

Combined Gaze-Angle and Vergence Variation in Infantile Nystagmus: Two Therapies That Improve the High-Visual-Acuity Field and Methods to Measure It

Alessandro Serra,^{1,2} Louis F. Dell'Osso,^{1,3,4} Jonathan B. Jacobs,^{1,3} and Robert A. Burnstine⁵

PURPOSE. To investigate the convergence-induced waveform and high-acuity-field improvements resulting from different therapies in two subjects with infantile nystagmus (IN) that was damped by convergence and to report a new finding in one of the subjects.

METHODS Infrared reflection was used to measure eye movements during fixation of targets at different gaze and convergence angles and the expanded nystagmus acuity function (NAFX) to evaluate the IN waveform's foveation quality at all fixation points.

RESULTS Recordings demonstrated that, at far, both subjects exhibited classic nulls (high NAFX values) with NAFX reduction at gaze angles lateral to the null. S1 was treated with prisms and S2 with surgery. When converged at near or at far with base-out prisms (S1) or after bimedial recession and bilateral tenotomy surgery (S2), NAFX was higher at both the null and lateral gaze angles; the null region was broadened. The longest foveation domain (gaze angles where the NAFX is within 10% of its peak) at near was three times wider than at far for S1 and two times wider after than before surgery for S2. The *therapeutic improvement domain* (gaze angles where the posttherapy NAFX is higher than pretherapy) was even broader. At fixed gaze angles in the central 20° of gaze, S1's NAFX variation with vergence exhibited *hysteresis*, higher during divergence than convergence; S2 exhibited no hysteresis after surgery.

CONCLUSIONS Damping IN by means of convergence, induced either surgically or with prisms, broadened the range of gaze angles with higher foveation quality, mimicking the null-broadening effects of tenotomy. The discovery of vergence hysteresis may reflect pulley movement and might allow higher acuity, if a near point is transiently fixated just before a far target. The acuity domains provide new and more comprehensive evaluations of both pre- and posttherapy visual function than do primary-position acuity measurements, suggesting that high-visual-acuity fields should be included in clinical measures of

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In some individuals with infantile nystagmus syndrome (INS),¹ the nystagmus damps at a specific gaze angle (null angle) or with convergence (convergence null) on a near target.^{2,3} Because the vergence angle damps the INS, the same result is obtained regardless of the stimulus inducing the convergence.^{4,5} This fact has been widely exploited therapeutically, either optically (e.g., prisms⁶⁻⁸) or surgically, to allow better visual acuity.⁹⁻¹⁹ It has been our experience that in binocular patients with both types of nulls, the vergence null is usually stronger than the gaze-angle null.²⁰ We may take advantage of that by the use of base-out prisms and -1.00 S (to converge the eyes and negate the induced accommodation) while viewing distant targets in primary position.² Alternatively, surgical recession of both medial rectus muscles (artificial divergence) requires convergence to realign the eyes, thereby damping the nystagmus.^{13,21-23}

The visual acuities of individuals with INS, or fusion maldevelopment nystagmus syndrome (FMNS) is directly related to the foveation characteristics of nystagmus waveforms (Guo S, et al. *IOVS* 1990;31:ARVO Abstract 83).²⁴⁻³⁶ Using these waveform characteristics (i.e., foveation-period duration, standard deviations of both mean foveation position and velocity, and number of cycles in an interval of fixation), we defined a mathematical function, the expanded nystagmus acuity function (NAFX), and incorporated it into a computer program to automate its application (Jacobs JB, et al. *IOVS* 1998;39:ARVO Abstract 697).³⁷ The NAFX is a repeatable, numerical measure of waveform foveation quality and estimation of the best-predicted visual acuity that a subject with nystagmus can achieve under benign real-world conditions. Its prior use in human (including a masked-data clinical trial) and animal studies has established its value as both a waveform quality measure and acuity estimator.^{18,34,38-40} We previously defined the *longest foveation domain* (LFD; the range of gaze angles in which the NAFX is within 10% of its peak value—that is, within 1 Snellen line of the best acuity).³⁷ The LFD identifies the range of gaze angles where high acuity is possible and provides a new and potentially important measure of visual function (a *high-visual-acuity field*) for patients with INS. To this, we add the therapeutic improvement domain (TID, range of gaze angles in which the NAFX is greater than the baseline). The TID is a therapeutic measure of *all* gaze angles with increased acuity.

One objective of this study was to investigate the observation that once IN is damped by convergence in a binocular subject, it remains damped over a broader range of gaze angles than when the subject is not converged (i.e., the damping is not confined to primary position).^{41,42} We wanted to investigate whether (1) the damping of IN by convergence also improves the waveform, yielding a higher potential visual acuity; (2) the beneficial effects of convergence apply across a wide range of gaze angles; and (3) either base-out prisms or bimedial recession surgery can produce similar therapeutic effects. We used the NAFX as a quantitative measure of wave-

From the ¹Daroff-Dell'Osso Ocular Motility Laboratory, Louis Stokes Cleveland Veterans Affairs Medical Center, and the Departments of ³Neurology and ⁴Biomedical Engineering, Case Western Reserve University and University Hospitals of Cleveland, Cleveland, Ohio; ²The Neuro-Ophthalmology Laboratory, Institute of Clinical Neurology, University of Sassari, Sassari, Italy; and ⁵Akron Pediatric Ophthalmology, Akron, Ohio.

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Corresponding author: Louis F. Dell'Osso, Daroff-Dell'Osso Ocular Motility Laboratory, Louis Stokes Cleveland Veterans Affairs Medical Center, 10701 East Boulevard, Cleveland, OH 44106; lfd@case.edu.

form quality. If the NAFX values increase under the above-imposed conditions or therapies, the hypotheses are supported; if they do not, the hypotheses are rejected. We present detailed data analyses from two representative INS subjects: One (S1) was treated with prisms and the other (S2) with surgery. Both demonstrated the same effects of vergence on potential visual function. We also present the unexpected finding that *hysteresis* exists in the effects of vergence on INS.

METHODS

Recording

Horizontal eye movement recordings were made using infrared reflection (Applied Scientific Laboratories, Waltham, MA). The system was linear to $\pm 20^\circ$ and monotonic to ± 25 to 30° with a sensitivity of 0.25°. The IR signal was calibrated monocularly with the other eye behind cover to obtain accurate position information and document small tropias and phorias hidden by the nystagmus. Eye positions and velocities (obtained by analog differentiation) were displayed on a strip-chart recording system (Type R612 Dynograph; Beckman, Fullerton, CA). The total system bandwidth (position and velocity) was 0 to 100 Hz. The data were digitized at 500 Hz with 12-bit resolution.

Subjects

Both subjects were treated with therapies that induced convergence on far targets; S1 using prisms and S2, a combination of bimedial rectus muscle recessions and bilateral muscle tenotomies. These therapies are contraindicated by strabismus and lack of stereopsis.

S1 was a 61-year-old man with INS and no other visual system deficits. The beneficial effects of base-out prisms on both the INS waveform and visual acuity have been documented.^{2,32} His observations of improved acuity at lateral gaze angles when using base-out prisms prompted this study. S1's horizontal-torsional waveforms were pendular with foveating saccades (PP_{fs}) and pseudopendular with foveating saccades (PP_{fs}), with well-developed foveation. In addition to a gaze-angle null at 2° left gaze, his IN damped with convergence; he is an experienced observer. He had no strabismus and normal stereopsis. His best corrected visual acuity improved from 20/40 OU to 20/25 OU with 7-D base-out prism therapy added to his refraction (presbyopia negated the need for -1.00 S to be added OU).

