INTRODUCTION

Four-muscle tenotomy and reattachment has demonstrated improvement of the foveation quality and damping of the waveforms of the infantile nystagmus syndrome (INS),\textsuperscript{1-4} acquired pendular nystagmus,\textsuperscript{5} and acquired downbeat nystagmus.\textsuperscript{6} Those demonstrations supported the hypothetical mechanism of action (ie, peripheral damping of the
A detailed presentation of the mechanisms, diagnoses, and treatments of nystagmus in infancy and childhood may be found elsewhere. Because the tenotomy and reattachment procedure improved diverse types of nystagmus (ie, in waveforms, etiologies, and brain sites), we concluded it would also benefit patients with strabismus and fusion maldevelopment nystagmus syndrome (FMNS, also known as latent/manifest latent nystagmus).

Of the patients with both strabismus and nystagmus, approximately 53% will have INS (due to its higher incidence), 35% will have FMNS (because strabismus is a necessary condition for FMNS), and 12% will have mixtures of the two. Classically, depending on the amount of deviation, horizontal strabismus surgeries have been confined to operating on one or both horizontal rectus muscles of the deviated eye or one horizontal muscle in both the deviating and the dominant eye. Three or four horizontal muscle surgeries are reserved for large-angle deviations (typically > 60 prism diopters of deviation). In contrast, nystagmus surgeries for INS should be applied to both horizontal rectus muscles of both eyes (whether the patients are binocular, exhibit alternating fixation, or have strabismus and monofixation). Currently, the only exception to this rule is in patients with binocular INS with convergence damping of their INS; in those cases, recessions of the horizontal medial rectus muscles of the two eyes (the so-called “artificial divergence” procedure) will suffice.

Operating on patients with both strabismus and INS requires the combination of strabismus and nystagmus procedures to simultaneously realign the eyes and damp the nystagmus, thereby improving visual function. Because the tenotomy and reattachment procedure is a peripheral therapy, its mode of action is independent of the source of the nystagmus. The efficacy of the tenotomy and reattachment procedure combined with strabismus recessions to accomplish both nystagmus damping and ocular alignment has already been demonstrated in INS and acquired nystagmus. Since its introduction in canines and then in humans, the tenotomy and reattachment procedure has been used successfully to treat hundreds of patients with INS. Because of its beneficial effects on different types of nystagmus (horizontal, vertical, pendular, jerk, acquired, and infantile), we have also routinely suggested adding the tenotomy and reattachment to all strabismus surgeries for patients with FMNS. That is, if fewer than all four horizontal rectus muscles are operated on to correct a deviation (as in the majority of cases), the remaining horizontal rectus muscles should receive a tenotomy and reattachment to damp the nystagmus. Strabismus is a necessary condition for FMNS and surgical procedures for these patients have classically been limited to strabismus procedures involving recessions, resections, or both. Because patients with FMNS usually require strabismus correction, the expected therapeutic effects on FMNS of a pure four-muscle tenotomy and reattachment procedure (ie, unaccompanied by muscle-moving recessions or resections) have never been demonstrated.

In this study, we present the effects of the tenotomy and reattachment procedure on a rare patient with accommodative strabismus and FMNS who did not require strabismus correction. Studying the ocular motility of this patient allowed us the unique opportunity to assess the isolated effects of a pure four-muscle tenotomy and reattachment procedure on FMNS waveforms and to compare the resulting improvements to those predicted by both model simulation and INS-based analysis.

PATIENTS AND METHODS

Patient

We studied the eye-movement changes before and after tenotomy and reattachment during target acquisition and fixation in a patient with FMNS who only required correction of her nystagmus, not her strabismus. The patient’s age, gender, clinical characteristics, and prior diagnoses are listed in the Patient History section.

Recording

Uncalibrated horizontal eye-movement recordings were initially made (at the age of 4 years old) using an infrared reflection system (Applied Scientific Laboratories, Waltham, MA). Subsequently, at the age of 9 years old, horizontal and vertical eye-movement recordings were performed using a high-speed digital video system (EyeLink II; SR Research, Mississauga, ON, Canada). The digital video system had a linear range of ±30 horizontally and ±20 vertically. System sampling frequency was 500 Hz, and gaze position accuracy error was 0.5° to 1° on average. The data from both systems were digitized at 500 Hz with 16-bit resolution. Eye positions and velocities (analog differentiation of the position channels) were also displayed on a strip chart.
The eye-position signal from each eye was calibrated with the other eye behind cover to obtain accurate position information and to document small tropias and phorias hidden by the nystagmus. Thus, with both eyes open, the eye-position traces of each eye clearly show if one or both eyes are on target, ensuring that we analyze only the fixating eye; because the eye movements of the non-fixating, deviated eye rarely duplicate those of the fixating eye, the results of analyses of the former would not be directly related to either potential or measured visual acuity. Throughout the recording, the patient was instructed to fixate on the laser target and follow the target steps in both directions.

