Magnetic Resonance Imaging of Human Extraocular Muscles in Convergence

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Demer, Joseph L., Reika Kono, and Weldon Wright. Magnetic resonance imaging of human extraocular muscles in convergence. J Neurophysiol 89: 2072–2085, 2003; 10.1152/jn.00636.2002. Extraocular muscle (EOM) paths during asymmetrical convergence were evaluated by tri-planar, contrast-enhanced magnetic resonance imaging of the orbits of eight young adults during binocular fixation of a target aligned to one eye at 800 and 15 cm distance. Cross-sections and paths of EOMs were determined from area centroids. In convergence, the aligned eye rotated and translated negligibly, while its inferior oblique (IO) muscle exhibited significant contractile thickening. There were no significant contractile changes in the cross-sections of aligned eye rectus or superior oblique (SO) muscles in convergence. The converging eye rotated nasally 22.4° but translated negligibly. The converging eye medial (MR) and lateral rectus (LR) muscles exhibited large contractile cross-section changes, and the IO showed significant thickening, while the vertical rectus muscles and the SO did not. Anterior paths of three aligned eye rectus EOMs could be determined in convergence and shifted consistent with a 1.9° extorsion of the rectus pulley array. Such extorsional reconfiguration of the rectus pulleys would move the pulleys in coordination with globe extorsion and avoid imparting torsional action to these EOMs. Extorsional rectus pulley shift in convergence is inconsistent with the reconfiguration predicted to explain the temporal tilting of Listing’s planes, instead suggesting that this temporal tilting is due to variations in oblique EOM innervation. Absence of globe translation in convergence argues against overall EOM co-contraction. The reconfiguration of EOM geometry in convergence has important implications for single-unit studies of neural control.

INTRODUCTION

Recent evidence suggests a connection between ocular kinematics and the geometry of the extraocular muscle (EOM) paths that is constrained by connective tissue pulleys first suggested by Miller (1989). More recent work has described these pulleys in detail. Each rectus pulley consists of an encircling ring of collagen located near the globe equator in Tenon’s fascia (Demer et al. 1995b), coupled to the orbital wall, adjacent EOMs, and equatorial Tenon’s fascia by sling-like bands containing collagen, elastin, and smooth muscle (SM) (Demer 2000; Demer et al. 1997; Kono et al. 2002b). Soft pulleys inflect rectus and inferior oblique (IO) EOM paths in a manner analogous to the way that the rigid trochlea inflects the path of the superior oblique (SO) tendon, yet the soft pulleys have the property of mobility in some directions. The coronal plane location of each rectus pulley has been shown by MRI to be highly uniform in normal subjects (Clark et al. 1997). All EOMs are bilaminar. Microscopic examination of serially sectioned human and monkey orbits suggests that the global layer (GL) of each rectus EOM, containing about half of total EOM fibers (Oh et al. 2001b), passes through the pulley and becomes contiguous with tendon to insert on the globe. The orbital layer (OL), containing the remaining about half of the EOM fibers, has an insertion on the pulley (Demer et al. 2000; Oh et al. 2001b).

The preceding anatomic features of pulleys are pivotal for ocular kinematics and neural control. It is important to recall that rotations of three-dimensional (3-D) objects are not mathematically commutative; consequently, final eye orientation depends on the order of rotations (Haslwanter 1995). This vexing conundrum for the neural control of ocular motility is avoided for all practical purposes if the ocular rotational axis shifts by half of the change in ocular orientation with respect to a primary position, for under these conditions, the effect of noncommutativity becomes negligible (Quaia and Optican 1998). This half angle behavior is equivalent to Listing’s Law (L1), a quantitative description of ocular torsion (Tweed and Vilis 1990). Precise locations and mechanical shifts in rectus pulley positions consistent with commutative half angle behavior were predicted by the active pulley hypothesis (APH) as diagrammed in Fig. 1, A, B, D, and E (Demer et al. 2000), and later quantitatively confirmed in humans by MRI in tertiary gaze positions (Kono et al. 2002a). The coordinated control postulate of the APH states that each rectus pulley is shifted anteroposteriorly in the orbit through the action of the OL to maintain a constant relationship, in an oculo-centric coordinate system, with the EOM’s scleral insertion. Thus the distance from the pulley to globe center D1 is equal to the distance from globe center to insertion D2 (Fig. 1, B, D, and E) (Kono et al. 2002a). This reasoning assumes trigonometrically small angles typical of the oculomotor range and requires each rectus pulley to make a posterior move during EOM contraction in coordination with rotation of the scleral insertion (Fig. 1, D and E). By so doing, the velocity vector produced by EOM contraction shifts by half of the change in ocular orientation from primary position (Fig. 1B). The IO muscle also has a pulley, mechanically coupled to the inferior rectus (IR) pulley (Demer et al. 1999), that moves anteroposteriorly by half as much as the IR pulley to maintain an half angle behavior for the IO
orthogonal to that of the rectus EOMs (Demer 2001; Demer et al. 2001).

