Longitudinal Study of Acuity and Stereopsis in Infants with or At-risk for Esotropia

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Grating acuity and stereopsis were measured longitudinally in five groups of infants: infantile esotropes, moderate hyperopes, high hyperopes, infants with a family history of strabismus or amblyopia and controls. Grating acuity was measured with a forced-choice preferential looking procedure. Stereopsis was assessed with a random-element stereogram. Testing was conducted when subjects were 3, 6, 9, 12, 18, 24, 30 and 36 months of age. No differences among groups in absolute acuity scores or interocular acuity differences were found until the infants reached 30 and 36 months of age. At these ages, treated infantile esotropes showed acuity scores that were, on average, 0.5 octave poorer than those of controls for both the eye showing the better acuity and the eye showing the worse acuity. Stereopsis testing indicated that few, if any, of the infantile esotropes showed stereopsis at any of the test ages. Over 30% of the high hyperopes developed strabismus by age 3 years, but none of the infants in the moderate hyperopia or family history groups developed strabismus. Invest Ophthalmol Vis Sci 30:1146–1158, 1989

One of the most common eye disorders of early childhood is strabismus, which has been estimated to occur in 1 to 5% of the population. In children less than 12 months of age, strabismus usually takes the form of an esodeviation and is termed infantile esotropia. After infantile esotropia, the most frequently diagnosed form of strabismus occurring in early childhood is accommodative esotropia, which is associated with a high hyperopic refractive error and/or a high AC/A ratio and typically appears when children are 2 to 3 years of age.

Young children with esotropia are at risk for two types of visual deficits. The first is amblyopia, a "decrease in visual acuity in one or both eyes which on physical examination appear normal. ..." In esotropia, the amblyopia is typically reported to be a visual acuity deficit in one eye, which is presumed to develop as an adaptive mechanism against the dissimilarity of foveal images in the two eyes. Clinically, amblyopia is usually diagnosed in infants as a fixation preference of one eye in comparison with the other eye. Recently, measures of grating acuity, including forced-choice preferential looking (FPL) procedures and the visually evoked potential (VEP), have been shown to be useful in detecting amblyopia in infants and in monitoring the changes in acuity that occur during amblyopia therapy.

The second visual deficit for which infants with esotropia are at risk is lack of binocularity, which presumably results from the disruption of simultaneous vision in the two eyes of these infants. Studies have indicated that if surgical alignment of the eyes occurs before age 2, a high percentage of esotropes will exhibit some degree of binocularity. However, the degree of binocularity reported varies from study to study, and appears to depend on the method of assessment, the adequacy of surgical alignment, and the length of time between surgery and assessment of binocularity.

Given the visual deficits that result from early-onset esotropia and the importance of early treatment, it is obvious that there is a need for identification of risk factors associated with esotropia. Studies of inheritance patterns have confirmed the common belief that strabismus tends to run in families. However, the inheritance appears to be multifactorial rather than simple Mendelian, which means that it...
is difficult to predict on the basis of family history which infants will develop strabismus. A second risk factor is the presence of high hyperopia during the first postnatal year. Ingram et al recently reported results of a follow-up examination at age 3 1/2 years of a large group of children who had been refracted at one year of age. The results indicated that 48% of children who had +4.00 D or more of meridional hyperopia (hyperopia along the most hyperopic meridian) at age one developed strabismus by age 3 1/2. Twenty-four percent of children with a moderate amount of meridional hyperopia (>= +3.00 D and < +4.00 D) had developed strabismus by age 3 1/2. However, only 4% of children who had less than +3.00 D of meridional hyperopia at age 1 developed strabismus.

The purpose of the present study was to follow visual development over a 3-year period in five groups of infants: (1) infantile esotropes; (2) infants at risk due to high hyperopia; (3) infants at risk due to moderate hyperopia; (4) infants at risk due to a family history of strabismus or amblyopia; and (5) a control group of infants. Monocular grating acuity and stereopsis were assessed behaviorally at 3- to 6-month intervals until children reached 3 years of age.

Materials and Methods

Subjects

Five groups of infants were enrolled in the study. Assignment to group was made on the basis of an eye examination and cycloplegic refraction performed by a pediatric ophthalmologist before each infant reached 8 months of age. Infants had no known developmental or neurological abnormalities, by parents’ report. The five groups and the criteria for inclusion in each group were:

2. High Hyperopia. No strabismus. Refractive error >= +4.00 D along one or more meridia.
3. Moderate Hyperopia. No strabismus. Refractive error between +3.00 D and +3.75 D along one or more meridia.
4. Family History. No strabismus. Refractive error between -0.75 D and +2.75 D along all meridia. Two or more close relatives (parents, siblings, grandparents, aunts, or uncles) with strabismus or amblyopia.
5. Controls. No strabismus. Refractive error between -0.75 D and +2.75 D along all meridia. No family history of strabismus or amblyopia.

At the time of their initial refraction, two of the 20 Esotropes showed anisometropia, defined as a difference of 1.00 D or more in spherical equivalent or cylinder between eyes. None of the infants in the remaining four groups were anisometropic at the time of the first refraction.

Subjects in the Esotropia group were recruited with the assistance of local pediatric ophthalmologists. Subjects in the other four groups were recruited by letters sent to parents listed in the birth announcements section of the newspaper and assigned to the appropriate group following their initial eye examination. Twenty infants were recruited into the Esotropia group, ten into the High Hyperopia group, 14 into the Moderate Hyperopia group, 14 into the Family History group, and 30 into the Control group.

