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Stability of near stereoacuity in childhood intermittent exotropia

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Abstract

Purpose—To investigate the course of near stereoacuity in a cohort of children with untreated intermittent exotropia.

Methods—A total of 95 children aged 2 to 16 years with untreated intermittent exotropia were identified who had measurements of near stereoacuity, using the Preschool Randot (PSR) test on at least two successive examinations, with no intervening treatment. Deterioration was defined as a drop of at least 3 octaves, based on test–retest data. Alternative secondary analyses were performed defining deterioration as a drop of at least 2 octaves or as a transition from normal to subnormal. The main outcome measure was the deterioration rate calculated at 1 and 2 years using a Kaplan-Meier survival analysis.

Results—For near stereoacuity, the rate of decreasing 3 or more octaves was 2% (95% CI, 0%-6%) at 1 year and 7% (95% CI, 0%-16%) at 2 years. The alternative secondary analyses revealed similar low deterioration rates. In most cases of apparent deterioration, near stereoacuity returned to baseline levels without treatment.

Conclusions—For children with untreated intermittent exotropia, deterioration in near stereoacuity at 1 and 2 years is infrequent. Therefore, performing surgery for intermittent exotropia to proactively prevent deterioration of near stereoacuity cannot be justified. Retesting stereoacuity is critical to determine whether any measured decrease in stereoacuity is real.

The optimal timing of surgery for intermittent exotropia remains controversial. Some authors have suggested that early surgery should be performed to preserve stereoacuity,¹⁻³ while others have posited that stereoacuity is preserved in the vast majority of cases without intervention.⁴ Although recent studies have evaluated distance stereoacuity as a potential measure of severity of intermittent exotropia,⁵⁻⁹ the functional importance of distance stereoacuity remains unclear, whereas the functional importance of near stereoacuity has been clearly established.¹⁰ The purpose of the present study was to evaluate the course of near stereoacuity in a cohort of children with intermittent exotropia.

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Subjects and Methods

Children with previously untreated distance-type (divergence excess or pseudo divergence excess) or basic-type intermittent exotropia and at least 2 consecutive measures of near stereoacuity measured using the Preschool Randot test without intervening treatment were retrospectively identified. Children with convergence insufficiency type intermittent exotropia were excluded (near angle more than 10^Δ greater than distance angle on prism and alternate cover test). In this retrospective study, all eligible children were identified using clinical databases. Participating clinicians had previously agreed to conservatively manage children with intermittent exotropia by following without treatment unless there was clear evidence of constancy of deviation, a drop in stereoacuity, troublesome symptoms of diplopia or asthenopia, or overwhelming parental or child concerns. This clinical approach was considered within the standard of care for children with intermittent exotropia. Two consecutive measures were required to determine whether or not stereoacuity had decreased; therefore no child was ineligible for this study due to treatment initiated for reduced stereoacuity. Such children were included in the study and then censored in Kaplan Meier analyses as described below. Institutional Review Board approval was obtained for retrospective review of patient records and all procedures and data collection were conducted in a manner compliant with the Health Insurance Portability and Accountability Act.

For each child, near stereoacuity was measured at each visit using the Preschool Randot test while wearing his or her refractive correction. The Preschool Randot test has thresholds that range from 800 to 40 arcsec. A “pass” at each level was defined as two of three correct responses.¹¹⁻¹³ If the child was able to name or point at the non-stereo black and white matching shapes but was unable to identify two of the stereo shapes at the 800 arcsec level, his or her stereoacuity was recorded as “nil.” For children able to identify the non-stereo shapes, testing continued with the 800 arcsec level and stopped when the child failed a level. Children were not included for analysis until they were able to understand the test, typically at age 3 years. In the Kaplan-Meier analysis, children were censored if they received any intervening treatment (occlusion, deliberate over-minus optical therapy, orthoptic exercises, or surgery). Control of exotropia was measured using a previously reported scale of 0-5 points, with 0 signifying pure phoria and 5 constant exotropia during a 30-second observation period.¹⁴

