A New Surgery for Congenital Nystagmus: Effects of Tenotomy on an Achiasmatic Canine and the Role of Extraocular Proprioception

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Purpose: Human eye-movement recordings have documented that surgical treatment of congenital nystagmus (CN) also produces a broadening of the null zone and changes in foveation that allow increased acuity. We used the achiasmatic Belgian sheepdog, a spontaneously occurring animal model of human CN and see-saw nystagmus (SSN), to test the hypothesis that changes induced by surgical interruption of the extraocular muscle afference without a change in muscle-length tension could damp both oscillations. ***Methods:*** An achiasmatic dog with CN and SSN underwent videotaping and infrared oculography in a sling apparatus and head restraints before and after all extraocular muscles (stage 1: 4 horizontal rectus muscles and stage 2 [4 months later]: 4 vertical rectus muscles and 4 oblique muscles) were surgically tenotomized and immediately reattached at their original insertions. ***Results:*** The dog had immediate and persistent visible, behavioral, and oculographic changes after each stage of this new procedure. These included damped CN and SSN, increased ability to maintain fixation, and increased periods of maintaining the target image on the area centralis over a broad range of gaze angles. ***Conclusions:*** Severing and reattaching the tendons of the extraocular muscles affect some as-yet-unknown combination of central nervous system processes producing the above results. This new procedure may prove effective in patients with CN with either no null, a null at primary position, or a time-varying null (due to asymmetric, (a)periodic, alternating nystagmus). We infer from our results in an achiasmatic dog that tenotomy is the probable cause of the damping documented in human CN after Anderson-Kestenbaum procedures and should also damp CN and SSN in achiasma in humans. It may also prove useful in acquired nystagmus to reduce oscillopsia. The success of tenotomy in damping nystagmus in this animal suggests that the proprioceptive feedback loop has a more important role in ocular-motor control than has been appreciated. Finally, we propose a modified bimedial recession procedure, on the basis of the damping effects of tenotomy. (J AAPOS 1999;3:166-82)

In 1979 the first oculographic analysis of the effects of extraocular muscle surgery in patients with congenital nystagmus (CN) appeared.[1] It was revealed and subsequently confirmed that the Anderson-Kestenbaum resection and recession procedure produced several beneficial *secondary effects* on the CN, in addition to the expected shifting of the null region to the straight-ahead position. This was a result of objectively measuring both the presurgical and postsurgical characteristics of the CN waveforms.[2-6] The breadth of the null region (ie, the range of gaze angles with damped CN) was markedly increased, and the off-null CN was also reduced in amplitude. The effects persisted during the 5 years of follow-up recordings.[3] On the basis of the data from the above studies, Figure 1 illustrates the predicted postsurgical variation with gaze angle of typical human CN compared with the actual results measured in the above studies. The presurgical variation is included as a baseline. Figure 1 is a composite of our findings.[1-3] The observed data suggest that the resulting lower slow-phase velocities and accelerations allowed increased foveation time per cycle and higher acuity in these patients.[7,8] In addition to this oculographically documented evidence, there are unpublished anecdotal reports of spontaneous damping of CN in patients

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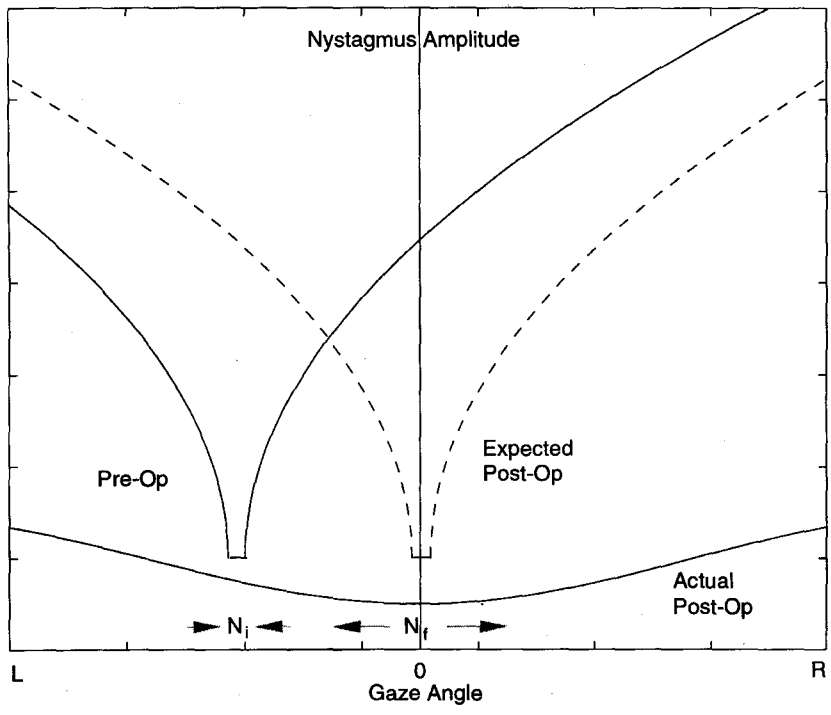

FIG 1. Illustration (based on recorded patient data) of expected null-shifting and actual, measured null-broadening and off-null damping effects of Anderson-Kestenbaum resection and recession procedure. *R*, Right gaze; *L*, left gaze; N_i, narrow initial null; N_f, broadened final null.

with strabismus after surgery specifically intended to correct only the deviation. There are also reports combining *nystagmus* and *strabismus* surgery.[9-11] The aim of strabismus surgery is to change the steady-state positions of the eyes to achieve alignment, whereas nystagmus surgery aims to move both eyes (conjugately or by means of induced divergence) to damp an ongoing oscillation, such as CN.

These unexpected and fortuitous secondary effects on CN provide a margin of error within which surgeons have been operating (ie, the calculation of the amount of eye rotation need not be precise) and help to explain the high success rate of the Anderson-Kestenbaum procedure, despite intersurgeon variability in the actual muscle relocations. More important, the secondary effects provide a broad range of gaze angles within which the patient could benefit from improved visual acuity without the need to align the eyes at a precise null angle, as it had been the case presurgically. The overall reduction in effort ("fixation attempt") further serves to damp the CN.[7]

The CN null region could be broadened, and the CN could be damped throughout the useful range of gaze angles by simply changing the level of afferent signals from the extraocular muscles. There might be no need to change the length-tension of the muscles by either recessing or resecting them to achieve these effects on CN. These long-lasting, beneficial, secondary effects in human patients, discovered after the Anderson-Kestenbaum procedure, led to the hypothesis that the broadening and damping could be achieved by simply tenotomizing the 4 horizontal rectus muscles and reattaching them at their original insertions. In the years since these observations, an animal model was sought on which the hypothetical procedure could be tried. In 1991 such a model appeared in achiasmatic members of a Belgian sheepdog family.[12] Studies of the eye movements of the affected dogs revealed horizontal (and sometimes vertical) CN plus a congenital see-saw nystagmus (SSN).[13,14] The hypothetical surgery could now be tested.[15] In this report we present the effects on CN of applying this surgical technique to the horizontal rectus muscles of both eyes in a single canine (stage 1) and also on SSN, after the vertical rectus muscles and both oblique muscles of both eyes were tenotomized (stage 2). The 2 stages were separated by 4 months to reduce the possibility of interruption of blood supply to the eyes.

We believe that the success of this procedure in its first application in the only available animal model of CN provides strong support for the above hypothesis that had been derived from recorded effects on human patients. The implications of and the questions raised by the effects of tenotomy on nystagmus may be found in the "Discussion" section.

METHODS

Recording

All applicable National Institutes of Health guidelines and regulations about the care and handling of the dogs are followed at the kennel and were adhered to in this study.

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Eye movements were recorded using infrared reflection systems and a sling apparatus described previously.[14] The dogs were encouraged to view blinking toys, light-emitting diodes, and noise-making toys at known gaze angles. Horizontal, vertical, or a combination of horizontal and vertical eye movements were recorded from both eyes simultaneously under binocular or monocular viewing conditions. Because of the cooperative nature of these sheepdogs, we were able to obtain eye-movement records from both dogs used in this study (MH1, who did not have nystagmus, and M5, who did) without the use of sedatives. Horizontal and vertical head motions were induced to test the conjugacy of the responses. Additionally, we were able to obtain good eye-movement data with the canine sitting on the floor in a more natural state instead of suspended in a sling. The data were equivalent, although not as well calibrated.