S2 was a 16-year-old girl with INS and no other visual system deficits. She was a naïve observer (unaware of the purposes of this study) and the characteristics of her IN included jerk (J), jerk with extended foveation (J_{ep}), pseudocycloid (PC), and PP_{fs} waveforms. Clinically, there was no gaze-angle null but convergence damped the IN. She had no strabismus and normal stereopsis. Her best corrected visual acuity was 20/40 OU. Therapeutically, minimal bimedial rectus muscle recessions (2 mm each) and bilateral rectus muscle tenotomies were performed, after which the eye-movement measures were repeated. After surgery, her visual acuity improved to 20/25 OU. No strabismus was induced by the surgery.

Protocol

Our study adhered to the Declaration of Helsinki. Written consent was obtained from the subjects before testing. All test procedures were carefully explained to the subjects and reinforced with verbal commands during the trials. The subjects were seated in a dimly lit room in a chair with headrest and a chin stabilizer, far enough from an arc of red LEDs to prevent convergence effects (>5 feet). At this distance, the LED subtended less than 0.1° of visual angle. The experiment consisted of seven convergence-divergence trials, one for each gaze angle (0° , $\pm 5^\circ$, $\pm 10^\circ$, and $\pm 20^\circ$). LED targets were placed on the arc for far (4.2 D) and on a stimulus bar, placed along the subject's line of sight, at eye level, at different increasing vergence angles (LED 5 = 19 D; LED 4 = 25 D; LED 3 = 33 D; LED 2 = 45 D; and LED 1 = 60 D). The exact vergence angles were calculated from the subject's IPD and distance to

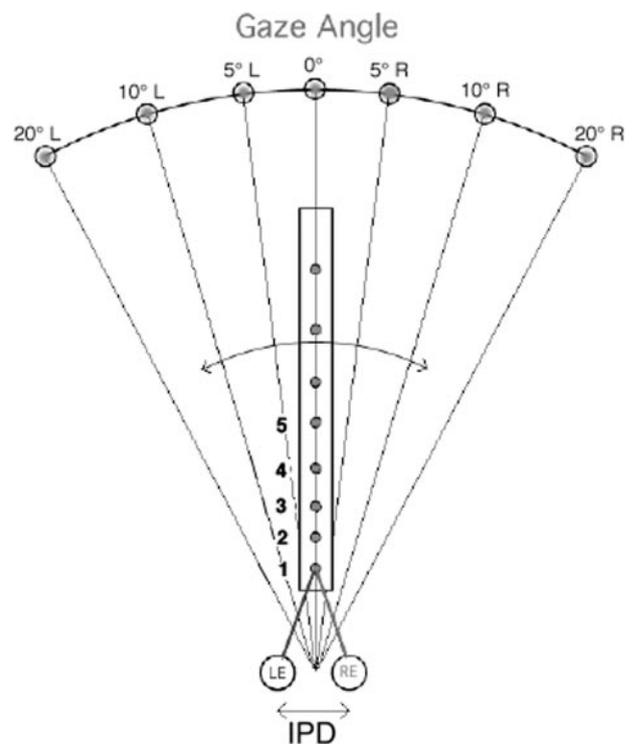


FIGURE 1. The experimental apparatus, including the arc with the seven LED far targets and the LED bar containing eight (numbered) convergence-divergence targets. The bar is shown aligned in primary position and is capable of being repositioned along any of the seven gaze angles used in this study. LE, left eye; RE, right eye; IPD, inter-pupillary distance.

the LED. For example, S1 (IPD = 64 mm) viewed LED 1 from a distance of 103 mm; the resultant vergence angle was 60 D. The comparable 60-D numbers for S2 were IPD = 59 mm and distance to LED 1 = 95 mm. During each trial, the targets were illuminated for 5 seconds, starting from far, coming successively closer (converging) to the near target, and then successively farther (diverging) to the far target. The trials were conducted at seven gaze angles, starting with 0° , and continuing with $+5^\circ$, $+10^\circ$, $+20^\circ$, and then with -5° , -10° , and -20° . Each trial lasted less a minute, with approximately 1 minute between them for the subject to rest. Trials were kept short to guard against boredom because IN intensity and foveation accuracy decrease with inattention. The stimulus bar and the stimuli paradigm are shown in Figure 1. For S2, only the far LEDs were used before surgery to assess the NAFX values at each gaze angle except in primary position, where the near LED was also used. After surgery, the above protocol was used.

Analysis

Data calibration, linearization, analysis (and filtering, if required), computation of means and standard deviations and graphic presentation were performed (MatLab software; The MathWorks, Natick, MA). The digitized data taken during monocular fixation of known targets were calibrated, and the calibration applied to all binocular records. Intervals of data (1.5–4 seconds) taken during fixation at each LED were analyzed by the NAFX and the results transferred to a spreadsheet. To be acceptable for NAFX analysis, fixation data intervals must be from the fixating eye (an obvious requirement for the NAFX to evaluate foveation quality); free of artifact (blinks or inattention); and not include postsaccadic drifts that may follow a refixation saccade. These restrictions are routinely applied to all other measures of ocular motility and were imposed on all data to be analyzed to ensure that the design criteria are met for the NAFX to reflect foveation quality and its

