Clinical and ocular motor complications of extraocular muscle extirpation for infantile nystagmus syndrome

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PURPOSE To describe the effects of extraocular muscle extirpation performed after previous eye muscle surgery in a 20-year-old woman with infantile nystagmus syndrome (INS) for whom we have 19 years of follow-up data.

METHODS Clinical examinations were performed. Eye movement data analysis was carried out using the eXpanded Nystagmus Acuity Function (NAFX) and longest foveation domain (LFD).

RESULTS The patient re-presented to the authors at age 20, 2 years after bilateral anterior myectomy of the horizontal rectus muscles, bilateral anterior nasal transposition of the inferior oblique muscle, and bilateral superior oblique recessions. Evaluation revealed deterioration in nystagmus at lateral gaze angles, new incomitant strabismus with severe loss of convergence, limited ductions, saccadic hypometria, slow saccades, and hypo-accommodation. Also, there was a pre- to post-extirpation minimal change of 21% in her peak NAFX, a 50% decrease in LFD, plus a predominant, asymmetric, multiplanar oscillation.

CONCLUSIONS It appears that in this patient, horizontal extirpation failed to abolish the nystagmus and caused significant, new, symptomatic deficits interfering with many of the patient's visual functions. (J AAPOS 2018;22:110-114)

The ability of the ocular motor system to shift and maintain gaze, align, and converge the eyes (in nonstrabismic patients), pursue moving targets, and stabilize gaze in the presence of head, body, or environmental movement are essential for good visual function in the real world. Arguably, the most effective surgical treatments for infantile nystagmus syndrome (INS)[1] are those that do not curtail ocular motor functions. The "maximal recession" procedure, which requires large recessions of all four horizontal rectus muscles, was an example of this negative effect.[2,3] Although that procedure was shown to damp the INS, it also significantly compromised the patient's ability to make accurate, rapid saccades, maintain eccentric gaze, align the eyes (especially in lateral gaze), converge the eyes, preserve stereopsis, pursue moving targets, or stabilize the eyes in the presence of head, body, or environmental motion. With the advent of the four-muscle tenotomy and reattachment (T&R) procedure, along with more traditional operations, homeostatic surgical algorithm for treatment of INS[4-8] were developed.[9-11] It has been demonstrated that the beneficial effects of the enthesial tenotomy portion (cutting the tendinous insertion) of any eye muscle surgery improves INS waveforms and dynamic visual functions and also prevents ocular motor system deficits seen in maximal extraocular muscle recessions.[4,12] In 2002 Sinskey extended the presumption underlying the maximal recession procedure to what he may have presumed to be a logical conclusion by proposing total *extirpation and disposal* of the anterior portions of the four horizontal rectus muscles.[13-17] The current case report presents clinical data collected over a 19-year period for a young woman with INS treated with standard eye muscle surgery and subsequently with muscle extirpation surgery.

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This work was supported in part by the Office of Research and Development, Medical Research Service, Department of Veterans Affairs.

Submitted September 16, 2017.

Revision accepted November 20, 2017.

Published online March 13, 2018.

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1091-8531/$36.00

https://doi.org/10.1016/j.jaapos.2017.11.007

Methods

Prior to the recent clinical intervention, the patient had been enrolled in a research protocol in which the collection and reporting of data followed institutional research approval via a research registry protocol with appropriate informed consent and US Health Insurance Portability and Accountability Act of 1996 regulatory requirements. Repeated, routine examinations were performed on a routine basis over a period of 19 years. Additional special testing included optical coherence tomography, fundus photography, electroretinography, visual evoked potentials, color vision, visual field, and contrast sensitivity. The recent muscle extirpation surgery was *not* part of this protocol.