Analysis

Graphic presentation, data analysis (and filtering, if required), and statistical computation of means and SDs were performed using either the ASYST (Keithley, Taunton, Mass) or MATLAB (MathWorks, Natick, Mass) software for scientific computing. Eye velocities were obtained by digital (2-point, central-difference algorithm) differentiation of the position signals. Further details on ASYST may be found elsewhere.[16]

We used *phase plane* analysis to study the simultaneous relationship between the position and velocity of the eye and, thus, of retinal image. A phase plane is a plot of 2 vector quantities: eye position on the x-axis versus eye velocity on the y-axis for either horizontal, vertical, or torsional motion. For horizontal motion, the upper right quadrant indicates rightward motion with the eye positioned to the right of the target (the eye moving away from the target). The upper left quadrant indicates rightward motion with the eye to the left of the target (the eye moving toward the target). For vertical phase planes, substitute upward for rightward and downward for leftward in the above explanation. All phase planes are plotted on "foveal" axes: the 0,0 point is centered on the stationary target, regardless of the absolute position of the target. This allows the phase plane to be interpreted as a retinal image position/motion plot and to relate the resulting trajectories to visual acuity, using the superimposed rectangular foveal window. The trajectories seen on phase plane plots are always in a *clockwise* direction, if the conventions of rightward direction and positive velocity are adhered to. Saccadic movements appear as high-velocity clockwise loops. Rightward saccades would show positive velocities and directions, whereas leftward saccades would be negative. The trajectories of respective slow movements would also appear clockwise with lower velocities. During fixation, phase planes enable immediate identification of those periods when the target image is both stable and on the fovea. During smooth pursuit or vestibulo-ocular reflex (VOR) analysis, phase planes of retinal image motion or gaze identify those periods of stability indicative of good pursuit or VOR, respectively. Further details on the use of phase planes may be found elsewhere.[8,17,18]

Figures

All figures containing eye movements versus time contain dashed lines indicating the extent of the area centralis in the appropriate place and plane (ie, horizontal or vertical). Relative comparisons can be made using the indicated extents of the area centralis, in addition to using the indicated scales to compare actual presurgical and postsurgical nystagmus magnitudes. Similarly, the phase planes contain dashed rectangular boxes indicating the boundaries of *centralisation* and, thus, good acuity, defined by the extent of the area centralis (x-axis) and retinal slip velocities of ± 4 degrees per second (y-axis).[8] Dogs have an elliptic area centralis, which corresponds to the human fovea, and it extends 6 degrees horizontally and 3 degrees vertically (ie, ± 3 by ± 1.5 degrees). The time the target image spends within this *centralisation window* is referred to as a *centralisation period* (*foveation* in humans).[13] Exceeding *either* the position or velocity boundary of the window degrades visual acuity. These additions allow the interpretation of both types of diagrams as indications of retinal image motion on the "stationary" retina, specifically across the area centralis on time plots and within the high-acuity centralisation window on phase planes.

Surgical Procedure (Stage 1)

Tenotomy of the Horizontal Rectus Muscles and Reattachment at Their Original Insertions. After the induction of general endotracheal anesthesia and the placement of intravenous access and monitors, both eyes were prepped and draped in sterile fashion for an ophthalmic surgery. The lids were retracted, and a 4-0 silk traction suture was placed through the nictitating membrane. Another 4-0 silk suture was placed through the episcleral tissue at the limbus at the 6-o'clock and 12-o'clock positions after the identification of the tendons of the medial and lateral rectus muscles through the conjunctiva. A conjunctival peritomy was made from the 2-o'clock to the 4-o'clock position at the limbus for access to the rectus muscle (medial rectus muscle OD and lateral rectus muscle OS). The tendon of the rectus muscle was isolated. The capsule, intermuscular membranes, and fascial attachments were dissected free for 5 to 7 mm posteriorly to the attachment of the tendon to the globe. A double-armed 6-0 Vicryl suture with an s-29 (Ethicon, Inc, Somerville, NJ) needle was placed 1.0 mm posteriorly to the insertion of the tendon of the rectus muscle in a whiplock fashion. The muscle was removed from the globe, and its tendon was reattached at the original insertion site in a double-crossed–swords fashion. The conjunctiva was then closed up to the limbus with interrupted 6-0 Vicryl suture. The eye was rotated in the opposite direction, and a conjunctival peritomy was made from the 8-o'clock to 10-o'clock position at the limbus for access to the antagonist rectus

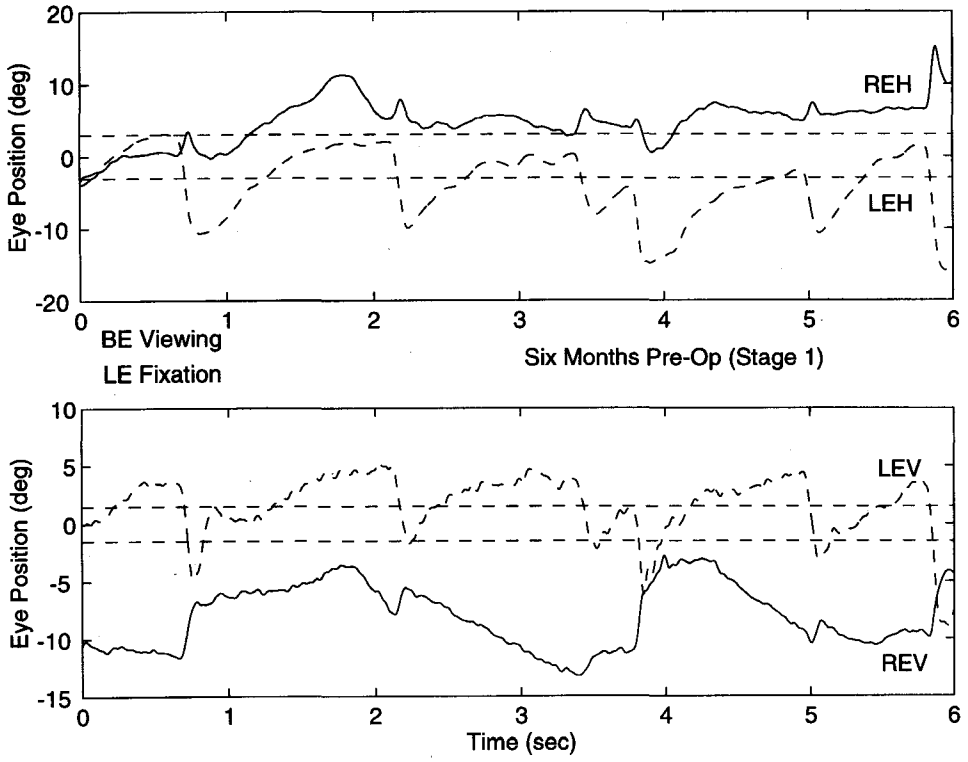

FIG 2. Horizontal CN and vertical SSN of M5 while fixating in primary position before stage 1 (horizontal rectus muscle) tenotomy. In this and following figures, dashed lines in time plots indicate the extent of horizontal (± 3 degrees) or vertical (± 1.5 degrees) area centralis. Upward (+) deflections indicate rightward (or upward) eye rotations. Viewing and fixation conditions are indicated on each figure. *BE,* both eyes; *H,* horizontal; *LE,* left eye (dashed tracing); *RE,* right eye (solid tracing); *V,* vertical (eg, REH, right eye horizontal data).

muscle (lateral rectus muscle OD, and medial rectus muscle OS). The tendon of the antagonist muscle was isolated, removed, and reattached as described above.

Surgical Procedure (Stage 2: 4 Months Later)

Tenotomy of the Vertical Rectus and Oblique Muscles and Reattachment at Their Original Insertions. We followed the same surgical procedures as in stage 1. However, the tendon complex of the rectus and oblique muscles is connected in the dog near the limbus and could be isolated as 1 unit.

After both the stage-1 and stage-2 procedures, each eye received topical antibiotic-steroid ointment. After each procedure, both the healthy (MH1) and achiasmatic (M5) animals were extubated and had the antibiotic-steroid ointment placed in both eyes twice a day for 5 days. There were no intraoperative or postoperative complications.

RESULTS

Presurgical (Stage 1) Ocular Motility

Before surgery, we had videotaped the eye movements of M5 and recorded his horizontal and vertical eye movements on numerous occasions over a period of 6 years. In both the videotape and on inspection, M5 had visibly evident horizontal CN and cyclovertical SSN. In both horizontal and vertical CN, the oscillations of the 2 eyes were phase locked. In contrast, the vertical components of SSN consist of disconjugate eye movements, whereas the torsional components are conjugate. The resulting motion is a rising and intorting eye coupled with a falling and extorting eye. Then, the motion reverses. In Figure 2 the mixture of both the horizontal and vertical CN and the vertical SSN of M5 can be seen; note the large scale differences between Figure 2 and the equivalent postsurgical figures (described below). From the presurgical recordings of M5 (made between 1992 and 1997), we identified both horizontal pendular and jerk CN with respective average frequencies of 2.9 and 2.8 Hz and peak-to-peak amplitude ranges of 1 to 12 degrees and 1 to 15 degrees.[13,14] Centralisation periods were usually less than 50 ms. The pendular and jerk SSN had average frequencies of 1 to 7 Hz and 0.7 to 3.5 Hz and peak-to-peak amplitudes of 0.5 to 8 degrees and 1.5 to 15 degrees, respectively. Of particular importance was the inability of M5 to maintain fixation on a target for more than 1 to 2 seconds, except on rare occasions. Presurgical phase planes were so irregular, because of both the high amplitudes of the CN and the lack of appreciable centralisation, that they are not shown.