Binocular viewing of near targets affords the potential visual advantage of stereopsis for depth perception. The geometric significance of interocular spacing relative to viewing distance not only provides the binocular sensory disparity that enables stereopsis, but it also poses challenges for the ocular motor system. It is kinematically appropriate to provide identical neural control to the two eyes when viewing a remote target so that the eyes move horizontally and vertically in a unison sometimes expressed as Hering’s Law. During viewing of distant targets with the head upright and stationary, the torsional position of each eye is governed by L1. A mathematically equivalent, familiar formulation of L1 states that all eye positions are reached from a primary position by rotation about a single axis lying in a plane, Listing’s plane, that is roughly horizontal or alternatively vertical, depending on choice of coordinate system) orientations of the two eyes. Vergences do not conform to Hering’s Law. Less obviously than for horizontal and vertical vergences, stereopsis requires adjustments in the torsional positions of the eyes to maintain alignment of corresponding retinal meridia (Schreiber et al. 2001). Allen and Carter used a photographic technique to demonstrate that asymmetric convergence produces excyclotorsion, violating L1 (Allen and Carter 1967). The finding of excyclotorsion in convergence has been repeatedly confirmed in humans (Bruno and van den Berg 1997; Mikhael et al. 1995; Minken and Van Gisbergen 1994; Mok et al. 1992; Somani et al. 1998) and monkeys (Misslisch et al. 2001). During asymmetrical accommodative or disparity-induced vergence, this temporal rotation occurs in both the aligned and converging eyes, independent of eye position (Steffen et al. 2000). Thus the classical form of L1 is not observed for near viewing: the Listing plane for each eye tilts temporally with convergence (Allen 1954; Kapoula et al. 1999; Minken and Van Gisbergen 1994; Mok et al. 1992;
Steffen et al. 2000), in a manner that has been described as L2, the binocular extension of Listing’s law (van Rijn and van den Berg 1993).

The temporal tilting of the Listing’s planes for the two eyes is roughly 1.6–2.2 times the vergence angle (Kapoula et al. 1999), corresponding to the relative excyclotorsion in depression and incyclotorsion in elevation (Somani et al. 1998; van Rijn and van den Berg 1993). This behavior depends quantitatively on visual characteristics of the targets employed (Kapoula et al. 1999). It is remarkable that during binocular viewing of near and far targets aligned on one eye, the Listing plane for that unmoving eye nevertheless tilts in association with the vergence movement of the other eye (Steffen et al. 2000). It has been proposed that a form of Herring’s Law of equal innervation exists for the vergence system, such that both eyes receive symmetric version commands for remote targets and mirror symmetric vergence commands for near targets (van Rijn and van den Berg 1993). Extending this idea, we proposed that this tilting of Listing’s plane during vergence might be due to binocularly symmetrical reconfiguration of rectus pulleys as diagrammed in Fig. 1: nasal shift of the vertical rectus pulleys (Fig. 1C), anterior shift of the MR pulley (Fig. 1F), and posterior shift of the LR pulley (Fig. 1F) (Demer et al. 2000). This predicted behavior of rectus pulleys in convergence constitutes an example of the differential control postulate of the APH wherein pulleys are supposed to be capable of motion not coordinated with that of the EOM insertions on the sclera (Kono et al. 2002a).

Knowledge of the mechanical configuration of the EOMs in convergence is important to interpretation of the neural commands that drive these eye movements, an area in which apparently reasonable assumptions have been shaken by empirical findings. Recording in the abducens nuclei of monkeys, Mays and Porter found that the mean decrease in firing in convergent adduction was only 62% of that in conjugate adduction (Mays and Porter 1984), similar to the value of 50% later found by another laboratory (Gamlin et al. 1989). Recording from abducens nerve rootlets, Zhou and King found that 66% of LR motor neurons were modulated in correlation with monocular movement of either eye (Zhou and King 1998). Even though the ipsilateral eye was immobile because the target was aligned on it, many LR motor neurons increased firing with addition of the contralateral eye (Zhou and King 1998). Assuming that EOM motor units constitute a final common pathway for both version and vergence eye movements, these findings would predict co-contraction of the MR and LR muscles in convergence. Miller et al. sought direct evidence of such co-contraction by implanting chronic force transducers on the MR and LR muscles of monkeys trained to perform asymmetrical convergence (Miller et al. 2002). Not only did Miller et al. fail to find the predicted MR and LR co-contraction, but actually observed slight co-relaxation!

Thus direct study of EOM forces and motor neuron discharge during convergence has failed to clarify the physiology. Another technical approach has now emerged, exploiting developments in orbital MRI that permit study of human EOM behavior during visual fixation. Miller first demonstrated the utility of MRI for quantitative assessment of normal rectus EOM contraction by measurement of the distribution of cross sectional area in relaxed and contracted gaze positions (Miller 1989). The method indicated reduced contractibility in denervated rectus EOMs (Demer and Miller 1999) as well as in normal and palsied SO (Clark et al. 1998a; Demer and Miller 1995; Demer et al. 1995a) and IO (Demer et al. 1999; Kono and Demer 2003) muscles. The current study aimed to evaluate the paths and contractility of all of the striated EOMs by MRI during the paradigm of asymmetric convergence so commonly employed in the human and animal literature. Asymmetric convergence aligns the target on one eye for both near and distant viewing, avoiding confounding changes in horizontal and vertical eye position while potentially disclosing changes due to convergence-related innervation that appears to be delivered equally to the two eyes (Allen and Carter 1967; Rashbass and Westheimer 1961; Steffen et al. 2000).

METHODS

Subjects

Eight presbyopic adult volunteers aged 24 ± 4 (SD) yr were recruited by advertisement and gave written informed consent according to a protocol conforming to the Declaration of Helsinki and approved by the Human Subject Protection Committee at the University of California, Los Angeles. All volunteers underwent complete eye examinations verifying normal corrected vision, normal ocular versions, orthotropia in all gaze positions, ability to maintain prolonged convergence to a target 15 cm away, and stereopsis of 40 arcsec by Titmus testing.

