Magnetic Resonance Imaging
of Human Extraocular Muscles During Static Ocular Counter-rolling

Extraocular Muscle MRI During Ocular Counter-rolling
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Abstract

The rectus extraocular muscle (EOM) pulleys constrain EOM paths. During visual fixation with head immobile, actively-controlled pulleys are known to maintain positions causing EOM pulling directions to change by half the change in eye position. This pulley behavior is consistent with Listing’s Law (LL) of ocular torsion as observed during fixation, saccades, and pursuit. However, pulley behavior during the vestibulo-ocular reflex (VOR) has been unstudied. This experiment investigated ocular counter-rolling (OCR), a static torsional VOR that violates LL but can be evoked during magnetic resonance imaging (MRI). Tri-planar MRI was performed in 10 adult humans during central target fixation while positioned in right and left side down positions known to evoke static OCR. EOM cross sections and paths were determined from area centroids. Paths were used to locate pulleys in 3-D. Significant (P<0.025) counter-rotational repositioning of the rectus pulley arrays of both orbits was observed in the coronal plane averaging 4.1 deg (maximum 8.7 deg) from right to left side down positions for the inferior, medial, and superior rectus pulleys. There was a trend for the lateral rectus averaging 1.4 deg. Torsional shift of the rectus pulley array was associated with significant contractile cross section changes in the superior and inferior oblique muscles. Torsional rectus pulley shift during OCR, which changes pulling directions of the rectus EOMs, correlates with known insertions of the oblique EOM orbital layers on rectus pulleys. The amount of pulley reconfiguration is roughly half of published values of ocular torsion during static OCR, an arrangement that would cause rectus pulling directions to change by less than half the amount of ocular torsion.
Introduction

In addition to their neural commands, the oculorotary actions of the extraocular muscles (EOMs) depend on their paths in the orbit. Miller first suggested that pulleys influence EOM paths (Miller 1989; Miller and Demer 1995). Over the past decade soft pulleys have been identified and described in detail that inflect rectus and inferior oblique (IO) EOM paths (Demer 2000; Demer et al. 1995; Demer et al. 1997; Kono et al. 2002b). The coronal plane locations of rectus pulleys have been shown by magnetic resonance imaging (MRI) to be uniform and stable with respect to horizontal and vertical gaze shifts in normal subjects (Clark et al. 1997). The global layer of each rectus EOM, containing about half of total fibers (Oh et al. 2001b), passes through the pulley and becomes contiguous with tendon to insert on the globe. The orbital layer of each rectus EOM, containing the remaining about half of the fibers, inserts on the pulley (Demer et al. 2000; Oh et al. 2001b). This arrangement allows rectus pulleys to move anteroposteriorly along the EOMs to maintain a constant distance from the scleral insertion during EOM activation.

The existence of orbitally-stabilized pulleys implies that the force directions of rectus EOMs change with eye position, and so has important implications for the neural commands required to control eye movements (Demer 2004; Miller 1989; Miller and Demer 1995; Raphan 1997, 1998). It has been argued that the fundamental basis of pulley properties is the problem of commutativity of the sequence of ocular rotations (Quaia and Optican 1998; Raphan 1998; Schnabolk and Raphan 1994a; Schnabolk and Raphan 1994b). One problem of non-commutativity is avoided if the ocular rotational velocity axis shifts by half of the change in ocular orientation with respect to a primary position, for under these conditions the effect of non-commutativity on EOM actions becomes negligible in neural computation of the relationship between the phasic and tonic components of the saccadic command (Quaia and Optican 1998; Raphan 1998). For eye positions beginning in primary position, half angle behavior is equivalent.
to Listing’s Law (LL), a quantitative description of ocular torsion whose corollary and original statement is that any eye orientation can be reached from a primary position by rotation about a single axis lying in Listing’s plane (LP) (Tweed and Vilis 1990). Recent neurophysiological observations in behaving monkeys suggest that LL has a mechanical basis: motoneurons innervating vertical rectus and oblique EOMs do not encode the torsion corresponding to half angle behavior during pursuit (Ghasia and Angelaki 2005), while direct electrical stimulation of the abducens nerve evokes horizontal saccades conforming to LL (Klier et al. 2005). Locations and mechanical shifts in rectus pulley positions underlying half angle behavior were predicted by the active pulley hypothesis (Demer et al. 2000), and later quantitatively confirmed in humans by MRI in tertiary gaze positions (Kono et al. 2002a). The IO muscle also has a soft pulley, mechanically coupled to the inferior rectus (IR) pulley (Demer et al. 2003b), that moves anteroposteriorly to maintain an analogous half angle behavior (Demer et al. 2003b). Despite its fixed pulley, it has been argued that because the path of the SO muscle’s reflected tendon is across the ocular diameter, the pulling direction of the SO also changes by half of horizontal and vertical eye position (Demer 2004).

