A Review of the Tenotomy Nystagmus Surgery: Origin, Mechanism, and General Efficacy

Z. I. Wang a, b, L. F. Dell'Osso b,c,d

a From the Daroff-Dell'Osso Ocular Motility Laboratory and Biomedical Engineering, Case Western Reserve University and University Hospitals of Cleveland, Cleveland, OH

b From the Daroff-Dell'Osso Ocular Motility Laboratory Louis Stokes, Cleveland

c Department of Veterans Affairs Medical Center and CASE Medical School, Cleveland, OH

d Departments of Neurology and Biomedical Engineering, Case Western Reserve University and University Hospitals of Cleveland, Cleveland, OH

Online Publication Date: 01 September 2007


To link to this article: DOI: 10.1080/01658100701647704

URL: http://dx.doi.org/10.1080/01658100701647704

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.informaworld.com/terms-and-conditions-of-access.pdf
A Review of the Tenotomy Nystagmus Surgery: Origin, Mechanism, and General Efficacy

Z. I. Wang, M.S.
From the Daroff-Dell’Osso Ocular Motility Laboratory and Biomedical Engineering, Case Western Reserve University and University Hospitals of Cleveland; Cleveland, OH

L. F. Dell’Osso, Ph.D.
From the Daroff-Dell’Osso Ocular Motility Laboratory, Louis Stokes Cleveland Department of Veterans Affairs Medical Center and CASE Medical School; and the Departments of Neurology and Biomedical Engineering, Case Western Reserve University and University Hospitals of Cleveland; Cleveland, OH

ABSTRACT
Tenotomy nystagmus surgery neither “weakens” nor “strengthens” the extraocular muscles; it is not strabismus surgery. Tenotomy effectively decreases the gain of the ocular motor plant to small, non-saccadic signals and was hypothesized to be efficacious for other types of nystagmus in addition to infantile nystagmus; it has subsequently been shown to damp various types of acquired nystagmus (pendular and jerk, horizontal and vertical) and reduce their associated oscillopsia. The eXpanded Nystagmus Acuity Function now allows visual acuity improvements to be estimated prior to surgery—something never before possible. More research into proprioceptive tension control should provide non-surgical methods to achieve the therapeutic improvements of tenotomy.

KEYWORDS
tenotomy; infantile nystagmus; acquired nystagmus; nystagmus surgery

THE ORIGIN OF THE TENOTOMY PROCEDURE

The history of the development of the four-muscle tenotomy nystagmus surgery is interesting because of its departure from that of its predecessors. Classically, ophthalmic surgeons developed methods to damp nystagmus based on the clinical characteristics of their patients and the approaches used in strabismus procedures (i.e., “weakening” or “strengthening” extraocular muscles). These procedures usually involved muscle recessions, resections, or their combination to either move both eyes conjugately opposite to a nystagmus “null” or to artificially create an exotropia in a binocular patient who had a convergence “null.” Because the surgical procedures were similar to those used in the correction of strabismus, they were referred to as strabismus surgery even though their purpose was not to correct a misalignment and, in the case of artificial divergence, was designed to produce one.

Tenotomy has very different roots; it was hypothesized based on pre- and post-Kestenbaum surgery eye-movement data analyzed by a non-surgeon (a biomedical engineer) and it does not involve moving the insertions of any muscle (i.e., it is not a strabismus procedure). The tenotomy procedure was the first nystagmus surgery proven effective on an animal model of...
Infantile nystagmus syndrome (INS, fka congenital nystagmus, CN). The concept of tenotomy was anathema to some classically trained ophthalmic surgeons, many of whom were vociferous in their skepticism, claiming it “could not work,” or “did nothing.” Never the less, in an NIH-sponsored, masked-data, clinical trial (the first such trial of a nystagmus surgery), tenotomy successfully improved INS waveforms and increased visual function. In addition to tenotomy’s efficacy in treating INS patients who either had no nulls or a primary-position null, (both populations are not candidates for the “muscle-moving” procedures) it has subsequently been shown to damp acquired nystagmus (both pendular and jerk, horizontal and vertical).