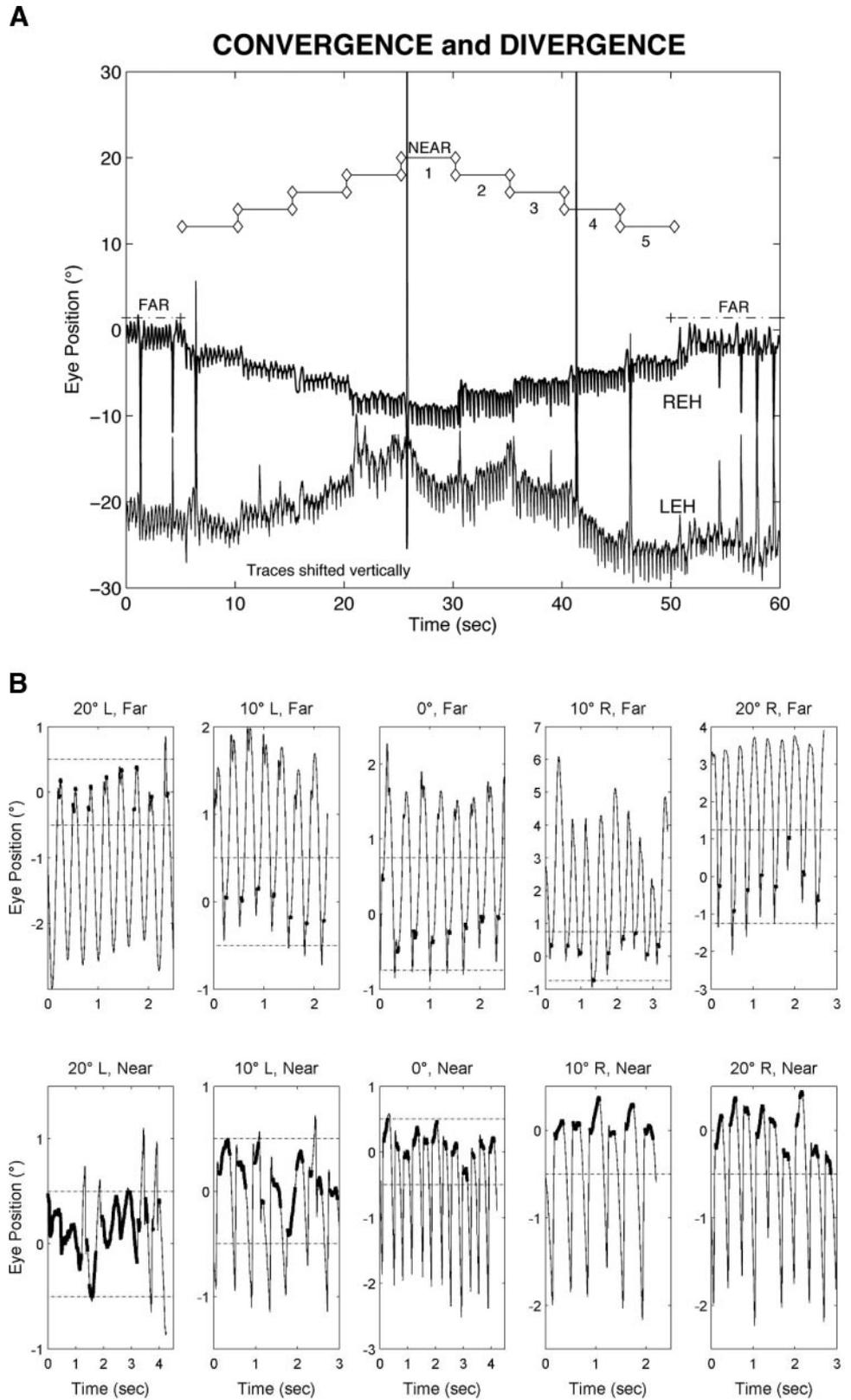


FIGURE 2. (A) A raw data recording of S1's right eye (REH) and left eye (LEH) horizontal eye movements along with a stimulus indicator showing the timing for each numbered LED target. Large vertical spikes in the eye-movement data indicate blinks. (B) Fixation data showing S1's waveforms and foveation periods (shown thickened) identified by the NAFX algorithm. Records at various gaze angles for both far and near targets are shown. *Dashed lines*, ranging from $\pm 0.5^\circ$ to $\pm 1.25^\circ$, indicate the foveation position window used to calculate the NAFX in each case.

effect on visual acuity. The uniform application of the same criteria to all fixation records also minimizes possible bias in the choice of data intervals, as is indicated by the repeatable values obtained by different individuals using the NAFX in our laboratory. Data were analyzed from both the convergence and divergence fixations at each gaze angle. Figure 2A illustrates a sample data file with stimulus change shown.

Right and left eye data are plotted against time during the convergence (stimulus change from far to near) and the divergence (stimulus change from near to far) steps of the trial.

There are three ways to identify or quantify broadened null regions (1) from the NAFX versus gaze-angle curves that are flatter at near than at far; (2) from the differences in NAFX values between near and far

NAFX, VERGENCE, and GAZE ANGLE

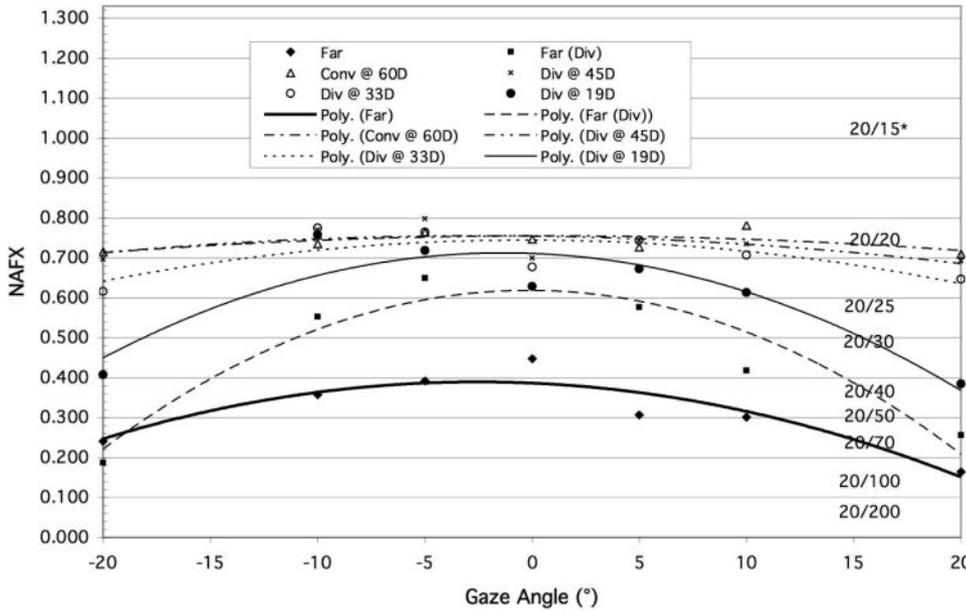


FIGURE 3. NAFX versus gaze-angle data and fitted polynomial trend curves for S1's fixation on far (pre-convergence and postdivergence), near (60 D), and intermediate (45, 33, and 19 D during divergence) targets. In this and Figures 4, 5, 7A, and 7B, Conv is convergence and Div is divergence (note that at 60 D, the convergence and divergence values are identical). In this and Figures 4 and 7, the positions of the NAFX-determined visual acuities are adjusted for the subject's age and the asterisk indicates the subject's acuity at the maximum NAFX value of 1.00.

that are larger at lateral gaze angles than at primary position; and (3) from the calculations of either the LFD or TID gaze-angle ranges (as defined in the introduction) that are larger at near than at far. In this article, we provide the data for all three methods.

RESULTS

NAFX for S1

The NAFX values, calculated at increasing and decreasing vergence steps (i.e., convergence and divergence) for each gaze angle (0°, ±5°, ±10°, and ±20°), were higher during fixation on near targets, either during convergence or divergence, than during fixation on far targets over the whole range of gaze angles we tested. The limited amount of patient data available precluded statistical testing, but the double and triple-digit improvements in near-versus-far measurements suggest that these improvements are medically significant. As shown in Figure 2B S1's nystagmus waveforms (P_{fs} at far and J_{er} at near) at all gaze angles had more well-developed foveation charac-

teristics for fixation on near targets as opposed to far targets. Foveation periods were more tightly clustered, and their durations were longer at near than at far. This occurred regardless of gaze angle, including instances when the amplitude of the IN did not damp appreciably.

During far fixation at 0°, NAFX of 0.448 (corresponding to a potential, age-adjusted visual acuity [VA] of 20/45+) was 14% to 172% higher than during far fixation at gaze angles in both lateral directions (ranging from 0.165 [VA 20/120-] to 0.392 [VA 20/50-]). Thus, S1 exhibited a classic NAFX peak ("null") looking at the far target in primary position with reduced NAFX (less damping) at gaze angles lateral to the peak.