Taken in isolation, orbital geometry might seemingly imply obligatory conformity of ocular kinematics to LL. However, the angular vestibulo-ocular reflex (VOR), which ideally produces ocular rotations opposite in direction to head rotation, could not do so if the axis of eye rotation were constrained to lie in any particular relationship to LP. The torsional VOR, in response to roll rotation about an anteroposterior axis, is an extreme case demonstrating violation of LL by ocular rotations nearly orthogonal to LP (Bockisch and Haslwanter 2001; Suzuki et al. 1997).

Although the dynamic torsional VOR clearly violates LL, static roll head tilt only torsionally offsets, but does not abolish, LP (Bockisch and Haslwanter 2001; Crawford and Vilis 1991; Furman and Schor 2003; Haslwanter et al. 1992; Hess and Angelaki 2003; Suzuki et al. 1997). Listing’s plane remains generally stable even during prolonged periods in darkness, albeit with some thickening in the torsional dimension during drowsiness (Suzuki et al. 1997). The
ocular torsion arising from static head tilt is known as ocular counter-rolling (OCR). An OCR of 3 – 7 deg (Bockisch and Haslwanter 2001; Markham and Diamond 2002-2003) results from 90 deg head inclination relative to gravity, illustrating that the typical gain (eye roll/head roll) of static OCR is only about 0.1 – 0.2 in monkey (Suzuki et al. 1997), and ranges from as little as 0.08 (Bockisch and Haslwanter 2001) to about 0.10 – 0.27 (Averbuch-Heller et al. 1997; Collewijn et al. 1985; Schworm et al. 2002) in humans.

While arising from the otolith organs (Schor et al. 1984), static OCR is not implemented via direct otolith input to the motorneurons, but via the neural integrator, whose inactivation in monkey abolishes OCR (Crawford et al. 2003b). Saccades during OCR are initiated from positions out of the LP prevailing with the head upright, leading to the supposition that the process responsible for LL is altered based upon otolithic input received via the neural integrator (Crawford and Guitton 1997; Glasauer et al. 2001). Mathematical models of the control of such saccades assume that the EOMs and associated orbital connective tissues constitute a “linear plant” that can be driven by an input that is the time derivative of eye position, rather than angular velocity, but that the configuration of this plant is otherwise unaltered by otolith input (Crawford et al. 2003a; Crawford et al. 2003b; Glasauer et al. 2001).

The current paper considers the possibility that otolith input may alter the configurations of the rectus EOMs in the orbit via repositioning of their pulleys. While the effect of static head tilt on rectus pulleys has not previously been investigated, MRI evidence of pulley behavior during binocular convergence suggests that the pulleys might shift transversely. Convergence in central gaze is associated with excyclotorsion (Allen and Carter 1967; Bruno and van den Berg 1997; Mikhael et al. 1995; Minken and Van Gisbergen 1994; Misslisch et al. 2001; Mok et al. 1992; Somani et al. 1998). The rotational axes of each eye remain in separate LPs that tilt 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 described as the binocular extension of LL (van Rijn and van den Berg 1993). Because orbital MRI in humans has demonstrated
extorsional repositioning of the rectus pulley array during convergence, it has been proposed that such pulley torsion may be coordinated with ocular torsion (Demer 2004; Demer et al. 2003a).

It is now recognized that under conditions where the head is free to move, LP shifts and tilts almost continuously (Crawford and Guitton 1997; Hess and Angelaki 1997a, b; Tweed et al. 1995). Most authors have considered this phenomenon to be a function of neural commands to a fixed ocular motor plant (Crawford et al. 2003a; Crawford et al. 2003b; Glasauer et al. 2001), perhaps via the coordinate reference system of the neural integrator (Hess and Angelaki 1997b). Based on pulley behavior during convergence, however, torsional reconfiguration of rectus pulleys has been alternatively postulated to account for some of the changes in ocular kinematics during vestibular stimulation (Demer 2004). Since systematic changes in rectus EOM pulling directions would affect all other eye movements that occur during static head tilt, the postulated torsional pulley reconfiguration would explain why static head tilt modulates several behavioral and neurophysiological features of ocular motor control. This includes LP orientation during visually-guided movements such as pursuit and saccades (Hess and Angelaki 2003), the preferred directions of midbrain saccadic burst neurons (Scherberger et al. 2001) believed common to the saccadic and pursuit systems (Cullen and McCrea 1993; Lisberger et al. 1994; Scudder and Fuchs 1992), the preferred saccadic directions of collicular neurons (Frens et al. 1998), and vestibular quick phases (Hess and Angelaki 1997b). Such putative changes in EOM pulling directions might account for errors in saccade direction during OCR (Klier and Crawford 1998), and for tilting of saccade axes during analogous torsional shifts of LP induced by unilateral inactivation of the rostral interstitial nucleus of the medial longitudinal fasciculus (riMLF) (Crawford and Vilis 1992). Nevertheless, since a 3-D sensorimotor transformation involving eye position is geometrically inevitable in central ocular motor processing, many investigators have favored models in which LL kinematics are not emergent properties of orbital mechanics, but instead are implemented neurally in 3-D, pre-motor commands to the EOMs (Angelaki 2003; Crawford et al. 2003a; Klier et al. 2003; Tweed and Vilis 1990, 1987). These pre-motor centers
have been proposed to receive atavistic otolith inputs tending to align LP with gravity (Hess and Angelaki 2003), and so would not need to be associated with rectus pulley repositioning.