THE MECHANISM OF THE TENOTOMY PROCEDURE

Initial observations of the secondary effects of the Kestenbaum procedure suggested that they were due to the tenotomy and reattachment of the muscles whereas, the shifting of the null was due to their repositioning. If that was so, then it was reasoned that the detachment and reattachment of the muscles left them less responsive to the unchanged nystagmus signal from the brain stem. That is, the gain to these relatively small signals (compared to the maximal signals driving saccades) was reduced. Examination of post-tenotomy saccades verified that saccades were unaffected and the gain changes were limited to small signals. Prior to the demonstrated damping of tenotomy, it had been thought that the extraocular muscle tendons contained no neural substrate that could affect muscle tension; tenotomy’s success suggested otherwise. Subsequent investigations into the anatomy of the enthesial tendons revealed such neural substrate. Thus, the anatomy exists for the hypothesized proprioceptive changes produced by tenotomy. Although proprioceptive tension control does not effect individual eye movements in real time (i.e., there is no stretch reflex), the long-term calibration and control of muscle tension is important for accurate ocular motor control and tenotomy appears to take advantage of altering this control by reducing the resting muscle tension and the plant gain determined by that tension.

THE APPLICABILITY OF THE TENOTOMY PROCEDURE

Infantile Nystagmus Syndrome

In 1998, the hypothesis of four-muscle tenotomy, i.e., detaching the muscles at the insertional end of the extraocular muscle tendons and reattaching them in the same place with absorbable sutures, was officially proposed based on the post-operative results of the Kestenbaum procedure. Depending on the plane of the dominant nystagmus component, the four-muscle tenotomy may be done on the medial and lateral rectus muscles (two per eye, four in total) for damping the horizontal component, or superior and inferior rectus muscles (two per eye, four in total) for the vertical.

The INS patients who underwent the Kestenbaum procedure had pre-operative null regions from 3°–9°; they were extended to 23°–25°. Primary-position visual acuities improved from 20/60–20/100 pre-operatively to 20/25–20/40 post-operatively. The net results of the procedure were: 1) moving the null regions to primary position and 2) damping the nystagmus at both the null and over a broader range of gaze angles. Although the exact mechanisms involved in these secondary effects were not clear at that time, the tenotomy procedure was hypothesized to benefit INS patients who have either a null point at or near primary position, no null, or a non-stationary null (asymmetric (a)periodic alternating nystagmus, APAN). This unexpected, generalized damping effect over a broad range of gaze angles suggested that the amount of surgical eye rotation might not need to be precise; it offered a margin of error in which the Kestenbaum procedure could achieve positive post-operative effects. This also helped to explain the high success rate of Kestenbaum procedure despite the different formulas used by individual surgeons to calculate the amounts of resections and resections they employed to shift the null position.

In 1991, an animal model appeared in an achiasmatic Belgian sheepdog family who had horizontal INS plus see-saw nystagmus (SSN). A two-stage tenotomy procedure was performed on one dog. In Stage 1, all of the horizontal rectus muscles were tenotomized and reattached at their original site. The post-surgical reduction was visibly obvious immediately after the operation. The ocular motility data documented a peak-to-peak amplitude reduction of 67% in the horizontal pendular component of the waveform and 65% in the jerk component. Post-surgical waveforms also had an
increased centralisation (i.e., within the area centralis) time per cycle, which resulted in long intervals of stable fixation. Such fixation periods were not seen in the pre-surgical record over the previous 6 years. These effects persisted for at least 1 year after the surgery. A control procedure was performed on 1 healthy member of the family, with no changes in ocular motility. Stage 2 of this operation (on the SSN component) will be reviewed in the next section.