Visual stimuli

Each subject briefly practiced the experimental task under conditions simulating those in an MRI scanner. While lying supine and looking upward, subjects wore a padded facemask containing a transparent faceplate and a dual-phased surface coil array (Medical Advances, Milwaukee, WI). A half mirror fabricated of transparent acrylic plate was mounted with its center 15 cm anterior to the eyes and angled approximately 45° to the vertical so that the reflected image of a distant, flashing red light-emitting diode (LED) at the opposite end of the room 600–800 cm away (depending on the individual MRI scanner) could be viewed as if centered vertically. The end of a single fine acrylic optical fiber was placed directly above the center of the half mirror so that when the fiber end was illuminated by an LED placed at its remote opposite end, it formed a small illuminated point 15 cm from the middle of the line connecting the two globe centers. The subject was then instructed to fixate the constantly illuminated near target, and the far, flashing target light was then moved until it was superimposed on the near target as seen by the designated aligned eye. The positions of the near and far targets were then fixed, and only illuminated alternately. With the far target illuminated, both eyes were in a conjugate position approximately 11° opposite to the side of the aligned eye. With the near target illuminated, the aligned eye was in the same position, but the opposite eye, designated as the converging eye, addducted without changing vertical position. Prior to MRI scanning, the ability of each subject to sustain the appropriate convergence was verified by visual inspection or video recording of eye position through the half mirror. Convergence to the near target was either achieved with high stability, or was grossly absent; no subject exhibited intermediate behavior. During MRI scanning sessions, actual eye positions were determined from the images themselves and are reported below for binocular viewing of both the near and far targets in various imaging planes.
High-resolution, T1-weighted MRI was performed using a 1.5 T General Electric Signa (Milwaukee, WI) scanner. Crucial aspects of this technique, described in detail elsewhere, include use of the dual-phased surface coil array (Medical Advances, Milwaukee, WI) to improve signal-to-noise ratio and fixation targets to avoid motion artifacts (Clark et al. 1998a,b, 1999; Demer and Miller 1999). Initially, a localizer axial scan was obtained at 3-mm thickness using a 256 × 192 matrix over a 10-cm square field of view (FOV). A true coronal image including both orbits was then obtained at 3-mm thickness using a 256 × 256 matrix over a 10-cm FOV. This true coronal image was used to place sets of 17 contiguous, 2-mm-thick axial images using a 256 × 256 matrix over a 9- to 10-cm FOV, minimally sufficient to view both orbits of each individual subject and yielding a pixel resolution of 350–390 μm. Axial images were repeated for the near and far targets and confirmed that the intended eye positions were actually achieved by each subject (Fig. 2). This verification of eye position was crucial because data from three additional subjects had to be discarded because axial images indicated gross failure to achieve convergence to the near target. The paramagnetic MRI contrast agent gadodiamide (0.1 mmol/kg total dose) was given intravenously in divided aliquots to improve the contrast of EOMs against connective tissue in the anterior orbit (Oh et al. 2001a) before most of the remaining scans. For both near and far target viewing, sets of 17 contiguous quasicoronal images perpendicular to the axis of each orbit were obtained with 2-mm slice thickness using a 256 × 256 matrix over an 8-cm square FOV, giving pixel resolution of 313 μm.

Figure 3 shows such quasicoronal scans obtained without contrast to illustrate better the posterior orbit because gadodiamide reduces image contrast of EOMs relative to the orbital fat posterior to the globe equator, while improving image contrast of EOM tendons relative to the surrounding pulley tissues more anteriorly. While gadodiamide enhanced images of the posterior orbit were less esthetic yet still adequate for analysis, in the anterior orbit gadodiamide made it possible to distinguish EOM tendons from the surrounding tissues.
with more posterior locations taken as negative and more anterior locations positive based on 2 mm image plane thickness (Clark et al. 1997). Anteroposterior distances for this purpose thus fell into 2-mm increments. Contractility was taken to be the change, in each image plane, in cross section from far to near target viewing.

The anteroposterior and mediolateral positions of the globe centers were determined from the area centroids in high-resolution axial images through the center of the lenses and optic nerves. Anteroposterior positions in axial images were corrected for small head translations by reference to bony landmarks. Gaze direction was determined relative to the MRI scanner coordinate system by projecting a line through the axis of symmetry of the lens to the sclera of each eye, and measuring the resulting angle using the function in National Institutes of Health Image. Accommodation was assessed indirectly from changes in lens shape by best fitting a bivariate ellipse to the lens outline in axial images. The minor axis of the elliptical fit was taken to represent anteroposterior lens thickness, which increases during accommodation. The major axis of the elliptical fit was taken to represent equatorial lens diameter, which decreases during accommodation.

**Results**

**Ocular rotation**

Axial MRI scans provided a clear demonstration of ocular changes during convergence from the far to the near target (Fig. 2). Resolution of MRI images was sufficient to verify appropriate binocular gaze shifts from far to near target viewing and to demonstrate lens changes appropriate to accommodation. It was considered reasonable to assume bifoveal fixation of the near and far targets because repeated questioning of subjects during scanning confirmed the absence of diplopia and because any significant eye movements during scan acquisition would have produced large and obvious motion artifacts (Demer and Miller 1999) that were conspicuously absent. Because, as for other laboratory methods of eye-position measurement, there was no means of determining absolute foveal direction from orbital MRI images, eye position data are reported as changes in angles of eye orientation from the far to near viewing conditions, with means and standard errors (SEM) for all eight subjects summarized in Table 1.

