Visual Acuity Development of Children with Infantile Nystagmus Syndrome

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PURPOSE. Infantile nystagmus syndrome (INS) can be idiopathic or associated with ocular or systemic disease. The ocular oscillation of INS directly contributes to loss of visual acuity. In this study, visual acuity development in patients with INS was examined.

METHODS. Children with INS were classified as having idiopathic INS ($n = 84$) or INS with an associated sensory deficit: INS and albinism ($n = 71$), bilateral optic nerve hypoplasia (ONH; $n = 23$), or congenital retinal disorder ($n = 36$). Visual acuity was assessed with Teller cards and/or optotypes, and the data were analyzed for three age groups (<24 months, $24-48$ months, and >48 months).

RESULTS. Patients with idiopathic INS showed mildly reduced visual acuity early in life and gradual maturation with age that paralleled a normative curve. Patients with albinism also showed a mild visual deficit early in life but failed to keep pace with the normative curve, showing a gradual increase in visual acuity deficit. Patients with ONH and congenital retinal disorders exhibited more severe visual acuity deficits during infancy. The ONH group displayed slow improvement of visual acuity with a plateau at 24 months through >48 months, with a small increase in visual acuity deficit. The congenital retinal disorder group had no significant change in visual acuity across age and had a rapid increase in visual acuity deficit.

CONCLUSIONS. The pattern of visual acuity development differs among children with INS, depending on the presence or absence of associated sensory system deficits. Careful characterization of visual system differences in patients with INS is important if visual acuity is an outcome in clinical trials. (*Invest*

Ophthalmol Vis Sci. 2011;52:1404-1411) DOI:10.1167/iov.09-4686

Infantile nystagmus syndrome (INS) is the early onset of nystagmus, characterized by an accelerating exponential slow phase followed by a rapid recovery movement in the opposite direction (jerk nystagmus) or symmetric sinusoidal horizontal movement of constant velocity (pendular nystagmus) on eye movement recordings. INS can be idiopathic or associated with albinism, bilateral optic nerve hypoplasia (ONH), or retinal disease. The prevalence of INS is not known with certainty, because of inconsistent reporting and classification systems, but it is undoubtedly higher than the oft-reported 1 in 1000 to 1 in 6000.^{1,2} Functional impairment in daily vision-related activities, assessed using the VF-14, is of a magnitude similar to that of patients with age-related macular degeneration.³

INS is associated with decreased visual acuity due to associated sensory system deficits, amblyopia, or ametropia and is a direct result of the inability to maintain stable foveal vision. In a recent study of 224 adult patients with INS, mean visual acuity was 0.4 logMAR (20/50) in the idiopathic group, 0.7 logMAR (20/100) in the albinism group, and 0.6 logMAR (20/80) in the ONH and ocular disease group.² However, there are few studies of visual acuity development in children with INS.

Surgical and pharmacologic treatment of the nystagmus itself can improve visual acuity by increasing the duration of foveation periods (i.e., the percentage of time during which a stable foveal image is present). This goal is based on the well-documented relationship between foveation time and visual acuity in adults.^{4,5} Theoretically, infants and young children benefit more than adults from treatment of INS, since treatment may increase foveation time. Treatment that yields longer foveation periods during the critical early years of visual development should have the additional benefit of minimizing visual deprivation amblyopia. However, to evaluate treatment success during the first years of life, knowledge of the natural history of visual acuity development in infants and children with INS is necessary. The purpose of this study was to define the natural history of visual acuity maturation in children with INS.

METHODS

Subjects

Two hundred fourteen children with INS were referred to the Retina Foundation of the Southwest by Dallas-Fort Worth area pediatric ophthalmologists. The classification of nystagmus was based on diagnostic clinical findings. Clinical evaluation included comprehensive eye examination, slit lamp evaluation, ocular motility evaluation, fundus examination, cycloplegic retinoscopy, pupillary responses, and intraocular pressure. Patients with neurologic disorders were excluded. All patients received routine care for refractive error, amblyopia, and

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Supported in part by National Institutes of Health Grants EY05236 and P30-EY008098 (Bethesda, MD); The Vision of Children Foundation; Eye and Ear Foundation (Pittsburgh, PA); and unrestricted grants from Research to Prevent Blindness (New York, NY).