The success of the animal model was followed by a clinical trial approved by National Eye Institute. Ten adult patients with varied associated sensory deficits as well as INS (including APAN) received the tenotomy surgery. Search-coil eye movement recordings were made before and 1, 6, 24, and 52 weeks after the operation. Masked-data analysis on the fixating eyes showed persistent, significant post-surgical increases in the eXpanded Nystagmus Acuity Function (NAFX) in 9 of the 10 patients (the NAFX is an objective measurement of nystagmus waveform foveation quality, which includes velocity and position thresholds for stable vision). Average foveation time increased in all 9 patients’ fixating eyes. Five of the 10 patients had more than a 5-letter increase, corresponding to at least a line’s increase in Snellen acuity. The NEI-VFQ-25 showed an improvement in vision-specific mental health in 9 patients. These post-surgical effects stabilized within 6 weeks and were shown to persist for at least 52 (see Figure 1 for 4 patients’ NAFX increases over the 52 weeks’ follow-up period). There were no adverse events. The one patient who had no increase in the NAFX had a good pre-surgical acuity, which indicated an upper bound beyond which no waveform improvement should be expected. This was supported by later studies.

In the second part of the NEI clinical trial, the same procedure and analysis protocol as in the first part were performed on 5 children with INS (including APAN) and sensory deficits. At a year after tenotomy and under binocular viewing conditions, two of the three patients whose NAFX could be measured had persistent and significant improvement, with an increase in average foveation time per cycle. Measured visual acuity improved in 4 children; the remaining one had retinal dystrophy. There were no adverse effects.

The animal model and the two-part NEI trial demonstrated the effectiveness of four-muscle tenotomy. However, the clinical standards for this procedure were not yet determined, i.e., when a patient should/should not have this procedure, how much post-surgical improvement the patient should expect to receive. In 2006, the effects of four-muscle tenotomy on foveation quality in both primary position and at lateral gaze angles were reported. Eye movements of 9 patients with INS were recorded using infrared reflection or high-speed digital video techniques. The NAFX was measured in primary position and at various gaze angles and the longest foveation domains (LFD) were measured from fitted NAFX curves. Three patients in this study showed moderate NAFX improvement (13.9–32.6%) in primary position, 5 showed large improvement (39.9–162.4%), and 1 showed no NAFX change (due to his high pre-tenotomy NAFX). The seven patients who had narrow, high-NAFX, gaze-angle regions pre-tenotomy showed broadening of these regions post-tenotomy. All patients had reductions in nystagmus amplitudes ranging from 14.6–37%. Foveation-period duration increases for all 9 patients ranged from 11.2–200%. The patient in Figure 2 had an NAFX increase of 39.9% (from 0.371 to 0.519) in primary position, and a much-broadened area of improved visual function post-surgically.

This study showed the percentage increases in both the NAFX and LFD decreased as their pre-tenotomy values increased respectively. Thus, the worse the presurgical NAFX is, the more percentage improvement the patient could expect to receive, both in terms of visual acuity elevation and high-acuity region broadening. Only patients with both a high primary-position NAFX (>0.6) and a large LFD (>25°) would not be expected to receive either NAFX or LFD improvement from tenotomy; all others remain candidates. The NAFX analysis, for the first time, enabled the prediction

FIGURE 1 Plots of NAFX data for 5 INS patients over the course of the NIH clinical trial. Avg = average of patients in each graph, Log = logarithmic curve fits of the NAFX vs. Post-Op Time data, NAFX = eXpanded Nystagmus Acuity Function.
FIGURE 2. NAFX improvement of one INS patient both in primary position and at lateral gaze angles. A much broadened postsurgical curve demonstrates elevated visual function over a larger visual domain.

See-Saw Nystagmus

The Stage 1 surgery performed on the sheepdog from the achiasmatic family only damped the horizontal component of the congenital nystagmus; the SSN component was unchanged. Stage 2 was performed 4 months after Stage 1; all four vertical rectus and all four oblique muscles were tenotomized and reattached at their original insertions. Reduction in the vertical and torsional nystagmus components was documented by post-surgical videotape, and eye movement recordings showed the absence of the vertical component over a 25-second fixation interval. The SSN was barely perceptible in primary position on visual inspection. These effects remained for at least 8 months when postmortem anatomic studies confirmed that the dog was an achiasmatic mutant.9 This 2-stage tenotomy procedure of all extraocular muscles provided a possible therapy for those rare individuals with INS and SSN that accompany human achiasma.31,38 Subsequently, this two-stage, all-muscle procedure has been successfully applied to two human achiasma patients to damp both their INS and SSN (R.W. Hertle, personal communication).