As noted in a recent review (Crawford et al. 2003a), it is impossible to adequately distinguish neural from mechanical contributions to ocular kinematics without a clear understanding of the EOM mechanics that neural signals command. No data have been available concerning rectus pulley behavior during any VOR. While the temporal resolution of MRI is inadequate for study of the more widely-studied dynamic VOR, the highly persistent (Suzuki et al. 1997) OCR of 3–7 deg (Bockisch and Haslwanter 2001; Markham and Diamond 2002-2003) mediated by the otoliths can be maintained indefinitely by 90 deg head inclination relative to gravity as in an MRI scanner. This OCR, which is a static torsional VOR, is associated with addition of a constant torsion to all eye positions, shifting LP along the torsional axis (Crawford and Vilis 1991; Frens et al. 1998; Haslwanter et al. 1992; Hess and Angelaki 2003; Suzuki et al. 1997). It is important in understanding and modeling eye head coordination to know if static OCR changes the pulling directions of the rectus EOMs, which would be the case unless the rectus pulleys shifted torsionally to exactly match ocular torsion. The current study aimed to address these issues by evaluating EOM paths and contractility by MRI during the paradigm of sustained, on-side head positioning.

**Materials and Methods**

**Subjects.** Ten adult volunteers aged 27 ± 5 yrs (mean ± standard deviation, SD) were recruited by advertisement and gave written informed consent according to a protocol conforming to the Declaration of Helsinki and approved by the Institutional Review Board 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, and normal stereopsis of 40 arcsec by Titmus testing.

**Magnetic Resonance Imaging (MRI).** 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; Clark et al. 1998b; Clark et al. 1999; Demer and Miller 1999). Subjects were scanned in both the right side down and left side down positions while lying on the scanner bed cushioned on folded linens. During imaging, subjects fixated at a distance of 2 cm the proximal end of a fine optical fiber illuminated from its distal end by a red light emitting diode. This afocal fixation target was presented to the upper eye in all cases as head supporting structures frequently occluded the lower eye. Initially, a triplanar (roughly axial, coronal, and sagittal) scan was obtained in 5 mm thickness image planes at 940 microns in plane resolution using a 256 x 256 matrix over a 24 cm square field of view (FOV). These images, axial examples of which are shown in the insets in Fig. 1, were used to verify correct head positioning relative to the earth-vertical coordinates of the scanner. If unsatisfactory, the subject’s head was repositioned and the triplanar scan repeated until positioning was verified to be correctly on side without other significant rotations. A true axial image including both orbits was then obtained at 3 mm thickness using a 256 x 256 matrix over a 10 cm FOV. This true axial image was used to place sets of 18 contiguous, 2 mm thick quasicoronal images in a plane perpendicular to the long axis of each orbit using a 256 x 256 matrix over an 8 cm FOV, yielding a pixel resolution of 312 microns (Fig. 1). This scan required 3 min, 40 s for acquisition. In most subjects the paramagnetic MRI contrast agent gadodiamide (0.05 mmol/kg) was given intravenously before the first quasicoronal scan in each left or right side down position to improve the contrast of EOMs against connective tissue in the anterior orbit (Oh et al. 2001a). Quasicoronal image sets were obtained first in the right, then in the left orbit. Sets of 17 contiguous, 2 mm thick quasisagittal images in planes parallel to the long axis of each orbit were then obtained using a 256 x 256 matrix over an 8 cm FOV, yielding a pixel resolution of 312 microns (Fig. 2). This scan required 3 min, 31 s for acquisition. Quasisagittal image sets were obtained first in the right, then in the left orbit.
**Analysis.** Digital MRI images were transferred to Macintosh® computers (Apple Computer, Cupertino, CA), converted into 8-bit tagged image file format (TIFF) using locally developed software, and quantified using the program *NIH Image* (W. Rasband, National Institutes of Health; available by ftp from zippy.nimh.nih.gov or on floppy disk from NTIS, 5285 Port Royal Road, Springfield, VA 22161, part number PB95-500195GEI).

