Early Treatment of Congenital Unilateral Cataract Minimizes Unequal Competition

Eileen E. Birch,1,2 David Stager,3 Joel Leffler,3 and David Weakley2,3

PURPOSE. Dense congenital unilateral cataracts may compromise visual development through visual deprivation and biased interocular competition, whereas dense congenital bilateral cataracts compromise visual development primarily through visual deprivation alone. Differences in sensory deficits between the two patient groups with these disorders may reflect the specific effects of unequal competition. To determine whether early treatment (at <8 weeks of age) minimizes the adverse effects of unequal competition, grating acuity deficits during the immediate posttreatment period and contrast sensitivity deficits at 6 to 8 years of age were assessed in 29 children with histories of dense congenital unilateral or bilateral cataracts who had had treatment between 1 and 8 weeks or 12 and 30 weeks. All children maintained good to excellent compliance with optical correction and occlusion therapy.

METHODS. Grating acuity was measured using a two-alternative forced-choice preferential-looking staircase protocol. Contrast thresholds at three spatial frequencies (0.38, 1.5, and 6 c/deg) were measured at each of two temporal frequencies (2- and 8-Hz sinusoidal counterphase modulation) using D6 grating patches.

RESULTS. Grating acuity deficits in the immediate posttreatment period were similar in patients with a history of unilateral cataract (n = 10) and those with a history of bilateral cataracts (n = 6) when treatment was provided during the first 8 weeks of life. With later treatment, patients with a history of unilateral cataract (n = 7) had significantly larger grating acuity deficits than patients with a history of bilateral cataracts (n = 6). Children with a history of dense congenital unilateral cataract had similar deficits in contrast sensitivity to children with a history of bilateral cataracts when treatment was initiated during the first 8 weeks of life. When treatment was initiated later (i.e., at 12–30 weeks), patients with a history of unilateral cataract showed greater deficits in contrast sensitivity and a dependence of the amount of spatial contrast sensitivity deficit on temporal frequency than did patients with a history of bilateral cataracts.

CONCLUSIONS. These findings support the hypothesis that only visual deprivation is active as an amblyogenic factor during the first weeks of life, but when unilateral deprivation is prolonged to 12 to 30 weeks, unequal competition also plays a role in amblyogenesis. (Invest Ophthalmol Vis Sci. 1998;39:1560-1566)

Adverse effects of dense congenital unilateral cataracts on the developing visual system of infants may result from the direct effects of visual deprivation and from competition with the normal eye in establishing cortical structure and function during a critical period in visual development. One approach to evaluating these two amblyogenic factors has been to compare the effects of unilateral and bilateral cataracts on visual development. The rationale is that a developing visual system with dense bilateral cataracts is affected primarily by early visual deprivation, whereas the developing visual system with a dense unilateral cataract is affected by visual deprivation and by competition with a normal eye.

Maurer and Lewis1 and Tytla et al.2 investigated the effects of deprivation and competition by evaluating contrast sensitivity deficits in children treated for unilateral or bilateral congenital cataracts at various ages, primarily at 12 weeks of age or older. They found a pattern of loss in children with a history of bilateral cataracts that was distinct from the pattern in children with a history of unilateral cataract. Although both groups of children showed increasing deficits with increasing spatial frequency, those with a history of unilateral cataract had deeper deficits and deficits across a wider range of spatial frequencies than those with a history of bilateral cataracts. In addition, children with a history of unilateral cataract had less spatial contrast sensitivity deficit at higher than at lower temporal frequencies, whereas children with a history of bilateral cataracts had similar deficits at high and low temporal frequencies. Thus, the unique effects of competition with a normal eye included an increase in the degree of deficit and a dependence on temporal frequency.

A second comparison of sensory outcome that is useful for evaluating the amblyogenic effects of deprivation and competition is prospective comparison of the depth of acuity deficits in patients with unilateral cataract with deficits in patients with

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bilateral cataracts immediately after treatment for congenital cataracts. If acuity deficits caused by congenital bilateral cataracts are primarily the result of early visual deprivation and acuity deficits caused by congenital unilateral cataract are the result of deprivation and competition, unilateral cases should always have larger acuity deficits than bilateral cases when matched for age at treatment.

