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Fixation instability in anisometropic children with reduced stereopsis

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Abstract

BACKGROUND—Hyperopic anisometropia in children can be associated with abnormal stereoacuity and “microstrabismus,” a small temporalward “flick” as each eye assumes fixation on cover testing. The prevailing hypothesis is that abnormal sensory experience leads to foveal suppression and, subsequently, secondary microstrabismus. This study investigated the hypothesis that disruption of bifoveal fusion by anisometropia directly affects ocular motor function.

METHODS—A total of 94 children with hyperopic anisometropia (ages 5–13 years) were evaluated prospectively between June 2010 and December 2012 with the use of the Nidek MP-1 microperimeter. Fixation instability was quantified by the area of the bivariate contour ellipse that included 95% of fixation points during a 30-second test interval. Each eye movement waveform during the 30-second test interval also was examined with the use of custom software and classified as normal, fusion maldevelopment nystagmus (FMNS), or infantile nystagmus. Finally, the Randot Preschool Stereoacuity Test (Stereo Optical Company Inc, Chicago, IL) was administered.

RESULTS—Stereoacuity was correlated with fixation instability (Spearman $r = 0.50$; 95% CI, 0.33–0.64); visual acuity was more weakly correlated ($r = 0.28$). All children with normal stereoacuity had stable fixation, children with subnormal stereoacuity had fixation instability, and those with nil stereoacuity had the most instability. Eye movement records during attempted fixation were of sufficient quality for classification in 81 children; 61% of those with reduced stereoacuity and 88% of those with nil stereoacuity had FMNS eye movement waveforms.

CONCLUSIONS—Our data support the hypothesis that the binocular decorrelation caused by anisometropia can disrupt ocular motor development, resulting in FMNS and its temporalward refoveating “flicks” that may mimic microstrabismus.

Hyperopic anisometropia in children may be associated with abnormal stereoacuity and a small temporalward flick as each eye assumes fixation on cover.^{1–6} The flick has been interpreted as evidence for the development of microstrabismus, that is, an “ultra small”-

angle heterotropia.^{1,3} The dominant hypothesis to explain the temporalward flick is that anisometropia leads to the development of foveal suppression and microstrabismus develops secondary to this foveal suppression.^{1,4,5,7} However, this hypothesis merely restates the observed association among foveal suppression, abnormal stereoacuity, and microstrabismus, with no rationale for why microstrabismus would be expected as a sequela of foveal suppression despite normal peripheral fusion, nor does it offer an explanation for why the flick is nearly universally observed to be temporalward (ie, consistent with esotropic microstrabismus). In this study we evaluated an alternative hypothesis for the flick observed during cover testing, namely, that disruption of bifoveal fusion by anisometropia has a direct effect on ocular motor function, which causes the temporalward flick observed during cover testing of children with anisometropia.

Methods

A total of 94 children ages 5–13 years with hyperopic anisometropia (spherical equivalent anisometropia) and 43 healthy control patients ages 5–13 years were enrolled in the prospective cross-sectional study, having been referred to the Retina Foundation of the Southwest by 14 pediatric ophthalmologists of greater Dallas between June 2010 and December 2012. None of the children had developmental delay or concurrent ophthalmic or systemic diseases. None of the children were born preterm earlier than 36 weeks. Informed consent was obtained from a parent before each child participated in the study. The research protocol was approved by the Institutional Review Board of the University of Texas Southwestern Medical Center and conformed to the requirements of the Health Insurance Portability and Accountability Act of 1996.

The Nidek MP-1 Microperimeter (Nidek Technologies, Padua, Italy), which combines an infrared video fundus camera with a liquid crystal display (ie, LCD) panel, was used to track horizontal and vertical eye position of the more hyperopic eye. Anatomical features (blood vessels) were marked in a fundus image reference frame that was obtained while the child fixated on the center of a 1-deg red fixation circle presented on the LCD panel. The child was asked to continue to fixate for 30 seconds with his or her head held steady by chin and forehead rests. MP-1 software tracked the reference landmarks and calculated shifts in x- and y-position between the reference frame and subsequent frames due to eye movements at 25 Hz. When tracking failed because the child blinked, the MP-1 automatically suspended its collecting of data until tracking could be resumed.