Excellent target positioning was confirmed for both eyes (Table 1). Axial scans showed mean adduction of the aligned eye during near target viewing of 0.3 ± 0.6° not significantly different from zero change from far target viewing. Quasi-sagittal scans (Fig. 4) showed mean supraduction during near target viewing of 0.6 ± 0.6° for the aligned and 0.5 ± 0.5° for the converging eye, not significantly different from zero change from far target viewing. The converging eye exhibited 22.4 ± 0.8° accommodation during near target viewing, geometri-

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<th>Table 1. Ocular changes with convergence</th>
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<td>Change With Convergence</td>
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<tr>
<td>Adduction, °</td>
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<td>Supraduction, °</td>
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<td>Anterior translation, mm</td>
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Values are means ± SE. * P < 0.001.
Ocular translation

The globes did not translate significantly during convergence (Table 1). Based on analysis of axial images, both eyes translated anteriorly: 0.2 ± 0.5 mm for the aligned eye, and 0.5 ± 0.5 mm for the converging eye (P > 0.05). Also based on axial images, both eyes translated nasally: 0.7 ± 1.2 mm for the aligned eye and 0.3 ± 0.8 mm for the converging eye (P > 0.05). There was an insignificant trend to reduction in interocular distance by 0.6 ± 0.3 mm with convergence (0.05 < P < 0.1). There was no significant vertical globe translation with convergence of either eye, as determined from quasi-coronal images by comparison of the globe center with the orbital centroid measured at the globe equator (Table 1).

Accommodation

The lenses of both globes changed shape significantly consistent with accommodation during convergence (Strenk et al. 1999). Anteroposterior lens thickness increased significantly by 0.6 ± 0.2 mm for the aligned and 0.5 ± 0.2 mm for the converging eyes (P < 0.001). Reductions in equatorial lens diameter of 0.1 ± 0.2 mm for the aligned and 0.2 ± 0.2 mm for the converging eye were not significant. Reduction of pupil size and ciliary body thickening were appreciated during convergence in some subjects but could not be analyzed quantitatively because these were not consistently within the resolution of the technique.

Extraocular muscle contractility

Contractility was evaluated by measurement using quasi-coronal images of the distribution of cross-sectional area along the length of each EOM (Fig. 3). To represent these data as true cross-sectional area perpendicular to the average linear path of each EOM, the cross-sectional areas measured in quasi-coronal image planes were adjusted by multiplying by the cosine of the mean angle between the EOM axes and the normal to the quasicoronal plane. This angle is also equivalent to half the angle formed by the intersections of the horizontal and vertical rectus pairs at the orbital apex. For the horizontal rectus EOMs, the correction angle determined from axial images was 20.2 ± 0.6° (mean ± SE, n = 16 orbits); for the vertical rectus EOMs, this angle determined from quasisagittal images was 20.2 ± 0.4°. All data below have thus been reduced by the cosine of this angle.

Behavior of EOMs in the converging eye is illustrated first to indicate the sensitivity of the technique, first for the MR muscle. Figure 5A plots mean (± SE) MR cross section for the converging eye as a function of anteroposterior distance in the orbit from 2-mm-thick image planes using the image plane containing the junction of the globe and optic nerve as reference plane zero (shown in 3rd row in Fig. 3). Most anteriorly as they approach their insertions, rectus EOMs thin and become noncontractile tendons (Fig. 2). As may be seen qualitatively in axial views such as Fig. 2, EOM cross section was greatest in the mid to deep orbit. Quantitatively, this is seen in Fig. 5A as a peak in the area distribution for distance viewing at −4 mm. Because the converging eye adducted during near viewing, the resulting MR contraction was evidenced by an increase in maximum cross section in the range of −6 to −16 mm (Fig. 5A). This contractile thickening may also be appreciated in Fig. 3, top, which contains images at −12 mm. Because the converging eye adducted, relaxation of its LR was evidenced by reduction in cross section in the range of −8 to −16 mm, as may be seen qualitatively in Fig. 3, top, and quantitatively in Fig. 5B.

Similar analyses of the horizontal rectus EOM cross sections were performed for the aligned eye. The posterior MR, which in the converging eye showed large contractile increases in cross section in multiple image planes, exhibited virtually no change in mean cross section during convergence in the aligned eye (Fig. 5C). The aligned eye LR showed no significant change in mean cross section during convergence (Fig. 5D).

Examination of the behavior of mean rectus EOM cross sections from multiple subjects has the disadvantage of being influenced by interindividual variations in EOM size. To minimize this effect, rectus EOM cross-section data were also analyzed as changes within individual subjects between far and near viewing. These changes are plotted for all eight rectus EOMs in Fig. 6, A–D, illustrating data for both the aligned and converging eyes on the same graphs for comparison. Recognizing that rectus EOM contractility is most evident in the mid to posterior orbit, convergence-related changes in pooled cross section were evaluated statistically in the six contiguous image planes extending posteriorly from the plane of maximum cross section in distance viewing. Statistical analysis was by paired, two-tailed t-test of differences from zero change using a 0.001 level of significance representing a Bonferroni adjustment from the usual level of 0.05 due to 48 simultaneous comparisons. For the converging MR, the expected significant contractile thickening in convergence was evident 10 and 12 mm posterior to the globe-optic nerve junction (Fig. 6A). For the converging LR, the expected significant relaxational thinning in convergence was evident posteriorly at −10 and −12 mm (Fig. 6B). Neither the aligned eye MR (Fig. 6A) nor LR (Fig. 6B) nor the vertical rectus EOMs in either eye (Fig. 6, C and D) showed significant changes in cross section during divergence.

The effect of convergence on oblique EOM cross sections is illustrated in Fig. 6, E and F. Because SO contractility is also best evaluated in the mid to posterior orbit (Demer and Miller 1995), the same statistical treatment was applied to it as for the rectus EOMs. There was no significant contractile or relaxational change in SO cross section during convergence in either the aligned or converging eye (Fig. 6E).

