Published in final edited form as:

J AAPOS. 2012 April ; 16(2): 156–160. doi:10.1016/j.jaapos.2011.11.007.

Fixation control and eye alignment in children treated for dense congenital or developmental cataracts

Eileen E. Birch, PhD^{a,b}, Jingyun Wang, PhD^{a,c}, Joost Feliuss, PhD^{a,b}, David R. Stager Jr, MD^{b,d}, and Richard W. Hertle, MD^e

^aRetina Foundation of the Southwest, Dallas, Texas

^bDepartment of Ophthalmology, University of Texas Southwestern Medical Center, Dallas, Texas

^cDepartment of Ophthalmology, Indiana University School of Medicine, Indianapolis, Indiana

^dPediatric Ophthalmology and Adult Strabismus, Plano, Texas

^eChildren's Hospital Vision Center, Children's Hospital Medical Center, Akron, Ohio

Abstract

BACKGROUND—Many children treated for cataracts develop strabismus and nystagmus; however, little is known about the critical period for adverse ocular motor outcomes with respect to age of onset and duration.

METHODS—Children who had undergone extraction of dense cataracts by the age of 5 years were enrolled postoperatively. Ocular alignment was assessed regularly throughout follow-up. Fixation stability and associated ocular oscillations were determined from eye movement recordings at 5 years old. Multivariate logistic regression was used to evaluate whether laterality (unilateral vs bilateral), age at onset, and/or duration of visual deprivation were associated with adverse ocular motor outcomes and to determine multivariate odds ratios (ORs).

RESULTS—A total of 41 children were included. Of these, 27 (66%) developed strabismus; 29 (71%) developed nystagmus. Congenital onset was associated with significant risk for strabismus (OR, 5.3; 95% CI, 1.1–34.1); infantile onset was associated with significant risk for nystagmus (OR, 13.6; 95% CI, 1.6–302). Duration >6 weeks was associated with significant risk for both strabismus (OR, 9.1; 95% CI, 1.9–54.2) and nystagmus (OR, 46.2; 95% CI, 6.0–1005). Congenital onset was associated with significant risk for interocular asymmetry in severity of nystagmus (OR, 25.0; 95% CI, 2.6–649), as was unilateral cataract (OR, 58.9; 95% CI, 5.1–2318).

CONCLUSIONS—Laterality (unilateral vs bilateral) and age at onset were significant nonmodifiable risk factors for adverse ocular motor outcomes. Duration of deprivation was a significant modifiable risk factor for adverse ocular motor outcomes. The current study demonstrated that reduced risk for nystagmus and strabismus was associated with deprivation 6 weeks.

Most studies of outcomes following surgery for dense congenital, infantile, or developmental cataracts have highlighted the importance of age at surgery, duration of

Copyright © 2012 by the American Association for Pediatric Ophthalmology and Strabismus.

Correspondence: Eileen E. Birch, PhD, Retina Foundation of the Southwest, 9900 North Central Expressway, Suite 400, Dallas, TX 75231 (ebirch@retinafoundation.org).

The authors have no conflicts of interest to disclose.

This work was presented as a poster at the 37th Annual Meeting of the American Association for Pediatric Ophthalmology and Strabismus, March 30–April 3, 2011, San Diego, California.

visual deprivation, and laterality (unilateral vs bilateral) as risk factors for poor visual acuity outcome.^{1–5} For dense congenital unilateral cataracts, surgery during the first 6 weeks of life is associated with improved visual acuity outcomes versus later surgery.^{6,7} It has been suggested that every 3 weeks of delay in surgery for dense congenital bilateral cataracts results in an average long-term loss of one line (0.1 logMAR) of visual acuity.^{8–10} Visual acuity outcomes following surgery for infantile and developmental cataracts are poorer when the duration of visual deprivation is lengthy.¹¹ Taken together, these studies support the hypothesis that the first months of life are a critical period for visual acuity maturation and that, during this critical period, even a brief period of visual deprivation can have profound and long-lasting consequences on visual acuity outcome.