Figure 3 shows the NAFX and visual acuity for near-fixation targets (19 D, 33 D, 45 D, and 60 D) plotted against gaze angle. NAFX values were 40.4%, 51.1%, 56%, and 66.7%, higher respectively at the null ($\approx 2^\circ$ left gaze during far fixation) and remained higher at gaze angles to both sides—that is, the null region was substantially broadened. Percentage improvements for all target positions are given in Table 1; at the peaks,

TABLE 1. Percentage of NAFX Improvements* and Null Broadening

Subject	Target	NAFX Increase at Gaze and Vergence Angles (%)							LFD (°)	TID (°)
		-20°	-10°	-5°	0°	5°	10°	20°		
S1	F†	0.241	0.358	0.392	0.448	0.307	0.301	0.165	20	—
	19D	68.9	111.7	83.4	40.4	119.2	103.7	132.7	22	>60
	33D	155.6	116.5	95.2	51.1	142.7	134.9	292.1	37	>80
	45D	189.2	115.4	103.6	56	142.3	144.2	320	55	>80
	60D	196.7	105.6	94.9	66.7	136.8	159.8	330.3	60	>80
S2	F (pre)†	0.271	0.431	0.429	0.466	0.434	0.460	0.224	20	—
	F (post)	125.1	43.2	36.6	8.6	20.5	-8.5	167.9	‡	>80
	32D	129.5	45.0	53.4	27.7	57.6	56.3	224.1	‡	>80
	44D	76.8	25.1	42.4	34.3	51.8	64.6	231.3	‡	>80
	60D	89.7	44.3	42.4	43.1	62.9	54.8	196.0	‡	>80

F, Far; D, diopters; LFD, longest foveation domain; TID, therapeutic improvement domain; pre, preoperative; post, postoperative.

* Measured with respect to baseline NAFX values at far (S1) or far (pre) (S2).

† Baseline NAFX values provided at each gaze angle.

‡ LFD calculations not applicable because of surgery-induced shapes of fitted curves.

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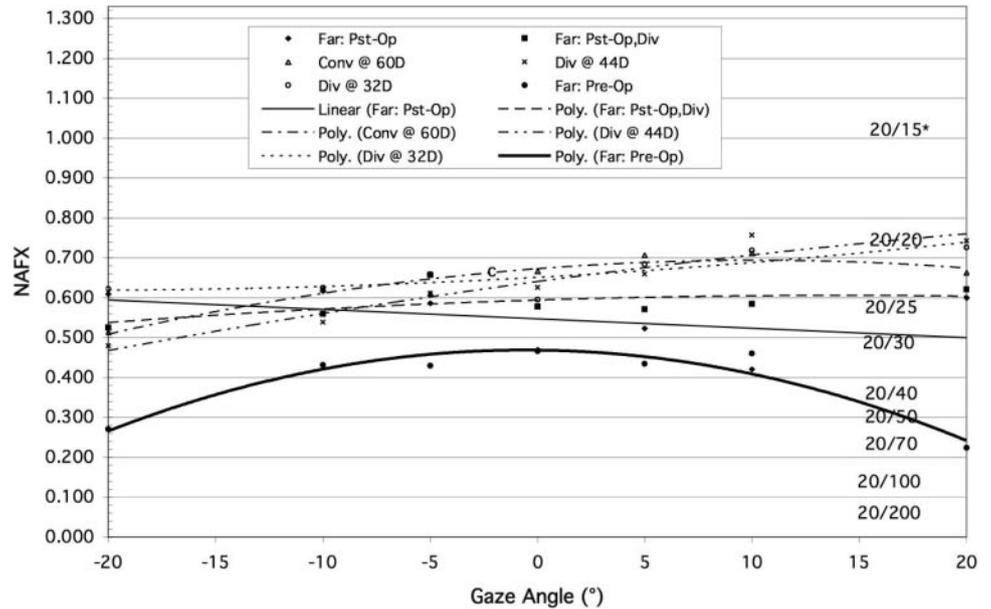


FIGURE 4. NAFX versus gaze-angle data and fitted polynomial trend curves for S2's fixation on far (pre- and post-op-pre-convergence; and post-op-postdivergence), near (60 D), and intermediate (44 D and 32 D during divergence) targets.

percentages increased with convergence, and they were even higher laterally.

NAFX for S2

Figure 4 shows that, before surgery, the far-fixation NAFX values were higher at primary-position than at lateral gaze angles, demonstrating an NAFX-measured null not seen clinically. They were also 39.5% higher on primary-position near targets (NAFX = 0.650; VA 20/20-) than on far targets (NAFX = 0.466; VA 20/30-). One year after surgery, the NAFX values were greater than before surgery for each gaze angle (0°, ±5°, ±10°, and ±20°); high values of convergence exhibited a saturation effect on the NAFX improvement (Fig. 4). For example, at far the NAFX improvements ranged from 8.6% to 167.9%. Percentage improvements for all target positions are given in Table 1. S2's nystagmus waveforms were improved at all gaze angles (i.e., more well-developed foveation characteristics). As Figure 4 also shows, NAFX values remained high across all gaze angles measured for all convergence values tested, including at far (i.e., the null regions were broadened) but increased less with convergence except at far left gaze.

Hysteresis

Figure 3 also shows how, during fixation at the far target, the NAFX values at central gaze angles were higher if S1 was looking at the target at the end of the trial (i.e., after diverging) rather than at the beginning (i.e., before converging). This was true for fixation at far as well as fixation on most of the remaining targets. There was improvement of the nystagmus waveform characteristics with longer lasting and more tightly clustered foveation periods for target fixation (at far or near), while diverging rather than during fixation of the same targets while converging. Figure 5 illustrates S1's waveform profiles during fixation at far (before convergence and after divergence), at 33 D (during both convergence and divergence), and at 60 D. Not only did the NAFX algorithm identify longer foveation periods (thickened regions) for nearer targets, but also for the same targets during divergence. In addition to these primary-position data, NAFX measured during fixation of targets at other central gaze angles was higher during divergence than during convergence, suggesting the presence of

hysteresis. When plotted for a fixed gaze angle, the variation of S1's NAFX with vergence exhibited hysteresis curves in the central 20° of gaze. The higher portions of the hysteresis curves occurred during divergence. Figure 6 shows S1's hysteresis (i.e., the vertical differences in the two curves in each pair) during target fixation at different gaze angles, more pronounced in the central 20° of gaze and minimal at ±20°. The dashed curves for data taken during divergence are higher than the solid curves from convergence.

The preoperative and early postoperative studies of S2 were made before the discovery of hysteresis in S1. Therefore, near and far recordings were made only in primary position as part of our standard INS protocol. Instead of small vergence steps from far to near and back to far, a target was moved slowly from far to near (~60 D) and back to far. Analysis of S2's preoperative eye-movement data during that paradigm did not reveal hysteresis. One year after surgery, S2 exhibited no hysteresis between convergence and divergence (using the current, stepped-target paradigm with the near target at 60 D).

LFD and TID

As used in this study, the LFD defines a *horizontal* region of high visual acuity. NAFX measurements at vertical gaze angles would expand this region into a high-visual-acuity field. As Figure 7A shows, S1's LFD at near (60 D) was 60°, approximately three times as wide as at far (20°). For targets requiring less convergence, the longest foveation domains were smaller but still greater than at far. Note that although the NAFX values at far postdivergence were greater than predivergence (due to hysteresis), there was no increase in the LFD (i.e., hysteresis increased acuity but did not change the high-visual-acuity field). The peaked shape of the NAFX versus gaze-angle curve is usually retained (albeit broadened) after prismatic and most surgical therapies, enabling posttherapy calculation of the LFD. However, the surgery in S2, skewed the curve, precluding its calculation.