Eye movement data were recorded at the Daroff-Dell'Osso Ocular Motility and the Visual and Ocular Motor Physiology Labs. The first recording was made when the patient was 1 year old using an Ober2 infrared system (Permobil, Timra, Sweden, 300 Hz). The video system used in 2001 and 2002 was an EyeLink II (SR Research, Mississauga, ON, Canada) that had a post-calibration linear range of ±30° horizontally and ±20° vertically. The data from these systems were digitized at 500 Hz with 16-bit resolution. Eye positions and velocities (obtained by analog differentiation of the position channels) were also displayed on a strip-chart recording system (Beckman Type R612 Dynograph). The system used when the patient was 6 and 9 years of age was an Ober2; when she was 15 and 20, an EyeLink II. The signal from each eye was calibrated with the other eye covered to obtain accurate position information; the foveation periods of each nystagmus cycle were used for calibration. The subject was seated in a chair with headrest and either a bite board or a chin stabilizer, far enough from an arc of red LEDs or a projection screen to prevent convergence effects (>5 feet). An experiment consisted of from one to ten trials, each lasting under a minute, with resting time allowed between trials.

Data Analysis

All analysis was carried out in MATLAB, using the eXpanded Nystagmus Acuity Function (NAFX)[18-20] and other OMtools software (omlab.org). Two-dimensional (radial) NAFX values were compared to those using the predominantly horizontal nature of the oscillations. The longest foveation domains (LFD) were calculated as the range of gaze angles, where the NAFX was ≥90% of the peak NAFX value.

Results

The patient's examinations have consistently and repeatedly shown normal color vision, visual field, lids, adnexa, anterior segment, and intraocular pressure; and abnormal (paradoxical) pupils, decreased foveal reflex, scattered peripheral, pigmentary disturbance, and mildly anomalous optic nerves. She always had a variable small-angle multiplanar strabismus (exotropia and hypertropia) and no stereopsis. She had no abnormal head posture.

At age 5, an associated congenital, stable, rod-cone dystrophy was diagnosed based on an abnormal electroretinogram and normal visual evoked potentials. Her best-corrected binocular visual acuity over 19 years' follow-up ranged between 20/80 and 20/60. She has had significant anisometropic astigmatism (at the time of this evaluation, −4.50 + 4.25 × 100 in the right eye and −4.50 + 2.00 × 170 in the left eye).

At age 6 years she underwent uncomplicated bilateral medial rectus T&R for the INS combined with a bilateral lateral rectus recessions of 3.0 mm for the exotropia, performed by one of the authors (RWH). After T&R surgery she was able to read easily and comfortably; she eventually obtained a driver's license and had no trouble driving. She did not have oscillopsia, head turn, or diplopia.

At age 18, believing her nystagmus could be stopped completely, she underwent an "anterior myectomy of the right and left medial and lateral rectus, anterior nasal transposition of the right and left inferior oblique and recession of the superior oblique right and left" at another institution. Each horizontal rectus was "allowed to retract into the sleeve where it disappeared from view" (from surgical notes). We are unaware of any IRB-controlled research protocol for that procedure.

At age 20, at the time of her most recent visit to our clinic, 2 years after extraocular muscle extirpations, she had the following subjective complaints: (1) persistent asymmetric, multiplanar oscillopsia and diplopia; (2) an anomalous and pronounced chin-down head posture; (3) incomitant vertical strabismus; (4) difficulty with reading and driving, and (5) motion sickness. Additionally, objective evaluation after extirpation revealed the following: (1) profound monocular asymmetry (right eye worse than left) in the horizontal, vertical, and torsional planes of the nystagmus (which increased in intensity at near); (2) incomitant strabismus (incomitant right hypertropia; (3) right head tilt; (4) no convergence, and incomitant exotropia; (5) limited ductions (see Figure 1); (6) a chin-down anomalous head posture; (7) saccadic hypometria; (8) low vestibular ocular reflex and horizontal pursuit gain; and (9) significant hypo-accommodation.

Eye Movement Data

The patient's eye movements were recorded six times, from 1 year to 20 years of age. A timeline for the recordings and two surgeries is provided in Table 1. The initial preoperative eye movement recordings, made when the patient was 1, 5, and 6 years of age, showed INS with both horizontal and vertical components (horizontal amplitudes usually greater than vertical), resulting in circular/elliptical/oblique motion. The horizontal components of both eyes were conjugate and the vertical components varied from 0° to 180°; when the vertical components were 180° out of phase, the oscillations had a see-saw component. The waveforms were pendular, pendular with foveating saccades, triangular, and pseudo-jerk. Neither horizontal nor vertical gaze changed the INS substantially; that is, there were no "nulls" in either plane. Figure 2 shows eye position versus time and scan paths of both eyes (before the standard surgery) during attempted right eye foveation of a target at 0° with the left eye with exotropia of about 10° and hypotropia of about 2°.