Defining Deterioration of Stereoacuity

For the primary analysis, deterioration of stereoacuity was defined as a drop in stereoacuity of 3 or more octaves from the best previous measure (3 doublings, eg 100–800 arcsec), based on 95% limits of agreement in children with intermittent exotropia.¹⁵ Two separate secondary analyses were performed, using alternative definitions of deterioration. In the first secondary analysis, deterioration was defined as a drop in stereoacuity of 2 or more octaves from the best previous measure (2 doublings, eg, 100–400 arcsec). This more conservative, 2-octave threshold was taken from stereoacuity test–retest data in a previously published study of subjects with constant (rather than intermittent), stable strabismus.¹⁵ In the subsequent secondary analysis, deterioration was defined as a change from “normal” stereoacuity (within normal range for age)¹⁶ to “subnormal” stereoacuity (below normal range for age) (Table 1).¹⁶

Monofixation versus Bifixation

Bifixation was defined as at least 60 arcsec since the frequency of bifixation in intermittent exotropia is similar when using definitions of at least 40 versus at least 60 arcsec for the Preschool Randot test.¹⁷ “Sensory monofixation” was defined, as “worse than published

age-specific normal thresholds.”¹⁶ We classified stereoacuity as “indeterminate” (with regard bifixation and monofixation) when it was worse than bifixation but was not below normal thresholds.¹⁷

Statistical Analysis

The risk of deterioration at 1 and 2 years was calculated using a Kaplan-Meier survival analysis. In each Kaplan Meier analysis, the first occurrence of deterioration of stereoacuity for each subject was taken as the event, with the assumption that a deterioration of stereoacuity was real. Additional descriptive analysis was performed to determine the frequency of apparent spontaneous recovery of stereoacuity after each event. The risk of deterioration was also compared between children with bifixation and monofixation (patients classified as “indeterminate” were not included in this particular analysis). Data from 30 subjects in the current study overlapped with data used in a previous study.¹⁷

Results

Ninety-five children with intermittent exotropia, aged 2 to 16 years (median 5, quartiles 4 and 7) were identified. The number of examinations per child ranged from 2 to 12 (median, 3; quartiles, 2 to 4) and the median duration between first and last observations was 15 months (range, 0.5 to 76 months; quartiles, 7 to 27 months). The median angle of deviation at the first examination using the prism and alternate cover test (PACT) at distance was 25^Δ (range, 10^Δ to 40^Δ) and at near was 15^Δ (range, 0^Δ to 40^Δ). The median control score was 2 (range, 0 to 5) at distance and 1 (range, 0 to 5) at near.

Stereoacuity at Baseline

stereoacuity at presentation ranged from 40 arcsec to “nil” (median, 100 arcsec; quartiles, 40 and 200 arcsec), with 32% having 40 arcsec (Figure 1). Of these, 49% met our definition of bifixation (40–60 arcsec) on their first measurable assessment. Applying previously published thresholds for normal Preschool Randot stereoacuity (Table 1),¹⁶ 27% met our definition of monofixation (subnormal stereoacuity); for 23% fixation status was indeterminate (within normal range but worse than 60 arcsec). Children with nil stereoacuity at baseline were not included in the following analyses of deterioration.

Risk of Deterioration of Near Stereoacuity

Using our primary definition for deterioration (a drop of 3 or more octaves), not all subjects started with a sufficiently fine stereoacuity threshold to allow for the possibility of deterioration. A 3-octave threshold required stereoacuity at the first examination to be at least 200 arcsec, leaving 75 of 95 subjects (79%) for analysis. Of these 75 subjects, 2 (3%) showed deterioration over the course of follow-up, yielding a Kaplan-Meier deterioration rate of 2% (95% CI, 0%-6%) at 1 year and 7% (95% CI, 0%-16%) at 2 years (Figure 2). The age of children who showed deterioration by dropping 3 octaves (median, 4 years; range, 4 to 4 years) was similar to the age of those who did not (median, 6 years; range, 2 to 15 years), $P = 0.1$, although the power of this comparison is limited by the low number of children who deteriorated.