The results of our recent studies suggest that the adverse effects of a dense congenital unilateral cataract are minimized when treatment is initiated during the first 6 to 8 weeks of life. One purpose of the present study was to determine whether children with a history of unilateral cataract who are treated during this critical period show the same pattern of spatial contrast sensitivity deficits as those treated at later ages. Specifically, if unilateral cases show larger spatial contrast sensitivity deficits than bilateral cases and dependence of deficit on temporal frequency, regardless of age at treatment, it would support the hypothesis that visual deprivation and unequal competition are amblyogenic factors, even during the first weeks of life. The alternative hypothesis is that children in unilateral and bilateral cases show similar deficits if treatment is initiated during the first weeks of life. This outcome would support the hypothesis that only visual deprivation acts as an amblyogenic factor during early weeks and that prolonged unilateral deprivation is necessary before adverse effects of unequal competition occur. A second purpose of the study was to determine whether children with a history of unilateral cataract show larger acuity deficits immediately after treatment than children with a history of bilateral cataracts, regardless of age at treatment. Specifically, if unilateral cases show larger acuity deficits than bilateral cases immediately after treatment, regardless of age at treatment, this outcome would support the hypothesis that visual deprivation and unequal competition are amblyogenic factors even during the first weeks of life. The alternative hypothesis is that unilateral and bilateral cases show similar acuity deficits if treatment is initiated during the first weeks of life. This outcome would support the hypothesis that only visual deprivation acts as an amblyogenic factor during the early weeks of life and that prolonged unilateral deprivation is necessary before adverse effects of unequal competition occur.

**METHODS**

**Patients**

Twenty-nine children aged 6 to 8 years participated in the study. Diagnosis was made and treatment initiated in all children treated between 1985 and 1990. Each had a history of dense fetal nuclear cataract more than 5 mm in diameter, with a fundus that was not visible on indirect ophthalmoscopy. Seventeen patients had unilateral cataract and 12 had bilateral cataracts. Cataract was noted in all by an ophthalmologist when the children were 1 to 10 days of age. Children were grouped by age at treatment (i.e., age at which surgery and optical correction were completed and occlusion therapy initiated), 8 weeks or younger (10 unilateral cataract and 6 bilateral cataracts) or 12 to 30 weeks old (7 unilateral cataract and 6 bilateral cataracts). In all cases, when treatment was delayed, it was because the parents chose to seek other medical opinions before surgery or because the parents refused surgery until their child was older.

**Table 1. Best Corrected Snellen Acuity in Children 6 to 8 Years of Age Obtained with a BVAT System at 20 feet**

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Eyes Tested</th>
<th>LogMAR</th>
<th>Snellen Acuity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilateral ≤ 8 weeks (n = 6)</td>
<td>Right</td>
<td>0.427 ± 0.252</td>
<td>(20/53)</td>
</tr>
<tr>
<td>Bilateral 12-30 weeks (n = 6)</td>
<td>Right</td>
<td>0.444 ± 0.162</td>
<td>(20/56)</td>
</tr>
<tr>
<td>Unilateral ≤ 8 weeks (n = 10)</td>
<td>Aphakic</td>
<td>0.383 ± 0.220</td>
<td>(20/48)</td>
</tr>
<tr>
<td>Unilateral 12-30 weeks (n = 7)</td>
<td>Aphakic</td>
<td>0.886 ± 0.371</td>
<td>(20/153)</td>
</tr>
</tbody>
</table>

BVAT, BVATII Video Acuity Tester (Mentor O & O Inc.); MAR, minimum angle of resolution.

There were no significant differences in the size or density of the cataracts in the unilateral versus bilateral cataract groups nor in the early versus late treatment groups. None of the patients had congenital malformations or infections, ocular abnormalities unrelated to the cataract, persistent hyperplastic primary vitreous, or neurologic dysfunction. All children had been treated with surgery, aphakic contact lens correction, and occlusion therapy (for unilateral cataract). Strabismus surgery was performed when indicated. When the children were aged 3 to 5 years, bifocal or multifocal spectacles were prescribed.