The scan paths of both eyes during attempted fixation of targets at 0° and ±20° horizontally and at 0° and ±10° vertically before standard surgery may be seen in eFigure 1. The scarcity or even absence of repeated cycles with accurate foveation illustrates the difficulty (more

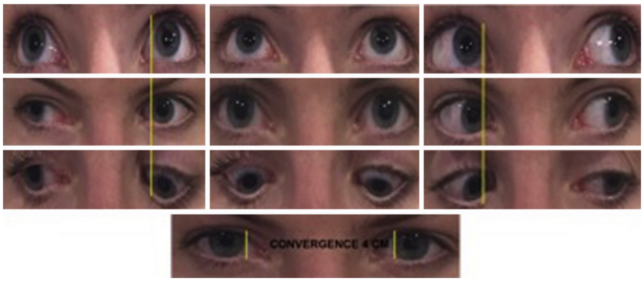

FIG 1. Clinical post-extirpation evaluation of versions and ductions showing limitation of adduction in the right and left eyes during left and right gaze, respectively (long vertical lines) and severe limitation of convergence during attempt to fixate a 4.0 cm (short lines).

Table 1. Patient timeline

Age, years	Notes
1	EMR
5	EMR
6	Standard surgery
6	EMR
9	EMR
15	EMR
18	EOM extirpation surgery
20	EMR

EMR, eye movement recording; *EOM*, extraocular muscle.

prevalent in both right gaze and upgaze) she had in acquiring targets and maintaining fixation. Peak-to-peak amplitudes ranged from 15° to 20°. The peak NAFX in primary position was 0.160, with an LFD of 17° (Figure 3).

After Standard Surgery

Initial recordings at age 9 years, after the standard surgery, showed that the INS waveforms were pendular, pendular with foveating saccades, and pseudo-jerk. Recordings made when the patient was 15 years of age (9 years after standard surgery) showed that waveforms remained unchanged and there was neither a "null" position (no head posture) nor a latent component. Near viewing did not damp the INS, which showed no changes with time over a 5-minute interval. These scan paths of both eyes during attempted fixation of targets at 0° and ±10° horizontally and vertically are given in eFigure 2. In contrast to the scan paths before surgery (eFigure 1), she was now easily able to accurately locate and foveate all five targets, with tight, repeated cycles containing accurate foveation. The reduced peak-to-peak amplitudes ranged from 5° to 10°. The peak NAFX was 0.265 (an increase of 65.6%) with an LFD of 28° (an increase of 65%, see Figure 3). Saccades, smooth pursuit, vestibulo-ocular, and optokinetic eye movements were unaffected by the standard surgery procedure.[9,21]

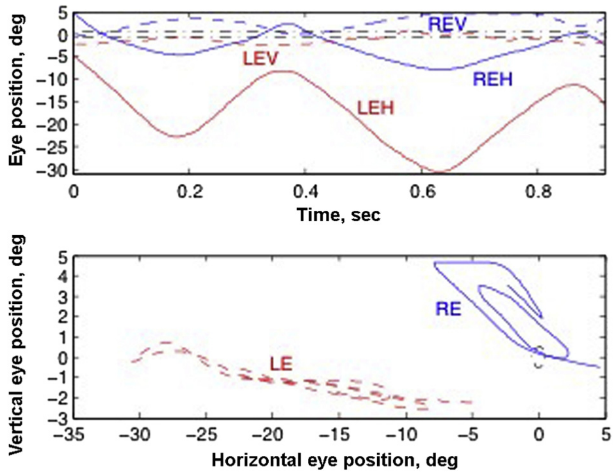

FIG 2. Before standard surgery eye position versus time and scan paths of both eyes during right eye fixation in primary position. The clockwise elliptical INS trajectories' major axes were from up and left to down and right, where the foveation periods of the right eye are located. The deviated eye has a larger, more horizontal trajectory. *RE*, right eye; *LE*, left eye; *H*, horizontal; *V*, vertical. The ±0.5° foveal areas are shown by the dash-dot lines and circles; in the scan paths, the fixating eye is solid and the deviated eye, dashed.