Fig. 1. Quasicoronal images at close to the rectus pulleys (approximate level shown on sagittal view in Fig. 2.) in central gaze from representative subject in right side down (upper row) and left side down (lower row) head positions. Images are conventionally depicted as would be seen from behind the subject, so that the right orbit is shown on the left, and left orbit is shown on the right. Axial insets demonstrate actual head position relative to gravity, while quasicoronal images have all been rotated upright for visualization. Green lines connect the centers of rectus EOM cross sections, and suggest that array of rectus pulleys counter-rotated in the coronal plane opposite the direction of head tilt. The effect was incyclotorsion of the rectus pulley array of the lower orbit, and excyclotorsion of the rectus pulley array of the upper orbit.
For quantitative analysis, images of left orbits were digitally reflected to the configuration of a right orbit. In MRI images analyzed, the cross section of each EOM was digitally outlined and its area automatically determined. The location of each rectus EOM was described by a single point in each quasicoronal image plane using the “area centroid” function of the *NIH Image* program. The area centroid of a cross-section is equivalent to the center of gravity of a shape of uniform density and thickness, and as first suggested by Miller (Miller 1989), represents the best estimate of the position of EOM force assuming uniform force distribution over cross sectional area (Clark et al. 2000). Next, approximating the globe as spherical, its 3-D center was determined to subpixel resolution in scanner coordinates using curve fitting to three separate cross-sectional images of the globe as previously described (Clark et al. 2000). Rectus EOM positions were then translated to place the 3-D coordinate origin at the computed globe center. The three Cartesian coordinates were positive lateral, positive superior, and positive anterior as illustrated in (Clark et al. 2000). All EOM path data were rotated into a standard orientation based on a previously published rotation matrix, using as orientation references the interhemispheric fissure of the brain and the junction of the superior ethmoid air sinus and the orbit (Clark et al. 2000). After data was transformed, the scanner coordinates were scaled to normalize each globe to the measured average diameter of 24.3 mm found by MRI in an earlier study of normal subjects (Clark et al. 2000). This permitted averaging of 3-D rectus EOM paths over the group of subjects in the manner previously published (Clark et al. 2000).

Torsion of EOM paths and pulleys was defined as rotation about the long axis of the orbit, analogous to the definition of ocular torsion as globe rotation around the line of sight. Intorsion was considered to represent medial shift of the SR, inferior shift of the MR, lateral shift of the IR, and superior shift of the LR.

Contractility of the oblique EOMs was inferred from distributions of cross sectional areas along their lengths. For evaluation of SO contractility, sets of coronal image planes were aligned on the globe-optic nerve junction for far target viewing, and averaged over all subjects for each
EOM and target location. The globe-optic nerve junction was designated as plane zero, 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. For evaluation of IO contractility, sets of quasisagittal image planes were aligned on the center of the IR crossing. The image plane containing the center of the IR crossing was designated to be image plane zero, with more medial locations taken as negative and more lateral locations positive based on 2 mm image plane thickness (Demer et al. 2003a; Demer et al. 2003b). For both the SO and IO EOMs, contractility was taken to be the change, in each image plane, in cross section from the right ear down to left ear down positions. Due to the highly curved path of the IO lateral to its pulley, however, IO contractility is reliably assessed only in image plane 0 (Demer et al. 2003a; Demer et al. 2003b).

Fig. 2. Quasisagittal MRI images from representative subject in ipsilateral side down and contralateral side down positions showed contractile thickening of the inferior oblique (IO) muscle contralateral to the lower orbit. This was designated image plane 0, the plane where the IO crossed the center of the inferior rectus (IR) muscle. The left side of these images is anterior, where the cornea and lens are evident. The approximate coronal plane of the rectus pulleys is indicated in green. LPS - levator palpebrae superioris muscle. ON - optic nerve. SR - superior rectus muscle.
Results