Horizontal and Vertical Acquired Pendular Nystagmus

A horizontal tenotomy was performed on a 50 year-old man with MS, in combination with a horizontal strabismus procedure (bilateral, lateral rectus muscle resections) to treat an existing exotropia.13 The patient had intractable oscillopsia that had been slowly progressing over the prior 8–9 years due to his multiplanar acquired pendular nystagmus (APN). A two-stage surgical approach was planned similar to that employed in treating the achiasmic Belgian sheepdog.9,39 Based on these experiences and those of others in patients (especially children), no anterior segment ischemia problems will occur if a second, vertical stage was done after circulation in the operated region has been re-established, although risks might be involved.40

Stage 1 was a four-muscle tenotomy of the horizontal rectus muscles combined with resections of both lateral rectus muscles (to correct his exotropia). Following the combined procedure, APN decreased by ∼ 50% and NAFX values in primary position increased by 34%. Measured Snellen visual acuity increased 100% from 0.125 to 0.25. Voluntary saccades and abducting saccadic pulses of INO were unaffected. The exotropia was reduced to less than 2°. In addition to damping the horizontal component of the APN, tenotomy also damped the vertical and torsional components to a lesser degree. The patient reported reduced oscillopsia after the Stage 1 operation.

Stage 1 was to be followed, in 4–6 months, by a Stage 2 procedure (vertical rectus-muscle tenotomies to damp the vertical component) if vertical oscillopsia was still interfering with the patient’s visual function. However, Memantine became available and was prescribed.41,42 The dosage increased over six weeks to a daily dose of 40 mg (twice the dose used for Alzheimer’s disease) without complication. After 6 weeks, the APN was damped an additional 69% and NAFX increased by an additional 9%. Visual acuity further increased to 0.4 (60%). Other drugs’ effects on damping nystagmus have also been investigated.43,44

In this case of multiplanar APN, the cumulative effects of tenotomy + memantine were: APN reduced by 82%; NAFX increased by 46%; acuity increased by 220%; and oscillopsia reduced by 75%. This dual-mode therapy, with the tenotomy damping the slow-phase eye movements peripherally and Memantine reducing the central nystagmus signal,
optimized the improvement of visual acuity and reduction of oscillopsia in this APN patient. No substantial post-operative changes in saccadic dynamics, smooth-pursuit, optokinetic, or vestibular eye movements were observed.

**Horizontal, Unicocular Acquired Pendular Nystagmus**

A two-muscle tenotomy was performed on a 39 year-old female with MS, who experienced reduced vision and intractable oscillopsia in her right eye. Her vision was 20/100 in the affected right eye and 20/20 in the normal left eye. A clinically evident horizontal pendular nystagmus was documented by videotape: the nystagmus was also only in her right eye. Six weeks after surgery, her right-eye nystagmus was substantially reduced (confirmed by video tape) and her visual acuity was 20/70 OD. She had no complications from the tenotomy. She also reported a marked reduction in the oscillopsia.
Acquired Downbeat Nystagmus

A vertical (Anderson + strabismus + tenotomy) procedure was performed on a 44 year-old man who had predominantly vertical nystagmus (downbeat nystagmus) and intractable oscillopsia for 14 years (the oscillopsia was resistant to drug therapy).\cite{15} The patient had a marked chin-down position and had right-eye hypertropia of 7° and esotropia of 3–5°. Superior rectus muscles were recessed asymmetrically to simultaneously rotate both eyes downward and reduce the right hypertropia; both inferior rectus muscles were tenotomized to complete the 4-muscle tenotomy.

This combined procedure elevated the patient’s primary-position NAFX values by 17% and visual acuity increased 25\% from 20/25 to 20/20+1. The reduction of vertical-component amplitude was \sim 46\%, which agreed with his post-surgical observations that the oscillopsia was reduced by half. Vertical NAFX values increased across the −10° to +5° vertical visual range, suggesting improved visual function in this region. His NAFX peak, which used to be at 10° up, was moved to primary position (eliminating the chin-down position). His INS foveation improvement and amplitude reduction are demonstrated in Figure 4. The time of the cycle spent in the dashed box (the foveation window) contributes to clear and stable vision; the much increased time in the foveation window post-surgically indicates elevated visual function. The right hypertropia was reduced to 3–4°. Figure 5 shows the reduction of strabismus on...
monocular viewing; also note that the amplitude of the downbeat nystagmus was greatly reduced. Combined strabismus and nystagmus surgeries provided individualized treatment for the patient’s visual function. As a simple, low-risk, one-time surgical therapy with no long-term side effects or costs, tenotomy should be considered for treatment plans of acquired nystagmus.