The TID is the range of gaze angles in which the NAFX is greater after than before therapy. Thus, for S1, the TID is the range of gaze angles in which the NAFX is greater when converged than when not converged. For S2, it is the range of gaze angles for a far target that the NAFX is higher after surgery

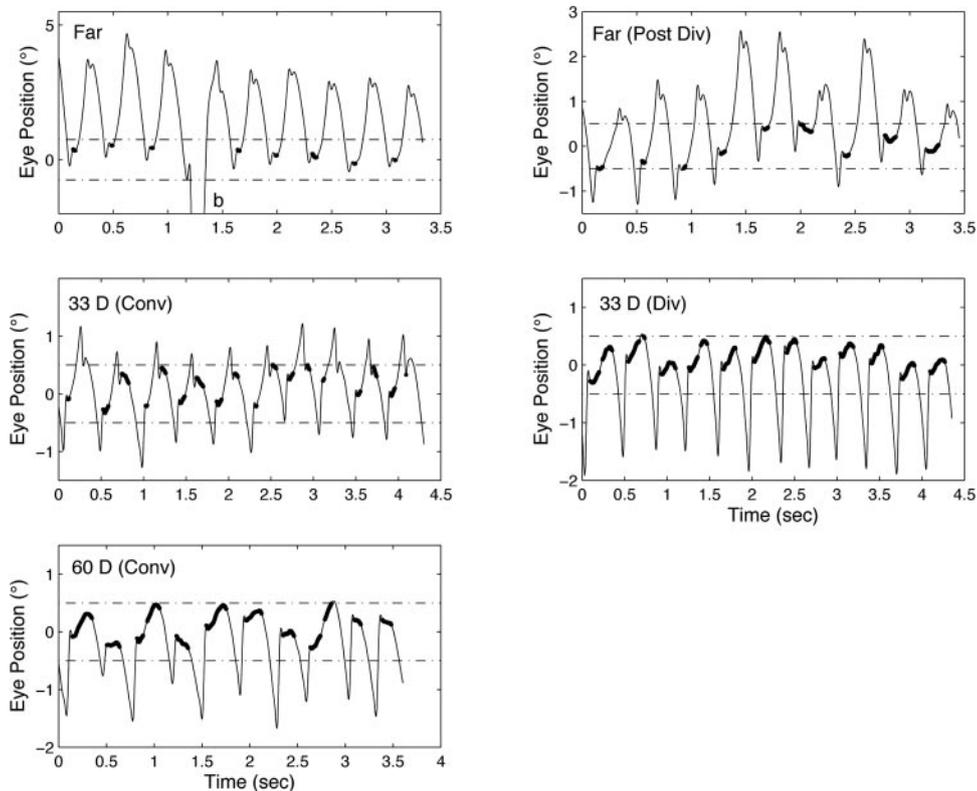


FIGURE 5. Fixation data showing S1's waveforms and foveation periods (shown thickened) identified by the NAFX algorithm. Records at various convergence angles in primary position during both convergence and divergence are shown. *Dashed lines*: ranging from $\pm 0.5^\circ$ to $\pm 1.0^\circ$, indicate the foveation position window used to calculate the NAFX in each case.

than before surgery. As Figure 7B shows, the TIDs are even greater than the LFDs and in contrast to the latter, for *all* of the near targets, the TID's encompassed the central 80° and for the postdivergence far target, the central 40° . That is, the convergence improvement in the NAFX is independent of gaze angle and the subject was able to achieve better visual acuity across the entire visual field (within a range of gaze angles of $\pm 40^\circ$) while converged. LFD and TID values for all vergence angles are given in Table 1; S1's LFD broadened with convergence and both subjects' TID encompassed $>80^\circ$.

DISCUSSION

The NAFX is a numerical method to quantify target foveation, predict visual acuity, and evaluate the effectiveness of therapies in subjects with INS, FMNS, or acquired pendular nystagmus (Dell'Osso LF, et al. *IOVS* 2005;46:ARVO E-Abstract 2403).³⁷⁻⁴⁰ It is calculated from data taken during an easy visual task. This minimizes the effect of anxiety (i.e., increased nystagmus intensity) such as might occur during a visual acuity test. Using the NAFX, we investigated the observation that once the nystagmus of a binocular INS patient is damped by convergence, it remains damped over a broad range of gaze angles. That is, convergence allows for a better potential visual acuity (higher NAFX) not only in primary position but also over a broader range of gaze angles than does unconverged fixation at distance. That results in improved visual function, even if the maximal acuity is unchanged; however, both subjects in this study also had their acuities improved by their respective therapies (see the Methods section). The importance to visual function of broadening the range of high-acuity gaze angles was first appreciated in patients who underwent Anderson-Kestenbaum procedures¹⁴ and has subsequently been attributed to tenotomy surgery in patients who had that procedure. Although this study of the data from two subjects does not include a statistical analysis, we have subsequently verified the

"null-broadening" effect in the 12 patients undergoing tenotomy thus far analyzed (study in progress).

S1's results showed that the NAFX increased with increasing convergence (albeit with a saturating effect) and that, during fixation on near targets at various gaze angles, they remained higher than during fixation on equivalent far targets. This supported the hypotheses that convergence, which reduces nystagmus, also raises the NAFX and potential visual acuity over a wide range of gaze angles. An increased NAFX was directly related to improvement of the subject's nystagmus waveforms (i.e., better foveation characteristics on near than on far targets) at all gaze angles. The increased saturation effect in S2 may have been due to the surgery.

Hysteresis

An interesting, unexpected, and potentially important finding of our study was the hysteresis (i.e., system output is dependent on both the current and previous inputs) exhibited by S1's NAFX. In the central 20° of gaze (0° , $\pm 5^\circ$, $\pm 10^\circ$) the NAFX measured for fixation on most targets was higher during divergence than during convergence—that is, the NAFX at a specific vergence angle was higher if the *previous* target was closer rather than farther away. Therefore, the mechanism underlying the convergence effects in raising the potential visual acuity (NAFX) of S1 was more effective during divergence at central gaze angles than during convergence. To investigate whether hysteresis was uncommon or dependent on fixation of stationary targets (e.g., the stepped-target paradigm), we examined the data of randomly selected prior subjects with INS with convergence damping. Four of five (80%) subjects exhibited hysteresis while fixating the slowly moving vergence target. Two subjects who fixated (5 seconds) stationary primary-position targets at different distances during convergence and divergence between far and near (20 D) targets did not. The effects of greater convergence (e.g., 60 D) were not measured; this, and any differences between vergence pursuit and ver-