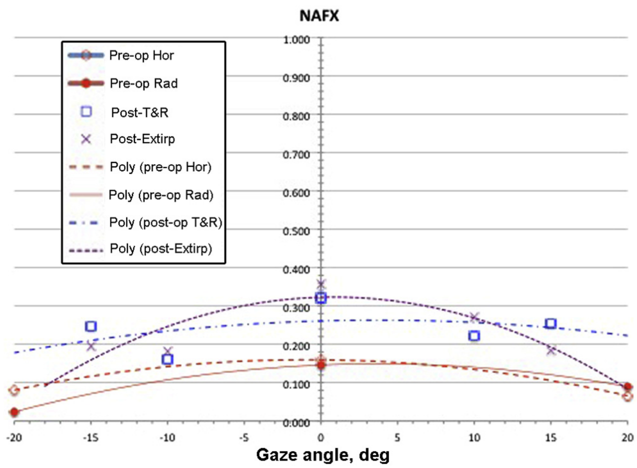

FIG 3. Plots of NAFX vs Gaze Angle from pre- and post-standard (*T&R*) surgery and post-extirpation (*Extirp*) surgery data. For the pre-standard surgery data, both horizontal (*Hor*) and biplanar (*Rad* [radial]) data are shown.

After Muscle Extirpation Surgery

Eye movement recordings at 20 years of age (2 years after extirpation surgery) showed an inability to accurately locate and foveate targets. INS waveforms were pendular, pendular with foveating saccades, and pseudo-jerk. Ocular motor analysis showed a new asymmetric, multiplanar oscillation that increased in lateral gaze and near. The superimposed scan paths of both the right and left eyes during attempted fixation of targets at 0° and ±10° horizontally and vertically are given in eFigure 3. In sharp contrast to the scan paths illustrated in eFigure 2 (after standard surgery), with the left eye she was now unable to accurately fixate the 10° left (4° above) and 10° down (10° left) targets. In fact, despite lower INS amplitudes, her scan paths were less accurate than they were before standard surgery (eFigure 1). Peak-to-peak amplitudes remained close to the range of 4°-10° after standard surgery. The recordings quantitatively document the subjective complaints of worsening. Further, despite the INS amplitude decreasing, the patient's condition worsened. The peak NAFX was 0.322 (an increase of 101% from the preoperative value but only 21.5% from value after standard surgery), with an LFD of 14° (a *decrease* of 18% from the preoperative value and a *decrease* of 50% from the value after standard surgery value; see Figure 3).

In addition, saccades of all amplitudes were slowed considerably, the peak velocities of 10° saccades averaged 700°/sec after standard surgery but dropped 57% to 400°/sec after extirpation.

Figure 2 and eFigures1-3 provide an overview of the observable changes in INS amplitudes and target-acquisition accuracies before surgery, after standard surgery, and after extraocular muscle extirpation. Both the absolute NAFX values and broad preoperative curvature were improved by the standard surgery procedure. As expected, the peak NAFX values improved after extraocular muscle extirpation but only in the central 20° and then decreased to preoperative values. The important range of high-acuity gaze angles decreased to less than the preoperative value.

Discussion

A recent retrospective study by Lingua and colleagues[22] on the effects of extraocular muscle extirpation (and partial extirpation, or, myectomy without reattachment) contained methodological errors and incomplete analysis, in our opinion.[22,23] Patients (including children) were subjected to experimentation with various types of extraocular muscle extirpations. The authors did not reference preceding studies.

The accumulation of objective ocular motor data over 19 years plus clinical evaluations of our patient has provided us with a unique opportunity to document the therapeutic effects of standard eye muscle surgery followed by the effects of extraocular muscle extirpation surgery for INS in this patient. Extirpation of the anterior portion of the horizontal rectus muscles combined with recession of the obliques failed to abolish the previously damped INS (after standard surgery). Meanwhile, significant new symptomatic deficits, including diplopia, oscillopsia, and anomalous head posturing along with vestibular and saccadic dysfunction, hypo-accommodation, and no convergence occurred. The 32% peak improvement in visual acuity noted after the original standard surgery was unchanged by extirpation. It should be noted that visual acuity, NAFX, and LFD values before and after standard surgery were consistent with our previously developed predictive curves relating these variables.[10]