Many children treated for dense cataracts develop strabismus, nystagmus, or both.^{4,12–15} Compared with our understanding of visual acuity outcome, little is known about the critical period for ocular motor outcomes. Nystagmus has been reported to be more prevalent among children with bilateral cataracts than in children with unilateral congenital and infantile cataracts.^{4,16,17} In addition to laterality, both age at surgery and duration of visual deprivation have been proposed as risk factors for the development of nystagmus.^{6–8,15,16,18} The majority of these studies did not report data on the incidence or prevalence of strabismus. Even when the incidence or prevalence of strabismus was addressed, there were inconsistencies among studies in methods of assessment and classification of strabismus and whether they reported the initial deviation or the deviation of the most recent visit. Even fewer studies used eye movement recording systems to assess fixation or the presence of associated ocular oscillations, relying on clinical observation despite the inadequacy of this approach for determining the presence or nature of any involuntary fixation instability or nystagmus.¹⁹ Therefore the critical period for adverse ocular motor outcomes remains ill defined. In this study, we evaluated whether age at onset, duration of visual deprivation, and/or laterality (unilateral vs bilateral) affected ocular motor outcomes following cataract surgery during the first 5 years of life.

Subjects and Methods

Children treated for dense congenital or developmental cataracts during the first 5 years of life were enrolled following cataract extraction. Participants with cataracts were referred to the study by eight Dallas–Fort Worth area pediatric ophthalmologists. Excluded from participation were children with posterior persistent fetal vasculature, glaucoma, congenital infections, metabolic diseases, syndromes, and developmental delay. Children who experienced sight-threatening intra- or postoperative complications were also excluded. Children with elevated intraocular pressure that was well controlled with medication were not excluded.

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. All data were gathered at the Retina Foundation of the Southwest in compliance with the Health Insurance Portability and Accountability Act.

Strabismus Outcome

Ocular alignment was assessed using simultaneous and alternate prism-and-cover testing at distance and near throughout follow-up, from the 6 week postoperative appointment through outcome at 5 years old. Horizontal ocular alignment was categorized as constant esotropia, intermittent esotropia, constant exotropia, or intermittent exotropia. Data on vertical deviations, dissociated deviations, patterns, or other incomitance were collected routinely as permitted by age and cooperation.

Ocular Motor Outcome

Horizontal and vertical eye movement recordings were accomplished on all patients using either a goggle embedded infrared reflection method sampled up to 500 Hz (Ober 2; Permobil Meditech, Woburn, MA) or a remote high-speed video eye tracker (EyeLink 1000; SR Research, Ontario, Canada). The child's head was stabilized using a chin rest and forehead rest. A series of stationary small (1.5 deg diameter) cartoon figures were presented at 115 to 135 cm from the child on a rear projection screen. Calibration was achieved by presenting the cartoon targets on the same screen at 0° and $\pm 10^\circ$ vertically and horizontally (5 seconds in each position; 20 seconds total). After calibration, the fixation target was presented in primary position (0°) with the child fixating binocularly, with the right eye only, and with the left eye only (20 seconds for each viewing condition; 60 seconds total).

Eye movement recordings were sent to one of the coauthors (RWH), who is experienced in the acquisition and analysis of these data, for masked evaluation. The types of any ocular oscillations or instabilities were classified according to those previously described and recorded, most recently in the Classification of Eye Movements and Strabismus (CEMAS) system.²⁰ All eye movement data were analyzed offline. The categories of ocular motor outcomes included normal fixation, saccadic oscillations, infantile nystagmus syndrome (INS, with and without a latent component), fusion maldevelopment nystagmus syndrome (FMNS, formerly "manifest latent nystagmus"), and mixed INS-FMNS (see CEMAS for definitions and characteristics). In addition, interocular differences in waveform type and/or oscillation intensity under monocular and binocular conditions were also recorded and analyzed.

Dichotomous Clinical Variables

Potential clinical risk factors for adverse ocular motor outcomes following pediatric cataract surgery during the first 5 years of life were based on literature review and included age of onset, laterality (unilateral vs bilateral), and duration of deprivation. These variables were coded as dichotomous variables for analysis, with cutoffs selected prior to data analysis: congenital (dense cataract present during the first week of life) versus developmental (dense cataract not present during neonatal examination but present at 9 weeks of age), infantile (dense cataract present at 12 months of age, including congenital) versus late onset (dense cataract not present at 12 months of age), unilateral versus bilateral, and duration of visual deprivation <6 weeks versus >6 weeks.