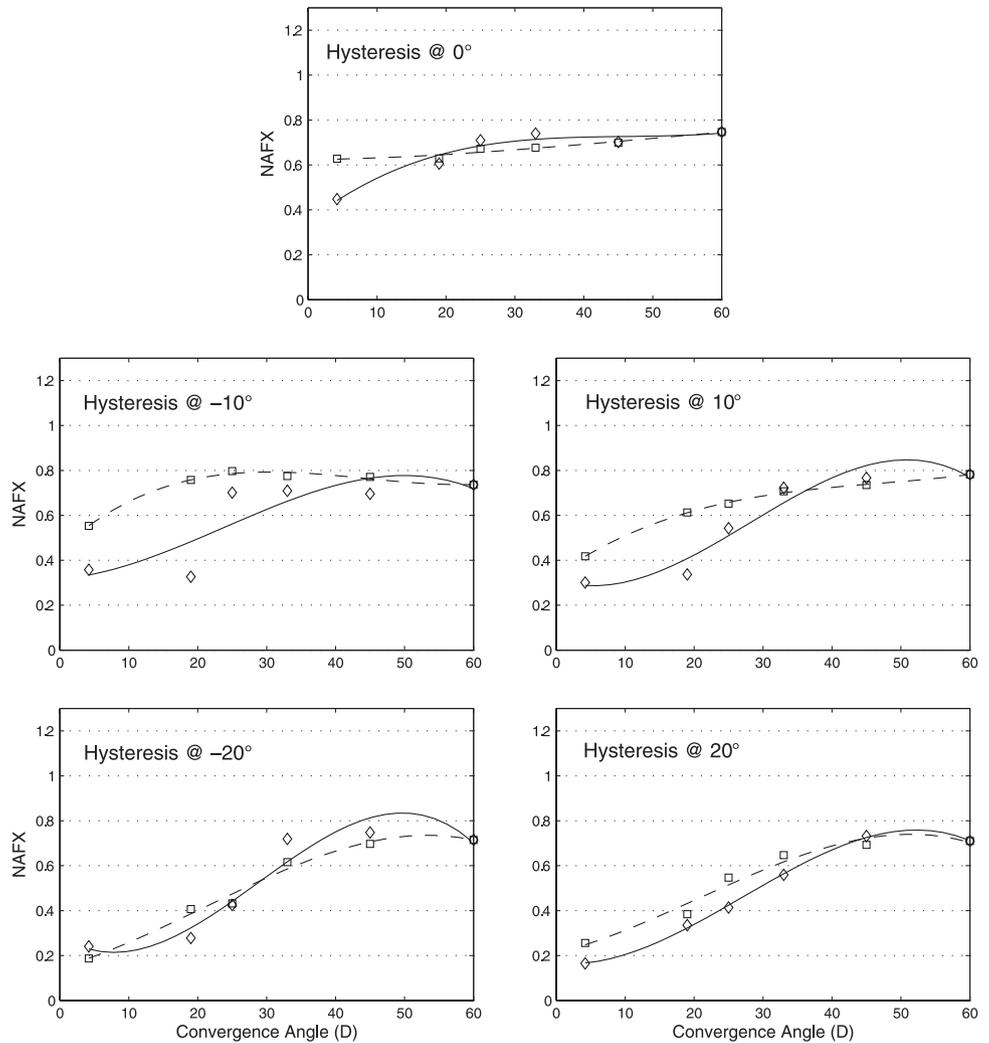


FIGURE 6. A set of hysteresis curves from S1's fixation data taken at different gaze and vergence angles (primary position, *middle top*; 10° and 20° of right gaze, *right top* and *bottom*, respectively; and 10° and 20° of left gaze, *left top* and *bottom*, respectively). Data from convergence (*diamonds*) and divergence (*squares*) form counterclockwise hysteresis curves.

vergence steps are currently being assessed as part of a study focused on hysteresis.

Possible Mechanisms

IN Convergence Damping. Although the mechanism responsible for convergence-induced nystagmus damping in IN is unknown, it has been attributed to co-contraction of both the lateral rectus and medial rectus muscles. Recent studies did not find this hypothesized extraocular muscle (EOM) co-contraction.⁴³ Therefore, it is improbable that it is a likely explanation for the convergence damping that we documented. It is not known whether peripheral or central mechanisms are responsible.

One possibility is a reduction in the plant's responsiveness (i.e., gain) during convergence, with a resultant damping of the nystagmus, which may be due to the repositioning of the muscle pulleys during convergence,⁴⁴ thereby reducing the effectiveness of the muscles in moving the globe itself. That diminishes the eye motion due to small signals such as the nystagmus input. Alternatively, a coinnervation of the antagonist muscles, even without muscle co-contraction, could account for the reduction in plant responsiveness by changing the gain in the proprioceptive loop responsible for steady state muscle tension.^{18,45,46} Further studies are needed to clarify the responsible or dominant mechanism.

NAFX-Vergence Hysteresis. S1's hysteresis caused higher NAFX values for a specific vergence target if the previous target

was nearer rather than farther away. It is tempting to interpret NAFX-vergence hysteresis as a finding that mimics the well-known "vergence asymmetry" (i.e., convergence is faster than divergence). The time constant of convergence is ~200 ms and of divergence, ~900 ms.⁴⁷ Because the time spent at each LED target during the experiment was 5 seconds, it is unlikely that this central mechanism is the explanation in our study.

Instead, we suggest that a peripheral mechanism, located either in the muscles or in the pulleys, is responsible for the hysteresis. If an increase in EOM stiffness during convergence were responsible for the nystagmus damping, the hysteresis we measured would imply a slower loss of stiffness during divergence. Further studies of nonstrabismic subjects whose IN damps with convergence are needed to determine the prevalence and time course of the hysteresis and explore possible mechanisms; also, nearest target positions ranging from 20 to 60 D should be used to quantify threshold effects.

Therapeutic Implications

For S1, conversation across a table (25 in.), viewing a computer screen (20 in.), face-to-face conversation (15 in.), reading (10 in.), and close inspection (5 in.) require vergence angles of 10, 13, 17, 25, and 49 D, respectively. The total value of the base-out prisms must be added to each of these numbers. Based on these requirements and the fitted trend curves in Figure 7, base-out prisms of 7 D OU are indicated. They would produce a high NAFX for distant targets while allowing for the