Submitted for publication September 24, 2009; revised January 7, June 25, August 24, and September 30, 2010; accepted October 7, 2010.

Disclosure: V.L.N. Fu, None; R.A. Bilonick, None; J. Felijs, None; R.W. Hertle, None; E.E. Birch, None

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strabismus, but none had surgery specifically for treatment of nystagmus. The children younger than 12 months of age were invited to return at 3-month intervals and those older than 12 months, at 6-month intervals. INS in these children was classified as idiopathic ($n = 84$; age, 2.4 months to 11.8 years) if there were no other associated sensory system deficits found on clinical testing or as INS with an associated sensory deficit: albinism ($n = 71$; age, 1.7 months to 15.6 years), bilateral ONH ($n = 23$; age, 2.0 months to 7.7 years), or congenital retinal disorders (achromatopsia, Leber congenital amaurosis [LCA], retinal degeneration, or foveal hypoplasia; $n = 36$; age, 3.3 months to 6.8 years). The age distribution for each of the four patient groups is shown in Figure 1.

In all children with achromatopsia ($n = 13$), LCA ($n = 8$), and cone-rod degeneration or cone dystrophy ($n = 9$), the diagnoses were confirmed with electroretinography. Two of the children with achromatopsia had blue cone monochromacy, and 11 had rod monochromacy. Two patients with achromatopsia were confirmed to have the *CBGB3* mutation, one with LCA was confirmed to have a *CRX* mutation, and another with cone dystrophy was confirmed to have the *ALMS1* mutation (Alström syndrome). Mutations in the remaining patients had not been identified at the time of the study.

Children with foveal hypoplasia ($n = 6$) all had abnormal fundus appearance in the macular area, with apparently normal pigmentation and no transillumination of the iris. Three of the patients had normal MRIs, and one showed optic chiasm glioma on MRI study.

Vision Testing

Visual acuity was assessed with acuity testing cards (Teller Acuity Cards [TACs]; Stereo Optical Company, Chicago, IL) in the younger children and with optotype acuity tests in the older ones. For all younger participants, testing began with the presentation of the 0.32 cyc/cm TACs at a distance of 55 cm. The cards were held vertically so that the gratings were horizontally oriented. A two-down-one-up, forced-choice, staircase protocol⁶ with eight reversals was used.^{6,7} Visual acuity was calculated as the average of the last six reversals in logMAR units [$\log\text{MAR} = -1 \times \log(\text{spatial frequency}/30)$]. In the older participants, optotype visual acuity was measured with crowded HOTV or ETDRS optotypes presented by the EVA system developed by the Pediatric Eye Disease Investigator Group,^{8,9} Lea symbols,¹⁰ or linear/isolated Allen symbols.¹¹ Testing distance was 3 m for optotype acuity tests, except in some cases of severe amblyopia, in which testing was conducted at 1.5 m. The number of data points in each age group that were obtained with each visual acuity testing procedure is pre-

sented in Table 1. Binocular visual acuity was recorded or, in strabismic children who were tested monocularly, the better monocular visual acuity was recorded; the percentages of binocular tests for each patient group are provided in Table 1. For children with strabismus, testing was attempted on each eye monocularly (right eye first) with an adhesive orthoptic eye patch on the fellow eye. All visual acuity data were converted to a common logMAR scale. Children wore their habitual optical correction (which had been prescribed recently and therefore was assumed to be close to the optimal correction) and were allowed to use their preferred head postures during the visual acuity testing.