Of the 20 Esotropes in the study, two (10%) had two or more close relatives (parents, siblings, grandparents, aunts, or uncles) with strabismus or amblyopia. Three (21%) of the Moderate Hyperopes and two (20%) of the High Hyperopes also had a family history of strabismus or amblyopia. Thus, if these children had not had strabismus or hyperopia, they would have qualified for inclusion in the Family History group.

Of the initial 88 infants, 16 in the Esotropia group, eight in the High Hyperopia group, nine in the Moderate Hyperopia group, nine in the Family History group, and 23 in the Control group remained in the study until they reached three years of age. The remaining subjects either moved out of the area (n = 14) or withdrew from the study (n = 9) before age three. All Esotropes who remained in the study until 36 months of age had undergone occlusion therapy and at least one surgical procedure for eye alignment by this age.

Test target ages, calculated from the infant's due date, were the following: 3, 6, 9, 12, 18, 24, 30 and 36 months. Infants 12 months of age and younger were tested within ±1 month of these ages, and children older than 12 months were tested within ±2 months of the target test ages.

Prior to beginning testing, the procedures were explained to the parent(s) and informed consent was obtained.

Apparatus

Visual acuity assessment: An automated forced-choice preferential looking (FPL) apparatus was used for assessment of grating acuity. This apparatus has been described in detail elsewhere. Briefly, the apparatus consisted of a gray cardboard (Crescent #651) screen containing two 8 cm circular stimulus apertures, the centers of which were located 17 cm to the
left and right, respectively, of a 4 mm central peephole. Grating stimuli (Intergraphics Incorporated, Kirkland, WA) were mounted in pairs located 180° apart on a 62 cm disk located behind the screen. Each pair of stimuli consisted of a high spatial frequency black-and-white square-wave grating (either 58 or 86 cycles/deg, depending on the test distance) and a second grating, the test grating, which differed in spatial frequency from pair to pair. Rotation of the disk was computer controlled, so that the pair of gratings and the left-right position of the gratings within a pair could be varied quickly from trial to trial. Behind the central peephole a video camera was mounted; this camera transferred an image of the subject’s face to a television monitor positioned above the FPL screen. When young infants were tested, this video system allowed the adult experimenter to hold the infant during testing and to serve as observer in the FPL procedure. When children reached the age where they preferred to be held by the parent, the camera could be swung away and the experimenter could observe the child’s face directly through the peephole.

A set of door chimes, a train whistle and a darkened plexiglas box that contained one of a variety of animated toys, were located to the left and right, respectively, of the stimulus screen. Activation of one or more of these items was used with subjects 6 months of age and older to reward them for looking at or pointing to the test grating and to maintain their interest in the test procedure.

For children tested at the oldest test ages (30 and 36 months), push panels and a cereal reinforcement system were added to the apparatus (see Fig. 1). The push panels were two 25 × 25 cm glass panels mounted 31 cm from the screen, directly in front of the stimulus apertures, with one panel located to the left and one panel located to the right of center. Pressure on a panel triggered a microswitch that activated one or more of the reinforcers and/or a food dispenser (Gerbrands) that released a piece of cereal through a plastic tube into a cup located at the lower outside corner of the push panel.

Although an attempt was made to use the FPL apparatus for all tests, some children would not cooperate long enough for testing to be completed. For test ages up to and including 24 months, we had no other option but to score these tests as incomplete. By the time most of the children in the study reached 30 months, the acuity card procedure had been developed. In 23 children at 30 months and three children at 36 months, we used acuity cards to assess acuity in children who refused to complete FPL testing.

The acuity cards used were 28 × 62 cm cardboard cards, each containing two 9° apertures, the centers of which were located 12° to the left and right, respectively, of a 4 mm central peephole. As in the FPL apparatus, a high spatial frequency "blank" grating was located behind one aperture and a second grating, the test grating, which varied in spatial frequency from card to card, was located behind the other aperture. During testing, the child was seated on the parent’s lap in front of a gray cardboard screen, and the experimenter presented the cards to the child by holding them up sequentially to a 20 × 46 cm opening in the screen. A more detailed description of the cards and screen can be found in McDonald et al.

Stereopsis: Stereopsis was tested with a dynamic random-element stereogram similar to that described by Shea et al. The stereogram was an anaglyph composed of two random-element matrices (red-black and green-black) presented on a 19 inch color television monitor. Element size averaged 30 min arc and all elements in each matrix were replaced randomly every 16 msec. On stereoscopic trials, the spatial position of a 12 × 13 cm (18° × 20°) portion of one matrix was shifted slightly, relative to the corresponding set of random elements in the other matrix, to produce a retinal disparity of 76 min visual angle at our test distance of 36 cm. To an adult viewing the display through chromatic filters, with a green (Wratten 58) filter in front of the right eye and a red (Wratten 29) filter in front of the left eye, the display had the appearance of a background of randomly moving spatial noise, with a rectangle of randomly moving spatial noise floating several centimeters in front of the background. Closure of one eye, so that display was viewed through only one chromatic filter, resulted in the disappearance of the rectangle. The control, or nonstereoscopic, stimulus consisted of a 12
The position of the rectangle on the stereogram display was under computer control. At the beginning of each trial, the rectangle was located at the center of the display. When the observer pressed a button to begin the trial, the computer moved the rectangle out to the left or the right edge, respectively, of the screen and then back to the center, according to a pseudorandom order. Total excursion time for movement of the rectangle out and back was approximately 5 sec. The computer also recorded the observer’s forced-choice judgment concerning the direction of target movement on each trial and provided feedback concerning the correctness of the judgment.