Rectus Pulley Positions. The axial images used to verify correct head positioning also indicated by the positions of the crystalline lenses the absence of gross convergence in all subjects (Fig. 1 insets). Quasi-coronal MRI images permitted rectus EOM cross sections to be traced anteriorly at least to the level of the pulleys, and with gadodiamide contrast nearly to the scleral insertions. In general, no single image plane contained all four rectus pulleys, but the anterior rectus EOM positions can be inspected in individual images to suggest approximate pulley locations. The four rectus paths near the pulleys were arrayed as roughly the arms of a cross. Representative quasi-coronal MRI images in Fig. 1 illustrate that this cross rotated in the quasi-coronal plane in the direction opposite head rotation. Qualitatively, it appeared that when the ipsilateral orbit was oriented downward, its SR pulley shifted nasally and its LR pulley shifted superiorly, its IR pulley shifted laterally, and MR pulley shifted inferiorly relative to when the ipsilateral orbit was oriented upward (Fig. 1). While the quasi-coronal imaging planes in Fig. 1 were chosen to approximate the plane containing the four rectus pulleys in central gaze, this arbitrary choice of imaging plane could not assure depiction of EOM cross sections at the pulleys. Differences in individual pulley locations relative to individual imaging planes could alter apparent EOM positions, and could alter apparent shifts in EOM positions due to head positioning, to differing degrees for the four rectus EOMs. For example, it cannot be determined from inspection of the single image plane of Fig. 1 if pulley shifts are equal for all pulleys in the same orbit, or are conjugate between orbits. For this reason, pulley behavior is better characterized by a 3-D analysis of contiguous image sets than by inspection of any single MRI plane. Precise determination of pulley locations required analysis of EOM cross sections in multiple image planes, as well as transformation of this data into a standardized coordinate system.
The rectus EOM paths were analyzed quantitatively by tracing their area centroids through the anterior orbits. Data for left orbits were mathematically reflected to the orientation of right orbits, and the quasicoronal plane coordinates for all rectus EOM pulleys were averaged across both orbits of all subjects for the ipsi- and contralateral ear downward positions. After transformation into the standard oculocentric coordinate system and pooling of data across all available orbits of all subjects, the superior coordinates of the horizontal rectus EOMs, and the lateral coordinates of the vertical EOMs, are plotted along the anteroposterior extent of the orbit in Fig. 3. The most striking effects on EOM path were evident for the medial rectus (MR) and superior rectus (SR) muscles. Linear regressions confirmed that the MR path illustrated in Fig. 3A was a nearly straight line regardless of which side was positioned down, but from the intercept term of the linear regressions can be seen to be offset 0.75 mm superiorly when the orbit was positioned upward as compared to downward. The SR path is depicted in Fig. 3B. In the standard coordinate system, the SR exhibited an oblique path due to the temporal orientation of each orbit relative to the midline. Linear regressions demonstrated that the SR followed a straight path, but that this path was offset 1.4 mm temporally when the orbit was positioned upward as compared to downward. It should be noted that imaging did not include approximately 14 mm of the EOM paths extending posteriorly to the anatomical origin in the annulus of Zinn, where presumably head position relative to gravity could not have had any effect on path. The anteroposterior locations of the human rectus pulleys have been determined by Clark et al. using identical analytical methodology in the standardized oculocentric coordinate system from inflections in EOM paths evident in this sort of graphical depiction in secondary gaze positions (Clark et al. 2000). The locations of the MR and SR pulleys have been marked by gray arrows in Figs. 3A and 3B. It is notable that there is no suggestion of EOM path inflections at the pulley locations, or anywhere else, for the MR and SR.

Like the MR, the lateral rectus (LR) path depicted in Fig. 3C is nearly horizontal in this coordinate system, but not as straight. Nevertheless, interpolated to the level of the LR pulley determined by Clark et al. (Clark et al. 2000) and noted by the gray arrow, the LR path was offset
approximately 0.5 mm inferiorly when the orbit was positioned upward as compared to downward. An inferior inflection in LR path is suggested at the approximate anteroposterior level of its pulley in both head orientations.

Fig. 3. Effect of lateral side positioning on mean rectus extraocular muscle (EOM) paths of 19 orbits. Data represent mean Cartesian coordinates of EOM area centroids relative to zero position at globe center. To illustrate torsional reconfiguration of EOM paths, the relevant superior coordinate is plotted for the medial (A) and lateral (C) rectus EOMs, while the relevant lateral coordinate is plotted for the superior (B) and inferior (D) rectus
EOMs. Vertical gray arrows indicate the anterior location of each rectus pulley as determined in this coordinate system from EOM path inflections in secondary gaze positions identified by Clark et al. (Clark et al. 2000). Note the absence of inflections in the four rectus EOM paths in both the upper and lower orbits, evidenced by good linear fits to the data.

Like the SR, the inferior rectus (IR) path depicted in Fig. 3D is oblique in the standard coordinate system due to the temporal orientation of the orbits. Linear regressions suggest that the IR path was straight regardless of which side was positioned downward, but that the anterior path shifted nasally when the orbit was positioned upward as compared to downward. Interpolated to the anteroposterior location of the IR pulley determined by Clark et al. (Clark et al. 2000) and noted by the gray arrow in Fig. 3D, this nasal shift was 0.8 mm. There was no suggestion of an inflection in IR path in either head orientation.