Data Analysis

All visual acuity data are expressed both as absolute values and as deviations from age-corrected norms (both in logMAR units) and were analyzed for three age groups (<24 months, 24–48 months, and >48 months). Visual acuity development for each group was compared with existing norms for TACs (Salomao SR et al. *IOVS* 1996;37:ARVO Abstract 4902),^{6,7,12,13} Allen symbols,¹⁴ Lea symbols,¹⁰ crowded HOTV optotypes,¹⁵ and the ETDRS chart.¹⁶ Normative data were chosen from the literature that matched both the stimuli and psychophysical methodology used in the present study. Normal and abnormal classifications were based on the lower limit of the 95% tolerance interval. Children who scored below the lower limit were classified as having abnormal visual acuity. Those who scored above the lower limit were classified as having normal visual acuity. Grating acuity is normally immature at birth and improves rapidly from 1.1 logMAR (20/260) to 0.6 logMAR (20/80) between 2 and 6 months of age. Grating acuity improves slowly by approximately 0.6 logMAR between the ages of 6 and 48 months. The rate of improvement averages 0.15 logMAR per month between 1 and 6 months and 0.015 logMAR between 6 and 48 months (Salomao SR, et al. *IOVS* 1996;37:ARVO Abstract 4902).^{12,13}

The cross-sectional normative data consisted of mean, SD, and sample size for acuity of normal subjects at various time points. These data were modeled by using weighted linear regression, where the weights were equal to the sample size, and age was logarithmically transformed so that the relationship with visual acuity was approximately linear (thereby accounting for the shape of the visual acuity growth curve which asymptotes beyond age 48 months). In addition, the SD for each age group tended to decrease with increasing age. Thus, the SD was modeled as a linear function of age, and this was used when estimating the 95% prediction interval bounds.

FIGURE 1. Number of tests across ages of the subjects at their first visits in four patient groups: idiopathic INS ($n = 84$), INS associated with albinism ($n = 71$), INS associated with ONH ($n = 23$), and INS associated with congenital retinal disorders ($n = 36$).

TABLE 1. Visual Acuity (logMAR) and Testing Method

	<24 Months	24–48 Months	>48 Months
Idiopathic			
VA, mean (SD)	0.79 (0.33)	0.45 (0.25)	0.29 (0.25)
Subjects, <i>n</i>	66	39	19
Visual acuity test method, <i>n</i> (%)			
TAC	66 (100)	27 (69)	4 (21)
Allen	0	10 (26)	10 (52)
Lea symbols	0	0	0
HOTV	0	2 (5)	3 (16)
ETDRS	0	0	2 (11)
Total tests, <i>n</i>	66	39	19
Binocular tests, <i>n</i> (%)	45 (68)	24 (62)	6 (32)
Albinism			
VA, Mean (SD)	0.87 (0.31)	0.66 (0.23)	0.52 (0.25)
Subjects, <i>n</i>	55	32	27
Visual acuity test method, <i>n</i> (%)			
TAC	55 (100)	29 (91)	6 (22)
Allen	0	3 (9)	12 (44)
Lea symbols	0	0	0
HOTV	0	0	5 (19)
ETDRS	0	0	4 (15)
Total tests, <i>n</i>	55	32	27
Binocular tests, <i>n</i> (%)	37 (67)	19 (59)	10 (37)
ONH			
VA, mean (SD)	0.95 (0.62)	0.58 (0.31)	0.54 (0.29)
Subjects, <i>n</i>	18	11	6
Visual acuity test method, <i>n</i> (%)			
TAC	18 (100)	9 (82)	2 (33)
Allen	0	1 (9)	3 (50)
Lea symbols	0	1 (9)	0
HOTV	0	0	1 (17)
ETDRS	0	0	0
Total tests, <i>n</i>	18	11	6
Binocular tests, <i>n</i> (%)	12 (67)	6 (55)	2 (33)
Retinal Disorders			
VA, mean (SD)	1.05 (0.27)	0.97 (0.45)	1.11 (0.39)
Subjects, <i>n</i>	28	19	16
Visual acuity test method, <i>n</i> (%)			
TAC	28 (100)	12 (63)	3 (19)
Allen	0	7 (37)	8 (50)
Lea Symbols	0	0	1 (6)
HOTV	0	0	4 (25)
ETDRS	0	0	0
Total tests, <i>n</i>	28	19	16
Binocular tests, <i>n</i> (%)	20 (71)	13 (68)	7 (44)