**Procedure**

**Visual acuity testing:** The Diagnostic Grating procedure was used to estimate monocular visual acuity. In this procedure, the subject is first tested with a low spatial frequency grating that has been shown to be well above threshold for a normal child of the subject's age. If the observer's FPL results meet certain prespecified criteria (six of the first six trials, eight of the first nine trials, or seven in a row correct), the subject is shown a series of trials of the "diagnostic" grating frequency appropriate for his/her age. At each age, the diagnostic grating frequency is the spatial frequency that 90 to 95% of normal children give evidence of detecting in an FPL acuity test procedure, as determined empirically. If the observer's results indicate that the child can see the diagnostic grating (ie, if the observer gets six of the first six, nine of the first ten, 13 of the first 15, or 15 of the first 20 trials correct), the child is tested next with a grating one octave higher in spatial frequency than the diagnostic grating. If the observer's results fail to indicate the child can see the diagnostic grating, the child is tested next with a grating one octave lower in spatial frequency than the diagnostic grating. In the current study, testing continued in this fashion until acuity threshold was bracketed by one spatial frequency on which the observer met criterion and an adjacent spatial frequency one octave higher on which the observer failed to meet criterion. If the observer remained cooperative, he/she was then tested with the middle spatial frequency, one-half octave away from the two bracketing spatial frequencies. Acuity was estimated to be the highest spatial frequency on which the observer met criterion.

Twenty-three (33%) of the 30-month-olds and three (5%) of the 36-month-olds could not be tested with the Diagnostic Grating procedure. Subsequently, 21 (81%) of these children were tested successfully with the acuity card procedure. The acuity card procedure used was identical to that described by McDonald et al, in which the observer tested the child with a subset of nine acuity cards, arranged in ascending order of spatial frequency and differing from one another in half-octave steps. The observer knew the relative order of spatial frequencies, but not the absolute spatial frequencies of the cards on each test. The back of each card was marked to indicate the position of the test grating and "blank" stimulus. Observers typically presented each card without knowing the position of the stimuli and then used the markings to confirm their judgment concerning stimulus location after the grating had been shown several times to the child.

Test distance from the peephole to the child's eyes was 31 ± 3 cm at the 3-, 6-, and 9-month test ages and 54 ± 3 cm for test ages older than 9 months.

Children who had been prescribed optical correction by their referring pediatric ophthalmologist wore their prescribed correction during testing.

**Stereopsis testing:** At the 6-month test age and all subsequent test ages, presence vs absence of stereopsis was assessed with the dynamic random-element stereogram. The child was seated on the parent's lap at a distance of approximately 36 cm from the stereogram screen. Glasses containing a red filter (Wratten #29) over the left eye and a green filter (Wratten #58) over the right eye were placed on the child. For children who already wore glasses, the filters were taped over their own lenses. The parent wore a pair of glasses with red filters over both eyes, which prevented detection of the stereoscopic target. The experimenter, who was masked to the direction of stimulus movement, observed the child's eye movements, head movements and reaching behavior and made a forced-choice judgment on each trial as to whether the stimulus had moved to the left or to the right. Observers also recorded whether or not the child reached for the stereoscopic stimulus.

Initially, the child was shown four trials with the control (green square on a dark background) target. If the experimenter correctly judged stimulus direction on at least three trials, testing with the stereoscopic stimulus was begun. Testing with the stereoscopic square continued until the experimenter met one of three criteria—five of the first five trials correct (Pass), eight of the first nine trials correct (Pass), or two trials incorrect (Fail)—or until the child refused to cooperate.

**Experimenters:** To minimize bias in acuity testing, the two experimenters who tested subjects were masked to the diagnosis of each subject and were allowed to see subjects only after they had been patched for monocular acuity testing. It was not pos-
Table 1. Clinical outcome at 36 months

<table>
<thead>
<tr>
<th></th>
<th>Esotropia</th>
<th>High hyperopia</th>
<th>Moderate hyperopia</th>
<th>Family history</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 16</td>
<td>8</td>
<td>9</td>
<td>9</td>
<td>23</td>
</tr>
<tr>
<td>Strabismus (# of children)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ortho</td>
<td>4</td>
<td>6</td>
<td>9</td>
<td>9</td>
<td>23</td>
</tr>
<tr>
<td>Deviation &lt;10Δ</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Deviation &gt;10Δ</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Single Surgery</td>
<td>13</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Multiple Surgeries</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hyperopia (# of eyes)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(most hyperopic meridian)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>None or Minimal</td>
<td>19</td>
<td>8</td>
<td>16</td>
<td>18</td>
<td>44</td>
</tr>
<tr>
<td>(+0.75 to -2.75 D)</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Moderate</td>
<td>5</td>
<td>2</td>
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<td>0</td>
<td>2</td>
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<tr>
<td>(+3.00 to +3.75 D)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>8</td>
<td>6</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>(&gt; +4.00 D)</td>
<td></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Astigmatism (# of eyes)</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>&lt;1.00 D</td>
<td>21</td>
<td>14</td>
<td>17</td>
<td>18</td>
<td>42</td>
</tr>
<tr>
<td>≥1.00 D</td>
<td>11</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Anisometropia (# of children)</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>&lt;1.00 D difference in</td>
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<tr>
<td>spherical equivalent or</td>
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<td></td>
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<tr>
<td>cylinder</td>
<td>12</td>
<td>7</td>
<td>9</td>
<td>9</td>
<td>23</td>
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<tr>
<td>≥1.00 D difference in</td>
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<td>spherical equivalent or</td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>cylinder</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>0</td>
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</tr>
</tbody>
</table>

