more likely to over-estimate than to under-estimate contrast sensitivity in amblyopic children (i.e., contrast sensitivity may be worse than the next higher level of contrast). Thus, we biased our scoring method against finding significant group effects (differences between NonA and astigmatic groups), so that any observed effects could not be attributed to bias in scoring methods. This method of scoring may have diluted any effects of stimulus orientation, as children who were unable to see the highest level of contrast for both vertical and horizontal stimuli were assigned the same value for both orientations. However, when we re-analyzed the V-H contrast sensitivity data excluding data from children who were unable to detect the highest level of contrast, there was no evidence of MA in HA and M/MA children, suggesting that the failure to observe MA was not related to bias in the method of scoring, unless orientation effects only occurred in the children with the most severe deficits.

Stereoacuity

The results of the present study showed poorer stereoacuity for subjects in the HA and M/MA groups than for subjects in the NonA group. We are aware of only one other study that provides evidence of reduced best-corrected stereoacuity in a subject with high astigmatism (Mitchell et al., 1973). One recent study reported reduced stereoacuity in the presence of simulated (lens induced) astigmatism (Chen, Hove, McCloskey, & Kaye, 2005), suggesting that the blur associated with uncorrected astigmatism may be sufficient to induce deprivation of the visual input necessary for normal levels of stereoacuity. While the results of the present study suggest that astigmatic blur disrupts the normal development of stereoacuity, we cannot rule out the possibility that the reduction in stereoacuity we have observed may be caused by the reduced best-corrected acuity found in the HA and M/MA groups, in a manner similar to the finding that blur associated with induced astigmatism affects stereoacuity.

Effects of Previous Treatment

A surprising result was the failure to find significant effects of previous eyeglass treatment on visual performance. That is, we expected that previously treated subjects might show less amblyopia if previous treatment had been at all successful. However, there was no evidence of this in the primary analyses. This failure to find significant evidence of effectiveness for previous treatment is most likely due to poor compliance with previous treatment, as only 26.7% (60/225) of the astigmatic children whose parents reported previous eyeglass wear were wearing eyeglasses upon arrival at the initial eye examination. The finding that previously treated astigmatic children who were compliant with their treatment (i.e., they were wearing their glasses upon arrival at the study eye examination) had significantly better best-corrected acuity than the previously untreated astigmatic children supports the idea that the null effects of previous treatment were due to poor treatment compliance.

Astigmatic Anisometropia

There were no significant effects of amount of astigmatic anisometropia in any of the analyses. This may be due to the fact that few of the astigmatic subjects had large amounts of astigmatic anisometropia (7/158 (4.4%) in the HA group and 20/172 (11.6%) in the M/MA group had astigmatic anisometropia ≥ 2.00 D).

Limitations

One limitation of the present study is the lack of refractive error data for our subjects during early development. In making our predictions with regard to expected patterns of deficits based on patterns of blur, we have assumed that our astigmatic subjects had astigmatism in early development that was similar to their present astigmatism, and there is evidence to support this assumption. Previous longitudinal analysis of astigmatic refractive error in this population indicated very little change in spherical or astigmatic refractive error during the preschool years (Dobson, Miller, Sherrill, & Harvey, 2003b; Miller, Sherrill, Dobson, & Harvey, 2003). Furthermore, a pilot study of astigmatism in infants and toddlers from this population indicated a prevalence of with-the-rule astigmatism in early development similar to that observed in preschool and school-age members of this population (Harvey, Dobson, Miller, Clifford, Lopez, & Adams, 2005), suggesting that it is likely that in this population, astigmatism is often present early in development, and persists into childhood. However, we have no direct measurements of early refractive error in the subjects whose data are presented here. An ongoing study of the development of refractive error and visual acuity in Tohono O'odham children between 6 months and 6 years of age will offer more definitive indication of the stability of astigmatic refractive error in Tohono O'odham infants and toddlers, as well as evidence as to when the presence of astigmatic refractive error begins to have a negative effect on visual development.