To control for the potentially intervening variable of compliance, only patients with good (>75% of prescribed number of hours) to excellent (>95% of prescribed number of hours) compliance with contact lenses or bifocal or multifocal spectacles and occlusion therapy of 6 to 8 h/d were included. Compliance was routinely evaluated in independent interviews by the surgeon and orthoptist, the contact lens specialist, and laboratory staff. These follow-up appointments occurred on different days at different sites. Volunteer participants in an independent research laboratory setting, in general, have good to excellent compliance. There were no significant differences in compliance between the unilateral and bilateral cataract groups or between the early and late treatment groups who met the compliance inclusion criteria for the study. The mean ± SD for best corrected Snellen acuity outcome at age 6 toconstituted the larger population of children with a history of congenital cataracts who are undergoing evaluation in an ongoing prospective study (N = 161).

Informed consent was obtained from one or both parents after the nature and possible consequences of the study were explained. This research protocol observed the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of the University of Texas Southwestern Medical Center.

**Contrast Sensitivity**

Contrast thresholds at three spatial frequencies (0.38, 1.5, and 6 c/deg) were measured at each of two temporal frequencies (2- and 8-Hz sinusoidal counterphase modulation) using D6 grating patches. D6 grating patches are spatially localized stim-
Forced-choice preferential-looking (FPL) acuity was measured for each eye using a two-alternative forced-choice preferential-looking protocol. All children were tested monocularly. In unilateral cases, the aphakic eye was tested first; in bilateral cases, the right eye was tested first. High-contrast (>90%) square-wave gratings and paired gray fields (72 cyc/deg gratings) were rear projected onto two 11.5”-diameter lenscreens (36° center-to-center separation; Polacoat Lenscreen™; 3M, Inc., Minneapolis, MN). Gratings and gray fields were photometrically matched in mean luminance (2.4 log cd/m²). All test sessions began with a low spatial frequency (0.4 cyc/deg), with approximate one-half octave steps between successive stimuli. A 2-down-1-up staircase procedure was used to converge on the acuity threshold in 10 reversals, and acuity was estimated as the geometric mean of the last 8 reversals.

All patients participated in FPL testing within 6 weeks of initial treatment and subsequently at approximately 3-month intervals until they reached 15 to 18 months of age. From 18 to 60 months, patients were evaluated at approximately 6-month intervals. Normative FPL acuity data for the right eyes (tested first) of children aged 0 to 5 years gathered as part of an earlier study were used for comparison.

Statistical Analyses

Contrast sensitivity data for the aphakic eyes of unilateral cases and for the right eyes of bilateral cases and healthy subjects were entered into the analyses. Data were analyzed by two-way analysis of variance to assess the main effects of diagnostic group (unilateral cataract, bilateral cataracts, or healthy) and spatial or temporal frequency. Tukey’s post hoc tests were used to determine pairwise differences. Forced-choice preferential-looking acuity data for the aphakic eyes of unilateral cases and for the right eyes of bilateral cases and healthy subjects were entered into the analyses. Immediate posttreatment FPL acuity deficits were calculated by computing the signed log difference between each patient’s logMAR (minimum angle of resolution) acuity measured within 6 weeks of the initial treatment and the mean normal logMAR acuity for age-matched infants. Acuity deficits were compared by t-tests to determine whether children with a history of unilateral cataracts and those with a history of bilateral cataracts in each treatment group had significantly different acuity deficits.

RESULTS

Contrast Sensitivity after Treatment at 12 to 30 Weeks

Spatial contrast sensitivity functions at 2 Hz and 8 Hz in children treated at 12 to 30 weeks of age are shown in Figure 1, along with data from age-matched healthy children. Also shown are the data replotted as log sensitivity deficit relative to the normative data. These data are consistent with the three major findings of the earlier study by Maurer and Lewis and Tytla et al. First, unilateral and bilateral cases show increasing acuity deficits with increasing spatial frequency (main effect of spatial frequency: F₁,₁₂ = 67.4, P < 0.001; F₈,₁₂ = 85.0, P < 0.001). Second, children with a history of unilateral cataract have significantly less acuity deficit at 6 cyc/deg at 8 Hz compared with that at 6 cyc/deg at 2 Hz (P < 0.05), whereas deficits are comparable at all spatial frequencies for both temporal frequencies in bilateral cases. Third, for the same period of visual deprivation (i.e., 12–30 weeks), children with a history of unilateral cataract show larger deficits and deficits across a larger range of spatial frequencies: That is, at 2 Hz, unilateral cases show significant deficits at 0.38 cyc/deg and 1.5 cyc/deg (P < 0.01); at 8 Hz, only unilateral cases show deficits at 0.38 cyc/deg (P < 0.01).