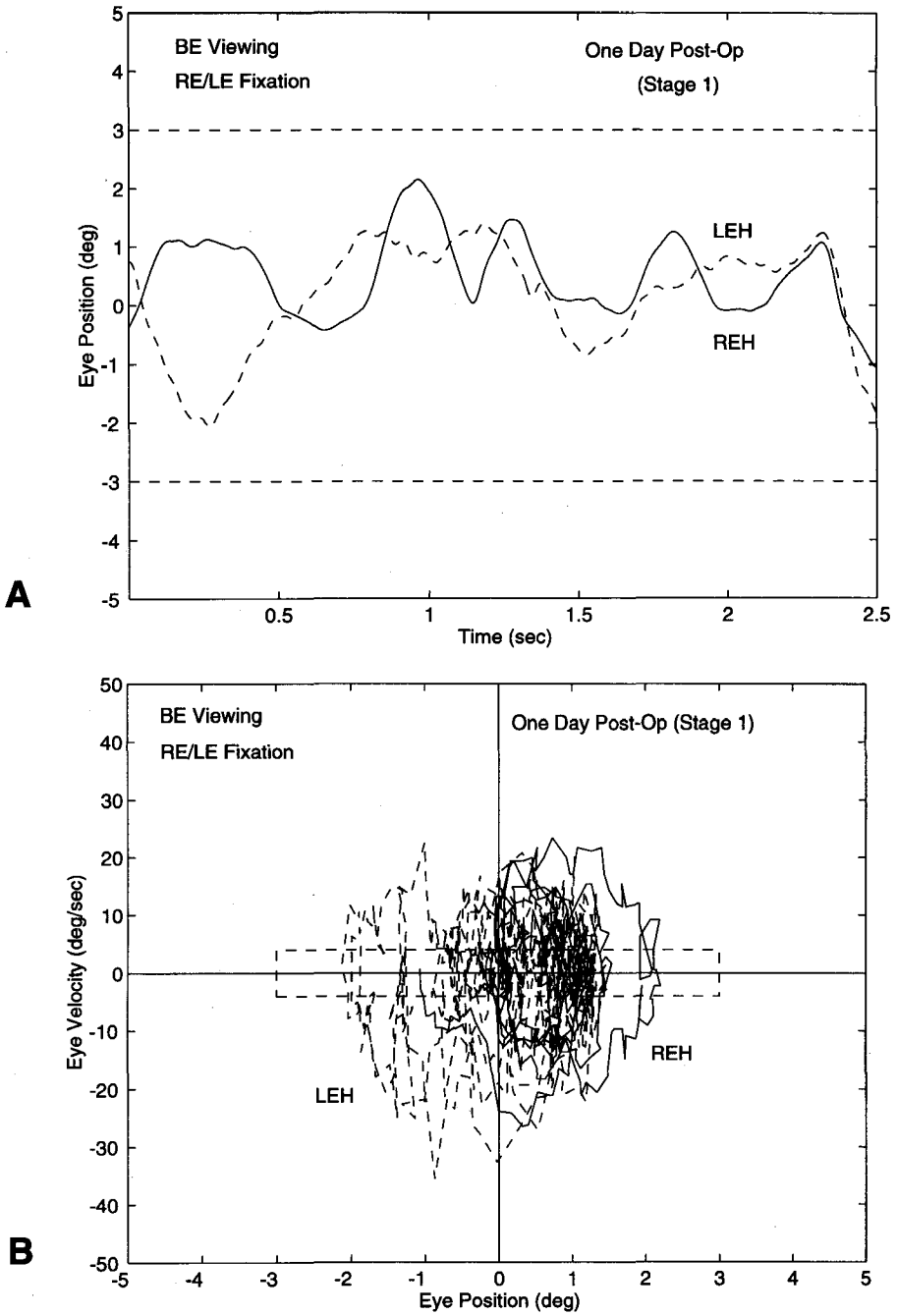

FIG 3. Horizontal CN of M5 while fixating in primary position on postsurgical (stage 1) day 1. **A,** 2.5 seconds of fixation with low-frequency and amplitude CN in both eyes and periods of extended centralisation (ie, flattened areas). **B,** Phase plane showing intervals within centralisation window at both right and left peaks of CN. In this and other figures, rectangular windows in phase planes indicate position (area centralis) and velocity (± 4 degrees/s) limits corresponding to good visual acuity. All phase planes are centered on area centralis, regardless of target position. In horizontal or vertical phase planes, right-eye trajectories are *solid* and left-eye trajectories are *dashed.* In phase planes showing both planes, horizontal trajectories are *solid* and vertical trajectories are *dashed.*

Surgery (Stage 1)

A preliminary control procedure was performed on 1 member of the family (MH1) who appeared to be healthy, with neither nystagmus nor any other ocular motor abnormalities, to familiarize ourselves with the specific anatomy of the extraocular muscles in the Belgian sheepdog. No changes in ocular motility were noted as a result of this procedure. After performing tenotomies and reattachments at their original insertions of all 4 horizontal rectus muscles on MH1 and examining the vertical rectus and

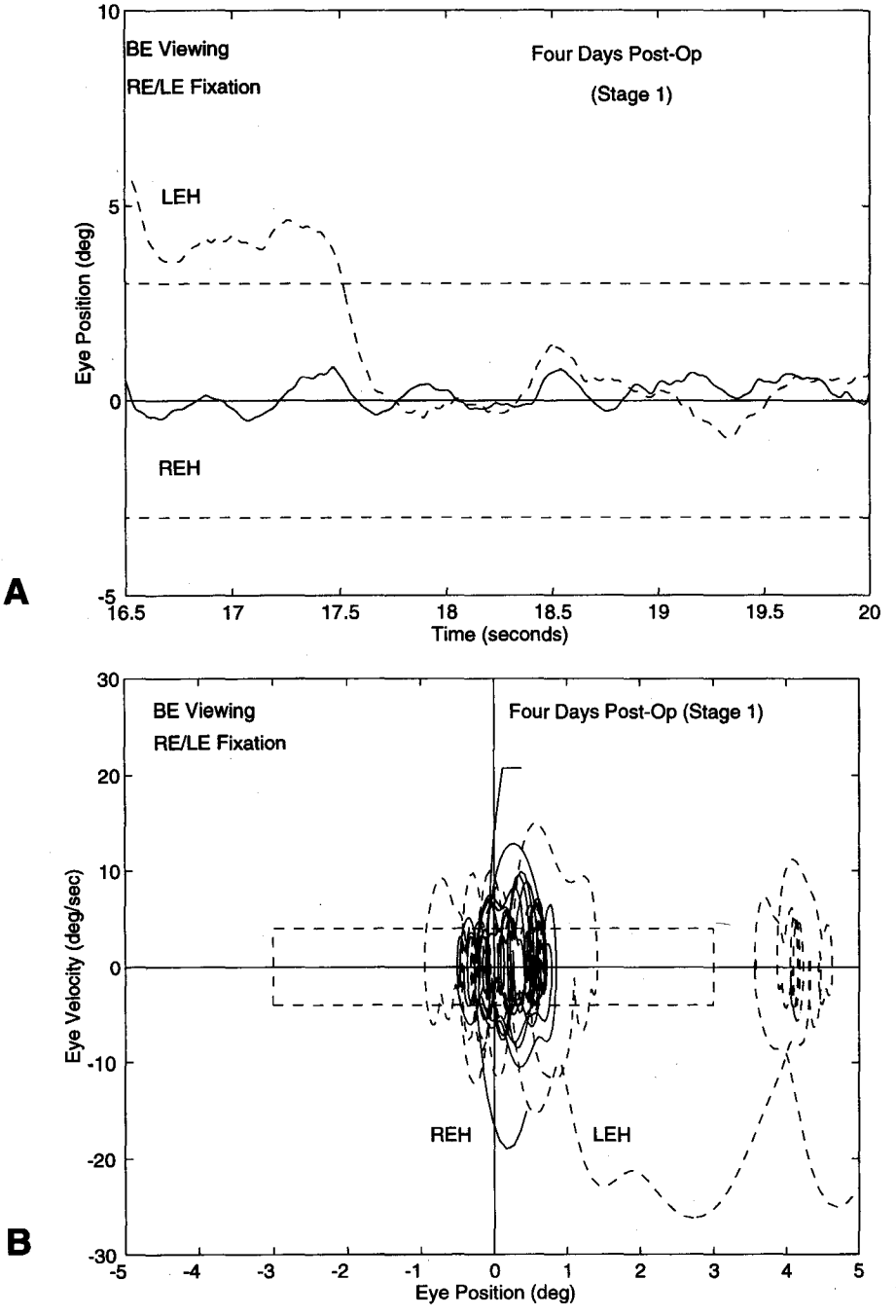

FIG 4. Horizontal CN of M5 while fixating in primary position on postsurgical (stage 1) day 4. **A,** 3.5-second interval of low-frequency and amplitude CN in both eyes and periods of extended centralisation. Disconjugacies are due to the strabismus in this canine. **B,** Phase plane showing intervals within the centralisation window at both peaks of CN.

oblique muscles, we performed the procedures described in the "Methods" section on M5, an achiasmatic mutant with CN and SSN.

Postsurgical (Stage 1) Ocular Motility

The reduction in M5's horizontal nystagmus was striking and visibly obvious on postsurgical day 1 and persisted throughout the initial 4-day recording interval. We recorded and videotaped M5 on postsurgical days 1 though 4 (stage 1). Figure 3, *A* shows the horizontal components of M5's CN on postsurgical day 1. The low-frequency, low-amplitude CN of both eyes remained within the horizontal extent of the area centralis for this 2.5-second interval. The corresponding phase plane demonstrates well-developed (ie, within the area centralis window on a cycle-to-cycle basis) centralisation occurring at *both* extremes of each CN cycle (ie, 2 centralisation periods per