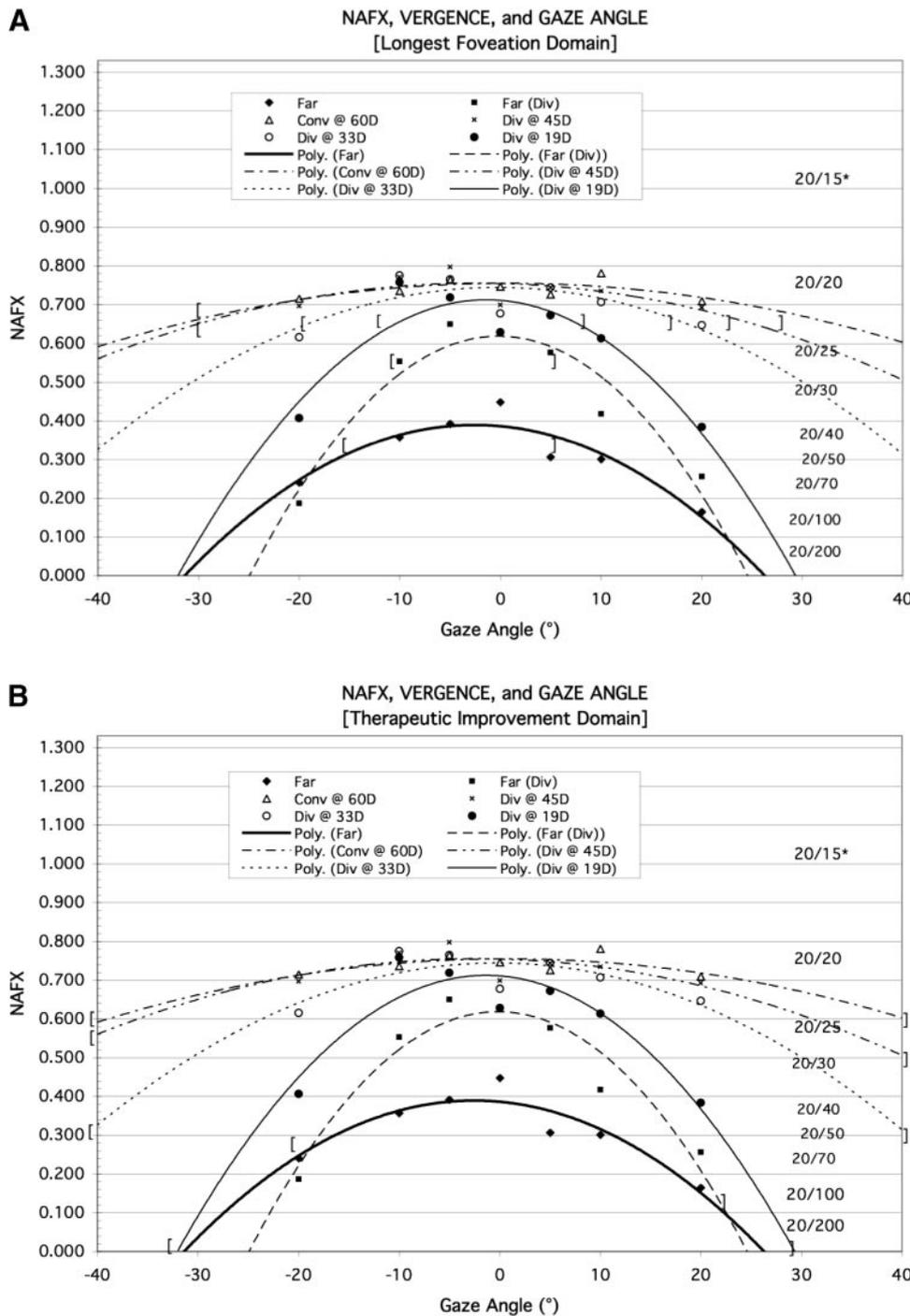


FIGURE 7. NAFX versus gaze-angle data and fitted polynomial trend curves with longest foveation domains (A) and therapeutic improvement domains (B) indicated by brackets for S1's fixation on far targets (preconvergence and postdivergence), near target (60 D), and intermediate targets (45, 33, and 19 D during divergence).

increased convergence needed for nearer tasks (e.g., 5 in. requires $49 + 14 = 63$ D). Increasing the base-out prism power beyond 7 D OU would not result in an appreciable increase in NAFX across the central gaze angles, would cause more distortion, and could preclude convergence on near targets, causing diplopia.

Damping IN by means of induced convergence, from either therapy, takes advantage of the vergence null and provides a broader range of gaze angles with higher potential acuity, mimicking the results recently discovered for tenotomy.^{18,19,39,40} The amount of convergence needed for distance vision should be chosen to be less than that which produced the greatest NAFX value, allowing for high acuity when reading, a condition requiring further convergence. Furthermore, the null-broaden-

ing effects of convergence negate the need to use composite prisms that combine the gaze-angle null with the vergence null.² This allows the same total amount of convergence to be achieved with less prism power (and distortion) on the adducting eye (e.g., 7 D base-out OU versus 3 D OS and 11 D OD; both provide 14 D of convergence). When applied to binocular recession surgery, our results suggest that, in binocular patients who have a stronger convergence than gaze-angle null, binocular recession surgery may provide superior results to the AK procedure alone. The report that a combination of the two surgeries is superior to binocular recession alone⁴⁸ may not be due to the addition of the AK shift, which our results suggest becomes irrelevant during convergence, but rather to the additional damping and null-broadening effects of tenot-

omy of all four muscles rather than just two.^{18,39,40} This suggests that bimodal recession plus bilateral tenotomy is a possible alternative therapy in these patients, eliminating the need for resections.

The hysteresis exhibited by S1 during vergence at central gaze angles raises the possibility that the acuity achieved when fixating a far target might be transiently improved by first fixating on a nearer point and then diverging to the target. There are times in daily life when this would be beneficial (e.g., trying to read a road sign while driving). It might be useful for a subject with convergence-damped INS to briefly fixate a near target first (e.g., the steering wheel) and then fixate the farther road sign. The prevalence of hysteresis and its usefulness in transient improvement of acuity are subjects worthy of further study.

Figure 7 demonstrates the broadening of the range of high-NAFX gaze angles. This has even greater clinical relevance if one considers that humans usually do not maintain eccentric fixation on targets beyond than 20°. They simply turn their head. However, within the central 40°, the use of saccadic eye movements is both more efficient and the preferred strategy to locate targets of interest. We suggest that the longest foveation (LFD) and therapeutic improvement (TID) domains are important new measures of overall visual function—equal to high primary-position visual acuity. The TID may always be calculated and the LFD (the high-acuity range) can be calculated in most cases, since most purely nystagmus therapies preserve the general shape of the NAFX versus gaze-angle curve. If either domain is small, as they usually are before therapy, the patient has only a restricted, head-fixed region in the visual field with maximal acuity. To scan the visual field for a target of interest (e.g., a face in a crowd), the head must constantly be moved to reposition that small region across the whole visual field to locate the target (like looking through a small hole in a mask fixed to the head). This is both inefficient and stressful, with the latter possibly increasing the IN to the further detriment of acuity.⁴⁹ If therapy broadens these measured domains, there is a greater portion of the visual field within which the patient can employ saccadic eye movements to scan with high acuity, as normal persons can without moving the head. A broad region of high acuity may provide even better visual function than a region of slightly higher acuity limited to a narrow region of gaze angles.

To assess accurately the direct, beneficial effects of therapies intended to improve IN waveforms, the LFD or TID should be used in addition to the primary-position NAFX. Together, they provide direct measures of potential acuity improvement over a broad range of gaze angles. Clinically, physicians should measure visual acuities at *different* gaze angles (producing a measured *visual acuity field* analogous to the classic visual field). Comparing pre- and posttherapy visual fields would provide a clinical measure of the broadening effects of the therapy on the high-visual-acuity field. In a recent paper, it was reported that measured visual acuities differed by two Snellen lines from their peak gaze angle to lateral angles, supporting the NAFX predictions.⁵⁰