The possibility of systematic globe translation during OCR was evaluated by comparing, in the quasicoronal plane, the horizontal and vertical coordinates of the globe center with those of the centroid of the bony orbit at approximately the level of the globe equator. The globe was $0.31 \pm 0.43$ mm more temporal and $0.14 \pm 1.29$ mm more inferior when the orbit was oriented upward than when downward. Neither of these values is statistically different from zero ($P > 0.1$), indicating absence of globe translation. This implies that rectus EOM paths can be analyzed for OCR in either an oculocentric or orbitocentric coordinate system, as path behavior will not differ systematically in the two coordinate systems.
Fig. 4. Mean rectus pulley positions in 19 orbits of 10 subjects, depicted in an oculocentric coordinate system as for a right eye viewed from anteriorly. Note counter-rotation of rectus pulley positions, with relative extorsion when the orbit was upward, and intorsion when downward. IR – inferior rectus. LR – lateral rectus. MR – medial rectus. SD – standard deviation. SR – superior rectus.

A graphical depiction of the effect of side down head position on the four rectus pulleys locations in the coronal plane is illustrated in Fig. 4 for an orbit-fixed coordinate system. Data in this figure were not obtained by interpolation, but by averaging the coordinates in each subject that were closest to the anteroposterior locations of each rectus pulley as determined by Clark et al. (Clark et al. 2000). Pulley coordinates could not be determined accurately for one orbit due to motion artifacts, so data for this orbit was excluded. Mean pulley coordinates confirmed the general impression of extorsion of the LR and SR pulleys when the orbit was upward, relative to when the orbit was downward.

The data of Fig. 4 include individual variability in initial rectus pulley positions that might obscure detection of individual changes. To avoid this confounding factor, changes in rectus pulley coordinates resulting from the downward to upward orbit positions were computed for each of the 19 orbits individually, and converted to a polar equivalent assuming the diameter of the rectus pulley array to be equal to that of the normalized globe at 24.3 mm as employed previously (Demer et al. 2003a). In polar form, all four rectus pulleys exhibited relative extorsional shift when the orbit was upward compared with downward (Fig. 5), although this
shift averaging $4.1 \pm 2.1$ deg was statistically significant only for the IR ($P < 0.025$), SR ($P < 0.01$), and MR ($P < 0.01$) pulleys.

Fig. 5. Relative extorsion with the ipsilateral orbit upward relative to downward for each of the four rectus pulleys of 19 orbits of 10 subjects, computed as changes within individual orbits. IR – inferior rectus. LR – lateral rectus. N.S. – not significant. MR – medial rectus. SR – superior rectus.

Since changes of oblique EOM cross section reflect contractile activity (Demer et al. 2003a; Kono and Demer 2003), the distributions of the IO and SO were compared in the right side down and left side down positions. Contractility of the IO is best assessed in the quasi-sagittal plane passing through the center of the IR, the plane designated zero. Nasal to image plane 0, IO bulk near its origin is small and so cannot increase greatly during contraction. Temporal to image plane 0, the IO inflects in its pulley to become variably tangential rather than perpendicular to the imaging plane, making temporal cross sections too variable for meaningful comparisons. The change in IO cross section associated with change in head orientation was first determined within individual orbits, and these changes were averaged at each image plane location across orbits. Although data for multiple quasi-sagittal image planes were computed, on a priori grounds only the cross section in image plane 0 is considered in assessing contractility. As illustrated in Fig. 2, the IO cross sections in image planes 0 and more medial were all greater when the orbit under consideration was upward than when downward. This difference, representing greater contractile thickening of the IO when the orbit was upward than when
downward, was statistically significant in plane 0 ($P < 0.01$, Fig. 6). Contractile thickening of the IO is consistent with its activity as an extorter of the globe.

Changes in SO cross section in the quasi-coronal plane reflect SO contractility (Demer and Miller 1995; Kono and Demer 2003). During large vertical gaze shifts, contractile change in the SO consists of a small increase in maximal SO cross section, and posterior shift in the location of maximum cross section. For the 18 orbits for which adequate quality images were collected, changes in the anteroposterior distribution of SO cross sections were evaluated along the length of the EOM, registering all data to the 2 mm thick image plane nearest the globe-optic nerve junction designated image plane 0. The change in SO cross section associated with change in head orientation relative to gravity was first determined within individual orbits, and these changes were averaged at each image plane location across all orbits. Absence of SO contractile activity would have been evident as a zero change in the cross section distribution along the EOM length, while on anatomic grounds contractile activity would be expected to produce reduction in cross section anteriorly, and increase in cross section posteriorly (Demer and Miller 1995). Contractile change in the SO would necessarily be zero at the origin in the orbital apex where EOM volume approaches zero, and also at the anterior end where the SO merges with its
non-contractile tendon. As seen in Fig. 7, as a result of downward positioning of the ipsilateral orbit, the SO cross section increased posteriorly, while it decreased anteriorly. It seemed reasonable to fit the non-monotonic behavior of SO contractility to the lowest order polynomial that could account for the bulk of the variance over the length of the SO. This distribution of cross section changes was better fit with a sixth order polynomial that accounted for $R^2 = 88\%$ of the variance, (F ratio 9.51, P < 0.003), than by lower order polynomials, but higher order polynomials did not account for appreciably more variance. This excellent fit indicated a significant effect of head positioning on SO cross section. The pattern is consistent with SO contraction during downward positioning of the ipsilateral eye, with an increase in posterior cross section, and a decrease in anterior cross section as the thin tendon moved posteriorly into the field of scanning.