Secondary Analyses of Deterioration Rates

Using the first secondary definition of deterioration as a 2-octave drop, 85 subjects (89%) had 400 arcsec or better on their first examination, allowing detection of such a decrease. In these 85 subjects, 6 (7%) showed deterioration over the course of follow-up, yielding a Kaplan-Meier deterioration rate of 8% (95% CI, 1%-14%) at 1 year and 12% (95% CI, 1%-21%) at 2 years (Figure 3).

Using the subsequent secondary definition of deterioration as change from normal to subnormal stereoacuity, 69 subjects (73%) had normal stereoacuity on their first examination using the Preschool Randot, allowing for the detection of a decrease in stereoacuity into the subnormal range. Of these 69 subjects, 11 (16%) showed deterioration over the course of follow-up, yielding a Kaplan-Meier deterioration rate of 12% (95% CI, 3%-20%) at 1 year and 25% (95% CI, 9%-39%) at 2 years (Figure 4).

Possible Misclassification of Deterioration Based on Retesting

Using our primary 3-octave criterion for deterioration, of the 2 subjects who deteriorated, only 1 had a subsequent measurement, and that patient achieved his original stereoacuity threshold with no intervening treatment.

Using the secondary definitions, the risk of misclassification was greater. For the 2-octave definition, 6 subjects deteriorated, but 4 of these (67%) had a subsequent measurement: all 4 achieved their original stereoacuity with no intervening treatment. For the normal to subnormal definition, 11 subjects deteriorated over follow-up, but 7 (64%) had a subsequent measurement: 5 (71%) showed a return to normal stereoacuity thresholds on a subsequent examination with no intervening treatment.

Effect of Monofixation versus Bifixation

Dividing subjects who had sufficient baseline near stereoacuity to deteriorate, into bifixation ($n = 47$) versus sensory monofixation ($n = 11$), deterioration rates were similar, although this comparison was limited by sample size. Using our primary definition of deterioration, a 3-octave decrease, the Kaplan-Meier deterioration rate was 0% (95% CI, 0%-11%) vs 0% (95% CI, 0%-52%) at 1 year and 0% (95% CI, 0%-26%) versus 0% (95% CI, 0%-84%) at 2 years.

For the first secondary definition, a 2-octave decrease, deterioration rates were also similar between bifixation and monofixation. The Kaplan-Meier deterioration rate was 0% (95% CI 0%-12%) versus 10% (95% CI, 0%-46%) at 1 year and 0% (95% CI, 0%-23%) versus 10% (95% CI, 0%-71%) at 2 years. The subsequent secondary definition of deterioration, a decrease from normal to subnormal, could not be used for this subanalysis, since no patient could have sensory monofixation and normal stereoacuity by our definitions.

Discussion

Deterioration of near stereoacuity was infrequent in untreated intermittent exotropia at 2 years of follow-up, based on both our primary and secondary analyses. Deterioration was particularly infrequent when considering that patients initially classified as deteriorated almost all returned to their original level without treatment.

The question of whether intermittent exotropia deteriorates without treatment has been the focus of previous reports¹⁸⁻²⁵; nevertheless, different definitions of deterioration and different periods of follow-up complicate interpretation. Most previous studies on deterioration of intermittent exotropia have evaluated angle of ocular deviation. Nusz and colleagues,¹⁸ using population-based methodology and defining deterioration as an increase in exotropic angle of 10^Δ or more, reported a Kaplan-Meier rate of deterioration of 23.1% at 5 years and 52.8% at 20 years. Subsequent work on variability of measurements of strabismus angle¹⁹ found that the 95% limits of agreement for a difference between two prism and alternate cover tests in children with 20^Δ or greater esotropia were $\pm 10.4^\Delta$ at distance and $\pm 11.7^\Delta$ at near, suggesting that some of the changes reported by Nusz and colleagues¹⁸ may have been within test-retest variability. Nevertheless, data on test-retest variability of angle of deviation in intermittent exotropia are not readily available.