Impact and Implications for Clinicians

The results of the present study suggest that astigmatism in early childhood places children at significant risk for the development of amblyopia. Furthermore, deficits in contrast sensitivity for middle spatial frequency stimuli indicate that the deficits include aspects of vision beyond visual acuity for high spatial frequency stimuli, a finding supported by a recent report that astigmatism disrupts global processing of stimuli (Polat, Bonneh, Ma-Naim, Belkin, & Sagi, 2005). Although the deficits are typically mild compared to those often reported for other forms of amblyopia, they may be large enough to introduce a significant educational obstacle.

The present study focused on children from a population with a high prevalence of astigmatism. While this population is certainly unique with regard to prevalence of astigmatism, it is not likely that the effects of uncorrected astigmatism on visual development observed in this

population would differ significantly from that which would be observed in astigmatic children from other populations. A recent report on data from a large-scale multicenter study of refractive error in school-age children found prevalences of high astigmatism (\geq 1.00 D, the criterion used in the present study) among non-Native American children ranging from 20% to 36.9%, depending on race and ethnicity (Kleinstein, Jones, Hullett, Kwon, Lee, Friedman, Manny, Mutti, Yu, & Zadnik, 2003).

Finally, while the present report provides a broad depiction of the patterns of deficits that result from astigmatism in early childhood, it does not directly address effectiveness of eyeglass treatment of the deficits. However, in addition to providing the data reported here, children participated in a longitudinal study of optical treatment of astigmatism-related amblyopia. Results of the treatment outcome aspect of this study are forthcoming, but preliminary results suggest that optical treatment is effective in reducing amblyopia in elementary school children who are within and beyond what was previously believed to be the sensitive period for successful treatment of astigmatism-related amblyopia (Cobb & MacDonald, 1978; Gwiazda et al, 1986; Harvey et al, 2004b; Mitchell et al., 1973).

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Figure 1.

Schematic representation of the locations at which the horizontal and vertical lines of a cross located at distance come into focus, with respect to the retina, in non-astigmatic eyes (a-c) and in eyes that have with-the-rule astigmatism (d-h) (from Harvey, 2002 and Harvey et al., 2004b, revised from Gwiazda, Mohindra, Brill, & Held, 1985).



Figure 2.

Mean letter acuity for children in the non-astigmatic (NonA, n=467), hyperopic astigmatism (HA, n=155), and myopic/mixed astigmatism (M/MA, n=168) groups. Bars indicate \pm 1 SEM. The NonA group had significantly better (p < 0.001) mean acuity than did both astigmatic groups.



Figure 3.

Letter acuity by amount of astigmatism (scatter plot), with regression line for entire sample. Although there was considerable variability in acuity results at each level of astigmatism, letter acuity was significantly related to amount of astigmatism for the overall sample and for the HA and M/MA groups (ps < 0.001).

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Figure 4.

Percentage of children with right eye acuity that met the criterion for amblyopia (best-corrected letter acuity of 20/40 or worse) by age, for children in the non-astigmatic (NonA), hyperopic astigmatism (HA), and myopic/mixed astigmatism (M/MA) groups. Significantly more children in the HA and M/MA groups than in the NonA group met the criterion for amblyopia (ps < 0.001). Percentages represented by each bar reflect the following sample sizes (for NonA, HA, and M/MA respectively, the number of children meeting amblyopia criterion/total number of children): For age 4 to < 6 years, 15/82, 30/52, 20/30; For age 6 to < 8 years, 6/127, 26/60, 35/47; For age 8 to < 10 years, 3/86, 9/21, 17/25; For age 10 years and older, 13/177, 8/25, 18/70.

Resolution (Grating) Acuity



Figure 5.