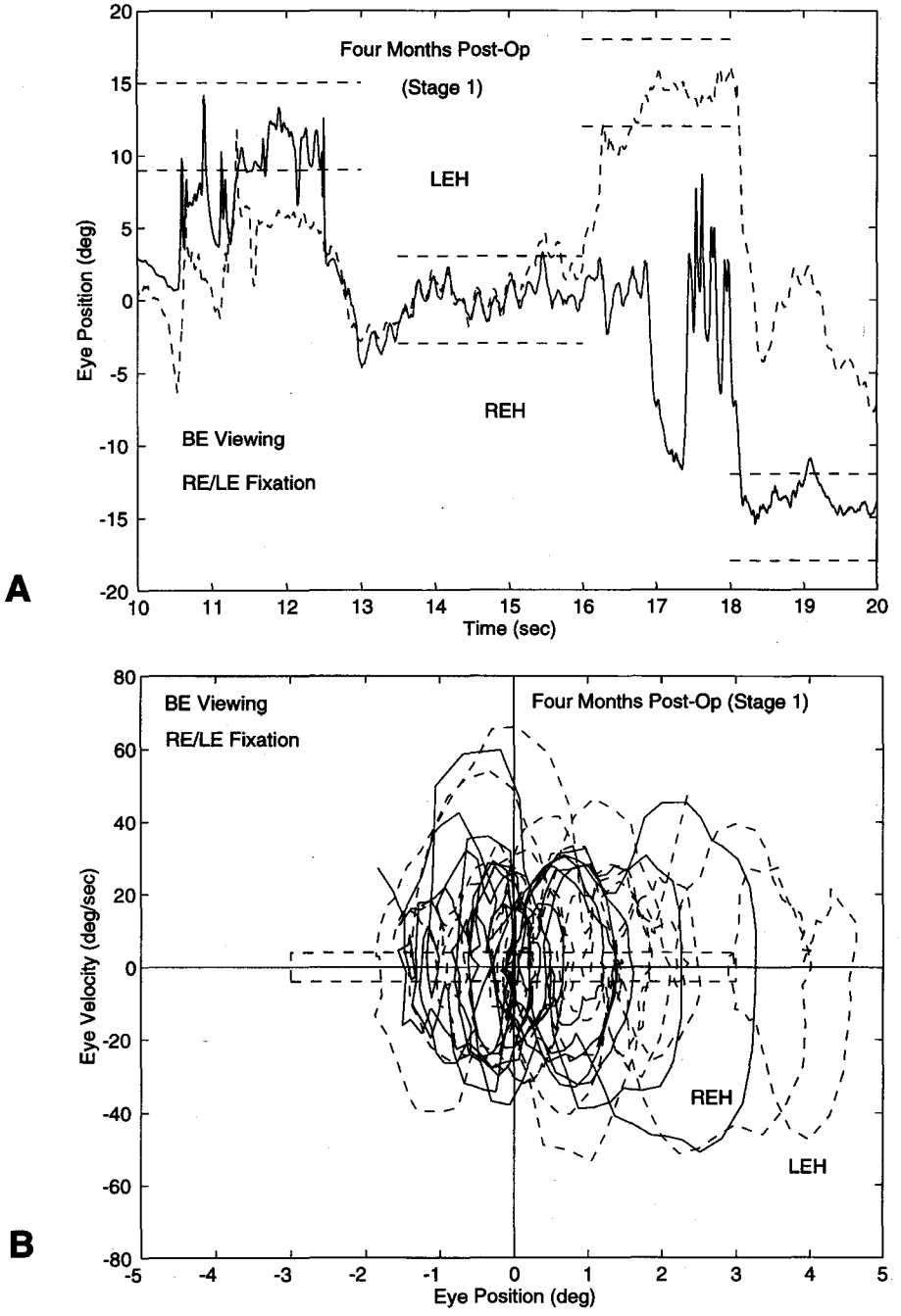

FIG 5. Horizontal CN of M5 4 months postsurgical (stage 1) and 1 day before stage 2 (vertical rectus and oblique muscles) tenotomy. **A,** 10-second record showing low-amplitude CN of the fixating eye in lateral gaze (± 15 degrees) and of both eyes at 0 degrees. M5 could fixate targets in both directions with either eye. **B,** Phase plane of primary-position segment (13-16 seconds) showing continued ability to use both peaks of CN cycle for centralisation.

CN cycle, one at each peak) (Figure 3, *B*). In Figure 4, *A* (from data taken on postsurgical day 4), a 4-second interval of steady fixation is shown. The right eye and, for the final 2.5 seconds, both eyes remained well within the horizontal extent of the area centralis. The phase plane of Figure 4, *B* reveals a tight fixation picture with 2 centralisation periods per CN cycle. These, and other (postsurgical) maintained fixation intervals (up to 60 seconds, see below) represented a dramatic departure from presurgical eye-movement recordings. The ocular motility data from M5 documented a large reduction in the horizontal CN. The pendular CN frequency averaged 2.5 Hz, and peak-to-peak amplitude averaged 1.8 degrees—a 67% reduction in CN amplitude. The jerk CN frequency averaged 2 Hz, and peak-to-peak amplitude averaged 2 degrees—a 65% reduction in CN amplitude. As Figure 3, *A* shows, the

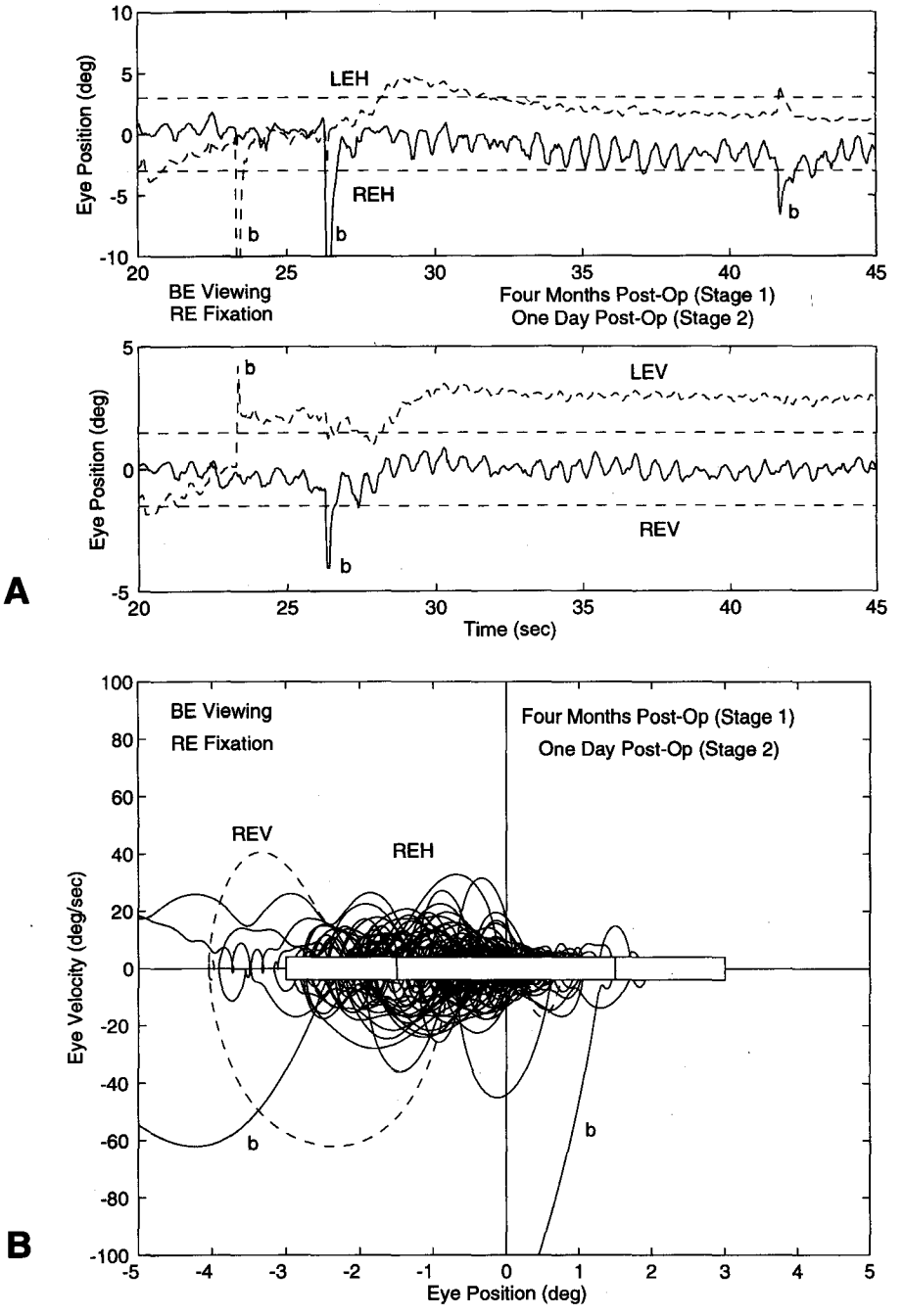

FIG 6. Horizontal and vertical CN of M5 while fixating in primary position 4 months postsurgical (stage 1) and 1 day postsurgical (stage 2). **A,** 25-second interval of steady, right-eye fixation in both planes with low-amplitude CN and no SSN. Both the ± 3-degree horizontal and ± 1.5-degree vertical areas centralis are shown. **B,** Phase plane of the fixating right eye in both planes showing well-developed centralisation. Data within both windows were deleted for clarity. In this and other figures, *b,* Blink.

waveforms also contained increased centralisation times of 200 to 400 ms per cycle. The SSN was unchanged from its presurgical levels.

Behaviorally, M5 appeared less tentative and more aware and interested in looking at us. He previously only glanced at us for short periods of time; now he looked directly at us for longer intervals. The horizontal component of his CN that had previously masked the SSN was now barely perceptible, and instead, the SSN became more visibly evident.