The highly curved path of the IO muscle requires a different analysis of contractility. Toward the origin more medially, the IO runs in a straight course perpendicular to the quasisagittal imaging plane but has small bulk. Lateral to the IR crossing at position 0 mm, the IO has significant bulk but curves out of the image plane to follow the globe circumference, and so cross-section measurements are unreliable. Contractility of the IO is thus best evaluated at mediolateral position 0, plane at the center of the IR crossing, the most temporal plane in which the IO path remains perpendicular to the sagittal plane (Demer et al. 1999). For both the converging and aligned eyes, the IO showed significant (P < 0.02, 2-tail t-test) contractile thickening at position 0 mm during convergence.
Rectus muscle paths

Cinematic presentation of quasicoronal images provides visualization of the changes described quantitatively in the following text and vividly demonstrates extorsion in convergence of the array of rectus EOMs in the aligned eye of the exemplary subject illustrated in Figs. 2-4. Cinematic presentation is also suggestive of extorsion of the rectus EOM array of the converging eye. However, quantitative EOM path analysis was not performed for the converging eye because path changes that might have been detected could not have been unambiguously assigned to the converged as opposed to the merely adducted state.

Centroid coordinates for aligned eye rectus EOMs were transformed into a normalized, oculocentric coordinate system before pooling across all eight subjects, enabling detection of small changes in paths. This transformation also compensates for variations in head position in the MRI scanner. It was possible to follow the anterior MR path reliably. The vertical position of the MR centroid \( \approx 20 \) mm posterior to globe center showed erratic changes (Fig. 7) attributable to a heavy representation of intramuscular motor nerve trunks observed histologically in this region in all of the rectus EOMs of human specimens (Lam et al. 2002). Because a central assumption of the use of the EOM area centroid as a surrogate for center of force is a uniform distribution of contractile fibers within it, the centroid data at least 20 mm posterior to globe center was not considered in extrapolating EOM paths in the much more anterior region of the pulleys. For the MR, linear regressions were taken of vertical centroid position against anteroposterior position (Fig. 7). During distance viewing, the slope of this regression was 0.009 ± 0.003 (mean ± SE, \( R^2 = 0.34 \)). During convergence, the slope of this regression was greater at 0.028 ± 0.004 (\( R^2 = 0.74 \)). Lack of overlap of the 95% confidence intervals for regression slopes indicates a significantly more superior path of the anterior MR in convergence than in distance viewing despite absence of any change in vertical eye position.

Due to interference from the lacrimal gland, it was not

![Diagram](https://example.com/diagram.png)
possible reliably to follow the anterior path of the LR. Linear regressions (not shown) on anterior path for both distant viewing and convergence accounted for less than 1% of the variance ($P > 0.7$).

Although more variable than the MR path, the anterior horizontal SR path could also be measured reliably during distance and converged viewing by the aligned eye (Fig. 8). As for the MR, linear regression of SR centroid position on anteroposterior position omitted data more than 18 mm posterior to globe center as the EOM centroids in the posterior region were influenced by dense intramuscular motor nerve arborization. During distant target viewing, the SR coursed...
medially with a slope of $0.049 \pm 0.016$ ($R^2 = 0.47$). During convergence, the slope of this regression was decreased to $0.020 \pm 0.021$ ($R^2 = 0.07$). Lack of overlap of the 95% confidence intervals for regression slopes indicates a significantly more lateral anterior SR path in convergence.

The anterior IR path could be reliably followed during distance and converged viewing by the aligned eye and showed a marked medial shift in convergence (Fig. 9). As for the other rectus EOMs, the most posterior part of the IR path was not included in linear regressions. During distance viewing, the IR coursed medially with a slope of $0.011 \pm 0.004$ ($R^2 = 0.27$). During convergence, the slope of this regression increased to $0.038 \pm 0.004$ ($R^2 = 0.70$). Lack of overlap of the 95% confidence intervals for regression slopes indicates a significantly more medial path of the IR in convergence.

**DISCUSSION**

The paradigm of asymmetric convergence has been a powerful tool in human behavioral studies as well as animal studies of neural control and proved suitable here for MRI investigation of human convergence. Analysis of high-resolution orbital MRI showed that precise horizontal and vertical target alignment could be maintained on one eye during binocular viewing of both a remote target and one requiring $22.4^\circ$ convergence. The near target employed here required 6 D accommodation. Resolution of MRI scans was sufficient to demonstrate anteroposterior lens thickening appropriate to accommodation (Table 1), confirming the finding of a study using an 8 D stimulus and a very small surface coil optimized for the anterior segment of the eye (Strenk et al. 1999).
Ocular translation during convergence

During alternate monocular viewing of aligned targets either remote or at 15 cm, Enright concluded from repeated photographic observations that the aligned eye translated temporally by as much as 200 μm during convergence (Enright 1980). While the present study’s single observation in each of eight subjects failed to show globe translations of either eye reaching statistical significance during binocular, asymmetrical convergence, the trend was for nasal, rather than temporal translation (Table 1). No significant vertical or anteroposterior globe translation was observed here. The current study employed binocular viewing with both accommodative and fusional convergence, while Enright’s experiment involved only accommodative convergence during monocular viewing of a near target. It is unclear if these or other methodological differences account for the differing findings from Enright.

Co-contraction in convergence?

In the current experiment, the converging eye adducted 22.4°. This large rotation was associated with significant contractile thickening in contiguous image planes representing the deep portion of the converging eye MR (Figs. 5A and 6A), and significant relaxational thinning in contiguous image planes representing the deep portion of the converging eye LR (Figs. 5B and 6B). These findings are not only not surprising but also required to confirm the sensitivity of the MRI technique. In the aligned eye, however, none of the rectus EOMs showed significant contractile changes in convergence (Figs. 5, C and D, and 6, A–D).