Data Analysis

To determine odds ratios, multivariate logistic regression was used to examine which of the dichotomous variables were associated with the adverse ocular motor outcomes of strabismus, nystagmus, and interocular asymmetry of the nystagmus. To eliminate nonsignificant risk factors, a backward stepwise strategy was used, eliminating the least significant variable in each step until all variables in the remaining final model had $P < 0.15$. The final regression output provided multivariate odds ratios and 95% confidence intervals for the remaining significant variables. All analyses were performed within the R Statistical Computing Environment.²¹

Results

A total of 41 children were enrolled in the study. Age at presentation, age at surgery, age at outcome test, and visual acuity are provided for each child in e-Supplement 1 and e-Supplement 2 (available at jaapos.org). Of the 41 children, 20 had congenital cataracts and 21 had developmental cataracts (9 infantile and 12 with onset >12 months). Eye alignment and fixation control outcomes are also provided for each child in e-Supplements 1 and 2. Of

the 20 children with congenital cataracts, 2 had primary intraocular lens (IOL) implantation and 18 initially were fitted with aphakic contact lenses, of whom 6 subsequently had secondary IOL implantation. Of the 21 children with developmental cataracts, 9 had primary IOL implantation and 12 initially were fitted with aphakic contact lenses, of whom 7 subsequently had secondary IOL implantation. All secondary IOLs were implanted after the child was 5 years old. All children with IOLs were provided spectacles to bring their refractive error near a target of -2.00 D during the first 18–36 months of life. At 18–36 months they were switched to bifocal or multifocal spectacle correction to provide clear vision for near work and at distance. Children with amblyopia were treated with occlusion therapy.

Strabismus

Twenty-seven children (66%) developed strabismus (21 esotropia [ET], 2 intermittent esotropia, 2 exotropia [XT], 2 intermittent exotropia). Congenital onset was associated with significant risk for strabismus (odds ratios [OR], 5.4; 95% CI, 1.1–34.1), as was visual deprivation >6 weeks duration (OR, 9.1; 95% CI, 1.9–54.2). Neither infantile onset nor laterality (unilateral vs bilateral) was associated with significant risk for strabismus. Overall, 10 children (24%) had one strabismus surgery, 8 (20%) had two surgeries, and 3 (7%) had three surgeries. At the outcome visit, 20 (49%) were judged to be orthotropic, 4 (10%) had dissociated deviations (3 vertical, 1 horizontal), 11 (27%) had intermittent tropia (2 esotropia, 2 hypertropia [HT], 7 exotropia), and 6 (15%) had small-angle constant tropia (1 ET, 1 HT, 1 ET+HT, 2 XT).

Ocular Oscillations

Twenty-nine children (71%) had nystagmus (18 predominantly INS, 11 predominantly FMNS); 12 (29%) had good fixation stability. None of the children had “latent nystagmus vera,” that is, eyes electrophysiologically quiet under binocular conditions and oscillations present under monocular conditions. Representative eye movement recordings from children with INS, FMNS, saccadic oscillations, and stable fixation are shown in Figure 1. Both INS and FMNS were associated with strabismus ($\chi^2 = 4.92$, $P = 0.03$, and $\chi^2 = 11.25$, $P = 0.0008$, respectively). Significant risk for nystagmus was associated with infantile (<12 months) onset (OR, 13.7; 95% CI, 1.6–302) and with visual deprivation >6 weeks duration (OR, 46.2; 95% CI, 6.0–1004). Neither congenital onset nor laterality (unilateral vs bilateral) was associated with significant risk for nystagmus.

Interocular Oscillation Symmetry

Fourteen children (34%) had asymmetric fixation instability: nine had interocular differences in amplitude, four had FMNS when fixing with one eye but both FMNS and INS when fixing with the other eye, and one had INS only when fixing with one eye but not when fixing with the fellow eye. Representative eye movement records from children with interocular asymmetry are shown in Figure 2. Significant risk for interocular difference in type or amplitude of nystagmus was associated with unilateral cataract (OR, 58.9, 95% CI, 5.1–2318) and with congenital onset (OR, 25.0; 95% CI, 2.6–649). Neither infantile onset nor duration of deprivation was associated with significant risk for interocular asymmetry of nystagmus.