DISCUSSION

The tenotomy procedure represents a new direction in nystagmus surgery. It is the antithesis of strabismus procedures that rely on movement of one or more muscles to achieve their desired repositioning of the eyes; tenotomy is an integral part of recessions or resections. It is the purest form of nystagmus surgery, relying only on reducing the plant gain to unchanged nystagmus signals without any muscle repositioning. As such, tenotomy is applicable to a population of individuals with INS who exhibit no gaze- or vergence-position improvements in waveform; prior to tenotomy, these patients would not have received any surgical therapy. In addition, because of its different mode of action, tenotomy works synergistically with muscle-moving procedures and should be combined with them to maximize nystagmus damping, waveform improvement, and potential acuity improvement (i.e., tenotomize the remaining muscles in the plane of action of the nystagmus along with the recessions and resections).

In conjunction with the NAFX method of waveform analysis, the visual acuity improvements of tenotomy can now be predicted a priori. That is, based on the pre-tenotomy NAFX value and the measured visual acuity, we can now estimate the percentage improvement in NAFX, and therefore, measured acuity, as a result of tenotomy. Figure 6 demonstrates the procedure used to estimate the post-tenotomy measured visual acuity from the pre-tenotomy NAFX and measured visual acuity values. The ability to inform patients how much their nystagmus may improve is unique in the history of nystagmus surgery and could not be done without the advent of the NAFX measure of waveform quality.

The NAFX at different gaze angles has provided a way to measure another visual-function benefit of tenotomy, the broadening of the range of gaze angles with higher quality waveforms and therefore, better acuity. The LFD measure graphically demonstrates improvements not evident from measures of primary-position visual acuity. As described above for the peak NAFX values, the LFD improvement can also be estimated.

FIGURE 6 Procedure for using pre-tenotomy NAFX and visual acuity measurements to estimate post-tenotomy visual acuity. First (top left), choose the proper age-matched NAFX vs. acuity line. Second (top right), plot the pre-tenotomy NAFX and potential and measured visual acuity points on the graph and draft a dashed line with the same slope as the solid line through the NAFX and measured acuity point. Third (bottom left), plot the estimated post-tenotomy point on the NAFX improvement curve and read off the percentage increase expected in the NAFX. Fourth (bottom right), calculate the expected post-tenotomy NAFX (e.g., 0.3 + 60% (0.3) = 0.48) and plot it on the dashed line. The estimated post-tenotomy measured visual acuity can then be read from the acuity axis of the graph.
a priori providing another benefit that can be discussed with the patient.

The demonstration that tenotomy affects only small signals to the ocular motor plant requires a reevaluation of commonly used linear models of the plant; they simply cannot simulate the effects of tenotomy. Despite the non-linear muscle force relationships, the plant may be approximated by a linear function for small signals because of the push-pull nature of the antagonist pairs of muscles. However, during saccades, the agonist muscle is fully on while the antagonist is turned off; thus, there is no push-pull action and no linearization of the agonist’s non-linear action. More accurate plant models that contain this dual-mode operation are needed.17

Now that the tenotomy procedure has demonstrated the power of using proprioceptive muscle tension control to damp nystagmus, other methods should be explored to alter the firing rate of the proprioceptive sensors in the extraocular muscle tendons. The approaches to altering the functions of the distal tendons might include: mechanical, merely suturing or otherwise mechanically changing them without actual tenotomy; cryogenic, heat or cold application; or pharmaceutical, microinjection. Thus, mechanical, cryogenic or pharmaceutical tenotomy might preclude the need for surgical tenotomy. Clearly more research into the proprioceptive tension control system and methods to alter it are needed to both better understand its function and use that knowledge therapeutically.

REFERENCES