At first it seems difficult to reconcile the single-unit data from monkeys in convergence (Gamlin et al. 1989; Mays and Porter 1984), which apparently predicts horizontal rectus co-contraction and globe retraction, with the direct observations of monkey MR and LR co-relaxation in convergence (Miller et al. 2002) and the present failure in humans to demonstrate significant posterior globe translation (Table 1). However, the reasoning underlying this conundrum assumes homogeneous EOM structure and behavior typical of a final common motor pathway (Miller et al. 2002). Several reasons to doubt such assumptions have been noted (Miller et al. 2002), including the APH’s proposal of specialization of the GL for ocular rotation and OL for pulley translation (Demer et al. 2000; Oh et al. 2001b). The studies in monkey correlated angular eye position with single-unit behavior, assuming that all abducens motor neurons are involved with ocular rotation. However, only 27% of all units innervating cat LR project to both the OL and GL, with the majority of units selective to only one layer or the other (Shall and Goldberg 1995). Based on the anatomy, tension recorded as by Miller et al. in the insertional tendons of rectus EOMs would be expected to be dominated by activity of GL units. To date, no study has selectively recorded such units, so that available data probably represent a mixture of OL and GL units.

The current data on EOM cross sections also fail separately to resolve GL and OL behavior. While the two layers can occasionally be distinguished using contrast perfusion MRI (Oh et al. 2001a) or by the adipose interlaminar septum usually visible in the human IR (Demer 2002), MRI lacks the spatial resolution required here. It is therefore possible that structurally compartmental behavior in aligned eye EOMs might have escaped detection. For example, in a given overall EOM cross section, GL relaxation might have been obscured by OL contraction and vice versa. Were this the case, GL force as measured at the insertional tendon by a transducer such as employed by Miller et al. might have indicated reduced EOM tension, while the overall impression from MRI might have been, as in this case for the aligned eye, unchanged horizontal rectus contractility in convergence. Besides OL and GL homogeneity, the LR appears to have superior and inferior subdivisions based on segregated patterns of innervation (Lam et al. 2002) and a distinct physical separation often directly visible in the deep orbit by MRI in living subjects (Demer and Kono, unpublished observations). These subdivisions might conceivably behave differently during convergence than during conjugate gaze. Finally, it is not clear if EOM contractility is

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\text{Inferior Rectus Path} & \\
\text{Distance} & \quad \text{Convergence} & \quad \text{Mean ± SE}
\end{align*}
\]

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\begin{align*}
\text{Horizontal Position} & \quad \text{mm} \\
\text{Lateral} & \quad \text{Medial} \quad \text{Anteroposterior Position} - \text{mm} \\
\text{Anterior} & \quad \text{Posterior}
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\[
\begin{align*}
\gamma = -0.011 x - 0.102 & \quad \text{r}^2 = 0.27 \\
\gamma = -0.038 x - 0.674 & \quad \text{r}^2 = 0.70
\end{align*}
\]
uniform along the anteroposterior lengths of EOMs, and it is further doubtful if EOM fiber tensions are uniformly transmitted from origin to insertion. While Mayr reported that the feline OL fibers run the entire extent of the EOM (Mayr et al. 1975), Alvarado found a variation in fiber number along the length of the feline IO muscle (Alvarado and Van Horn 1975). Gradual distal reduction in the number of IR and LR fibers has been reported in rabbit (McLoon et al. 1999). Quantitative human data suggest a region of relative constancy in the number of fibers in each of the rectus EOMs in the region 9–21 mm from the orbital apex, but there is no zone of relative constancy in monkey MR (Oh et al. 2001b). In both humans and monkeys, there is a gradual decline in the number of fibers over the anterior 6 mm of the OL and the anterior 4–12 mm of the GL (Oh et al. 2001b). Such numerical variation along EOM length suggests that the fibers posteriorly bifurcate and more anteriorly reunitie in myomymous junctions (McLoon et al. 1999). Series and parallel couplings of fibers would imply that transmission of the contractile force of any one fiber to aggregate EOM force would depend on the contractile state of other fibers (Miller et al. 2002). This is consistent with the observation in cat LR that simultaneous stimulation of multiple motor units in about 25% of cases generates less total tension than the sum of the tensions of each motor unit stimulated separately, a form of nonlinear summation (Goldberg et al. 1997). It seems doubtful that any single currently available technique, neither GL tension measurement at the inserational tendon nor MRI of EOM cross sections, could fully characterize the complex EOM contractile behavior in a manner that would correlate closely with motor neuron firing. Multiple complementary techniques will be required to understand neural control of EOMs.

Kinematics of extorsion in convergence

Early investigators considered only direct oculorotary actions of the EOM insertions on the sclera. Allen and Carter attributed the extorsion in asymmetrical convergence to IO contraction (Allen 1954). Enright considered the supposition that differential activity in the IO and SO might cause the extorsion (Enright 1980). Single-unit recordings in monkey trochlear nucleus showed a greater reduction in activity in convergence than conjugate adduction, prompting Mays et al. to propose that SO relaxation mediates excyclotorsion in convergence and, because a tertiary action of the SO is abduction, might also compensate for insufficient LR relaxation (Mays et al. 1991).

Later recognition that pulleys influence the directions of rectus EOM force led to the suggestion that L2 and excyclotorsion in convergence could be mediated by shifts in rectus pulley locations (Demer et al. 2000). Shifts of any rectus pulley out of anteroposterior alignment with the scleral insertions would, in theory, impart a torsional action. Appropriate anteroposterior pulley shift could then maintain mechanical behavior consistent with a temporally tilted Listing’s plane. An explicit, binocularly symmetric reconfiguration of rectus pulleys (Fig. 1F) was proposed to account for L2 (Demer et al. 2000): the vertical rectus pulleys were proposed to shift nasally, the horizontal rectus pulleys were proposed to shift temporally. The present findings rule out that proposed mechanism as the basis for L2. Paths of three of the rectus EOMs of the aligned eye shifted significantly to reflect shifts of their pulleys, but only the IR shifted nasally as predicted. In convergence, the MR shifted superiorly, and SR temporally, for an overall extorsional shift paralleling the presumed ocular extorsion. The anterior LR path in the aligned eye could not be adequately resolved to be confident of any effect, but the qualitative impression from images of the converging eye suggested that a similar extorsional shift occurred bilaterally.