Discussion

There was a high prevalence of postoperative strabismus and nystagmus among children who had extraction of dense cataracts during the first 5 years of life. Congenital onset and visual deprivation >6 weeks were associated with significantly higher risk for strabismus; infantile onset and visual deprivation >6 weeks were associated with significantly higher

risk for nystagmus. Congenital onset and unilateral cataracts were associated with higher risk for interocular asymmetry in amplitude or nature of nystagmus.

Because the head was held still while the child fixated on cartoon targets in primary positions, eye movement responses recorded likely reflect primarily the integrity of the fixation control system; that is, the ability to detect retinal image drift and to program appropriate corrective eye movements. Abnormal fixation control may result in saccadic oscillations or nystagmus. Because saccadic oscillations are common in normal children and adults,^{22–25} they were not categorized as an adverse ocular motor outcome for statistical analyses, although some children in the present study had saccadic oscillations that were both larger in amplitude (ie, $>3^\circ$) and more frequent than normal (ie, 1–3 per minute or short bursts).^{22–25} Thus we may have underestimated the prevalence of adverse ocular motor outcomes in our cohort. These saccadic types of fixation instabilities have been reported to occur more frequently in amblyopic eyes.²⁶

Only one prior study used eye movement recording to evaluate adverse ocular motor outcomes in children who had extraction of a dense cataract before 5 years of age: Abadi and colleagues²⁷ reported adverse ocular motor outcomes for 17 children who were followed from the age of 10 months to 4.5 years; 88% developed strabismus and 71% developed nystagmus. Of those who developed nystagmus, only one had true latent nystagmus; the remainder had FMNS (“manifest latent nystagmus”). The Abadi and colleagues²⁷ prevalence estimates for strabismus and nystagmus are not significantly different from the present study for a similar cohort of 41 children followed to age 5 years. We also confirmed that FMNS is always associated with strabismus, but our report additionally found that INS can also be associated with strabismus.

Following extraction of a dense cataract in children 5 years old, duration of visual deprivation >6 weeks was the only modifiable risk factor identified that was associated strongly with increased risk for strabismus and nystagmus, either INS or FMNS.

Congenital onset, infantile onset, and laterality (unilateral vs bilateral) were identified as nonmodifiable risk factors for strabismus, nystagmus, or interocular asymmetry in ocular oscillations. However, unlike prior informal observations that nystagmus may be more prevalent among children treated for bilateral cataracts than unilateral cataracts,⁴ eye movement recording and risk factor analysis in the present study revealed no significant association between laterality and risk for nystagmus. Laterality was associated with interocular asymmetry in ocular oscillations but not overall prevalence.

INS and FMNS (old latent nystagmus) are two of the most common ocular oscillations in infancy and childhood. These oscillations are always binocular and result from developmentally anomalous neural communication between immature afferent and efferent visual systems. Any early-onset afferent system anomaly, either unilateral or bilateral, is capable of sufficient disruption of the neural communication process to result in the oscillations of INS or FMNS. Thus a unilateral congenital cataract with its profound disruption of the visual afferent (spatial acuity, contrast, motion perception, stereopsis, visual field) and efferent (binocular, saccadic, fixation, pursuit asymmetry) systems is easily capable of creating the developmental scenario resulting in either INS or FMNS. There are often significant interocular differences (asymmetry) of these oscillations, sometimes so profound as to appear “clinically silent” in one of the two eyes. This is often the case with large discrepancies in interocular acuity. Using ocular motor recordings in patients with clinically “unilateral” oscillations often reveals the binocular, but asymmetric, presence of this motor anomaly.