sible, however, to completely mask the experimenter to latent nystagmus, extreme deviation or the presence of the optical correction.

The experimenter for stereopsis testing was not the same experimenter who conducted acuity testing. This experimenter knew the diagnosis of the child and, of necessity, viewed the child when the child was not wearing a patch.

Eye Examinations

In addition to the initial eye examination, performed when the child entered the study, each child in the High Hyperopia, Moderate Hyperopia, Family History and Control groups received an eye examination and cycloplegic refraction by a pediatric ophthalmologist when they reached 1, 2, and 3 years of age. Children in the Esotropia group and children in the High Hyperopia group who developed strabismus received examinations as required by clinical protocol.

Results

Clinical Outcome at Age Three Years

The clinical outcome at age 3 of the children in each of the five groups is summarized in Table 1. Several general conclusions can be drawn from Table 1. First, the only children who became strabismic after 8 months of age were three children in the High Hyperopia group, who developed strabismus ≥ 15 prism diopeters between 21 and 29 months of age. Of the three, one underwent surgery at 33 months, spectacle correction eliminated the esotropia in one and the third had not yet undergone surgery by age 3.

Second, all children in the Esotropia group had undergone at least one surgical procedure for eye alignment by 3 years of age. Despite surgical intervention, 12 continued to show some deviation.

Third, a significant reduction in the amount of hyperopia present occurred between infancy and age 3, as evidenced by the finding that 16/18 eyes in the Moderate Hyperopia group and 8/16 eyes in the High Hyperopia group showed minimal or no hyperopia at age 3. The two children in the High Hyperopia group who continued to show high hyperopia in both eyes and one of the two children who showed high hyperopia in one eye and moderate hyperopia in the other eye developed esotropia ≥ 15 prism diopters between 21 and 29 months. All three had received spectacle correction between 14 and 24 months, one at 14 months, prior to any strabismus, one at 14 months, when 4 prism diopters of esotropia was noted, and one at 24 months, when esotropia of 15 prism diopters was noted.

† A small angle deviation (4 prism diopters) was noted for one of these children at 14 months. A deviation of 30 to 40 prism diopters developed by 24 months.
The initial refraction of subjects in the Esotropia group, conducted when subjects were between one and eight months of age, revealed that 12 infants had no significant refractive errors in either eye, five had moderate hyperopia in one or both eyes and three had high hyperopia in both eyes. At age 3, the incidence of moderate and high hyperopia in this group had increased, in contrast to the Moderate Hyperopia and High Hyperopia groups, both of which showed a decrease in the incidence of hyperopia at age 3.31

Fourth, all groups except the Esotropia group showed a reduction in the incidence of astigmatism ≥1.00 D by age 3. The prevalence of astigmatism ≥1.00 D in one or both eyes at the time of the initial refraction was 55% (11/20) in the Esotropes, 20% (2/10) in the High Hyperopes, 21% (3/14) in the Moderate Hyperopes, 14% (2/14) in the Family History group and 13% (4/30) in the Control group. At age 3, nine of the Esotropes (56% of those refracted at age 3) had at least 1.00 D of astigmatism in one or both eyes; six of the nine were in the group of 11 Esotropes who had ≥1.00 D of astigmatism at the time of the initial refraction.

Finally, four of the 16 Esotropes showed anisometropia ≥1.00 D spherical equivalent or cylinder at age 3. Two of the four were the only two children in the study with anisometropia at the time of the initial refraction. Only one other child (one of the High Hyperopes who became strabismic) developed anisometropia by age 3.

Visual Acuity Results

Success rates: The percentage of children from whom one or both monocular acuity estimates could be obtained varied widely across the various test ages. Table 2 shows for each test age the percentage of eyes that reported previously for binocular testing of children at these ages.32 The success rates at 18 and 24 months in the present study were so low that it is unlikely that the data obtained provide a representative sample of visual acuity in the five groups of subjects. Therefore, we did not analyze the monocular acuity data at these two ages.

Overall success rates for the five groups were 88%, 91%, 83%, 90% and 93% for the Esotropia, High Hyperopia, Moderate Hyperopia, Family History and Control groups, respectively. For the 30- and 36-month test ages, where acuity differences between the Esotropes and Controls were found, the success rate was 100% (64/64 tests) for the Esotropia group and 99% (95/96 tests) for the Control group.