Protocol

This study was approved by the local institutional review board and written consent was obtained from the patient before testing. All procedures were carefully explained to the patient before beginning and were reinforced with verbal commands during the trials. The patient was seated in a chair with a 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 room light could be adjusted from dim down to blackout to minimize extraneous visual stimuli. Experiments before and after tenotomy and reattachment consisted of 5 to 10 trials, each lasting less than a minute with time allowed between trials for the patient to rest.

Analysis

All of the analysis was done using MATLAB environment (The MathWorks, Inc., Natick, MA) and OMtools software (available from http://www.omlab.org). Only eye position was sampled directly; velocity data for analysis were obtained from the sampled position data by a central-point differentiator with \( n \) equal to 3 (ie, using third points pre- and post-center). Position data were low-pass filtered with a fourth-order Butterworth filter with the cut-off frequency of 50 Hz to reduce the noise while minimally affecting the saccades. Data were filtered forward and backward to eliminate phase distortion. Analysis was done on the fixating eye. Segments with inattention or blinking were not used for this analysis.

The eXpanded Nystagmus Acuity Function (NAFX) was used to measure tenotomy and reattachment-induced foveation changes in the nystagmus at primary position and various gaze angles.\(^{17,19}\) It is an objective and repeatable measure of INS waveform foveation quality that is directly proportional to potential Snellen decimal visual acuity in patients with no additional visual sensory deficits and the changes after therapy that are directly proportional to visual acuity changes in all patients with INS, irrespective of the presence of afferent visual sensory deficits (as shown in the figures of Chapter 7,\(^ {20}\) the NAFX program provided potential visual acuities as a comparison).\(^ {10,15}\) Details of the NAFX’s theory and application may be found elsewhere.\(^ {17}\) In this study, each plotted NAFX point represents an average of several fixations, each consisting of 3 to 10 cycles (1 to 3 seconds) of steady foveation immediately following target acquisition.\(^ {21}\) Although “unblinded,” all analyses adhered to long-established and refined procedures in our laboratory.

Model Simulation

Preoperative and postoperative model simulations of FMNS were performed using our behavioral OMS model, constructed in MATLAB Simulink (The MathWorks, Inc.). We used the current version (1.5) of the model with an improved fixation block containing the added position criteria to its velocity nulling output that was originally suggested in our prior simulation of FMNS.\(^ {22}\) Postoperative simulation was accomplished by reducing the small-signal gain of the ocular motor plant by 50%, the same method we previously employed to simulate the effects of tenotomy and reattachment on INS.\(^ {23}\) Several versions of the OMS model, including the most current (1.5), may be downloaded from http://www.omlab.org.

Patient History

The patient was a 9-year-old girl with a history of nystagmus and achromatopsia, both noted at birth and observed in our clinic. In early infancy, she had nystagmus and head nodding and was thought to have spasmus nutans. Hyperopia, accommodative esotropia, and possibly Leber congenital amaurosis were also noted. Electroretinography performed at 1 year old was thought to be abnormal, but a second electroretinogram performed at 2.5 years old was normal, eliminating that possibility. Her eye movements were first recorded at the age of 4 years (ruling out spasmus nutans) and later repeated at the ages of 8.75 and 9 years. No genetic testing was done.

Preoperatively, her best-corrected visual acuity was 20/125; uncorrected visual acuity was 20/200.
in both eyes. She preferred right gaze for her best visual acuity and occasionally exhibited a left head turn. Pupillary examination was normal, as was slit-lamp and fundus examination. With glasses on, she appeared to be orthophoric at near and at distance, whereas without glasses at near, she had up to 30 prism diopters of esotropia. Her stereoacuity was worse than 400” of arc and she alternated her fixating eye. Because of her orthophoria with glasses, she was thought to be a good candidate for the four-muscle tenotomy and reattachment procedure, performed in an attempt to improve both her nystagmus and her visual function.