![Fig. 7. Mean change in superior oblique muscle cross sectional area distribution along its length due to downward positioning of the ipsi-minus contralateral orbit. Anteroposterior position is referenced at zero to the image plane containing the junction of the globe and optic nerve. Data represents 18 orbits. A sixth order polynomial (gray dotted line) accounted for 88% of the variance (P < 0.003)](image)

**Discussion**

**Torsion of Rectus Pulley Array.** Prior concepts, embodied in quantitative models (Crawford et al. 2003a; Crawford et al. 2003b; Glasauer et al. 2001; Robinson 1985), of OCR have given little explicit consideration to the possibility that this phenomenon might be associated with changes
in the deep orbital paths of the rectus EOMs as influenced by their pulleys. While static OCR is a small effect, averaging of the data of 10 subjects positioned in left and right side down positions in an MRI scanner allowed the demonstration in the current study of a similarly-directed counter-rolling of the paths of the rectus EOMs, which at the anteroposterior level of the rectus pulleys averaged 4.1 deg difference between the right and left side down positions. The finding of rectus pulley shifts in response to change in head position relative to gravity represents a novel functional anatomic correlate of OCR, which is an otolith-mediated, static torsional VOR.

It was not possible in the current experiments to measure OCR directly in the MRI scanner, partially because the required instrumentation is incompatible with the magnetic field and radio frequency energy in the scanner environment. Static OCR is a relatively small effect that is difficult to measure accurately even under ideal environmental conditions. However, two recent investigations have used reliable techniques to report OCR under conditions of whole-body rotation to side down positions, and in human subjects comparable to the current experiment. Bockisch and Haslwanter used scleral magnetic search coil recording system mounted on a motorized, whole-body gimbal system to measure OCR over the full range of roll rotations (Bockisch and Haslwanter 2001). This study, performed in six adults of average age 35 ± 2 yrs, found a mean of 4.8 deg OCR from upright to the on-side position after exclusion of data in which the scleral coil lead might have artifactiously reduced the effect (Bockisch and Haslwanter 2001). Markham and Diamond used video-oculography to measure OCR in 19 humans of mean age 38 ± 19 yrs (Markham and Diamond 2002-2003). Video-oculography is not susceptible to the torsional artifacts of search coils. These investigators found mean static OCR from the upright of 3 deg in right and 4 deg in left side down positions, as well as a mean disconjugacy averaging 1.5 deg with one side down (Markham and Diamond 2002-2003). Example subjects did not have symmetrical responses between the right and left side down positions (Markham and Diamond 2002-2003), correlating with the apparent disconjugacy suggested by Fig. 1 of the current study. Careful studies measuring static OCR under optimal conditions in humans thus have found mean values of 3 – 5 deg change from the upright position,
representing a peak-to-peak change of 6 – 10 deg. In monkeys implanted with search coils that presumably could not slip, the mean difference in static OCR between the right and left side down positions found by Frens et al. was $8.1 \pm 0.2$ deg (Frens et al. 1998), while Crawford et al. found a static OCR from the upright to side down position of 8.5 deg (Crawford et al. 2003b). The current study compared the difference in torsional positions of the rectus pulley between the right and left side down positions, finding a maximum counter-rolling effect of about 6 deg for the SR, and a mean effect of 4.1 deg across all four rectus pulleys.

Visual conditions, particularly convergence, are known to influence the torsional VOR (Misslisch et al. 2001). The axial images obtained in the current experiment rule out the occurrence of significant convergence that might otherwise have suppressed OCR. Simultaneous determination of the OCR during MRI would be required for certainty on the issue of how much the rectus pulley array changes position relative to the globe, but such a determination is currently a technical impossibility. Given that the variability in the present MRI technique requires pooling of data from multiple subjects to determine rectus pulley positions during OCR, it is unlikely that attempts to correlate magnitude of OCR with pulley positions in individual subjects would be successful. It can nevertheless be concluded that OCR in the side down positions is associated with a similarly-directed torsional repositioning of the rectus pulley array of humans that is, on average, is roughly half of published values for ocular torsion under similar conditions.