Table 2. Success rates of acuity and stereopsis testing

<table>
<thead>
<tr>
<th>Age (months)</th>
<th># Eyes tested successfully</th>
<th>%</th>
<th># Successful tests*</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>113/126</td>
<td>90</td>
<td>54/60</td>
<td>90</td>
</tr>
<tr>
<td>6</td>
<td>147/158</td>
<td>93</td>
<td>44/57</td>
<td>77</td>
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<tr>
<td>9</td>
<td>144/168</td>
<td>86</td>
<td>37/60</td>
<td>62</td>
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<tr>
<td>12</td>
<td>128/160</td>
<td>80</td>
<td>31/64</td>
<td>48</td>
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<tr>
<td>18</td>
<td>65/149</td>
<td>44</td>
<td>34/71</td>
<td>48</td>
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<tr>
<td>24</td>
<td>45/144</td>
<td>31</td>
<td>34/71</td>
<td>48</td>
</tr>
<tr>
<td>30</td>
<td>128/138†</td>
<td>93</td>
<td>53/64</td>
<td>83</td>
</tr>
<tr>
<td>36</td>
<td>124/126†</td>
<td>98</td>
<td>52/59</td>
<td>88</td>
</tr>
</tbody>
</table>

* Child completed enough trials to yield an observer's score of 5/5 or 8/9 correct, or two or more incorrect.

† Success rate at 30 and 36 months include tests performed with the acuity card procedure. Forty-six tests of 30-month-olds and six tests of 36-month-olds required use of the acuity cards. At 30 months, 38 (83%) of the acuity card tests yielded an acuity estimate, and at 36 months, acuity estimates were obtained in 4 (67%) of the acuity cards tested.

Monocular acuity results: For the data obtained at 3, 6, 9, 12, 30 and 36 months, the acuity results from the five groups at each age were compared using a Kruskall-Wallis test. At each age, one test was conducted on data from the eye showing the better acuity score, and a second test was conducted on data from the eye showing the worse acuity score. For data obtained at 3, 6, 9 and 12 months, the results of the Kruskall-Wallis test showed no difference among groups in the distribution of acuity scores from either the eye showing the better acuity score or the eye showing the worse acuity score.

At 30 and 36 months, there was a significant difference in the distribution of acuity scores across groups, both for the eye showing the better acuity score (H = 11.92, P < 0.02 at 30 months, and H = 12.55, P < 0.02 at 36 months) and for the eye showing the worse acuity score (H = 11.20, P < 0.05 at 30 months, and H = 17.16, P < 0.01 at 36 months). Subsequent analysis with Mann-Whitney U-tests (adjusted for multiple comparisons)33 comparing the distribution of acuity scores from the Control group with the distribution of acuity scores from each of the experimental groups indicated a significant difference between the distribution of acuity scores of the Controls vs. the Esotropes for the eye showing the better acuity score at 30 months and the eye showing the better acuity score at 36 months (z = 3.01, P < 0.05 at 30 months, and z = 2.63, P < 0.05 at 36 months) and for the eye showing the worse acuity score at 30 months and the eye showing the worse acuity score at 36 months (z = 2.93, P < 0.05 at 30 months, and z = 3.90, P < 0.05 at 36 months). There were no significant differences between the results of the Control group and the results of any other group.
The distributions of acuity scores obtained at each test age for Controls vs. Esotropes for both the eye showing the better acuity score and the eye showing the worse acuity score are plotted in Figure 2. For data obtained at 3, 6, 9 and 12 months, there are no differences between the distributions of acuity scores for the Controls vs. Esotropes for either the eye showing the better acuity score or the eye showing the worse acuity score at each age. At 30 and 36 months, however, the Esotropes show, on average, significantly poorer acuity scores than do the Controls. The difference between groups in the mean acuity value for the eye showing the better acuity score is 0.54 octave at 30 months and 0.49 octave at 36 months. For the data of the eye showing the worse acuity score, the difference in the mean acuity shown by the Esotropes vs. Controls was 0.59 octave at 30 months and 0.70 octave at 36 months.

Because children were tested with optical correction only when it was prescribed by their referring ophthalmologist, some children with significant uncorrected hyperopia or astigmatism may have performed poorly on the acuity test. To determine whether data from uncorrected subjects may have accounted for the acuity differences between the Control and Esotropic groups, we reanalyzed the data, excluding from analysis data from eyes with uncorrected hyperopia $\geq +4.00$ D or astigmatism $\geq 1.00$ D. This reanalysis was done only at the 36 month test age, because refractions were not performed at 30 months. Mann-Whitney U-tests confirmed the previous findings that the acuity scores of the Controls and Esotropes were significantly different ($z = 2.54$, $P < 0.05$ for the eye showing the better acuity score, and $z = 3.70$, $P < 0.001$ for the eye showing the worse acuity score). Thus, uncorrected hyperopia or astigmatism did not account for the differences in monocular acuity between Esotropes and Controls.

**Interocular acuity differences:** Among the esotropic subjects, interocular acuity differences greater than 1.0 octave were not found in any children at the 3-, 6-, and 9-month test ages, and were found in only one of 11 children tested at 12 months, one of 16 children tested at 30 months and one of 16 children tested at 36 months. These results are not significantly differ-
Fig. 2. Part 2. See Figure 2, Part 1, for details.

Fig. 2. Part 3. See Figure 2, Part 1, for details.
The purpose of the present study was to examine prospectively monocular visual acuity and stereopsis development in infants who had or who were at risk from the percentages of Controls who showed interocular differences greater than 1.0 octave at these ages (1/17 at 3 months, 2/23 at 6 months, 1/23 at 9 months, 1/21 at 12 months, 0/24 at 30 months and 0/23 at 36 months). Kruskall-Wallis tests showed no differences in interocular acuity differences among the five groups at any of the test ages.