Data are the mean (SD) for visual acuity results, the number of data points, the number of subjects, the visual acuity testing procedures used, and the percentage of monocular versus binocular tests for each of the patient groups: idiopathic INS and INS associated with albinism, bilateral ONH, or congenital retinal disorders (achromatopsia, LCA, retinal degeneration, and foveal hypoplasia). One patient in the idiopathic INS group and two in the congenital retinal disorder group had visual acuity of light perception.

Visual acuity was modeled as a function of age (log month) and diagnosis (idiopathic INS or INS associated with albinism, ONH, achromatopsia, LCA, retinal degeneration, or foveal hypoplasia). To account for repeated measurements over time for each subject, longitudinal linear mixed-effects (LME) models with random intercepts and random slopes (for age) were estimated, using maximum likelihood the method. In these models, age was logarithmically transformed so that the relationship with visual acuity was approximately linear. Com-

putations were performed using the *R* statistical programming language and environment¹⁷ and the *nlme* *R* library.¹⁸ The fixed-effects slope (i.e., the slope for the typical subject) for log months for each diagnosis was used to compare with the slope computed based on the normative data. The 95% confidence interval (CI) for the true fixed-effect slope of each diagnosis was computed. Slope values for each diagnosis outside the range of the corresponding CI were implausible for the true slope. Slope values within the CI were plausible as values for the true slope. Therefore, if treating the estimated normative slope as a constant known value, if the normative slope fell outside the CI for a diagnosis, the slope for the diagnosis was considered significantly different from the normative slope.

Human Subjects

This protocol was approved by the Institutional Review Board at the University of Texas Southwestern Medical Center. For all children younger than 18 years of age, the parent was asked to provide written consent. Written assent was also obtained from children between 10 and 18 years of age. The protocol was conducted in compliance with the guidelines in the Declaration of Helsinki.

RESULTS

Idiopathic INS

Patients with idiopathic INS showed mildly reduced visual acuity before 24 months of age and a gradual maturation of visual acuity with age after 24 months (Fig. 2A; Table 1). There was little change in the amount of visual acuity deficit compared with the norms across ages (Table 2). In fact, most of the visual acuity test results were within the 95% normative tolerance limit before 48 months of age (Table 2). After 48 months of age, visual acuity improved (Table 1), even though only half of the visual acuity test results were within the 95% normative tolerance limits (Table 2). Figure 3A shows the visual acuity data from patients who had three visits (*n* = 7). Most (6/7 patients) showed gradual maturation in visual acuity and had visual acuity within the 95% normative tolerance limit across age before 48 months of age (both grating and optotype acuity). However, five patients had abnormal visual acuity (two grating acuity and three optotype acuity) after 48 months of age.

The longitudinal linear mixed-effects model was used to examine the rate of visual acuity improvement among patients with idiopathic INS (Fig. 4). The rate of maturation for the typical patient with idiopathic INS was -0.27 logMAR/log months—that is, a typical improvement of 0.09 logMAR (1 line) for each doubling of age (Table 3). The slope of the normative cohort was -0.23 , which fell within the 95% CI for idiopathic INS (Table 3). Therefore, the slopes were not significantly different between idiopathic INS and norms. Hence, the rate of visual acuity maturation may be similar in the patients and the normative cohort (-0.23 logMAR/log months; 0.08 logMAR improvement for each doubling of age). In other words, patients with idiopathic INS gradually improved their visual acuities with age.