RESULTS

Behavioral OMS Model Simulation

We used our behavioral OMS model to simulate FMN, including both the Alexander’s law variation of the jerk nystagmus (minimum in the direction of the slow phase and maximum in the direction of the fast phase) and its transition to saccadic pulses in abduction when the slow-phase velocity exceeded a threshold value. The preoperative tenotomy and reattachment plots in Figure 1A show the transition to occur at 24.5° for right-eye fixation. We used the model to predict the effects of the tenotomy and reattachment procedure on FMN. Figure 1A shows the model’s prediction of a postoperative tenotomy and reattachment reduction of slow-phase amplitudes and velocities (and nystagmus frequencies) at all gaze angles and a broadening of the low-amplitude range of gaze angles, plus movement further into abduction of the transition angle from nystagmus to saccadic pulses. Figure 1B demonstrates the effects of these improvements on the model’s simulated slow-phase velocities (ie, the post-tenotomy and reattachment velocities were reduced).

Eye-Movement Recordings

Even prior to our analysis of the data, the preoperative eye-movement recordings revealed that the patient had difficulty in both acquiring and maintaining fixation on targets as they were presented. As the preoperative tenotomy and reattachment top traces in Figure 2 show (at all gaze angles and for both alternating direction and stepping targets), there was switching of the fixating eye during attempted steady fixation, thereby limiting the duration of steady fixation, or an inability to acquire the target with either eye; this was worse in left gaze. A comparison with the postoperative tenotomy and reattachment bottom traces in Figure 2 shows that not only was the
nystagmus decreased but also the patient’s ability to rapidly acquire and maintain fixation on targets markedly improved, not only in right gaze but even more so in left gaze. Both before and after tenotomy and reattachment there was a tendency to fixate with the left eye in right gaze. Figure 2B (bottom panel) shows right-eye fixation as the target stepped rightward from primary position was replaced by left-eye fixation at 25° and remained so even as the target stepped back to primary position. There did not appear to be a marked Alexander’s law amplitude variation with gaze angle for fixation with either eye.

NAFX Variation With Gaze Angle

We plotted the NAFX values at each gaze angle under monocular viewing conditions for each eye both before and after tenotomy and reattachment. Figure 3 shows the Alexander’s law decrease with abduction of the left eye before tenotomy and reattachment was essentially eliminated after tenotomy and reattachment. We used the old terminology of “LN” to unambiguously identify this FMN as true “latent” nystagmus during monocular viewing. For the right eye, the reversed preoperative tenotomy and reattachment Alexander’s law variation...
(ie, better NAFX in abduction than adduction of the right eye) was improved enough in left gaze (right eye adducted) to produce a normal Alexander's law variation. In both cases, the postoperative tenotomy and reattachment improvements were greater for the lower NAFX values, mimicking the improvements demonstrated by patients with INS. The net effect for the preferred left eye was a raising and broadening of the high-acuity gaze angle region across the ±30° range. Also, the NAFX improvement of right-eye fixation in adduction was sufficient to provide the same potential acuity for either eye in left gaze. The plots of foveation time mimicked the NAFX improvements (Figure 3).

In Figure 4, we plotted the NAFX values for the fixating eye at each gaze angle under binocular viewing conditions both before and after tenotomy and reattachment. We used the old terminology of "MLN" to unambiguously identify this FMN as "manifest latent" nystagmus during binocular viewing. The differential improvements in NAFX values (greater for lower pre-tenotomy and reattachment NAFX values) again resulted in raising and broadening the range of high-acuity gaze angles. The estimated improvements, based on our data from patients with INS, were approximately the same as those realized for the higher preoperative tenotomy and reattachment NAFX values but less than those realized for the lower values. The plots of foveation time again mimicked the NAFX improvements (Figure 4).

Figure 5 shows the percent improvements in both the estimated (from preoperative surgical data) and realized (from postoperative surgical data) NAFX values from Figure 4. Both trend lines show approximately a 20% or 30% increase at the higher preoperative tenotomy and reattachment NAFX values.
values (in right gaze) and greater increases (estimated = 40% and realized = >140%) for the lower values in left gaze. Thus, the realized increases in left gaze exceeded those estimated using criteria derived from INS preoperative and postoperative tenotomy and reattachment data taken from many patients. The actual, measured increase of Snellen decimal best-corrected visual acuity to 20/100 falls between the estimated (20%) and measured (30%) increases in the NAFX.