### Stereopsis Results

**Success rates:** Assessment of stereopsis with the dynamic random dot stereogram was attempted at the 6-month and all subsequent test ages. As indicated in Table 2, the percentage of subjects on whom presence vs absence of stereopsis could be determined, based on the forced-choice preferential looking criteria of 5/5 or 8/9 correct or two incorrect by the observer, ranged from 48% at 18 and 24 months to 90% at 6 months. Success rates for individual groups were 82% for the Esotropes, 66% for the High Hyperopes, 60% for the Moderate Hyperopes, 75% for the Family History group, and 67% for the Control group. Incomplete tests were largely due to the unwillingness of children to wear the red-green glasses.

**Stereopsis data:** The percentage of testable subjects in each group who showed evidence of stereopsis according to the forced-choice preferential looking criteria of 5/5 or 8/9 correct is shown in Table 3 for the seven test ages. The stereopsis results from each of the four experimental groups were compared with the data from the Control group at each of the test ages using the Chi-Square Test when sample sizes in all or all but one cell were five or greater or the Fisher's Test when sample sizes were small. Analyses revealed significant differences between the prevalence of stereopsis in the group of Esotropes as compared to the Controls at test ages of 24, 30 and 36 months. No significant differences were found between the remaining experimental groups and the Control group.

In addition to making a judgment about whether the stereoscopic square moved to the left or right on each trial, observers also recorded other indications that the child could detect the stereoscopic square, such as following the square with the eyes or hand, or reaching for the square in front of the screen. Some children would cooperate for only a few trials, but would reach for the stereoscopic square in front of the screen and follow its movement for one or two trials. Others would seem to discover the stereoscopic square after several trials and suddenly reach for it or follow it. By strict forced-choice preferential looking criteria, the results from such children were scored as a failure to exhibit stereopsis or an incomplete test. However, it was clear from their behavior that they could detect a target moving in front of the screen.

Therefore, we also analyzed the data based on the observer's judgment concerning whether or not a child exhibited any evidence of stereopsis. These results are presented in Table 4. Overall, many more children showed evidence for stereopsis than was evident from Table 3. Nevertheless, Chi-Square Tests and Fisher's Tests comparing the results of each experimental group with the results of the Control group confirmed the results from Table 3, that only the Esotropia group showed a significantly lower prevalence of stereopsis than the Control group.

Examination of the results of individual children in the Esotropia group revealed that only one child showed evidence of stereopsis at more than one test age (at 18 and 30 months, although not at 24 and 36 months), and this child was also the only child in the Esotropia group who met the forced-choice criteria for stereopsis (with a score of 7/7 correct). In the High Hyperopia group, none of the three children who developed strabismus showed stereopsis at any of the ages at which they were tested.

### Discussion

The purpose of the present study was to examine prospectively monocular visual acuity and stereopsis development in infants who had or who were at risk...
Table 4. Percentage of subjects with stereopsis based on all available information, including percent correct, reaching behavior, and looking behavior

<table>
<thead>
<tr>
<th>Test age</th>
<th>6 mo.</th>
<th>9 mo.</th>
<th>12 mo.</th>
<th>18 mo.</th>
<th>24 mo.</th>
<th>30 mo.</th>
<th>36 mo.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Esotropia</td>
<td>0*</td>
<td>(11)</td>
<td>11</td>
<td>(9)</td>
<td>9</td>
<td>(11)</td>
<td>13*</td>
</tr>
<tr>
<td>High</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hyperopia</td>
<td>20</td>
<td>(5)</td>
<td>13</td>
<td>(8)</td>
<td>20</td>
<td>(5)</td>
<td>80</td>
</tr>
<tr>
<td>Moderate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hyperopia</td>
<td>60</td>
<td>(10)</td>
<td>33</td>
<td>(6)</td>
<td>80</td>
<td>(5)</td>
<td>100</td>
</tr>
<tr>
<td>Family</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>history</td>
<td>22</td>
<td>(9)</td>
<td>33</td>
<td>(6)</td>
<td>63</td>
<td>(8)</td>
<td>78</td>
</tr>
<tr>
<td>Control</td>
<td>42</td>
<td>(19)</td>
<td>40</td>
<td>(15)</td>
<td>50</td>
<td>(10)</td>
<td>75</td>
</tr>
</tbody>
</table>

* P < 0.05.
† P < 0.001.

for strabismus and amblyopia. On the basis of an eye examination and cycloplegic refraction conducted before they reached 8 months of age, infants were enrolled into one of five groups: (1) Esotropes; (2) High Hyperopes; (3) Moderate Hyperopes; (4) Infants with a Family History of strabismus or amblyopia; and (5) Controls.