Presurgical (Stage 2) Ocular Motility

At 4 months postsurgery (stage 1) and 1 day presurgery (stage 2), we again videotaped and recorded the eye movements of M5. Figure 5, *A* documents persistence of the initial reductions in horizontal CN, recorded over the initial 4-

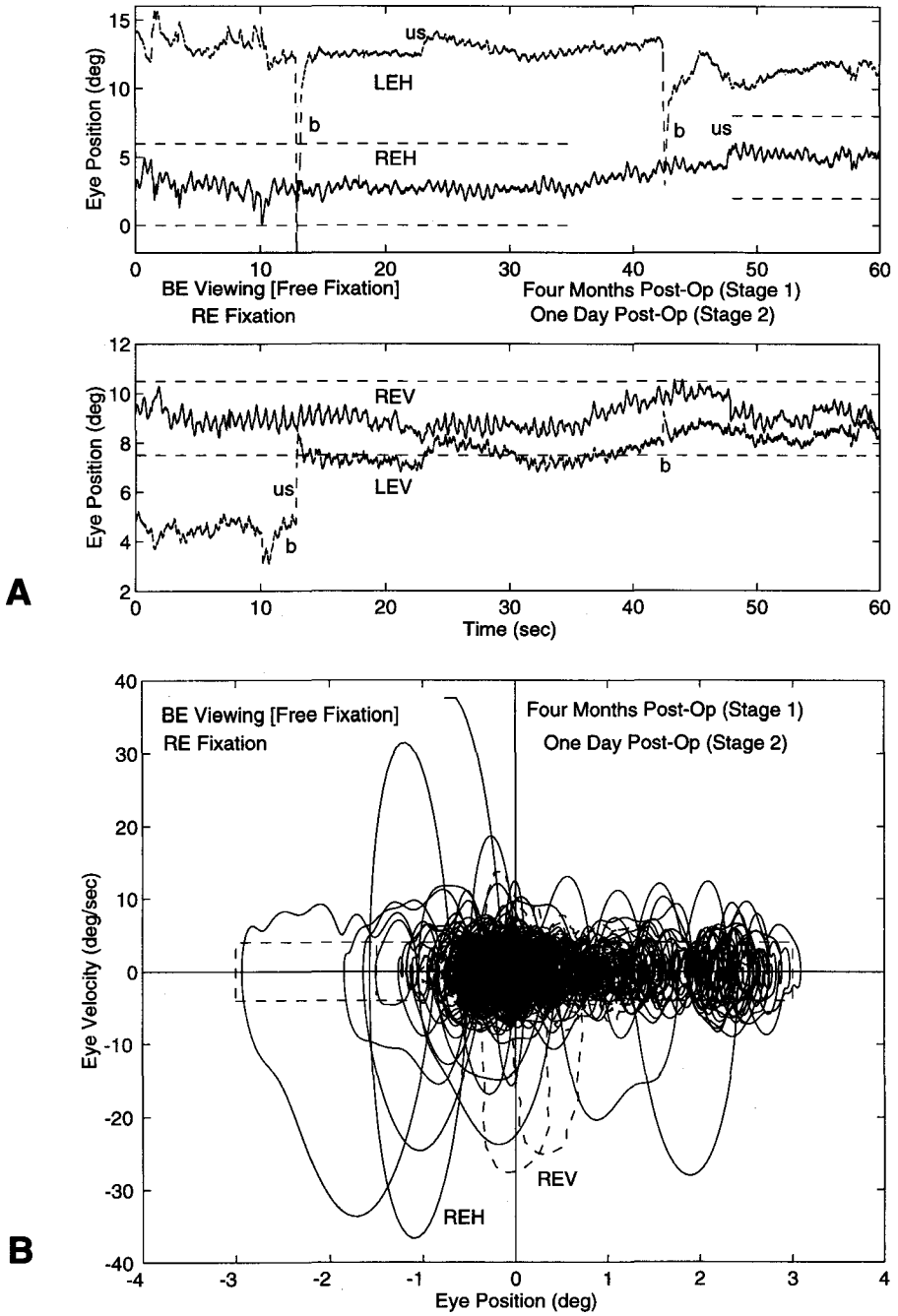

FIG 7. Example of horizontal and vertical CN of M5, made during free fixation at 3 to 5 degrees right and 9 degrees up while comfortably seated on the floor, 4 months postsurgical (stage 1) and 1 day postsurgical (stage 2). **A,** 60-second interval of steady, right-eye fixation in both planes with a 2-degree horizontal shift at 48 seconds; CN was of low amplitude, and no SSN was present. **B,** Phase plane of the fixating right eye in both planes showing well-developed centralisation at both the initial fixation point (3 degrees) and at 5 degrees, where the canine spontaneously fixated. In this and other figures, *us,* uniocular saccade.

day postsurgical observation period and the null-broadening effects of tenotomy (CN damped in lateral gaze). The CN was damped in lateral gaze (± 15 degrees) as well as at 0 degrees. Fixation was possible with either or both eyes. The phase plane of Figure 5, *B* demonstrates continued, well-developed centralisation by both eyes for the 2.5 seconds at 0 degrees. The pendular CN frequency averaged 3.1 Hz, and peak-to-peak amplitude averaged 1.3 degrees—a 76% reduction in CN amplitude. The jerk CN frequency averaged 1.5 Hz, and peak-to-peak amplitude averaged 1.5 degrees—a 74% reduction in CN amplitude. The postsurgical (stage 1) prominence of the SSN remained.

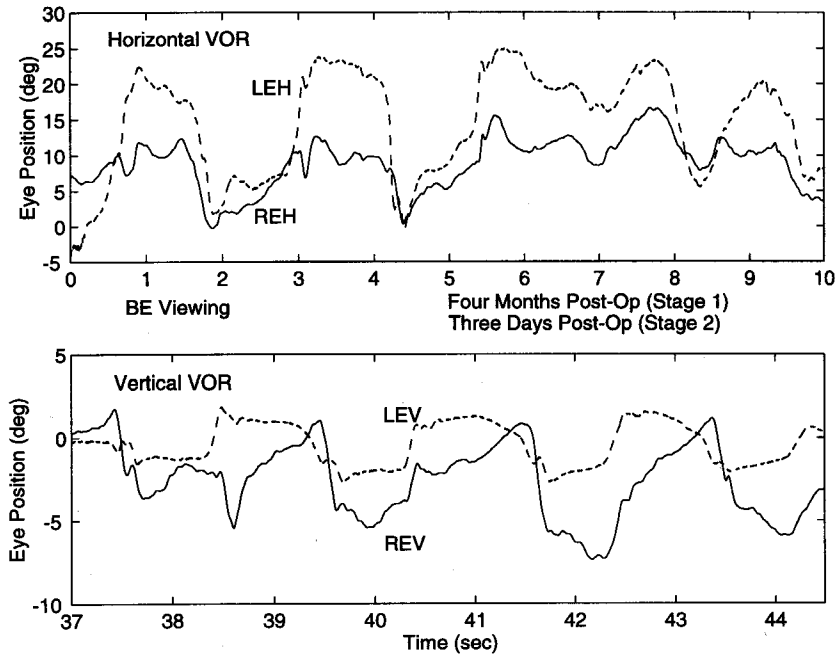

FIG 8. Demonstration of intact horizontal and vertical VOR in response to passive rapid and slow head rotations, 4 months postsurgery (stage 1) and 3 days postsurgery (stage 2). Note 2 beats of SSN (37.5 and 38.5 sec).

Surgery (Stage 2)

We performed tenotomies and reattachments at their original insertions of all 4 vertical rectus muscles and all 4 oblique muscles on M5 as described in the "Methods" section.

Postsurgical (Stage 2) Ocular Motility

The reduction in M5's cyclovertical nystagmus was again striking and obvious by inspection on postsurgical day 1 and persisted throughout the second 4-day recording period. We videotaped and recorded M5 on postsurgical days 1 through 4 (stage 2), 4 months postsurgically (stage 1). The videotape documented the reduction in both components (vertical and torsional) of the SSN. Figure 6, *A* documents the *absence* over a 25-second fixation interval of the vertical component of the SSN as a result of stage 2 of this surgery; only conjugate vertical CN was seen. The corresponding phase plane of Figure 6, *B* verifies the well-developed centralisation in both planes for this interval. Figure 7, *A*, recorded 4 months postsurgically (stage 1), shows an even more remarkable 60 seconds of steady fixation by the right eye, including a slight horizontal refixation at 48 seconds. Again, *there was no SSN*, only the conjugate CN. Note the uniocular saccades in both planes shown in Figure 7, *A*. The phase plane diagram of the whole interval demonstrates the excellent fixation in both the primary horizontal fixation area (at 3 degrees) and the secondary fixation area (at 5 degrees) (Figure 7, *B*).

The conjugacy of the eye-movement responses to horizontal and vertical head perturbations (ie, VOR) is shown in Figure 8. The vertical data are somewhat confounded by some SSN cycles present in addition to the conjugate vertical VOR.

There was only 1 instance of pendular SSN recorded in this 4-day period. The jerk frequency averaged 1.6 Hz, and peak-to-peak amplitude averaged 1.9 degrees—a 67% decrease in SSN amplitude. Recordings made 3 months postsurgery (stage 2) confirmed the continued absence of SSN, especially the null-broadening effects of tenotomy recorded in downgaze (damped CN) (Figure 9). As Figure 9, *A* shows, eye movements (including saccades) could be conjugate. The phase plane of the 10-second fixation interval at –10 degrees (downgaze) demonstrates well-developed centralisation of the target (Figure 9, *B*). At that point, which corresponds to 7 months postsurgery (stage 1), the horizontal CN remained damped. The horizontal pendular frequency averaged 3 Hz, and peak-to-peak amplitude averaged 1.4 degrees—a 74% decrease in CN amplitude. No jerk CN was recorded in this 4-day period. During the only intervals when SSN was recorded (usually elicited by loud noises), there either was a low-frequency pendular (Figure 10, *top*) SSN or a low-frequency and low-amplitude jerk SSN (Figure 10, *bottom*). Phase planes (not shown) verified well-developed centralisation of the fixating eye for both types of SSN.