**Clinical Improvements**

There was a modest improvement in peak Snellen decimal best-corrected visual acuity of 25% (20/125 to 20/100) in either right or left gaze. Stereoacuity improved by 50% (400” to 200” of arc). Clinical examination 3 years after tenotomy and reattachment demonstrated that, consistent with the results from other types of nystagmus, the tenotomy and reattachment improvements were permanent.

**Patient’s Parent’s Reports**

Despite the modest improvements in the patient’s measured peak visual acuity, the patient’s mother reported the following improvements after tenotomy and reattachment:

1. She no longer requires a slant board for reading.
2. She discontinued cane training because she can now see the sidewalk.
3. She can now view the television from several feet away.
4. She can now successfully perform activities of daily living, such as pouring her own drink, buttoning or zipping clothing, and locating items.
5. She can now use 12-point font for reading, whereas she formerly needed 14- to 16-point fonts.
6. She can now ride a two-wheeled bike several miles with her family.
7. She now notices and comments on things in her environment from within the car.
8. She now sees and differentiates colors better.

**DISCUSSION**

The primary aim of this study was to provide ocular motor data that documented the predicted effects of the tenotomy and reattachment procedure on foveation quality in FMNS. Such data could either support or contradict our general recommendation that, for patients with FMNS and strabismus, a tenotomy and reattachment should be performed on all horizontal rectus muscles not recessed or resected to correct the strabismus. That is, even lacking eye-movement data, should the physician feel confident in adding the tenotomy and reattachment nystagmus procedure to the strabismus procedure?

Specifically, what changes in FMNS waveforms and characteristics should we expect from a four-muscle tenotomy and reattachment procedure? The effects it has on INS and on different forms of acquired nystagmus may suggest the answer. In INS, ocular motor data has shown that the tenotomy and reattachment improves the foveation quality of the waveforms by a percentage related to the preoperative NAFX value that is independent of age or associated visual afferent deficits. Thus, ocular motor research data contradict the unfounded and incorrect speculation of some that, in patients with afferent visual sensory deficits, visual function would not improve after INS therapy. Put more directly, the presence of a sensory deficit in addition to INS is not a contraindication to therapeutic intervention aimed at improving visual function. In acquired pendular nystagmus, the amplitude is reduced, thereby improving visual function and decreasing oscillopsia. In acquired jerk nystagmus (eg, downbeat), the improvements are the same as in acquired pendular nystagmus. The net results in INS are a reduction in the peak NAFX with a concurrent increase in visual acuity and, more importantly, a broadening of the peak of the NAFX versus gaze angle curve (ie, a broadening of the high-acuity “nystagmus field”).

However, FMNS does not exhibit a true peak NAFX (ie, a “null” in the nystagmus). Rather, the slow-phase velocity of the linear jerk waveform is minimal when the fixating eye is in adduction and linearly increases as it is brought into abduction (Alexander’s law). Thus, the NAFX is maximal in adduction and minimal in abduction if the FMNS waveform remains jerk with a linear slow phase. However, in many patients, that waveform changes abruptly to a saccadic pulse train at some idiosyncratic abduction gaze angle. The saccadic pulses take the fixating eye off target and their decelerating slow drifts return it to the target, allowing the fixation mechanism to further slow the eye movement.

If the waveform remains jerk with a linear slow phase across all gaze angles, one might presume that the nystagmus-damping effects of the tenotomy
and reattachment might simply raise the level of the NAFX versus gaze angle line. However, if the improvements conform to the results demonstrated in INS, we should expect the tenotomy and reattachment to have less effect on the NAFX in adduction (high NAFX) and a greater effect as the fixating eye is brought into abduction (lower NAFX). Thus, the slope of the NAFX versus gaze angle line should be less after tenotomy and reattachment than it was before tenotomy and reattachment, but remain anchored near the high-NAFX point in adduction. The net result of such improvements would be a broadening of the high-acuity nystagmus field that mimics the broadening found in INS. Such a reduction in the rate of change of the NAFX with gaze angle should shift any existing preoperative transition from linear nystagmus to saccadic pulses laterally farther into abduction. These were our expectations prior to this study (in fact, the above portion of the Discussion section was written prior to either simulating the tenotomy and reattachment on our model or performing an NAFX analysis of the patient data).

Our previous model simulation of the effects of tenotomy and reattachment on INS was an accurate predictor of its effects on patients.\textsuperscript{23,26} The model’s FMNS simulation predicted that, as a result of the tenotomy and reattachment procedure, for linear (ie, constant velocity) FMN, the slope of the slow-phase velocity versus gaze angle plot would be reduced and the amplitudes of slow-phase velocities would be reduced. Thus, we expected the amplitudes of the FMN to be reduced in primary position and as a reduction in their rate of increase as gaze of the fixating eye went from adduction to abduction. These predicted improvements in FMNS mimicked those documented for INS.