Romanchuk²⁰ reported on 109 patients followed for a mean of 9 years (range, 5-25 years) and found no significant change in the mean angle of exodeviation. Increasing frequency of deviation, sometimes referred to as loss of control, has been suggested by some clinicians as an indication for surgery, but Romanchuk found change in control in the distance from initial to final visit was favorable in 26%, showed no change in 51%, and was unfavorable in 23%, with 17% deteriorating to a constant exotropia at distance fixation. Nevertheless, recent studies of control²⁶ suggest marked variability throughout the day in some patients, making single assessments of control unreliable. Romanchuk²⁰ found only 2 patients with initially good stereoacuity had no measurable stereoacuity on the final visit (because of decompensation to a constant exotropia at both near and distance). Von Noorden²¹ is one of the few authors who reported high rates of deterioration (75% over an average of 3 years follow-up [n = 51]), but provided few details. Other authors²²⁻²⁵ report most cases remain stable, based on motor alignment. Taken together with data from the present study, it appears that deterioration of intermittent exotropia is infrequent over a one- or two-year time period, whether based on angle, control, or stereoacuity.

Defining deterioration of stereoacuity is fraught with problems. Applying retrospective chart review methods for the current study, we were obliged to use single measures of stereoacuity at each clinic visit. Nevertheless, we have previously reported that in an individual patient with intermittent exotropia²⁷ stereoacuity thresholds can vary over one day, from visit to visit, and even in stable strabismus.¹⁵ To account for this test-retest variability in our analyses, our primary definition (and one of our secondary definitions) required change in stereoacuity exceeding 95% limits of agreement, previously published for the Preschool Randot test in intermittent exotropia and in stable strabismus.¹⁵ The values for the 95% limits of agreement are large,^{15,27} which creates two challenges: first, the cohort “at risk” for deterioration is only a subset of the total number since there needs to be enough room to drop that number of octaves; second, the required drop is very large. We also performed a secondary analysis using a more conservative, 2-octave threshold based on previously reported limits of agreement for stereoacuity in stable strabismus.¹⁵ Using this alternative threshold of dropping 2 octaves expanded the cohort “at risk” and resulted in somewhat higher estimates of deterioration rate. Nevertheless, the weakness of this alternative, more liberal, definition, is a higher risk of misclassifying deterioration, illustrated by 4 of 4 patients with additional follow-up returning to baseline thresholds. Therefore, such apparent reductions were not true deterioration but rather corollaries of variability.^{15,27} These findings reinforce the need to retest stereoacuity, if deterioration is suspected.

One additional problem with using 95% limits of agreement to define an occurrence of a rare event is that the rate of a real observed event becomes indistinguishable from the expected rate of the event by variability alone. By definition, 2.5% of observations will lie on either side of the 95% limits of agreement. Therefore, a low real observed event rate, for example 2%, may be indistinguishable from the 2.5% event rate by chance alone, unless the sample size was very large. This phenomenon is illustrated by our own data in the recovery of stereoacuity for most patients meeting the initial definitions of deterioration with a single test, again illustrating the need for a retest to confirm real deterioration.

Deterioration of near stereoacuity in intermittent exotropia may be a function of suppression or motor misalignment or both. In some cases a measured reduction of near stereoacuity may indicate tenuous motor fusion rather than sensory deterioration. Apparent loss of stereoacuity or recovery on subsequent testing may similarly reflect motor alignment at that moment, hence the importance of repeat testing in the case of apparently reduced stereoacuity. The best measurement of near stereoacuity in intermittent exotropia may most closely approximate the patient’s best stereoacuity status at a central sensory level, whether

bifixational or monofixational. Consistent with this hypothesis is our observation that simply performing a stereotest can trigger binocular motor alignment, allowing a patient with tenuous fusion to momentarily control his or her exodeviation and achieve high levels of stereoacuity. It also seems likely that any selective measured deterioration of distance stereoacuity is a function of motor misalignment at that distance, or suppression at that distance, or both, since the sensory substrate for stereoacuity should remain the same regardless of fixation distance.