Calibration of the MP-1 by the manufacturer provided the degree to pixel ratio of 1:16.048. The MP-1 provided a graphical display of fixation on Cartesian axes and quantified fixation instability by determining three bivariate contour ellipses (BCEs) that circumscribe the areas within which 68%, 95%, and 99% of fixations occurred during the 30-second test period.^{8,9} The area of the 95% bivariate contour ellipse (ie, BCEA, in deg²) was used in this study as a quantitative measure of fixation instability. Examples of MP-1 fixation data from 3 children with anisometropia are shown in Figure 1.

Data from the 30-second test period could also be exported as a video or as numerical array for additional analysis of eye movements during fixation. Waveforms were classified as

consistent with infantile nystagmus syndrome, fusion maldevelopment nystagmus, square wave oscillations, or normal using published criteria.^{10–14} The Randot Preschool Stereoacuity Test (SO-007; Stereo Optical Company Inc, Chicago, IL) was also administered to each study participant.

Analyses

BCEA (fixation instability) was compared among subgroups of anisometropic children with different levels of stereoacuity defined as bifixation (< 60 arcsec), monofixation (100–800 arcsec), or nil stereoacuity by pairwise *t* tests. The Bonferroni adjustment for multiple comparisons was $P = 0.05/3 = 0.017$. BCEA data within each subgroup did not violate the normality assumption using the Shapiro-Wilks test. Some authors have used log BCEA rather than raw BCEA to normalize their data; all statistically significant differences in BCEA found among subgroups were also present when the analysis was repeated with log BCEA. The association of BCEA and stereoacuity was evaluated with the Spearman rank-order correlation.

Results

All children with normal stereoacuity (< 60 arcsec) had stable fixation, with nearly all 750 fixation points obtained during the 30-second test occurring within the 1-deg fixation circle (Figure 2). For children with normal stereoacuity, mean ($\pm$ SD) 95% BCEA was 2.3 ± 1.2 deg², which was not significantly different from that of age-matched healthy control patients (2.5 ± 0.3 deg²). Anisometropic children with subnormal stereoacuity (100–800 arcsec) had more unstable fixation; mean 95% BCEA was 4.2 ± 3.5 deg², with a trend to greater instability than anisometropic children with normal stereoacuity ($P = 0.08$). Anisometropic children with nil stereoacuity had the most instability (95% BCEA = 7.4 ± 4.2 deg²), significantly more than either of the other two anisometropic groups ($P < 0.001$ for both comparisons). Overall, fixation area (95% BCEA) was correlated with stereoacuity (Spearman $r = 0.50$; 95% CI, 0.33–0.64). Fixation area was more weakly correlated with visual acuity of the poorer-seeing eye ($r = 0.28$). Fixation area was correlated with stereoacuity even when the analysis was restricted to nonamblyopic children ($r = 0.47$; $n = 26$).

Figure 3 provides two examples of the eye movement records obtained from anisometropic children. The first example is an 8-year-old boy with stable fixation. Overall, his fixation was accurate, with the exception of a brief saccadic oscillation. Also shown in Figure 3 is an example of an eye movement record obtained from a 6-year-old anisometropic girl with significant fixation instability. Her eye position record shows the classic waveform of fusion maldevelopment nystagmus (FMNS), that is, slow drift nasalward, with a rapid refixating temporalward saccade, and this pattern repeated. Video records of eye movements for the children shown on Figure 3 are available as an online supplement (Videos 1 and 2, available at jaapos.org).

Eye movement records during attempted fixation were of sufficient quality for waveform classification in 81 children. All of the children with normal stereoacuity (< 60 arcsec) had stable fixation, with only an occasional small amplitude saccadic oscillation (Figure 4). In

contrast, 61% of children with subnormal stereoacuity (100–800 arcsec) and nearly all of the children (88%) with nil stereoacuity had FMNS waveforms in their eye movement records.