INS Associated with Albinism

Patients with albinism also showed only a mild deficit in visual acuity early in life (<24 months; Fig. 2B; Table 2). The maturation of visual acuity with age was more modest than in patients with idiopathic INS after 24 months of age (Fig. 2B; Table 1). The visual acuity deficit compared with the norms increased significantly with age (Table 2). Few of the visual acuity test results at <24 months were below the 95% normative tolerance limit but, by 24 to 48 months, nearly half of the visual acuity test results were below normative tolerance lim-

FIGURE 2. Visual acuity scores for individual visits in children with (A) idiopathic INS, (B) INS associated with albinism, (C) INS associated with bilateral ONH, and (D) INS associated with congenital retinal disorders. *Shaded area:* tolerance limits of norms of visual acuities measured by TACs (●) (Salomao SR, et al. *IOVS* 1996;37:ARVO Abstract 4902).^{6,7,12,13} *Dashed line:* mean monocular acuity measured by crowded HOTV optotypes (▼).¹⁵ *Solid line:* mean monocular acuity measured by EITDRS chart (●).¹⁶ *Dotted line:* mean acuity measured by Lea symbol (○),¹⁰ linear Allen (△) symbols,¹⁴ and isolated symbol (□) acuity tests.

its, and, by 48 months, most fell below the 95% normative tolerance limits (Table 2). Figure 3B shows the visual acuity in patients with three visits ($n = 13$). Most had grating acuity within normal range at <24 months (11/13 patients). However, only four patients had normal visual acuity by 24 to 48 months (all grating acuity). Most patients (12/13) tested after

TABLE 2. Visual Acuity Deficit in Each of the Four Groups

	<24 Months	24–48 Months	>48 Months
Idiopathic			
VA deficit, mean (SD)	0.11 (0.07)	0.12 (0.11)	0.25 (0.22)
Total tests, n	66	39	19
Number (%) below normative tolerance limit	12 (18)	11 (28)	11 (58)
Albinism			
VA deficit, mean (SD)	0.10 (0.07)	0.19 (0.17)	0.33 (0.26)
Total tests, n	55	32	27
Number (%) below normative tolerance limit	12 (22)	17 (53)	25 (93)
ONH			
VA deficit, mean (SD)	0.39 (0.45)	0.19 (0.20)	0.43 (0.25)
Total tests, n	18	11	6
Number (%) below normative tolerance limit	7 (39)	5 (46)	5 (83)
Retinal Disorders			
VA deficit, mean (SD)	0.28 (0.21)	0.58 (0.43)	0.95 (0.40)
Total tests, n	28	19	16
Number (%) below normative tolerance limit	16 (57)	15 (79)	16 (100)

Data are the mean (SD) of visual acuity deficit (logMAR) below normal for the age, the number of tests, and the percentage below the normative tolerance limit for each of the four patient groups, as described in Table 1.

FIGURE 3. The courses of the patients who had three consecutive visits. (A) Idiopathic INS ($n = 7$), (B) INS associated with albinism ($n = 13$), (C) INS associated with bilateral ONH ($n = 3$), and (D) INS associated with congenital retinal disorders ($n = 8$). Shaded area: tolerance limits of norms of visual acuities measured by TACs (●) (Salomao SR, et al. IOVS 1996;37:ARVO Abstract 4902).^{6,7,12,13} Dashed line: mean monocular acuity measured by crowded HOTV optotypes (▼).¹⁵ Solid line: mean monocular acuity measured by ETDRS chart (●).¹⁶ Dotted line: mean acuity measured by Lea symbol (○),¹⁰ linear Allen (△) symbols,¹⁴ and isolated symbol (□) acuity tests.

48 months of age fell below the 95% normative tolerance limit for both grating and optotype acuities.