Contrast Sensitivity after Treatment between 1 and 8 Weeks

Spatial contrast sensitivity functions at 2 Hz and 8 Hz in children treated between 1 and 8 weeks are shown in Figure 2 along with data from age-matched healthy children. Also shown are the data replotted as log sensitivity deficit relative to the normative data. Children with a history of unilateral or bilateral cases show increasing acuity deficit with increasing spatial frequency (main effect of spatial frequency: F₁,₁₂ = 214.1, P < 0.001; F₈,₁₂ = 214.1, P < 0.001). There are no significant differences in the depth of acuity deficits at any spatial–temporal frequency between unilateral cases and bilateral cases. There are no significant differences in the depth of deficits at 2 Hz and 8 Hz in unilateral cases. Note that with the current sample size, there is 0.8 power to detect differences of 0.3 log unit (1 octave) at α = 0.05.

Forced-Choice Preferential-Looking Acuity

Forced-choice preferential-looking acuity after treatment for congenital cataract is shown in Figure 3, along with data from age-matched healthy children. During the first weeks immediately after treatment, children with a history of bilateral or unilateral cataracts treated by 8 weeks of life had similar FPL acuity deficits of approximately one-half octave (0.20 ± 0.09 and 0.18 ± 0.07 log deficit, respectively; [NS] not significant). In contrast, among the children treated between 12 and 30 weeks, unilateral cases had significantly larger FPL acuity def-
FIGURE 1. (A) Contrast sensitivity of children treated for bilateral (n = 6) or unilateral (n = 7) congenital cataracts between 12 and 30 weeks of age. Also shown are normative data (n = 29). Vertical bars indicate ±1 SEM. (B) Acuity deficits in contrast sensitivity relative to age-matched healthy children derived from (A). Vertical bars indicate ±1 SEM; (--) 2 SEs for the normative population.

Conclusions
Children with a history of dense congenital unilateral cataract had similar deficits in contrast sensitivity to children with a history of bilateral cataracts when treatment was initiated during the first 8 weeks of life. When treatment was initiated later (i.e., between 12 and 30 weeks), unilateral cases showed greater deficits in contrast sensitivity and dependence of the amount of spatial contrast sensitivity deficit on temporal frequency. These findings support the hypothesis that only visual deprivation is ac-

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tive as an amblyogenic factor during the first weeks of life but, when unilateral deprivation is prolonged to 12 to 30 weeks, unequal competition also plays a role in amblyogenesis.

Although the contrast sensitivity data are consistent with a model of visual development in which unequal competition has little or no amblyogenic effect during the first weeks of life, the contrast sensitivity data are also consistent with a model in which competition has an amblyogenic effect during the first weeks of life. Its effects, however, are reversible by early treatment. The prospective FPL acuity data pertain to these alternative models of visual development. If unequal competition is an active amblyogenic factor during the first weeks of life, visual acuity should be poorer

**Figure 2.** (A) Contrast sensitivity of children treated for bilateral ($n = 6$) or unilateral ($n = 10$) congenital cataracts between 1 and 8 weeks of age. Also shown are normative data ($n = 29$). Vertical bars indicate $\pm 1$ SEM. (B) Acuity deficits in contrast sensitivity relative to age-matched healthy children derived from (A). Vertical bars indicate $\pm 1$ SEM; (- - -) $2$ SEs for the normative population.
in children with a history of unilateral cataract than in those with a history of bilateral cataracts immediately after treatment, regardless of age at treatment. Instead, the prospective FPL acuity data presented here show that treatment during the first 8 weeks of life yields similar small FPL acuity deficits in unilateral and bilateral cases immediately after treatment. Treatment between 12 and 30 weeks yields a significantly larger FPL acuity deficit in unilateral cases than bilateral cases immediately after treatment. Thus, the prospective FPL acuity data support the hypothesis that only visual deprivation is active as an amblyogenic factor during the first weeks of life.

The data of the present study are also consistent with the findings of several recent studies in which good acuity outcomes were attained when treatment was initiated in affected children between 6 and 8 weeks of age. In addition, a recent statistical analysis of Snellen acuity outcome data supports a bilinear model of treatment effectiveness in which treatment during the initial 6 weeks is maximally effective, whereas the effectiveness of treatment rapidly diminishes between weeks 12 and 52.

References