There may be different subtypes of exotropia based on the longitudinal stereoacuity profile: for example, (1) stable normal, (2) stable subnormal, and (3) fluctuating. Nevertheless, any future classification into such subtypes would increase the complexity of determining whether an individual patient had deteriorated since different criteria for deterioration would almost certainly be needed for each subtype and classification of subtype would be required before applying a specific set of rules for deterioration. For example, subjects with confirmed stable normal stereoacuity might in fact require less change in stereoacuity to confirm deterioration, whereas a patient with fluctuating stereoacuity would require a greater change. If this were true, the “3-octave change” rule would be unreasonably stringent for a cohort that included subjects with stable normal stereoacuity. The rule was derived from an analysis of 95% limits of agreement from test–retest data in a relatively small cohort of children with intermittent exotropia²⁷ who were examined three or four times during the course of a day. Re-examining those previous data,²⁷ it is apparent that the study included subjects with both stable and unstable stereoacuity. It is likely that intermittent exotropia patients with stable normal stereoacuity would behave like subjects with stable constant strabismus, and their threshold for real change may be only 2 octaves,¹⁵ not 3 octaves. Regardless of whether or not future studies confirm our speculation of different subtypes of intermittent exotropia based on the longitudinal stereoacuity profile, we advocate repeat testing of stereoacuity on the same clinic visit if reduction from the previous visit is apparent. Repeat testing is necessary to minimize misclassification of normal/subnormal stereoacuity, minimize misclassification of monofixation/bifixation,¹⁷ and reduce the threshold needed for a change to exceed test–retest variability. A practical definition of deterioration in near stereoacuity is a 2-octave decrease requiring a confirmatory retest.

One weakness of our study was the retrospective method of data collection. Nevertheless, we had previously standardized data collection for subjects with intermittent exotropia and the participating clinicians had previously agreed that subjects would be followed without treatment unless there was clear evidence of constancy of deviation, a drop in stereoacuity, or overwhelming parental or child concerns. Despite this approach, we still had a small proportion of subjects who received intervention during the course of their condition. Of the 18 patients who had an intervention (patching, over-minus lenses, or surgery) during follow-up, and who were therefore censored in the Kaplan-Meier analysis, very few met the definition of deterioration prior to initiation of treatment (1 for the 3-octave definition, 3 for the 2-octave definition, and 4 for the normal/subnormal definition). Using a Kaplan-Meier survival technique allows us to account for loss to follow-up due to intervention, but there may have been a bias toward intervention in the more severe cases. An additional weakness is that we estimated the rate of deterioration over only a two-year period, and longer follow-up would provide more useful natural history data.

Based on our data, deterioration of near stereoacuity occurs infrequently in intermittent exotropia and therefore will only rarely be an indication for surgery, but there are other reasons to proceed with strabismus surgery, including symptoms of diplopia, constancy of the exodeviation, and social concerns. Intermittent exotropia can effect a child’s quality of life,²⁸ and we now have developed quality of life instruments to evaluate these effects in individual subjects.²⁹ Awareness of exodeviations appears to increase with age³⁰ and in

adults there are clearly psychosocial effects of strabismus.³¹ One advantage of delaying or avoiding surgery for intermittent exotropia in younger children is avoidance of prolonged consecutive esotropia, with possible risk of permanent loss of stereoacuity.² Nevertheless, it is unclear whether some cases of postoperative subnormal stereoacuity may be due to undetected preoperative sensory monofixation,³² where subnormal postoperative stereoacuity may be inevitable.