The rate of visual acuity maturation for the typical patient with INS associated with albinism was -0.17 logMAR/log months (Fig. 4)—that is, a typical improvement of 0.06 logMAR (0.6 lines) for each doubling of age (Table 3). The slope of the normative cohort was -0.23 which fell outside the 95% CI for INS associated with albinism (Table 3). Therefore, the slopes were significantly different. Hence, the rate of visual acuity maturation in patients may be different from the normative cohort. Visual acuities of INS patients associated with albinism failed to improve with age.

INS Associated with ONH

The group with ONH exhibited more severe deficits in visual acuity early in life (<24 months) and had a plateau in visual acuity maturation at 24 to 48 months through >48 months (Fig. 2C; Tables 1, 2). The visual acuity deficit increased significantly with age (Table 2). Figure 3C shows the three patients with three consecutive visits. Two showed improvement in visual acuity before 24 months of age with grating acuity. Two patients showed little or no improvement in acuity after 48 months of age (one grating acuity and one optotype acuity).

The rate of visual acuity maturation for the typical patient with INS associated with ONH was -0.29 logMAR/log

months—that is, 0.097 logMAR improvement for each doubling of age (Fig. 4). The slope of the normative cohort was -0.23 , which fell within the 95% CI for INS-associated ONH (Table 3). Therefore, the slopes were not significantly different. Hence, the rate of visual acuity maturation in this patient group may not be significantly different from the acuity maturation in the normative cohort. Patients with nystagmus and ONH had significantly poorer acuity than the normative group, even during early infancy.

INS Associated with Congenital Retinal Disorders

Patients with INS associated with congenital retinal disorders had the poorest visual acuity among all patient groups early in life (<24 months; Table 1). The mean visual acuity was consistently lower than the norm, with no significant change in visual acuity across ages (Fig. 2D, Table 1). As a consequence, visual acuity deficit compared with the normative curve showed a rapid increase with age (Table 2). Among the four main subdivisions of the congenital retinal disorders group (retinal degeneration, achromatopsia, LCA, and foveal hypoplasia), all subgroups showed modest improvement in mean visual acuity before 48 months (Table 4). However, after 48 months of age, visual acuities in the LCA and retinal degeneration subgroups deteriorated. Figure 3D shows all patients who had three consecutive visits ($n = 8$). Although five of the eight

FIGURE 4. Visual acuity (logMAR) plotted as a function of age in months (on a logarithmic scale) for each subtype (idiopathic INS, INS associated with albinism, INS associated with bilateral ONH, achromatopsia, LCA, retinal degeneration, foveal hypoplasia) to illustrate the approximate linear trends. *Solid black lines:* longitudinal linear mixed-effect model fixed-effects predictions. *Solid gray line:* linear regression prediction based on the normative data. *Dashed gray lines:* denote the 95% prediction interval for patients in the normative group. *Open colored circles:* crossed-sectional data from individual subject. *Circles connected by colored lines:* longitudinal data from individual subjects.

patients showed an improvement of visual acuity before 24 months of age (four grating acuity and one optotype acuity), optotype acuities of most patients (6/8) either did not improve or deteriorated thereafter.

The congenital retinal disorder group was subdivided into four main subgroups (retinal degeneration, achromatopsia, LCA, and foveal hypoplasia) for statistical analysis. The rates of

TABLE 3. Rate of Visual Acuity Maturation for Three INS Groups and Four Congenital Retinal Disorder Subgroups

Groups	Slope	Lower Limit	Upper Limit
Normal	−0.23		
Idiopathic	−0.27	−0.33	−0.22
Albinism	−0.17*	−0.22	−0.12
ONH	−0.29	−0.39	−0.19
Retinal degeneration	0.14*	−0.02	0.31
Achromatopsia	−0.11	−0.26	−0.11
LCA	0.18*	0.0	0.35
Foveal hypoplasia	−0.10	−0.34	0.13

Data are expressed in log–log scale for three patient INS groups and four subgroups of congenital retinal disorder. See Table 1 for the groups.