Acuity for vertical (black symbols), horizontal (white symbols), and oblique (gray symbols) gratings for children in the non-astigmatic (NonA, n=468), hyperopic astigmatism (HA, n=152), and myopic/mixed astigmatism (M/MA, n=166) groups. Bars indicate \pm 1 SEM. For all three orientations, mean acuity in the NonA group was significantly better than mean acuity in the HA and M/MA groups (ps < 0.001). In comparison to results from the NonA group, both the HA and M/MA groups showed evidence of MA (ps < 0.001), with the HA group showing better acuity for horizontal than for vertical gratings, and the M/MA group showing better acuity for vertical than for horizontal gratings.

Vernier Acuity



Figure 6.

Vernier acuity for vertical (black symbols), horizontal (white symbols), and oblique (gray symbols) stimuli for children in the non-astigmatic (NonA, n=466), hyperopic astigmatism (HA, n=151), and myopic/mixed astigmatism (M/MA, n=165) groups. Bars indicate \pm 1 SEM. For all three orientations, mean vernier acuity was significantly better for the NonA group than for the HA and M/MA groups (ps < 0.001). Neither the HA nor the M/MA group showed evidence of MA.



Figure 7.

Contrast sensitivity for 1.5, 6.0, and 18.0 cy/deg sinewave gratings for horizontal and vertical stimuli for children in the non-astigmatic (NonA, n=435), hyperopic astigmatism (HA, n=135), and myopic/mixed astigmatism (M/MA, n=156) groups. Bars indicate \pm 1 SEM. The NonA group had significantly better contrast sensitivity than the HA and M/MA groups for 6.0 and 18.0 cy/deg vertical and horizontal stimuli (all ps < 0.05 after Bonferroni correction), but contrast sensitivity in the astigmatic groups did not differ from that of the NonA group for 1.5 cy/deg stimuli. Neither the HA nor the M/MA group showed evidence of MA.



Figure 8.

Stereoacuity for children in the non-astigmatic (NonA, n=466), hyperopic astigmatism (HA, n=153), and myopic/mixed astigmatism (M/MA, n=168) groups. Bars indicate \pm 1 SEM. Children in the NonA group had significantly better stereoacuity than did children in either the HA or the M/MA group (ps < 0.001).

Table 1

Refractive error criteria for the non-astigmatic control (NonA), hyperopic astigmatism (HA), and myopic/mixed astigmatism (M/MA) groups.

Group	Refractive Error Criteria	
Non-astigmatic Control (NonA) Group [*] Hyperopic Astigmatism (HA) Group [*] Myopic or Mixed Astigmatism (M/MA) Group [*]	< 0.75 D cylinder in RE and LE ≥ 1.00 D cylinder in RE, RE sphere (plus cyl) ≥ 0 ≥ 1.00 D cylinder in RE, RE sphere (plus cyl) < 0	

No ocular abnormalities other than high refractive error and no anisometropia (> 1.50 D difference in spherical equivalent between eyes).

Table 2

Summary of information on NonA children who met the criterion for amblyopia.

Age Group	N	Outcome
	(% of Age Group)	
	12 (80%)	Normal on retest*
4 to < 6 years (n=15)	2 (13%)	Normal on re-examination**
	1 (7%)	No further information available
	4 (67%)	Normal on retest*
6 to < 8 years (n=6)	1 (17%)	Normal on re-examination**
	1 (17%)	No further information available
8 to < 10 years (n=3)	3 (100%)	Normal on retest*
10 years and older (n=13)	7 (54%)	Normal on retest*
	5 (38%)	Normal on re-examination **
	1 (8%)	Over-corrected hyperope
Overall (n=37)	26 (70%)	Normal on retest *
	8 (22%)	Normal on re-examination **
	2 (5%)	No further information available
	1 (3%)	Over-corrected hyperope

* Best-corrected acuity retested approximately 1 month later was better than 20/40.

** Met the criterion for amblyopia on retest, but upon re-examination by pediatric ophthalmologist refraction was verified and no ophthalmic abnormalities noted.