Data from nonhuman primate models support the hypothesis that FMNS results primarily from a loss of binocularity in the middle temporal and middle superior temporal visual areas when there is misalignment of the visual axes during an early critical period.^{28,29} Nevertheless, the predominant model of INS posits that the degraded visual experience as a result of cataract during an early critical period induces an adaptive ocular motor response that leads to INS.^{28,29} Because INS develops in the presence of multiple sensory system diseases, it has been hypothesized that INS may be the result of failure of a portion of the smooth pursuit system to calibrate its own internal gain during a critical period of development.^{28,29} The results presented here, that is, that dense cataracts present during the first 5 years of life were associated with either FMNS or INS, suggests that each motor outcome is a result of its own critical combination of time, duration, and type of associated visual system perturbation. Moreover, persistent asymmetry in monocular afferent visual system maturation after the onset of the ocular motor anomaly may result in interocular asymmetry in motor development.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work was supported by grants from the Gerber Foundation (EEB) and the National Eye Institute EY05236 (EEB).

References

1. Chak M, Wade A, Rahi JS. Long-term visual acuity and its predictors after surgery for congenital cataract: Findings of the British congenital cataract study. *Invest Ophthalmol Vis Sci*. 2006; 47:4262–9. [PubMed: 17003414]
2. Ejzenbaum F, Salomao SR, Berezovsky A, et al. Amblyopia after unilateral infantile cataract extraction after six weeks of age. *Arq Bras Oftalmol*. 2009; 72:645–9. [PubMed: 20027402]
3. Gouws P, Hussin HM, Markham RH. Long term results of primary posterior chamber intraocular lens implantation for congenital cataract in the first year of life. *Br J Ophthalmol*. 2006; 90:975–8. [PubMed: 16597661]
4. Hussin HM, Markham R. Long-term visual function outcomes of congenital cataract surgery with intraocular lens implantation in children under 5 years of age. *Eur J Ophthalmol*. 2009; 19:754–61. [PubMed: 19787594]
5. Parks MM, Johnson DA, Reed GW. Long-term visual results and complications in children with aphakia. A function of cataract type. *Ophthalmology*. 1993; 100:826–40. discussion 840–41. [PubMed: 8510894]
6. Birch EE, Stager D, Leffler J, Weakley D. Early treatment of congenital unilateral cataract minimizes unequal competition. *Invest Ophthalmol Vis Sci*. 1998; 39:1560–66. [PubMed: 9699545]
7. Birch EE, Stager DR. The critical period for surgical treatment of dense congenital unilateral cataract. *Invest Ophthalmol Vis Sci*. 1996; 37:1532–8. [PubMed: 8675395]
8. Birch EE, Cheng C, Stager DR Jr, Weakley DR Jr, Stager DR Sr. The critical period for surgical treatment of dense congenital bilateral cataracts. *J AAPOS*. 2009; 13:67–71. [PubMed: 19084444]
9. Lundvall A, Kugelberg U. Outcome after treatment of congenital bilateral cataract. *Acta Ophthalmol Scand*. 2002; 80:593–7. [PubMed: 12485278]
10. Jain S, Ashworth J, Biswas S, Lloyd IC. Duration of form deprivation and visual outcome in infants with bilateral congenital cataracts. *J AAPOS*. 2010; 14:31–4. [PubMed: 20227619]
11. Lesueur LC, Arne JL, Chapotot EC, Thouvenin D, Malecaze F. Visual outcome after paediatric cataract surgery: Is age a major factor? *Br J Ophthalmol*. 1998; 82:1022–5. [PubMed: 9893592]
12. Brown SM, Archer S, Del Monte MA. Stereopsis and binocular vision after surgery for unilateral infantile cataract. *J AAPOS*. 1999; 3:109–13. [PubMed: 10221805]