* Significantly different from normal cohort (falls outside the 95% CI).

visual acuity maturation for the typical patient with INS associated with retinal degeneration and LCA were 0.14 and 0.18 logMAR, respectively (Fig. 4, Table 3). Both subgroups showed reduction in visual acuities across ages: a 0.05- to 0.06-logMAR decrease in acuity in the retinal degeneration and LCA subgroups, respectively, for each doubling of age. The slope of the normative cohort fell outside the 95% CIs for INS associated with these two subgroups (Table 3). The slopes were significantly different. Hence, the rates of visual acuity maturation in these two subgroups may be radically different from the acuity maturation in the normative cohort. Patients with INS associated with retinal degeneration and INS associated with LCA showed rapid deterioration in visual acuity with age.

The rates of visual acuity maturation for the typical patient with INS associated with achromatopsia and foveal hypoplasia were −0.11 and −0.10 logMAR, respectively (Fig. 4, Table 3). Both subgroups showed visual improvement across ages—that is, a 0.04- and 0.03-logMAR improvement for each doubling of age in the achromatopsia and foveal hypoplasia subgroups, respectively. The slope of the normative cohort fell within the 95% CIs for these two subgroups (Table 3). The slopes were not significantly different. Hence, the rates of visual acuity maturation in these two subgroups were not significantly different from the acuity maturation in the normative cohort. Patients with INS associated with achromatopsia or with foveal

TABLE 4. Visual Acuity Deficit in the Four Subgroups of Retinal Disorders

	<24 Months	24–48 Months	>48 Months
Achromatopsia			
VA deficit, mean (SD)	0.35 (0.24)	0.43 (0.43)	0.73 (0.36)
Total tests, <i>n</i>	10	7	6
Number (%) below normative tolerance limit	7 (70)	5 (71)	6 (100)
LCA			
VA deficit, mean (SD)	0.29 (0.21)	0.59 (0.51)	1.75
Total tests, <i>n</i>	8	4	2
Number (%) below normative tolerance limit	5 (63)	4 (100)	2 (100)
Retinal Degeneration			
VA deficit, mean (SD)	0.14 (0.12)	0.67 (0.46)	1.07 (0.26)
Total tests, <i>n</i>	4	6	7
Number (%) below normative tolerance limit	2 (50)	5 (83)	7 (100)
Foveal Hypoplasia			
VA deficit, mean (SD)	0.22 (0.17)	0.82	0.6
Total tests, <i>n</i>	6	2	1
Number (%) below normative tolerance limit	3 (50)	1 (50)	1 (100)

Mean (SD) for visual acuity (logMAR) deficit, the number of tests, and the percentage below the normative tolerance limit for each of the four subgroups of patients with retinal disorders: achromatopsia, LCA, retinal degeneration, and foveal hypoplasia. Two patients with LCA had a visual acuity of light perception.

hypoplasia had significantly poorer acuity than the normative group throughout their lives.

DISCUSSION

Most children with INS had subnormal vision after 48 months of age. However, maturational trends differed significantly among patient groups. Most patients with idiopathic INS and albinism had visual acuity within the normative range during infancy. However, idiopathic INS maturation paralleled with normative curves, whereas albinism failed to keep pace with rates of normal maturation after 24 months. On the other hand, patients with ONH had poor acuity during infancy and a slow improvement in visual acuity. Finally, patients with congenital retinal disorders had very poor visual acuity during infancy and showed virtually no change in visual acuity with age.