References

- CEMAS_Working_Group. A National Eye Institute Sponsored Workshop and Publication on The Classification of Eye Movement Abnormalities and Strabismus (CEMAS). *The National Eye Institute Publications* (www.nei.nih.gov). Bethesda, MD: National Institutes of Health, National Eye Institute; 2001.
- Dell'Osso LF, Gauthier G, Liberman G, Stark L. Eye movement recordings as a diagnostic tool in a case of congenital nystagmus. *Am J Optom Arch Am Acad Optom*. 1972;49:3-13.
- Ukwade MT, Bedell HE. Variation of congenital nystagmus with viewing distance. *Optom Vis Sci*. 1992;69:976-985.
- Dickinson CM. The elucidation and use of the effect of near fixation in congenital nystagmus. *Ophthalmic Physiol Opt*. 1986; 6:303-311.
- Dell'Osso LF. Nystagmus, saccadic intrusions/oscillations and oscillopsia. *Curr Neuroophthalmol*. 1990;2:147-182.
- Dell'Osso LF. Fixation characteristics in hereditary congenital nystagmus. *Am J Optom Arch Am Acad Optom*. 1973;50:85-90.
- Dell'Osso LF. Improving visual acuity in congenital nystagmus. In: Smith JL, Glaser JS, eds. *Neuro-Ophthalmology Symposium of the University of Miami and the Bascom Palmer Eye Institute*. Vol. 7. St. Louis: CV Mosby Co.; 1973:98-106.
- Dell'Osso LF, Flynn JT, Daroff RB. Hereditary congenital nystagmus: an intrafamilial study. *Arch Ophthalmol*. 1974;92:366-374.
- Anderson JR. Causes and treatment of congenital eccentric nystagmus. *Br J Ophthalmol*. 1953;37:267-281.
- Kestenbaum A. Nouvelle operation de nystagmus. *Bull Soc Ophthalmol Fr*. 1953;6:599-602.
- Kestenbaum A. A nystagmus operation. *Acta XVII Council Ophthalmol (Canada, US)*. 1954;1:1071-1078.
- Schlossman A. Nystagmus surgery. *Int Ophthalmol Clin*. 1966; 613:723-726.
- Cüppers C. Probleme der operativen Therapie des okulären Nystagmus. *Klin Monatsbl Augenheilkd*. 1971;159:145-157.
- Dell'Osso LF, Flynn JT. Congenital nystagmus surgery: a quantitative evaluation of the effects. *Arch Ophthalmol*. 1979;97:462-469.
- Flynn JT, Dell'Osso LF. The effects of congenital nystagmus surgery. *Ophthalmol AAO*. 1979;86:1414-1425.
- Flynn JT, Dell'Osso LF. Surgery of congenital nystagmus. *Trans Ophthalmol Soc UK*. 1981;101:431-433.
- Abadi RV, Whittle J. Surgery and compensatory head postures in congenital nystagmus: a longitudinal study. *Arch Ophthalmol*. 1992;110:632-635.
- Dell'Osso LF, Hertle RW, Williams RW, Jacobs JB. A new surgery for congenital nystagmus: effects of tenotomy on an achiasmatic canine and the role of extraocular proprioception. *J Am Assoc Pediatr Ophthalmol Strabismus*. 1999;3:166-182.
- Dell'Osso LF, Hertle RW, FitzGibbon EJ, Miles FA, Thompson D, Yeng D. Preliminary results of performing the tenotomy procedure on adults with congenital nystagmus (CN): a gift from "man's best friend." In: Sharpe JA, ed. *Neuro-ophthalmology at the Beginning of the New Millennium*, Englewood, NJ: Medimond Medical Publications; 2000:101-105.
- Dell'Osso LF. Nystagmus, saccadic intrusions/oscillations and oscillopsia. *Current Neuro-Ophthalmology*. 1991;3:153-191.
- Roggenkamper P. Combination of artificial divergence with Kestenbaum operation in cases of torticollis caused by nystagmus. In: Reinecke RD, ed. *Strabismus II*. Orlando, FL: Grune & Stratton; 1984:329-334.
- Sendler S, Shallo-Hoffmann J, Mühlendyck H. Die Artifizielle-Divergenz-Operation beim kongenitalen Nystagmus. *Fortschr Ophthalmol*. 1990;87:85-89.
- Shallo-Hoffmann JA, Visco F, Jr, Tusa RJ. Misuse of the artificial divergence operation to treat congenital nystagmus in a patient with infantile strabismus and acromatopsia: analysis of eye movement recordings. In: Sharpe JA, ed. *Neuro-ophthalmology at the Beginning of the New Millennium*. Englewood, NJ: Medimond Medical Publications; 2000:125-129.
- Keesev UT. Effects of involuntary eye movements on visual acuity. *J Opt Soc Am*. 1960;50:769-774.
- Abadi RV, Sandikcioglu M. Visual resolution in congenital pendular nystagmus. *Am J Optom Physiol Optics*. 1975;52:573-581.
- Funahashi K, Yabumoto M, Nakai M, Miyamoto E, Fujii T, Komai N. Relations between visual acuity and waveform on electronystagmograms (ENG) of congenital nystagmus. *Neuroophthalmol Jpn*. 1984;1:414-419.
- Abadi RV, Worfolk R. Retinal slip velocities in congenital nystagmus. *Vision Res*. 1989;29:195-205.
- Bedell HE, White JM, Abplanalp PL. Variability of foveations in congenital nystagmus. *Clin Vision Sci*. 1989;4:247-252.

29. Currie DC, Bedell HE. Visual acuity in normal subjects with simulated nystagmus. *Optom Vis Sci.* 1989;66:145.
30. Bedell HE, Loshin DS. Interrelations between measures of visual acuity and parameters of eye movement in congenital nystagmus. *Invest Ophthalmol Vis Sci.* 1991;32:416-421.
31. Dell'Osso LF. Eye movements, visual acuity and spatial constancy. *Neuroophthalmol.* 1991;11:151-156.
32. Dell'Osso LF, Van der Steen J, Steinman RM, Collewijn H. Foveation dynamics in congenital nystagmus I: Fixation. *Doc Ophthalmol.* 1992;79:1-23.
33. Currie DC, Bedell HE, Song S. Visual acuity for optotypes with image motions simulating congenital nystagmus. *Clin Vis Sci.* 1993;8:73-84.
34. Sheth NV, Dell'Osso LF, Leigh RJ, Van Doren CL, Peckham HP. The effects of afferent stimulation on congenital nystagmus foveation periods. *Vision Res.* 1995;35:2371-2382.
35. Chung STL, Bedell HE. Effect of retinal image motion on visual acuity and contour interaction in congenital nystagmus. *Vision Res.* 1995;35:3071-3082.
36. Chung STL, Bedell HE. Velocity criteria for 'foveation periods' determined from image motions simulating congenital nystagmus. *Optom Vis Sci.* 1996;73:92-103.
37. Dell'Osso LF, Jacobs JB. An expanded nystagmus acuity function: intra- and intersubject prediction of best-corrected visual acuity. *Doc Ophthalmol.* 2002;104:249-276.
38. Averbuch-Heller L, Dell'Osso LF, Leigh RJ, Jacobs JB, Stahl JS. The torsional component of 'horizontal' congenital nystagmus. *J Neuro-Ophthalmol.* 2002;22:22-32.
39. Hertle RW, Dell'Osso LF, FitzGibbon EJ, Thompson D, Yang D, Mellow SD. Horizontal rectus tenotomy in patients with congenital nystagmus: results in 10 adults. *Ophthalmology.* 2003;110:2097-2105.
40. Hertle RW, Dell'Osso LF, FitzGibbon EJ, Yang D, Mellow SD. Horizontal rectus muscle tenotomy in patients with infantile nystagmus: a pilot study. *J AAPOS.* 2004;8:539-548.
41. Dell'Osso LF. Nystagmus and other ocular motor oscillations and intrusions. *Neuroophthalmology.* 1984;3:157-204.
42. Dell'Osso LF. Development of new treatments for congenital nystagmus. *NY Acad Sci* 2002;956:361-379.
43. Miller JM, Bockisch CJ, Pavlovski DS. Missing lateral rectus force and absence of medial rectus co-contraction in ocular convergence. *J Neurophysiol.* 2002;87:2421-2433.
44. Demer JL, Miller JM, Poukens V, Vinters HV, Glasgow BJ. Evidence for fibromuscular pulleys of the recti extraocular muscles. *Invest Ophthalmol Vis Sci.* 1995;36:1125-1136.
45. Büttner-Ennever JA, Horn AKE, Graf W, Ugolini G. Modern concepts of brainstem anatomy: from extraocular motoneurons to proprioceptive pathways. *Ann NY Acad Sci.* 2002;956:75-84.
46. Hertle RW, Chan C, Galita DA, Maybodi M, Crawford MA. Neuroanatomy of the extraocular muscle tendon enthesis in macaque, normal human and patients with congenital nystagmus. *J AAPOS.* 2002;6:319-327.
47. Schor CM, Ciuffreda KJ. *Vergence Eye Movements: Basic and Clinical Aspects.* Woburn, MA: Butterworth-Heinemann; 1983.
48. Zubcov AA, Stärk N, Weber A, Wizov SS, Reinecke RD. Improvement of visual acuity after surgery for nystagmus. *Ophthalmology.* 1993;100:1488-1497.
49. Tkalcevic LA, Abel LA. The effects of increased visual task demand on foveation in congenital nystagmus. *Vision Res.* 2005;45:1139-1146.
50. Yang D, Hertle RW, Hill VM, Stevens DJ. Gaze-dependent and time-restricted visual acuity measures in patients with Infantile Nystagmus Syndrome (INS). *Am J Ophthalmol.* 2005;139:716-718.