The SSN was also barely perceptible in primary position on visual inspection. The eyes appeared still to the casual observer. Both the vertical and torsional components had been reduced. Both the CN and SSN could again be seen, consistent with a broadened null region, when taken in far lateral gaze. Also, whenever the animal was anxious or in some discomfort, the nystagmus became more visible. The

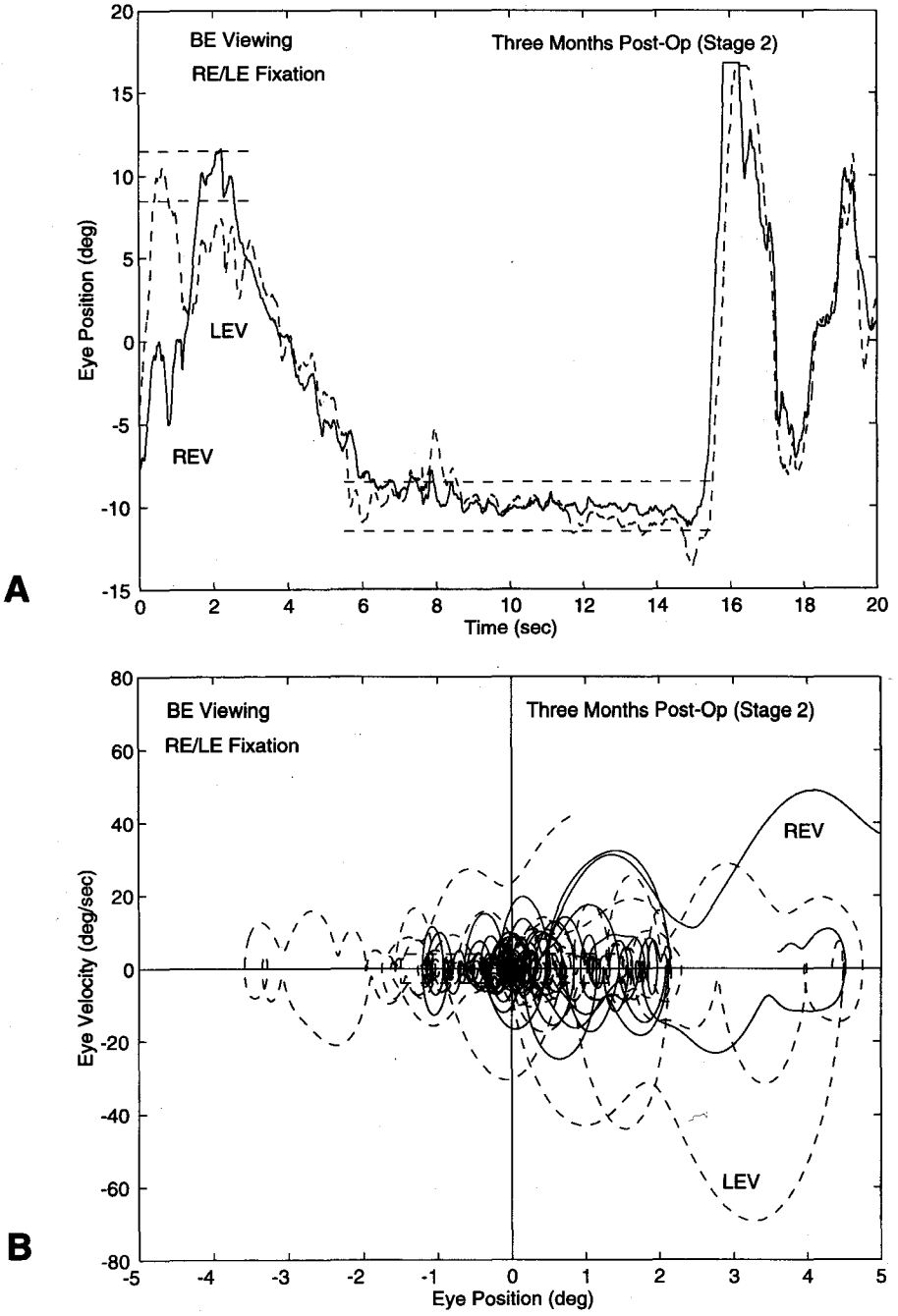

FIG 9. Example of vertical CN of M5 3 months postsurgical (stage 2). **A,** 20-second interval containing both up and down gaze (± 10 degrees) with conjugate nystagmus and saccades during final 17 seconds. **B,** Phase plane of 10-second interval of downgaze shown in **A.** Both eyes exhibited well-developed centralisation.

SSN became greater than the horizontal CN. An independent assessment of the striking effects of these operations on M5 was made by the veterinary and support staff at the animal facility. They expressed amazement at both the visible reduction in M5's nystagmus and the changes in his behavior, now that he appeared to be able to see things better.

Table 1 summarizes the ocular-motor effects of tenotomy on CN and SSN. Both the means and ranges of nystagmus amplitudes (especially the upper ranges) were greatly diminished postsurgically for CN (Table 1, *A*) and SSN (Table 1, *B*). The prevalence of jerk CN and SSN in primary position was also reduced, as the "ND" (no nystagmus data recorded) and "NR" (no ranges of data recorded) entries suggest. In both Tables 1, *A* and 1, *B*, the time lines for each stage of this procedure are indicated with the relevant stage and nystagmus in bold type. Because of the absence of pendular SSN in all but 1 post–stage-2 recording in the first 4 days, no average data

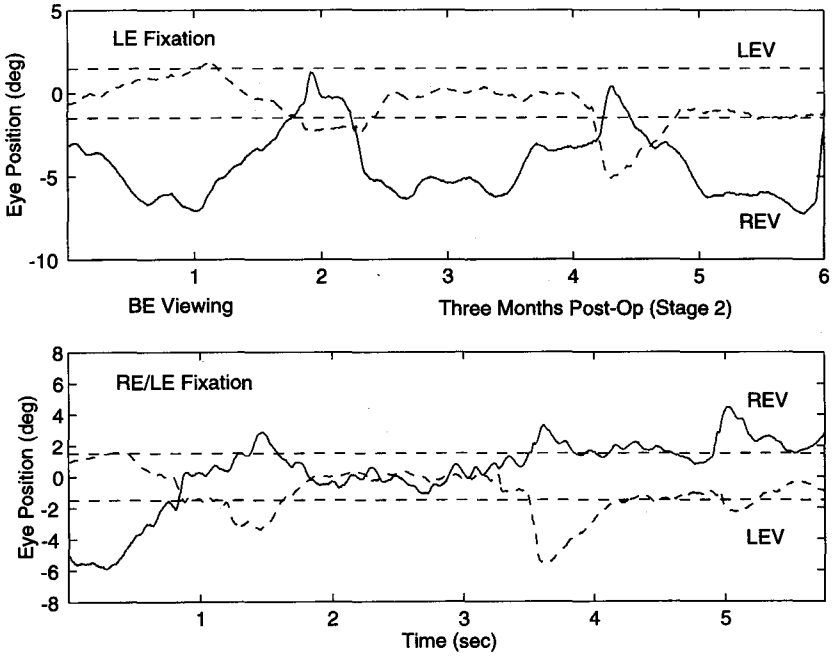

FIG 10. Example of vertical SSN elicited by loud noises to arouse M5 while fixating in primary position 3 months postsurgical (stage 2). Approximately 6-second intervals of low-frequency pendular SSN *(top)*, not seen preoperatively and jerk SSN *(bottom)*. In both records, there were extended periods of centralisation verified by phase planes.

appear in Table 1, *B*. Similarly, at 3 months post–stage 2, we only elicited SSN by arousing M5 with loud noises. Therefore, no comparable average data were available.

Both CN and SSN remained damped a year postsurgical (stage 1) and 8 months postsurgical (stage 2). Postmortem anatomic studies confirmed that M5 was an achiasmatic mutant. The corpus callosum and anterior and posterior commissures were found to be intact and of approximately normal size. Brain weight was normal, and there was no suggestion of holoprosencephaly. Cytoarchitecture of the pretectum, midbrain, and pons appeared normal.

DISCUSSION

Using videotape and digitized infrared ocular-motility recordings, we documented the damping of both CN and SSN that was obvious by inspection and the waveform changes. The data establish that tenotomy alone is sufficient to diminish both canine CN and SSN, thus, duplicating the secondary effects demonstrated in humans 2 decades previously.[1] Tenotomy directly changed only peripheral factors (ie, tendon and its insertion). The well-known variation of CN amplitude with changing psychologic input remained, but the baseline nystagmus was reduced. In M5, CN and SSN were greatly reduced; SSN was entirely absent many times. However, arousal appeared to bring back his SSN more than his CN, and the elicited SSN was a slow pendular or jerk oscillation (Figure 10). M5's SSN mimicked the slow SSN of M4, a previously studied animal that was subsequently used for neurophysiologic and anatomic studies.[13,14] The presurgical, high-frequency see-saw tremor was absent. In human CN, damping sufficient to allow target foveation twice per CN cycle results in increased visual acuity.[8] Such damping, evident in Figures 3 through 7 and 9, plus the positive postsurgical changes in M5's behavior suggest that the same beneficial effects on his acuity have occurred. As pointed out in the "Results" section, Figures 5 and 9 demonstrate the null-broadening effects of tenotomy on both horizontal (Figure 5, *A*) and vertical (Figure 9, *A*) CN. That is, the nystagmus remained damped in lateral/downward gaze, as it had been previously observed in the postsurgical recordings made of human patients who underwent Anderson-Kestenbaum procedures.[1-3] Comparison of presurgical and postsurgical recordings also confirmed the visual observations that M5 was able to maintain fixation for longer periods of time after the procedures. Figures 6 and 7 demonstrate long intervals of maintained fixation. Such intervals were not seen in the preoperative records taken over during the previous 6-year period.