The INS waveform improvements over a broad range of gaze angles that resulted from the standard procedure were apparently adversely affected by the extirpation procedure. Target acquisition and fixation ability at lateral gaze angles deteriorated to worse than before standard surgery, and saccadic velocities dropped by 50%-60%. Although the peak NAFX increased 21.5% from the value after standard surgery, the more important LFD decreased by 50%. As is evident from Figure 3, outside of the central ±10°, the NAFX fell below values after standard and, at $< \pm 20°$, fell below values before standard surgery.

Significantly, the INS was *not* eliminated by extirpation; in fact, the nystagmus was not greatly reduced from what was already achieved by standard surgery. Initially, the patient had greater difficulty in fixating the vertical targets (see eFigure 1), but after the standard surgery procedure, all targets were easily fixated (see eFigure 2). However, after extirpation, the difficulty in fixating vertical targets returned (see eFigure 3).

Each extraocular muscle is part of a brain-controlled, muscle-tension control system in addition to brain-controlled, vision-determined eye position, alignment, and velocity control systems. Thus, whatever is done to affect the response of the extraocular muscle will trigger automatic brain responses via each ocular motor control system that will act to return the systems to homeostasis and efficient operation. Standard strabismus eye muscle operations are usually not designed or performed to limit extraocular muscle function but to improve eye position, restore comitance, or release restrictions. The few exceptions include anterior transposition of the inferior oblique, orbital myopexy, and sharing procedures, all of which have clear indications and known complications. Lowering the small-signal gain of the tension control system allows both increased NAFX and LFD. At high values of NAFX (eg, produced by the standard surgery), visual acuity cannot be increased significantly, as was the case after extirpation. However, destruction of the tension control system by extirpation eliminated the large LFD increase produced by standard surgery.

The most successful surgical approaches to INS damping and improvement in foveation quality have been those that replicate standard techniques. The goals of these procedures are to change eye position (or compensatory head position) and improve the nystagmus characteristics by simultaneously reducing the small-signal gain of the extraocular muscle while *maintaining* all of the required ocular motor functions.

Extraocular muscle extirpation failed to improve this patient's INS and also introduced symptomatic deficits not associated with current surgical therapies for INS. We suggest that full or partial extraocular muscle extirpation to treat INS in human patients, is, at this time, premature and may risk inducing symptomatic deficits.

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Seeing Is Believing

When eyesight is deficient, as in disease or in darkness, imagination is never tardy to supply the wants of an imperfect ocular function. However, once the imagination is let go, there is no telling what bizarre delusions it might incur: a lamp shade becomes a burnt parrot perched atop a ship's mast, and a desk turns into the cadaver of an ox whose throat has been slit. Hence the unbearable tension and enhanced terror of an object that is both deemed suspect and imperfectly visualized. Every detail in its outline threatens; a riotous fancy discovers a ghoulish menace in the blandest of its features.

—F. Gonzalez-Crussi, *On Seeing: Things Seen, Unseen and Obscene* (New York: Overlook Duckworth, Peter Mayer Publishers, 2006), 175.