Could pulley reconfiguration still underlie extorsion in convergence? The anteroposterior locations of normal human rectus pulleys have been determined from EOM path inflections in unconverged secondary gaze positions for the same coordinate system employed here (Clark et al. 2000). The MR pulley was 3 mm posterior to globe center in that study, a point at which the linear regressions illustrated in Fig. 7 of the current paper indicate a 0.3-mm superior shift of the MR path with convergence. The SR pulley was 7 mm posterior to globe center, a point at which the linear regressions illustrated in Fig. 8 of the current paper indicate a 0.4-mm lateral shift of the SR path with convergence. The IR pulley was 6 mm posterior to globe center, a point at which the linear regressions illustrated in Fig. 9 of the current paper indicate a 0.4-mm medial shift of the IR path with convergence. It may be concluded that each of the rectus pulleys for which reliable data were available shifted about the same amount with convergence, 0.3–0.4 mm. Data on EOM paths anterior to the pulleys are sparse and often contributed by a single observation at each anteroposterior location rather than a more reliable average of several observations available more posteriorly. It is thus not possible to determine from MRI images if the torsional shift of the scleral insertions on the globe exceeded the torsional shift of the pulleys because the most anterior data points in Figs. 7–9 are represented by only one or a few individual subjects. However, previously published data on pulley locations indicates that they are located as if on the circumference of a circle roughly 24.5 mm in diameter, almost identical to globe diameter, but 8 mm posterior to the equator and thus 16 mm posterior to the rectus insertions on the sclera. A pulley shift of 0.4 mm along a circumference of this diameter represents about 1.9° extorsion. This amount is similar to but slightly less than the value of 1.68 ± 1.12° ocular extorsion observed for 37° convergence using a photographic technique (Allen and Carter 1967).

Effectors of pulley repositioning in convergence

The anteroposterior movements of rectus pulleys appear to be actively coordinated with ocular rotations through the action of the OL of each rectus EOM (Demer et al. 2000; Kono et al. 2002a). Quantitative analysis of pulley shifts during convergence suggests for several reasons that this is a coordinated, active process as well. First, anatomic considerations make it impossible for the rectus pulleys simply to be dragged by the extorting globe surface. Being 8 mm posterior to the globe equator and radially displaced from the globe surface, the rectus pulleys must allow the posterior globe surface to slide freely beneath them during horizontal and vertical ocular rotations. This is consistent with anatomical evidence of absence
of direct tissue connections between the globe and pulleys (Demer et al. 1995b; Kono et al. 2002b). Second, each rectus pulley is about 16 mm posterior to the scleral insertion (Demer et al. 2000; Kono et al. 2002a). If torsional pulley shift was simply due to passive dragging of the four rectus pulleys by the insertions of the torting globe 16 mm more anteriorly, the pulleys would shift a much smaller distance than the insertions. The preceding analysis suggests that the rectus pulleys actually shift by about the same distance as their scleral insertions, consistent with active pulley repositioning as diagrammed in Fig. 10. A third reason that torsional pulley shift in convergence is likely to be active is that the pulleys exhibit a strong mechanical resistance to transverse displacement. Even after surgical transposition of the MR insertion about 10 mm (1 tendon width) superiorly on the sclera that would correspond to globe torsion of 47°, postoperative MRI showed that the MR pulley shifted superiorly only about 0.5 mm (Fig. 5 of Clark et al. 2000; Kono et al. 2002a). If torsional pulley shift was actually due to insufficiency of the technique or to an actual lack of MR relaxation. However, in the monkey there was reduced single-unit firing in the trochlear nucleus during 16° convergence associated with 1.05° excyclotorsion (Mays et al. 1991), consistent with SO relaxation. No direct SM or striated EOM insertions exist to superiorly displace the MR pulley during convergence. However, the MR pulley is elastically coupled to both the SR and IR pulleys (Kono et al. 2002b), both of which as noted in the preceding text receive direct coupling from oblique EOM OLs.

Two muscle mechanisms appear capable of putative active torsional pulley repositioning. Smooth muscle (SM) exists in the pulley suspensions, particularly in a dense band from the IR to MR pulleys that appears suited to medially displace the IR pulley (Demer et al. 1997; Kono et al. 2002b; Miller et al. 2003). However, the orbital SM is not uniformly distributed among the four rectus pulley suspensions and is minimal in the suspensory band from the IR to the LR pulleys. The bulk of any active torsional shift of rectus pulleys is likely to be accomplished by the oblique EOM OLs, which are bilaminar similar to rectus EOMs. Fibers of the IR OL insert on the conjoined IO-IR pulley, on the connective tissue sheath of the IO temporal to the IR pulley, and even on the inferior aspect of the LR pulley (Demer 2002; Demer et al. 2001; Kono et al. 2002b). Contraction of the IO OL would displace the IR pulley nasally and the LR pulley inferiorly, thus extorting half of the rectus pulley array in a manner that could naturally coordinate with extorsion produced by the IO GL. The current MRI data showed a contractile increase in IO cross section at image plane 0 during convergence, consistent with this mechanism of torsional pulley repositioning. The OL of the SO terminates posterior to the trochlea on the SO sheath, which along with the SO tendon is reflected through the trochlea (Demer 2001). While the SO tendon inserts on the sclera to transmit the force of GL contraction, the SO sheath inserts on connective tissues, including the medial aspect of the SR pulley (Demer 2001). Thus contraction of the SO OL would translate the SR pulley nasally as appropriate to intorsion, and relaxation of the SO OL would allow suspensory tissue elasticity to translate the SR pulley temporally as associated with extorsion. Nasal repositioning of the SR pulley would naturally coordinate with globe intorsion produced by the SO GL. The current MRI data did not indicate significant reduction in SO cross-sectional area during the pulley excyclotorsion associated with convergence; this may simply be due to insufficient sensitivity of the technique or to an actual lack of SO relaxation. However, in the monkey there was reduced single-unit firing in the trochlear nucleus during 16° convergence associated with 1.05° excyclotorsion (Mays et al. 1991), consistent with SO relaxation. No direct SM or striated EOM insertions exist to superiorly displace the MR pulley during convergence. However, the MR pulley is elastically coupled to both the SR and IR pulleys (Kono et al. 2002b), both of which as noted in the preceding text receive direct coupling from oblique EOM OLs.