Visual acuity results indicated that subjects in the Esotropia group showed significantly poorer monocular acuity scores than did the Controls at the 30- and 36-month test ages. This difference was significant for data from the eye showing the better acuity score of each subject, as well as for data from the eye showing the worse acuity score of each subject, and was not due to uncorrected refractive errors. Previously, two groups of researchers compared the absolute acuity scores of the eye showing the better acuity score in esotropic vs. nonesotropic infants 12 months of age and younger. One group tested acuity in 3- to 14-month-olds with an FPL procedure and found no difference between esotropic vs. nonesotropic infants' acuity in the eye showing the better acuity score. Our results for infants in the 3- to 12-month age range are in agreement with these FPL results. In contrast, the other group of researchers, who measured acuity with the visual evoked potential (VEP), showed reduced acuity in esotropes less than one year of age, when the esotropes' results were compared with data obtained from nonesotropic infants tested with the same procedure. The magnitude of the acuity reduction found was large enough (1.04 octaves for the right eye, 1.06 octaves for the left eye, and 0.75 octave for binocular testing) that one would expect it to be detectable in FPL, as well as VEP, acuity testing. The fact that neither of the two FPL studies reported a significant acuity deficit in the better eye of esotropes less than 1 year of age suggests that young esotropes may have an acuity deficit that is present at the level of the visual system tapped by the VEP, but not present at a reduced magnitude, at the level of the visual system tapped by FPL testing.

At our oldest test ages, 30 and 36 months, the FPL results did show an acuity deficit in both the better eye and the worse eye of former esotropes. A recent reanalysis of behavioral acuity data obtained by Ing from treated esotropes tested at 5 and 11 years of age suggested that Ing, too, found reduced acuity in the better eye of a significant number of former esotropes. The cause of this bilateral acuity defect is unclear. On the one hand, it could be the behavioral manifestation of the deficit detectable with VEP testing during the first year of life. On the other hand, the acuity deficit could be the result of the occlusion therapy that our esotropes and the esotropes in the Ing study received during infancy and early childhood. Research on reverse occlusion in kittens has shown that early occlusion of a nondeprived eye can result in bilateral amblyopia. In either case, it is unfortunate that we were unsuccessful in testing subjects at 18 and 24 months, since it would be of interest to know how early the acuity defect was detectable with behavioral testing.

Although both esotropic infants and infants with high hyperopia are known to be at risk for amblyopia, there were no differences among groups at any age in the distribution of interocular acuity differences obtained. Analysis of the data indicated that at each of the 3-, 6-, 9-, 12-, 30- and 36-month test ages, no more than one Esotrope showed an interocular acuity difference of greater than one octave. The failure to find significant interocular differences at 3 and 6 months is not unexpected, since even infants who show a fixation preference typically do not show FPL interocular acuity differences before 7 to 8 months of age. The failure to find significant interocular acuity differences in older infants and young children in our study is undoubtedly related to the fact that all children in the Esotropia group were under treatment for strabismus and amblyopia. On the basis of an eye examination and cycloplegic refraction conducted before they reached 8 months of age, infants were enrolled into one of five groups: (1) Esotropes; (2) High Hyperopes; (3) Moderate Hyperopes; (4) Infants with a Family History of strabismus or amblyopia; and (5) Controls.
by the time they reached the 9-month test age. In addition, research with older amblyopes has indicated that grating acuity tasks may be less sensitive than recognition or localization acuity tasks to the presence of strabismic amblyopia. Therefore, it is possible that some of our former esotropes have a residual interocular acuity difference that will appear clinically when they reach an age at which recognition acuity, for example, the E Test or Snellen letters, can be assessed.

Absolute acuity scores for subjects in our High Hyperopia group were not significantly different from those of the Control group at any of the test ages. This result is in contrast to data reported recently by Atkinson and colleagues, who showed a significant reduction in the acuity of high hyperopes tested at 6 to 9 months of age and at 3½ to 4 years of age. It is likely that the data of Atkinson and colleagues are more representative of the acuity status of high hyperopes, since approximately 100 children were tested in their study while our study enrolled only ten high hyperopes.

A striking finding of the present study was that none of the 36-month-olds in the Esotropia group showed evidence of stereopsis. This failure to show stereopsis is in contrast to the results of several studies in which the percentage of esotropes who had achieved early alignment and who demonstrated stereopsis ranged from approximately 20% to over 40%. Examination of the test conditions used in the studies of stereopsis in treated infantile esotropes suggests that these differences among the reported percentages of children with stereopsis in the various studies may be largely due to differences among the test stimuli used to assess stereopsis. For example, in most of the studies that reported the presence of stereopsis in a substantial proportion of former esotropes, a static stereogram and polarizing separation were used for stereopsis testing. In contrast, two of the three previous studies in which dynamic stereograms and anaglyphic separation, similar to that of the present study, were used to assess stereopsis in former infantile esotropes have shown a prevalence of stereopsis between 0 and 10%. Cooper and Feldman have suggested that the difference in the presence of monocular cues in the static stereograms. The only study in which dynamic stereograms were used and a high proportion of former esotropes showed stereopsis is a study by Rogers and colleagues, in which infants were tested two weeks after strabismus surgery. Recent results of Archer and colleagues indicate that stereopsis in these infants is confined to the immediate postoperative period and is not detectable after longer follow-up intervals. Thus, our results that few, if any, former esotropes show stereopsis when tested with a dynamic random dot stereogram are consistent with the results of other studies that have used similar stimuli to evaluate infantile esotropes who underwent surgery months or years prior to stereopsis testing.