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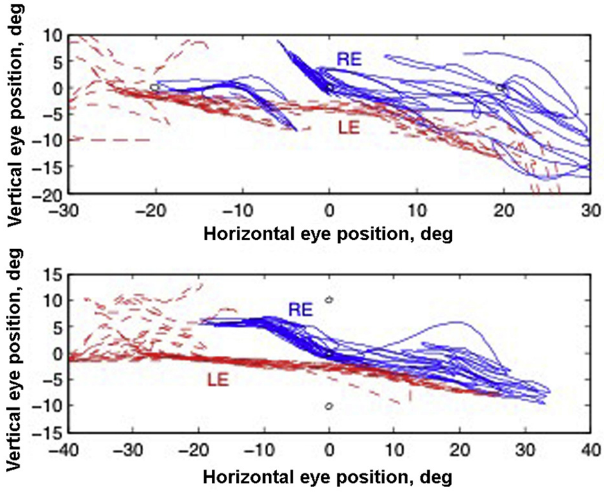
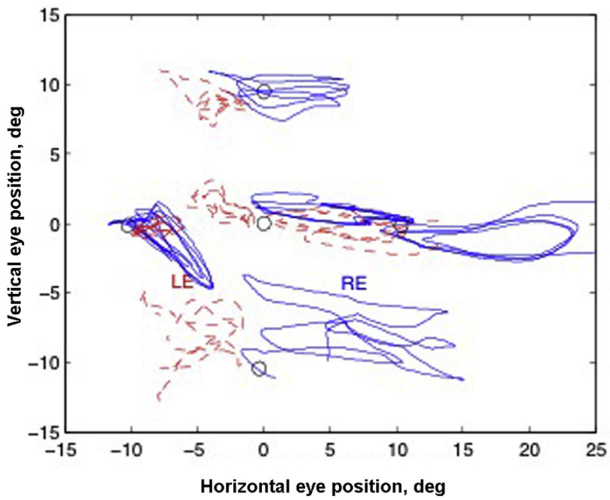
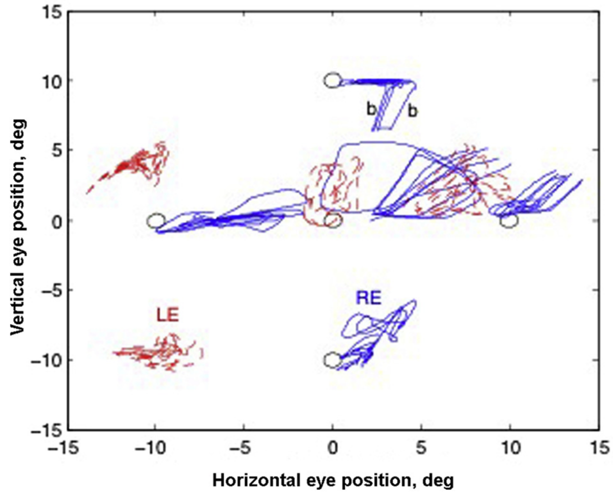


eFIG 1. Scan paths before standard surgery of both eyes during attempted fixation at 0° and ±20° horizontally (top) and 0° and ±10° vertically (bottom). The foveation periods are located at the leftward portion of the INS cycles of the right eye during these fixation intervals. During right eye foveation of a target at 0°, the deviated left eye was about 10° of exotropia and about 5° of hypotropia. At the other positions within the central ±20° horizontal and ±10° vertical, it varied from 5° to 20° of exotropia and 5° to 10° of hypotropia. Peak-to-peak amplitudes ranged from 15° to 20°. The ±0.5° foveal areas are shown by circles; in the scan paths, the fixating eye is solid and the deviated eye dashed, respectively.



eFIG 2. Post-standard surgery scan paths of both eyes during attempted fixation at: 0° and ±10° horizontally and vertically. Data from left-eye fixations also demonstrated accurate fixation at all five target positions. The foveation periods are located at the leftward portion of the INS cycles during these fixation intervals. During right-eye foveation of a target at 0°, the left eye varied from 0° to 5° exo- and 0° to 1° hypotropic. At the other positions within the central ±10°, it varied from 0° to 10° exo- and 0° to 2° hypotropic. The reduced peak-to-peak amplitudes ranged from 5° to 10°. The ±0.5° foveal areas are shown by circles; the fixating eye is solid and the deviated eye, dashed.



eFIG 3. Following extirpation surgery scan paths of both eyes during attempted fixation at 0° and ±10° horizontally and vertically. She was unable to locate the 10° up target. Unlike Figures 2, e1, and e2, the data shown for both eyes were collected during attempted fixation with that eye (the deviated eye is not shown). The foveation periods that were produced are located at the leftward or bottom-leftward portions of the INS cycles during the fixation intervals of the right eye and, for the left eye, at the bottom (0° target) and rightward (10° right target) portions. During right-eye foveation of the 0° target, the left eye was about 5° of exotropia and about 0° of hypotropia. At the other positions within the central ±10°, it varied from 5° to 20° of exotropia and 3° to 8° of hypotropia. *b*, blinks. The ±0.5° foveal areas are shown by circles; the right eye is solid and the left eye, dashed.