Previous studies have described decreased grating visual acuity in patients with idiopathic INS,¹⁹ albinism,^{19–22} bilateral ONH,¹⁹ and generalized retinal degeneration.²³ Our data for idiopathic INS differ from those of Weiss and Kelly¹⁹ in that we found little or no acuity deficit during the first 2 years of life, whereas they reported a mean deficit of 0.49 logMAR in the first year of life. One methodologic difference between our study and theirs that may account for this discrepancy is that all our patients wore their habitual optical correction during testing, whereas few patients in Weiss and Kelly's younger group (<3 years old) wore optical correction during visual acuity testing. It may be that those children with INS who have refractive errors outside the normative range would benefit from early optical correction and would be more likely to develop normal or close to normal visual acuity. We speculate that early optical correction may prevent the possible additive effect of refractive amblyopia to the disturbance of visual development which has already been imposed by the ocular oscillations. Weiss and Kelly¹⁹ also reported that the rate of acuity development was similar to the normal rate of development, and we obtained the same results as Weiss and Kelly. When we reanalyzed our data including only grating acuity data obtained with TACs in children from birth to 48

months, we obtained the same observations as Weiss and Kelly (Table 5).

Our visual acuity data from patients with albinism are consistent with those in reports of visual acuity within the normal range during the first months of life^{22,24} and a 0.4- to 0.5-logMAR deficit after 4 years of age.^{19–21} However, there is less agreement about visual acuity development between these two time points; we report a mean deficit of 0.33 logMAR at 2 to 4 years of age, which is smaller than the deficits that were reported by Weiss and Kelly,¹⁹ Whang et al.,²⁰ Summers,²⁴ and Louwagie et al.²¹

Most patients with INS associated with ONH had poor visual acuities in our study and in the study by Weiss and Kelly.¹⁹ However, our patients' averaged deficits of 0.19 to 0.43 logMAR across the three age ranges, while Weiss and Kelly's patients averaged a 0.79-logMAR deficit. Both studies found that the rate of visual acuity maturation for patients with ONH was similar to the normative rate of maturation. Moreover, our study shows a wide spectrum of visual acuities in the ONH group ranging from very low vision to nearly normal vision. This wide spectrum contributes to a wide scatter of acuities in Figures 2C and 4. As the result, the longitudinal data

TABLE 5. Rate of Grating Visual Acuity Maturation

	Slope	SE	Intercept	r ²	Data Points
Birth to 4 years					
Idiopathic	−0.59	0.25	1.34	0.40	92
Albinism	−0.44	0.24	1.28	0.33	84
ONH	−0.79	0.48	1.72	0.25	27
Retinal degeneration	0.22	0.47	0.73	0.03	7
Achromatopsia	−0.16	0.37	1.25	0.02	14
LCA	0.18	0.34	0.96	0.04	11
Foveal hypoplasia	−0.64	0.35	1.53	0.21	7
Normal	−0.62	0.07	1.21	0.93	20

Data are expressed in log-log scale (logMAR/log months) for three patient groups and four subgroups of congenital retinal disorder from birth to 4 years of age (see Table 1 for the groups).

for individual patients with ONH may provide a better description of visual maturation than the maturation curve of group data.

In the congenital retinal disorders groups, there was no apparent overall change in acuity with age, consistent with Mayer et al.²³ Both studies found abnormal visual acuity to be present in early infancy, with a progressive increase in the deficit with age (from 0.28 to 0.95 logMAR in our study and from 0.57 to 1.2 logMAR in Mayer et al.²³). However, by subdividing this patient group into four main subgroups, we found that there was a subtle difference in visual maturation. INS with retinal degeneration had a relatively better visual acuity in early infancy than the other three subgroups, whereas INS with LCA had the worst visual acuity across ages compared with visual scores from the other subgroups (Tables 3, 4). Visual acuities of the retinal degeneration and LCA subgroups decreased gradually with age, whereas visual acuities of the achromatopsia and foveal hypoplasia subgroups tended to improve with age (Table 3, Fig. 4). However, caution should be taken for this analysis because the sample size became small when we subdivided this patient group.

The results of this study indicate that children with INS and associated sensory system disease are characterized by different developmental courses of visual acuity maturation. Treatment success is dependent on normative or natural history data if visual acuity measures are used as treatment outcomes. It is only by collecting and studying these data in patients with INS and associated sensory system diseases that we can reliably depend on acuity as an outcome measure in interventional or observational clinical trials.

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