**FIG. 10.** Diagrammatic illustration of proposed coordinated pulley torsion consistent with current data. Top: path of MR muscle during distance viewing (left) and convergence (right). Coordinated extorsion of the globe and pulley maintains a vertical rotational axis for the MR in convergence, leaving unchanged the distances and geometric relationships consistent with half angle shifts in velocity axis diagrammed in Fig. 1, A and B, and D and E.
Kinematics of coordinated pulley torsion

The simplest interpretation of the present findings is that ocular extorsion in convergence is associated with quantitatively similar, coordinated extorsion of the rectus pulley array (Fig. 10, bottom right). This arrangement has important kinematic implications. While with fixed rectus pulleys globe torsion imparts a new torsional action to each of the rectus EOMs (Miller et al. 1999) that would surely complicate neural control, coordinated pulley and globe torsion would not do so. In convergence, none of the essential geometric relationships of the APH (Fig. 1, A, B, D, and E) would be altered for each eye considered individually; the change would merely be in the differing torsional orientations of each eye’s globe and orbit in primary position (Fig. 10). In conjunction with well-documented anteroposterior coordination of rectus pulley position during horizontal and vertical gaze shifts (Demer et al. 2000), coordinated pulley and globe torsion would result in shifts of the velocity axis of each EOM equal to half the shifts in ocular orientation (Fig. 10). This is a necessary and sufficient condition for compliance with Listing’s Law L1 if one assumes a simple torsional offset of Listing’s plane equal to pulley array torsion and preserves the advantage of commutativity with respect to the order of horizontal and vertical rotations. A single torsional offset of Listing’s plane does not amount to L2, however, because L2 specifies a temporal tilt in the orientation of the Listing’s planes for the two eyes representing a systematic change in torsion with vertical eye position. It appears that L2 requires a vertical gaze-dependent change in coordinated pulley positions with predicted greater rectus pulley extorsion in convergence looking down and less extorsion, or even intorsion, when looking up. Orbital MRI during asymmetrical convergence at different vertical elevations might test this prediction.

Another instance of ocular torsion that violates L1 is the vestibuloocular reflex (VOR), which stabilized images on the retina during head rotation or tilt from the upright position. While L1 specifies a shift in the ocular rotational axis half that of the shift in ocular orientation, an ideal VOR has an axis fixed in the head, and thus independent of ocular orientation. During head rotations, the VOR velocity axis rotates by 0% (Misslisch and Hess 2000; Palla et al. 1999) to 25% (Misslisch et al. 1994) of the ocular angle, contrasting with a 50% rotation required by L1. Non-Listing VOR kinematics cannot be explained by anteroposterior shifts in rectus pulley locations (Misslisch and Tweed 2001). For the VOR, the oblique EOMs must play important roles. The oblique EOMs are configured to maintain a half angle behavior orthogonal to rectus half angle behavior, appropriate to commanded violations of Listing’s Law as during the VOR (Demer 2001). Observed VOR kinematics are consistent with high gain pitch and yaw responses mediated by mechanisms consistent with the coordinated control postulate of the APH, but a lower gain roll response consistent with the observed behavior of the torsional VOR (Misslisch and Tweed 2001). Another instance of the VOR is static ocular counter-rolling in response to maintained head tilt relative to gravity. Recordings from burst neurons in monkeys are compatible with torsional shift of rectus pulleys transverse to the EOM axes in the direction of ocular counterroll induced by static head tilt (Scherberger et al. 2001), analogous to the coordinated torsional pulley shift observed here in convergence. In monkeys the displacement plane for 3-D eye positions during pursuit and saccades also shifts opposite to changes in head orientation relative to gravity (Hess and Angelaki 2002). Another way of describing the proposed overall arrangement is coordinated control of the rectus pulleys consistent with a Listing’s plane with supplementary coordinated torsion of the rectus pulley array mediated by neural commands to the oblique EOMs providing instantaneous torsional offset to Listing’s plane as required by vestibular or binocular sensory demands.

An interesting problem for the VOR is presented by extorsion in convergence. Simultaneous extorsion of the rectus pulley arrays of the two eyes misaligns the pulling directions of their MR-LR pairs. In a caninotopic reference, the extorsion would give the LR a depressing action and the MR an elevating action. A skewing, with elevation of the adducting eye, would result from the horizontal VOR in response to pure yaw rotation unless complex innervalritional adjustments were simultaneously made in innervation to all of the cyclovertical EOMs. Projections of the semicircular canals to the antagonist EOM pairs have been represented in matrix form that reflects EOM geometry (Robinson 1982; Smith and Crawford 1998). This matrix would require modification in convergence to avoid a skewing of the converged VOR. It is not clear whether such skewing is actually avoided for the yaw VOR in convergence.

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