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

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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 visual function in nystagmus. (Invest Ophthalmol Vis Sci. 2006;47:2451–2460) DOI:10.1167/iovs.05-1320

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.15,21–23

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 85).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-
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 ±20° and monotonic to ±25 to 30° with a sensitivity of 0.25°. The IR signal was calibrated monocularly with the other eye held behind a 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.2-3 He observed improvements of acuity at lateral gaze angles when using base-out prisms prompted this study. S1’s horizontal–torsional waveforms were pendular with foveating saccades (Psv) and pseudopendular with foveating saccades (Psvf), 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 naive observer (unaware of the purposes of this study) and the characteristics of her INS included jerk (j), jerk with extended foveation (jfe), pseudopendular (PC), and Pfs 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°, ±5°, ±10°, and ±20°). 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 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°, +10°, +20°, 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
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
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 (Pfs at far and Jef at near) at all gaze angles had more well-developed foveation characteristics 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 (2° 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,
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.
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 ±40°) 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°.

**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).<sup>37–40</sup> 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) and potential visual acuity over a wide range of gaze angles. An increased NAFX was directly related to improvement of the subject’s nystagmus waves (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°, ±5°, ±10°) 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 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-
gence 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. 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, 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 coinervation 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. 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. 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 DO U are indicated. They would produce a high NAFX for distant targets while allowing for the
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.\textsuperscript{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-broadening effects of convergence negate the need to use composite prisms that combine the gaze-angle null with the vergence null.\textsuperscript{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 bimedial recession surgery, our results suggest that, in binocular patients who have a stronger convergence than gaze-angle null, bimedial recession surgery may provide superior results to the AK procedure alone. The report that a combination of the two surgeries is superior to bimedial recession alone\textsuperscript{48} 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-
tery of all four muscles rather than just two.18,39,40 This sug-
gests that bimedial recession plus bilateral tenotomy is a pos-
sible 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 re-
levance if one considers that humans usually do not maintain
eccentric fixation on targets beyond 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 improve-
ment (TID) domains are important new measures of overall
visual function—equal to high primary-position visual acu-
ity. 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 maxi-
mal 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 mov-

ing 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 ther-
apies 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
visual acuity 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

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