In humans, CN is affected by both its driving force (fixation attempt) and other psychologic inputs.[7] The entries in Table 1 suggest that similar drives may have a diminished ability to increase CN above its baseline level, postoperatively. Both the lower ends and, to a greater extent, the upper ends of the ranges were reduced by tenotomy. As noted above, some of the SSN we recorded postsurgically was elicited by making loud noises to arouse M5. The data recorded out of the sling, while M5 was sitting quietly on the floor, are at the other end of the CN spectrum (Figure 7). Comparison of the eye-movement data during this

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TABLE 1, *A.* Effects of tenotomy on congenital nystagmus (M5)

		Stage 1 <4 months> Stage 2			
Surgery		**Before**	**After**		
Congenital		≥1 d	1-4 d	4 mo	7 mo
Magnitude (degrees)	P	5.4 (1-12)	1.8 (0.5-6)	1.3 (<0.5-5)	1.4 (<0.5-4)
	J	5.7 (1-15)	2 (NR)	1.5 (NR)	(ND)
Frequency (Hz)	P	2.9 (1-4)	2.5 (0.5-4)	3.1 (1-5)	3 (1.5-5)
	J	2.8 (1-4)	2 (NR)	1.5 (NR)	(ND)
Change (%)*	P		–67	–76	–74
	J		–65	–74	(ND)

*Changes from presurgical amplitudes.
Data expressed are means and (ranges).
J, Jerk; *ND,* no data; *NR,* no range; *P,* pendular.
Bold type indicates time of stage 1 and type of nystagmus affected.

TABLE 1, *B.* Effects of tenotomy on SSN (M5)

		Stage 1 <4 months> **Stage 2**		
Surgery		**Before**	**After**	
See-Saw		≥1 d	1-4 d	3 mo*
Magnitude (degrees)	P	2.4 (0.5-8)	(see text)	(see text)
	J	5.8 (1.5-15)	1.9 (0.8-3)	
Frequency (Hz)	P	2.9 (1-7)	(see text)	(see text)
	J	1.7 (0.7-3.5)	1.6 (0.7-3)	
Change (%)†	P			
	J		–67	

*Data taken during loud noises to arouse dog.
†Changes from presurgical amplitudes.
Data expressed in means and (ranges).
J, Jerk; *P,* pendular.
Bold type indicates time of stage 2 and type of nystagmus affected.

period with similar presurgical data revealed a 300.6% increase in average centralisation time (fewer, longer periods—sometimes across several CN cycles) and a 24% increase in the "expanded" nystagmus acuity functions that were calculated using the canine window (± 3 degrees by ± 4 degrees per second for horizontal data) instead of the human foveal window.[19,20] Even when M5 was sitting quietly, the effects of tenotomy were evident. The postoperative numbers in Table 1, *B* are from SSN, elicited only occasionally and with arousal. Therefore, the percent-change calculations do not accurately reflect the success of tenotomy in reducing SSN because they fail to include the many times that SSN was not present.

The nature of the achiasmatic mutation (ie, a midline abnormality at the optic chiasm) and the presence of uniocular saccades in all mutants recorded raised the possibility of additional midline maldevelopment in brainstem ocular-motor pathways.[13,14] However, as Figure 8 demonstrates, both the horizontal and vertical VORs were conjugate. This and the presence of conjugate saccades and nystagmus suggest normal, intact, brainstem-level connections and are consistent with the absence of anatomic abnormalities in midline structures, other than at the chiasm in M5 and other mutants.[21-23]

Tenotomy was effective in damping both the CN and the vertical-torsional SSN in a Belgian sheepdog with achiasma. Our results may have clinical application for both CN and acquired nystagmus. They do have theoretic implications about the ocular-motor muscles and their control. We discuss the possible clinical usefulness of tenotomy, followed by theoretic considerations, and conclude with a suggested modification to an existing procedure that would take advantage of the damping produced by tenotomy alone.

From the Research Lab to the Operating Room

The tenotomy procedure did not evolve from the kind of analysis that led to either the Anderson-Kestenbaum resection and recession or the bimedial recession ("artificial divergence") procedures.[24-26] Instead, accurately recording the effects of the Anderson-Kestenbaum procedure and measuring the CN at all gaze angles (preoperatively and postoperatively) led to the observations of the beneficial secondary effects discussed above. That prompted the hypothesis that the beneficial secondary effects of the surgery could be produced by tenotomy alone to emerge from the eye-movement data.[15] In the absence of such recordings, it is doubtful that this new procedure would ever have come to light and the value of objective, quantitative eye-movement data, already demonstrated for accurate diagnoses and therapies of both congenital and acquired ocular-motor disturbances, was further reinforced.

CN Patient Population Affected

Tenotomy is presumably a muscle-sparing procedure that, unlike large recessions, does not provoke a confounding central response (see below).[15] We wish to clarify at this point that this new procedure is *not* offered as a substitute for either the Anderson-Kestenbaum or bimedial recession procedures. Rather, it is an *addition* to the arsenal of surgical therapies available to treat patients with CN. Tenotomy, *like all other procedures,* should only be used in those cases indicated by the *patient's* specific CN characteristics. However, the tenotomy procedure does extend the possibility of surgical therapy to several different classes of patients with CN for whom other procedures are contraindicated. A theoretic (but untested) protocol for nystagmus surgery in humans is outlined in Table 2, depending on the degree to which one can extrapolate from the canine to the human. Both the indicated nystagmus characteristics for commonly used surgical procedures and those characteristics for which tenotomy may prove to be applicable are included. These are patients whose CN either does not null, nulls at 0 degrees but not with convergence, or exhibits asymmetric, (a)periodic alternation with no convergence null. Both the earlier data from humans and the tenotomy-induced CN damping in an animal model provide a strong foundation for further

evaluation of this procedure in those specific patients for whom it is indicated.

Large recessions of the 4 horizontal rectus muscles have previously been suggested as a procedure to damp CN.[27-31] We believe that consideration of this controversial procedure should be confined solely to those patients in whom the Anderson-Kestenbaum or bimedial recession is contraindicated, with the further requirement that they *have strabismus*.[32] We regard the danger of induced diplopia in lateral gaze in binocular patients (anecdotally observed in Germany and in the United States) as a contraindication for large recessions. Large recessions disturb ocular-motor-system homeostasis by reducing the moment arm of the muscles, thereby reducing both the overall gain of the subsystem (saccadic, pursuit, optokinetic, or vestibulo-ocular) driving an eye movement and the fine control required, especially in lateral gaze. Peripheral deficits in gain due to either palsy or neuromuscular junction disease are known to produce an increase in central gain because of the plasticity of the ocular-motor system.[33-37] Thus, large-recession surgery may actually provoke a commensurate and *counterproductive* increase in the nystagmus signal itself. Finally, the loss of fine control may result in long-term ocular-motor problems as patients age. Currently, none of these problems have been adequately studied using recorded eye-movement data.

Now that the damping effects on CN of tenotomy alone have been quantitatively demonstrated, it remains to be determined whether the extent to which the initial CN damping observed after large-recession surgery is actually caused by the previously unrecognized benefits of the muscles undergoing tenotomy as part of that procedure. Clearly, if the damping is substantially the result of tenotomy, this muscle-sparing and homeostasis-maintaining procedure should emerge as the preferred conservative therapy for these patients with CN. Currently available eye-movement data suggest that tenotomy be considered the method of choice, when both the Anderson-Kestenbaum and bimedial recession procedures are contraindicated, and that large recessions should only be attempted in those patients with strabismus in whom tenotomy has failed to damp their CN. We expect the latter to be a rare occurrence.

Patients with either gaze-angle or convergence nulls (or both) should continue to be treated by either the Anderson-Kestenbaum or bimedial recession procedures, respectively. Only those in other categories should be candidates for the tenotomy procedure, as indicated in Table 2. In our laboratory, 3 decades of recording hundreds of patients with CN have consistently demonstrated the measured damping effects of convergence to be greater than those of gaze angle (in patients who exhibit both gaze-angle and convergence nulls). Furthermore, once the eyes are converged, gaze angle has little effect on the already damped CN. This effectively provides a broad null region extending laterally from primary position. Therefore, the most effective surgical therapy in these patients remains bimedial recession and nonsurgical, base-out prisms with −1.00 spheres OU added to prepresbyopic refractions.[38] The Anderson-Kestenbaum procedure can be combined with bimedial recession to achieve additional damping in some patients.[39] Finally, it should be remembered that the beneficial effects of tenotomy are *incorporated* in the Anderson-Kestenbaum procedure. It was the null-broadening and off-null damping, measured in human eye-movement recordings, that led to the hypothesis that tenotomy was responsible and would be successful in this animal model of CN.[15]

TABLE 2. Addition of tenotomy to standard surgical procedures for congenital nystagmus

Nystagmus	Procedure
Only gaze-angle null	A-K resection and recession
Only convergence null*	Bimedial recession (+ bilateral tenotomy)
Both types of null	Bimedial recession (+ A-K resection and recession)
No nulls	Horizontal rectus muscle tenotomy†
Null at zero degree	Horizontal rectus muslce tenotomy†
APAN‡	Horizontal rectus muscle tenotomy†
SSN	Vertical rectus muscle and inferior and superior oblique muscle tenotomy

*Including APAN.
†If unsuccessful and patient has strabismus, large recessions of the horizontal rectus muscles may be indicated.
‡With no convergence null.
A-K, Anderson-Kestenbaum; *APAN,* asymmetric (a)periodic alternating nystagmus *SSN,* see-saw nystagmus.