Monitoring near stereoacuity is reasonable in children with intermittent exotropia, but apparent deterioration of stereoacuity should always be confirmed by retesting. Because the rate of loss of near stereoacuity is very low, we cannot justify performing surgery for intermittent exotropia to proactively prevent loss of stereoacuity's central substrate.

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FIG 1.

Distribution of baseline stereoacuity thresholds at presentation. Black shading indicates subjects with subnormal stereoacuity (sensory monofixation). Applying previously published age-specific thresholds for normal Preschool Randot stereoacuity (Table 1),¹⁶ 49% had bifixation (40–60 arcsec) on their first measurable assessment, 23% indeterminate (within normal range but worse than 60 arcsec) and 27% monofixation (subnormal). Note that depending on child age, a threshold of 100 to 400 arcsec could either be normal, and therefore indeterminate regarding monofixation/bifixation, or subnormal, and therefore consistent with sensory monofixation (Table 1).

FIG 2.

Kaplan-Meier plot of deterioration in near Preschool Randot stereoacuity defined as a reduction in stereoacuity of 3 octaves. At initial examination, 75 of the cohort (79%) had 200 arcsec or better stereoacuity and were therefore at risk for deterioration using this definition. Dots above the line indicate when a subject was censored for no further follow-up or intervening treatment. At 1 year, 46 subjects were still at risk of deterioration; at 2 years, 18. The 1-year rate of deterioration was 2% (95% CI, 0%-6%), and the 2-year rate was 7% (95% CI, 0%-16%). Of the 2 subjects that met deterioration criteria, 1 had a subsequent measurement and passed their original stereoacuity threshold with no intervening treatment.

FIG 3.

Kaplan-Meier plot of deterioration in near Preschool Randot stereoacuity defined as a reduction in stereoacuity of 2 octaves. At initial examination 85 of the cohort (89%) had stereoacuity of 400 arcsec or better and were therefore at risk for deterioration by this definition. Dots above the line indicate when a subject was censored for no further follow-up or intervening treatment. At 1 year, 50 subjects were still at risk of deterioration; at 2 years, 20. The 1-year rate of deterioration was 8% (95% CI, 1%-14%), and the 2-year rate was 12% (95% CI, 1%-21%). Of the 6 subjects that met deterioration criteria, 4 (67%) had a subsequent measurement and all 4 passed their original stereoacuity threshold with no intervening treatment.

FIG 4.

Kaplan-Meier plot of deterioration in near Preschool Randot stereoacuity defined as a change from normal to subnormal stereoacuity. At initial examination, 69 of the cohort (73%) were normal and were therefore at risk for deterioration by this definition. Dots above the line indicate when a subject was censored for no further follow-up or intervening treatment. At 1 year, 43 subjects were still at risk of deterioration; at 2 years, 16. The 1-year rate of deterioration was 12% (95% CI, 3%-20%), and the 2-year rate was 25% (95% CI, 9%-39%). Seven (64%) of the 11 subjects that met deterioration criteria had a subsequent measurement and 5 (71%) of 7 returned to normal stereoacuity on a subsequent examination with no intervening treatment.

Table 1

Normal and subnormal Preschool Randot stereoacuity values in children with intermittent exotropia, with baseline stereoacuity values used to define monofixation and bifixation in children with intermittent exotropia when bifixation was defined as at least 60 arcsec.

Age (years)	Preschool Randot (arcsec)				
	Normal stereoacuity	Subnormal stereoacuity	Assigned bifixation vs monofixation status based on stereoacuity at baseline		
			Bifixation	Indeterminate ^a	Monofixation ^b
3	40-400	800	40-60	100-400	800-nil
4	40-200	400-800	40-60	100-200	400-nil
5	40-200	400-800	40-60	100-200	400-nil
6	40-100	200-800	40-60	100	200-nil
7	40-60	100-800	40-60		100-nil
8-17	40-60	100-800	40-60		100-nil

^a Stereoacuity values worse than 60 arcsec but still within normal range for age.

^b Monofixation was defined as stereoacuity below age-referenced normal thresholds published by Birch et al.¹⁶