The failure of most infants in the present study to show evidence of stereopsis by the FPL criteria of 5/5 or 8/9 correct before 18 to 24 months of age may seem surprising, since studies using similar stimuli and procedures have indicated that normal infants show stereopsis by 6 months of age. However, examination of results from the Shea et al study, which presented data of individual infants, revealed that none of the infants in that study would have met the FPL criteria for stereopsis used in the present study, since observers scored two or more incorrect trials for each infant. Because infants completed 10 to 20 trials, Shea et al were able to use criteria for stereopsis that allowed more incorrect trials than did the criteria of the present study. In contrast to the infants in the Shea et al study, most infants in our study would not cooperate for 10 to 20 trials. This is probably because they were tested after completion of two monocular acuity tests, and therefore were tired of testing in general, especially with a stimulus (the stereoscopic square) that may have been less compelling than the black-and-white gratings used for acuity testing.

Three groups of subjects in the present study—the Moderate Hyperopia, High Hyperopia and Family History groups—were selected because previous research has suggested that infants in these groups are at risk for the development of strabismus and/or amblyopia. Results from Ingram et al, based on refractions conducted when infants were 12 months of age, predict that approximately one-fourth of infants in our Moderate Hyperopia group would have developed strabismus by age three. However, none of our Moderate Hyperopes developed strabismus, perhaps because infants were assigned to the Moderate Hyperopia group on the basis of a refraction conducted prior to eight months of age rather than at 12 months of age, as in the Ingram et al study. It is also possible that one or more of the five Moderate Hyperopes who dropped out of the study developed strabismus.

Evidence that infants in our High Hyperopia group were at risk for strabismus comes from two previous studies. Ingram et al reported that 48% of infants with +4.00 D or more of meridional hyperopia developed strabismus by age 3½ and Atkinson et al found that approximately 16% of infants with meridional hyperopia of +4.00 D or more at 6 to 9 months of age had developed strabismus by age 4 years. Our results are in agreement with these two studies, in that
three (38%) of the eight High Hyperopes whom we followed for more than 2 years developed strabismus.

It would be of interest to know why some infants with high hyperopia become strabismic and others do not. In our sample, four infants showed a reduction in hyperopia to below +4.00 D in both eyes by age 17 months. None of the four became strabismic. However, three of the four infants who retained hyperopia \( \geq +4.00 \) D in one or both eyes became strabismic. Atkinson et al.\(^{38,39}\) reported that infants with oblique-axis astigmatism were more likely to remain hyperopic and more likely to become strabismic than were nonastigmatic infants. However, in our sample, only two of the High Hyperopes showed more than 1.00 D of astigmatism at the time of the initial refraction and only one of these infants became strabismic. Thus, in our sample, it is unclear why some infants retained their hyperopia and became strabismic, and others showed a significant reduction in hyperopia by 1 to 2 years of age. Our data provide a small amount of evidence that high hyperopes who show evidence of stereopsis do not develop strabismus, since none of the three High Hyperopes who developed strabismus showed stereopsis at any test age. However, failure of an infant to show stereopsis is not necessarily predictive of future strabismus, since there were several High Hyperopes who failed to exhibit stereopsis in infancy but did not go on to develop strabismus by age 3 years.

The presence of a genetic component in the occurrence of strabismus has been reported.\(^{21}\) The finding that none of the children in our Family History group developed strabismus by age 3 does not necessarily contradict the presence of a genetic component, since two of the children in our Esotropia group had two or more close relatives with strabismus or amblyopia. It could be argued that the genetic factor associated with strabismus is associated with early onset of strabismus, so that infants who developed strabismus in conjunction with a family history did so early enough that they were included in the Esotropia rather than the Family History group in the study. In addition, it is possible that one or more of the five infants in the Family History group who dropped out of the study could have developed strabismus after leaving the study. Of the three infants in the High Hyperopia group who developed strabismus, only one had a family history of strabismus and/or amblyopia. Thus, it is likely that factors other than simple genetic transmission influenced the development of strabismus in this group.

In summary, we followed five groups of infants prospectively, to examine the development of visual acuity and stereopsis in infants with esotropia and in infants at various degrees of risk for strabismus or amblyopia. Our results showed no differences in absolute acuity scores or in interocular acuity differences among groups of infants until the 30- and 36-month test ages, when the group of children who had been treated for infantile esotropia showed below normal acuity in both the eye with the better acuity score and the eye with the worse acuity score. Stereopsis testing with a dynamic random-element stereogram showed evidence of stereopsis in no more than one or two children in the infantile esotropia group at any test age, and no evidence of stereopsis in any of the former esotropes at 36 months.

None of the nonstrabismic infants at risk due to a family history of strabismus or amblyopia and none of the infants with moderate hyperopia (\( \geq +3.00\) D and \( \leq +3.75\) D along the most hypotropic meridian) diagnosed by age 8 months developed strabismus over the 2- to 3-year follow-up. However, over 30% of the infants with hyperopia greater than +4.00 D along the most hyperopic meridian before age eight months developed strabismus by age 3 years. This finding confirms previous reports\(^{22,36,39}\) that infants with high hyperopia are at significant risk for strabismus and highlights the importance of continued follow-up of infants who show high hyperopia at an early age.

**Key words:** visual acuity, stereopsis, esotropia, hyperopia, infants

**Acknowledgments**

We thank Melvin Carlson, MD and Howard Freedman, MD for referring the esotropic infants, Melvin Carlson, MD for performing eye examinations on non-strabismic subjects, MaryAlice McDonald, PhD for assistance in testing subjects, Carol Jerome for illustrations, and Luisa Mayer, PhD for comments on the manuscript.

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