Potential Applications of the Tenotomy Approach

We believe that the success we have demonstrated in damping SSN—a disconjugate, vertical oscillation with a conjugate torsional component—suggests that tenotomy alone will prove effective in some types of acquired nystagmus.

Patients with oscillopsia, who are unresponsive to other forms of therapy, should benefit from surgical damping of their acquired nystagmus. As in patients with CN, this procedure is indicated for those types of acquired nystagmus not damped by other means (eg, convergence damping of downbeat nystagmus or gabapentin for acquired pendular nystagmus).[40,41] Tenotomy may also prove to be effective in damping acquired SSN, thereby reducing oscillopsia. These possibilities require postoperative eye-movement data to assess the effectiveness of the procedure in each venue.

Tenotomy in Human Achiasma

Because we have effectively damped both CN and SSN in canine achiasma, we regard the 2-stage tenotomy of all extraocular muscles as a possible therapy for those rare (currently 4) individuals with the CN and SSN that accompany human achiasma.[14,42] The horizontal CN should be treated according to Table 2 and the SSN by tenotomy of the vertical rectus and oblique muscles. If the horizontal strabismus of patients with achiasma was large enough to require correction, suitable recessions or resections of specific horizontal rectus muscles could be included in the procedure. In the

case of the first achiasmatic human studied using ocular-motor recordings, Dell'Osso et al[14] found a slight CN null and an increased nystagmus acuity function in primary position.[19] Because her strabismus is not very noticeable, this patient is a candidate for tenotomy of her horizontal rectus muscles, followed (after 4-6 months) by tenotomy of her vertical rectus and oblique muscles. The damping of both the CN and SSN resulting from tenotomy should allow better waveforms (ie, greater foveation time per cycle) and higher acuity in this patient (and others) with achiasma.

Mechanisms

Our current observations appear to be therapeutically effective but theoretically unexplained. We believe that the *most probable* explanation is that tenotomy may have changed the dynamics of the proprioceptive loop known to exist for all peripheral muscles, including the extraocular muscles (see below). Other possible mechanisms are that we have changed the extraocular "plant" dynamics, or we have changed the gain of the extraocular muscle pulley system.[43] It is possible that plant dynamics (ie, the extraocular muscles, tendons, fascia, and globe) could have been affected by altering the connection of the tendons to the globe or by irreversible changes resulting from the interrupted blood supply to the muscles. Alternatively, the preparations before actually tenotomizing an extraocular muscle (for this and other procedures) first require opening the space around the muscle by dissecting it from the surrounding fascia. There is a small possibility that this may have altered the positions or attachments of the extraocular muscle pulleys, thereby changing the gain of the system.

There is an abundance of basic science and some clinical evidence supporting a hypothesis that central nervous system gain-modulation of the oscillation may be due to afferent changes from the extraocular muscles after the procedure.[44,45] The primary afferent neurons providing sensory innervation of the mammalian extraocular muscles are located in the trigeminal ganglion. After primary afferent projection, extraocular muscle afferent information is distributed broadly within the central nervous system.[44,46] Afferent fibers from V1 (ophthalmic branch of the trigeminal nerve) either directly connect to or influence brainstem, cerebellar, and cortical areas associated with eye-movement control.[44,45,47-54] Afferent fibers also affect binocularity, strabismus, spatial localization, and adaptive control of eye movements.[47,55-61]

Given these numerous studies, it is likely that afferent information from the extraocular muscles (either as proprioceptive signals or as other sensory information) serves as a continuous and long-term calibration signal. The underlying pathophysiologic cause of CN has been attributed to a high-gain instability in the pursuit system.[38,62] The clinical and electrophysiologic consequences of extraocular muscle tenotomy in this animal model (and in patients) with CN may be due to interruption of the afferent proprioceptive loop, producing a damped *peripheral* ocular-motor response to the nystagmus signal. Two observations suggest that we have not reduced the central (ie, smooth pursuit) gain driving the CN. First, the well-documented psychologic effects on the nystagmus remained postoperatively. Second, the transient head tremor also remained. Proprioception has been shown to affect smooth pursuit gain (the source of CN), raising the alternate possibility that tenotomy may have reduced the baseline CN motor signal itself while preserving its variability with fixation attempt or other central inputs.[62,63]

Implications for the Ocular-Motor Plant

Despite the evidence for an ocular-motor proprioceptive loop, the absence of a stretch reflex has led to its (mis?)characterization in computer models as a simple 1- or 2-pole (with or without a zero) transfer function. This study provides dramatic evidence in support of previous indications that afferent signals play an important, albeit not yet understood, role in the ocular-motor system.[19,58,64] It suggests that we may need to significantly expand this portion of our models (the plant) to contain a proprioceptive feedback loop. Specifically, when the afferent signal is perturbed, the results may be altered plant dynamics and reduced gain. This effect has been exploited therapeutically by either passive or active afferent stimulation (both have been shown to damp CN) and now, by tenotomy.[19,64]

Remaining Questions

There are some important unanswered questions (with practical consequences) raised by these observations. Is it necessary to tenotomize *both* antagonist-pair muscles of each eye in the plane of action, or will one suffice? The architecture of the ocular-motor system is a bilateral, push-pull arrangement, whereby activation in 1 direction (ie, 1 side of the brainstem) is accompanied by inhibition in the other. This suggests that 2-muscle tenotomy would be required on each eye for maximal effect, but this remains to be shown; perhaps 2 antagonist muscles, one in each eye (eg, both lateral rectus muscles), might suffice. A remote but distinct possibility is that the proprioceptive endings in the tendons could be altered by simply pinching them with a hemostat, thereby producing similar damping effects on nystagmus.

Although the reductions shown in Table 1 are large, the effects in humans may differ quantitatively and show inter-patient variability. Our data suggest that tenotomy was the most probable cause of the previously documented changes in human CN.[1-3] The CN damping effects reported for the Anderson-Kestenbaum procedure led Drews[65] to attempt bimedial resections in 5 patients with esotropia with undiagnosed "nystagmus."[1] The results of such an apparently counterproductive approach were mixed, with damping in 3 of the 5 patients. Without eye-movement recordings, neither the author nor the reader can determine which patients had CN with a latent component and which had latent/manifest latent nystagmus. Primary-position nystagmus reversal does *not* establish the diagnosis of latent/man-

ifest latent nystagmus on alternate cover. Because the reversal of CN with a latent component is due to an entirely different mechanism (ie, a shift in the neutral zone), we should not expect any procedure to have the same damping effect in both types of nystagmus.[66] Drews realized this and so stated. We can only presume that the 3 patients in whom the procedure was effective had CN, but there is no proof. Because a 2-antagonist muscle operation did have a damping effect, we need only determine if a greater effect is produced by a 4-muscle procedure.

Although tenotomy in a given plane (horizontal or vertical) has no more effect on the blood supply to the eye than conventional 4-muscle surgery, the case of human achiasma is special. If all 12 muscles are to be tenotomized in an attempt to damp both the horizontal CN and SSN, as we did with this canine, the surgery must be done in 2 stages, separated by 4 to 6 months. Procedures to spare the blood supply might be advisable to prevent anterior segment ischemia. Depending on the patient's age and the status of the patient's cardiovascular system, ischemia can still occur despite waiting this recommended amount of time.[67]

Proposed Modified Bimedial Recession Procedure

A strong inference from this study is that the beneficial damping effects of tenotomy on CN are primarily responsible for the overall CN damping measured after the Anderson-Kestenbaum procedure. Therefore, we hypothesize that the damping effects of bimedial recession can also be further enhanced by a simple addition to the procedure. We propose a *modified* bimedial recession, consisting of bimedial rectus muscle recession plus bilateral rectus muscle tenotomy. This slight modification would provide the added damping of the tenotomy of this antagonist pair to that of convergence in the same manner as it does in the Anderson-Kestenbaum procedure, in which all 4 muscles are tenotomized. Given our observations about the null-broadening effects of convergence and that tenotomy is inherent in the Anderson-Kestenbaum procedure, it is possible that the increased damping observed when the Anderson-Kestenbaum procedure was added to bimedial recession was due to tenotomy of the lateral rectus muscle rather than null shifting.[39] As stated above, once CN is damped by convergence, it is not affected by a coexisting gaze-angle null; the CN remains damped regardless of gaze angle.

In conclusion, surgical procedures will be more uniformly successful in patients with nystagmus who have had their oscillations properly diagnosed by eye-movement recordings. The shotgun approach, based solely on clinical impression, can only continue to have mixed results. Different types of nystagmus are due to separate mechanisms, have different characteristics, and respond best to therapies specifically tailored to them. Applying less-than-optimal therapies to poorly diagnosed or undiagnosed diseases in patients (eg, "nystagmus") contributes little to our scientific understanding, cannot accurately determine the utility of each procedure, and is a disservice to the patient.

We regard *neither* tenotomy nor large recessions as appropriate substitutes for the standard bimedial recession or null-shifting procedures; the latter 2 exploit naturally occurring nulls in CN, do not radically alter ocular-motor homeostasis, and do not provoke counterproductive increases in central gain. Both the clinical and mechanistic hypotheses underlying the damping effects of tenotomy remain to be tested in future studies. Presently, we urge that this procedure be limited to those accurately diagnosed patients indicated in Table 2 (for whom neither bimedial recession nor null shifting is indicated) and that both preoperative and postoperative eye-movement data be collected for analysis. The ultimate use and successful application of this procedure, born from eye-movement data, should be determined by objective data, not by anecdotal reports of its application to poorly diagnosed patients with nystagmus.

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Digitized videos of M5's preoperative and postoperative nystagmus may be found at http://med-aapos.bu.edu/newnystagsurg/newnystagsurg.html.

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