Eye-movement data provided an explanation for the patient’s preferred use of her left eye in adduction before tenotomy and reattachment and for her subsequent ability to use either eye across all gaze angles after tenotomy and reattachment. The tenotomy and reattachment procedure applied to a patient with FMNS achieved similar improvements in waveform foveation characteristics across a broadened range of gaze angles (nystagmus field), as has been demonstrated in INS. In this patient, the better waveforms found in right gaze before tenotomy and reattachment were both improved and extended across the whole ±30° range of gaze angles studied. The predicted improvements based on preoperative tenotomy and reattachment NAFX values from INS data were achieved. Measured improvements either matched or exceeded those estimated using curves derived from INS data. Thus, as we found in patients with INS, this patient with FMNS was able to see “better, more, and faster” postoperatively even though peak acuity was only moderately improved. It should be noted that this “standard” clinical measure (peak visual acuity) is usually taken with a free head (ie, at either an INS null or with the fixating eye in abduction in FMNS) precisely where the NAFX is highest and therefore the least improvement is expected to occur.

The largest improvements, and those resulting in the greatest improvements in visual function, are those in left gaze, where preoperative tenotomy and reattachment NAFX values were lowest (Figure 5). These correspond to the large, bilateral, “off-null” improvements in INS that also make the most difference in the patient’s visual function improvement.

Both the model’s predicted improvements and the patient’s measured improvements support, and extend to FMNS, the proprioceptive mechanism hypothesized to be responsible for the improvements produced by the tenotomy and reattachment procedure in INS, acquired pendular nystagmus, and acquired downbeat nystagmus.\textsuperscript{7–10} They also support our prior recommendation that adding the tenotomy and reattachment procedure to all strabismus surgeries in patients with FMNS can present further benefit. Because tenotomy and reattachment is homeostatic and muscle sparing, it does not preclude any subsequent strabismus procedure that might become necessary at some future date (ie, the muscles that received a tenotomy and reattachment may subsequently be recessed or resected).

Finally, the marked clinical improvements in this patient’s behavior were far greater than suggested by the modest improvements in the two commonly relied on clinical measures (ie, best-corrected visual acuity and stereoacuity). That is because those measures reflect only the patient’s best values (ie, when the fixating eye is in adduction). But, as in INS, those are the values that are not expected to increase the most. Therefore, in both FMNS and INS, these two “gold standards” of clinical evaluation are severely limited and potentially misleading measures in determining the initial or predicting postoperative visual function in patients with either type of nystagmus. Measuring visual acuity in either INS or FMNS at five gaze angles eliminates that inadequacy. Comparison of preoperative and
postoperative acuities at all gaze angles provides the most important measure of visual function in patients with nystagmus (the breadth of their peak gaze angle vs acuity function). In FMNS, those patients with pronounced Alexander's law variation of their nystagmus will benefit the most from tenotomy and reattachment therapy. That is, those whose nystagmus damps significantly in adduction of the fixing eye (perhaps causing a head turn) will benefit most.

Based on her eye-movement data, we attribute the dramatic improvements in the patient's lifestyle to her postoperative tenotomy and reattachment ability to more rapidly and more consistently acquire new targets and, once acquired, to maintain fixation for longer durations with damped nystagmus over a broader range of gaze angles. Most patients with INS do not usually exhibit an inability to acquire targets; the NAFX improvements reflect the increase in foveation quality and visual acuity. In this patient with FMNS, the visual function improvements exceeded those estimated because the tenotomy and reattachment also allowed rapid acquisition and prolonged fixation on targets across the measured range of gaze angles. The secondary improvement in stereoaucuity also contributed to the patient's improved lifestyle.

The four-muscle tenotomy and reattachment procedure has the same beneficial clinical and ocular motor effects on FMNS that have been repeatedly demonstrated for INS. Both model predictions and patient data analysis now provide objective evidence supporting our prior recommendation for the use of this procedure, either alone or in conjunction with strabismus procedures, in cases of FMNS. Treatment of FMNS should no longer be limited to the correction of the associated strabismus, especially because improvements in the nystagmus waveforms may have far more beneficial effects on the patient's visual function.

REFERENCES
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