Discussion

The primary characteristic of FMNS is nasalward slow drift with a temporalward refoveating fast-phase microsaccade. The data presented here suggest that the temporalward refoveating FMNS “flicks” are common in anisometropic children. The magnitude of FMNS was correlated with stereoacuity. The temporalward flicks of FMNS may mimic microstrabismus during cover testing but are actually an ocular motor abnormality that results from decorrelated visual experience.¹⁵

Not unexpectedly, fixation instability also was weakly correlated with visual acuity of the poorer seeing eye. González and colleagues¹⁶ recently reported increased fixation instability in 13 amblyopic adults; however, the magnitude of instability was not correlated with visual acuity of the amblyopic eye. All of the amblyopic adults in the González and colleagues¹⁶ study also had abnormal stereoacuity, so it is not possible to determine whether stereoacuity or amblyopia was more strongly associated with the fixation instability.

In the present study, fixation instability was strongly correlated with stereoacuity even when the analysis was limited to nonamblyopic children. Hyperopic anisometropia is but one of many pediatric eye disorders, including strabismus, unilateral congenital cataract, neonatal vitreous hemorrhage, unioocular corneal clouding, and so forth, that may prevent normal binocular experience during visual development. Although many of these disorders can also cause amblyopia, visual acuity impairment is not a prerequisite for the development of FMNS; the necessary and sufficient factor is binocular decorrelation.¹⁵

If FMNS is causing the temporalward flick that is seen during cover testing, why is the nystagmus only noticeable during cover testing? First, it can be very small in amplitude, making it difficult to appreciate clinically except with close observation, as is the case during cover testing to determine whether microstrabismus is present. More importantly, in most children with anisometropia, we observed FMNS only in intermittent, small-amplitude bursts. The video record of eye movements for a typical child with anisometropia who shows only occasional FMNS is provided as an online supplement (Video 3, available at jaapos.org).

Our results are consistent with the model of FMNS proposed by Tychsen and colleagues¹⁵ in which correlated visual experience is necessary for the development of stereopsis and balanced gaze. In a nonhuman primate model, they demonstrated that decorrelated visual experience during visual development caused stereoacuity deficits and the fixation instability of FMNS.¹⁵ The stereoacuity data presented here support the hypothesis that the disruption of ocular motor development by anisometropia is associated with abnormal binocular visual experience and reduced stereoacuity.

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FIG 1.

Examples of MP-1 data from 3 children with hyperopic anisometropia acquired during 30 seconds of fixation. A, A child with stable fixation and nearly all fixation points inside the 1-deg circle. B, A more typical anisometropic child, with moderate instability. C, A child with extreme fixation instability. Red 1-deg circle shows the location of the fixation target in the reference frame. A small blue dot marks the location of fixation every 0.04 seconds; for the 30-second test, this resulted in a cloud of 750 fixation blue fixation points. Pale blue BCEs on each image enclose 68%, 95%, and 99% of the fixation points. The 95% BCE has been highlighted in yellow; the 95% BCEA is 0.8 deg^2 (A), 5.9 deg^2 (B), and 10.8 deg^2 (C).

FIG 2.

Mean ($\pm$ SD) fixation instability (bivariate contour ellipse area) of 94 anisometropic children (5–13 years old). Children were divided into 3 subgroups based on stereoacuity. Also shown is the mean fixation instability of 43 age-matched healthy control children (horizontal line) and 95% tolerance limits for the normative data (gray area). Aniso-metropic children with subnormal stereoacuity showed a trend toward greater fixation instability than children with normal stereoacuity ($P = 0.08$) and anisometropic children with nil stereoacuity had significantly more fixation instability than either of the other two groups ($P < 0.001$ for both comparisons).

FIG 3.

Eye movements recorded by the Nidek MP-1 during attempted steady fixation from two anisometropic children. A, An 8-year-old anisometropic boy with stable fixation (same boy shown in Figure 1A). Overall, his fixation was accurate, with the exception of a brief saccadic oscillation. B, A 6-year-old anisometropic girl with significant fixation instability (same girl shown in Figure 1C). Her eye position record showed the classic waveform of FMNS syndrome, that is, slow drifts nasalward, with rapid refixating temporalward saccades.

FIG 4.

Percentage of children with FMNS waveforms identified in eye movement records obtained with the Nidek MP-1 during 30 seconds of attempted steady fixation. Children are grouped by their stereoacuity measured with the Randot Preschool Stereoacuity Test.