13. Jeffrey BG, Birch EE, Stager DR Jr, Stager DR Sr, Weakley DR Jr. Early binocular visual experience may improve binocular sensory outcomes in children after surgery for congenital unilateral cataract. *J AAPOS*. 2001; 5:209–16. [PubMed: 11507579]
14. Magli A, Iovine A, Bruzzese D, Giani U, Fimiani F. Strabismus in developmental cataract. *Eur J Ophthalmol*. 2008; 18:540–3. [PubMed: 18609471]
15. Watts P, Abdolell M, Levin AV. Complications in infants undergoing surgery for congenital cataract in the first 12 weeks of life: Is early surgery better? *J AAPOS*. 2003; 7:81–5. [PubMed: 12736618]
16. Lambert SR, Drack AV. Infantile cataracts. *Surv Ophthalmol*. 1996; 40:427–58. [PubMed: 8724637]
17. Wright KW, Christensen LE, Noguchi BA. Results of late surgery for presumed congenital cataracts. *Am J Ophthalmol*. 1992; 114:409–15. [PubMed: 1415449]
18. Taylor D. The Doyne Lecture. Congenital cataract: the history, the nature and the practice. *Eye (Lond)*. 1998; 12(Pt 1):9–36. [PubMed: 9614513]
19. Hertle RW. Examination and refractive management of patients with nystagmus. *Surv Ophthalmol*. 2000; 45:215–22. [PubMed: 11094245]
20. Classification of Eye Movement Disorders and Strabismus (CEMAS). National Eye Institute; Committee for the Classification of Eye Movement Abnormalities and Strabismus Workshop. Available at: <http://www.nei.nih.gov/news/statements/cemas.pdf>
21. R Development Core Team. R: A language and environment for statistical computing. Version 2.12.1. Vienna, Austria: R Foundation for Statistical Computing; 2010. Available at: <http://www.R-project.org/>
22. Abadi RV, Gowen E. Characteristics of saccadic intrusions. *Vision Res*. 2004; 44:2675–90. [PubMed: 15358063]
23. Gowen E, Abadi RV. Saccadic instabilities and voluntary saccadic behaviour. *Exp Brain Res*. 2005; 164:29–40. [PubMed: 15754180]
24. Gowen E, Abadi RV, Poliakoff E, Hansen PC, Miall RC. Modulation of saccadic intrusions by exogenous and endogenous attention. *Brain Res*. 2007; 1141:154–67. [PubMed: 17313940]
25. Sharpe JA, Fletcher WA. Saccadic intrusions and oscillations. *Can J Neurol Sci*. 1984; 11:426–33. [PubMed: 6518425]
26. Zhang B, Stevenson SS, Cheng H, et al. Effects of fixation instability on multifocal VEP (mfVEP) responses in amblyopes. *J Vis*. 2008; 8:16.1–16.14. [PubMed: 18484822]
27. Abadi RV, Forster JE, Lloyd IC. Ocular motor outcomes after bilateral and unilateral infantile cataracts. *Vision Res*. 2006; 46:940–52. [PubMed: 16289271]
28. Tychsen L, Richards M, Wong A, Foeller P, Bradley D, Burkhalter A. The neural mechanism for latent (fusion maldevelopment) nystagmus. *J Neuroophthalmol*. 2010; 30:276–83. [PubMed: 20818206]
29. Dell'Osso L. Biologically relevant models of infantile nystagmus syndrome: the requirement for behavioral ocular motor system models. *Semin Ophthalmol*. 2006; 21:71–7. [PubMed: 16702072]

FIG 1.

Representative horizontal eye movement data obtained with binocular fixation in primary position. For each example, right eye (gray) and left eye (black) horizontal positions are shown. Upward deflections correspond to eye movement to the right and downward deflections correspond to eye movement to the left. A, Normal fixation without oscillations, interrupted only by blinks. B, Fixation and refixation interrupted by back-to-back, conjugate, symmetric saccades with an intersaccadic interval typical of saccadic oscillations (SO). C, Jerk right fusion maldevelopment nystagmus syndrome (FMNS). D, Mixed jerk left FMNS and jerk right infantile nystagmus syndrome (INS).

FIG 2.

Representative horizontal eye movement obtained with binocular fixation in primary position from children with interocular asymmetry in ocular oscillations. For each example, right eye (grey) and left eye (black) horizontal position are shown. Upward deflections correspond to eye movement to the right and downward deflections correspond to eye movement to the left. A, Oscillation intensity asymmetry that remained consistent throughout the recording, showing a preferred left eye. The waveforms are jerk with extended foveation and pseudopendular waveforms consistent with INS. B, Spontaneous change in fixation from the right to the left eye, with changes in oscillation direction and type from jerk left with extended foveation infantile nystagmus syndrome (INS) when the right eye was fixing to jerk right fusion maldevelopment nystagmus syndrome (FMNS) when the left eye was fixing.