**Effectors of Pulley Torsion.** Potential effectors of torsional repositioning of the rectus pulleys during OCR include both passive dragging of pulleys due to ocular torsion, and active repositioning by forces exerted directly on pulleys by the orbital layers of the oblique EOMs. During visually-guided fixation in secondary and tertiary gaze positions, rectus pulley positions are highly stable in the quasi-coronal plane (Clark et al. 1998a, 1997, 2000; Kono et al. 2002a). This suggests a high coronal plane resistance to passive displacement in the rectus pulley suspensions. During visual fixations conforming to LL, however, there is no consistent ocular torsion tending to displace the pulleys, which might during that condition be stabilized due to
their extensive mutual connective tissue interconnections (Kono et al. 2002b). Since the current data suggest that the torsional shift of the rectus pulley array is only half of ocular torsion, some degree of passive torsional dragging of the pulley array by the eye seems probable. Whether acting only via passively transmitted ocular torsion or directly on the rectus pulleys themselves, the obvious candidates for effectors of rectus pulley array counter-rolling are the oblique EOMs. Both the SO and IO insert on the globe to produce torsion (Demer 2000). The orbital layer of the IO is known to insert on both the IR and LR pulleys in a manner that would produce extorsional shift in their positions during IO contraction, although this insertion degenerates over the human lifespan (Demer et al. 2003b; Kono et al. 2002b). The IO’s antagonist, the SO, has an orbital layer that indirectly acts on the medial border of the SO pulley via an insertion on the SO tendon sheath (Demer 2004; Kono et al. 2002b). Using large visually-guided changes in eye position, MRI has been used to demonstrate changes in SO cross section that correlate with behavioral measures of normal (Demer et al. 2003a; Demer and Miller 1995) and impaired SO function (Kono and Demer 2003), and presumably constitute measures of contractility. Similarly, MRI has demonstrated changes in IO cross section at the point of crossing of the IR muscle that correlate with extorsion during convergence (Demer et al. 2003a), and with normal visually-guided elevation in adduction (Kono and Demer 2003). The contractile changes in the oblique EOMs demonstrated here by MRI are likely to be the causes of the rectus pulley array torsion during head tilting.
Fig. 8. Diagrammatic representation of effects of head tilt on rectus pulley shifts in lateral (top row) and frontal (bottom row) views. In upright head position, the inferior (IR), lateral (LR), medial (MR), and superior rectus (SR) pulleys are arrayed in frontal view as along the arms of a cross. The MR passes through its pulley, represented as a ring, to its scleral insertion. The rotational velocity axis imparted by the MR is perpendicular to the segment from the pulley to the insertion. If during globe extorsion in contralateral head tilt the MR pulley shifts superiorly by the half the distance the insertion shifts, then the rotational axis imparted by the MR would change by one quarter the angle of ocular torsion.

A possible direct mediator of active pulley array torsion is the inframedial orbital muscle, a smooth muscle band extending from the IR to the MR pulleys (Miller et al. 2003). Contraction of the inframedial orbital muscle would displace the IR pulley nasally, as appropriate to extorsion, and this motion could be elastically coupled to the other rectus pulleys via known connective tissue bands (Kono et al. 2002b). While innervation of the orbital smooth muscles is
autonomic (Demer et al. 1997), the vestibular system has influences on autonomic functions (Radtke et al. 2003).

**Kinematic Implications.** A parsimonious interpretation of the present findings is that ocular torsion during the VOR is associated with some degree of coordinated torsion of the rectus pulley array similar to that postulated to occur during convergence (Fig. 8). This arrangement has important kinematic implications. With fixed rectus pulleys, globe torsion would impart a new torsional action to each of the rectus EOMs (Miller et al. 1999). Since rectus pulleys are located as far posterior to globe center as the insertions are anterior to globe center, and subject to the trigonometrically small angle approximation, pulleys that did not move at all during ocular torsion would have caused the rectus EOM pulling directions to tilt anteroposteriorly by half of the ocular torsional angle. This half angle dependency would have been analogous to LL behavior for ocular torsion, but the current data excludes this behavior during OCR. Despite imprecision in our ability to estimate the amount of rectus pulley relative to globe torsion, the current MRI data indicate that the pulley array torsion is non-zero, and is in the same direction of ocular torsion. The more closely pulley array torsion matches ocular torsion, the less ocular torsion would influence rectus EOM pulling directions. The present data suggest that during OCR, the rectus pulley array’s torsional shift might be about half of ocular torsion. Were this to be the case, small angle geometry suggests that rectus pulling directions would change by one quarter of ocular torsion (Fig. 8). During head tilt, this would not appreciably change the geometric responsible for the half angle dependence of rectus EOM pulling direction on horizontal and vertical eye position. There would, however, be a shift in torsional orientation of the globe and rectus pulley array in primary position (Fig. 8). Consistent with this idea, static roll tilts of the head are well known to evoke a parallel shift of LP in the torsional direction (Crawford and Vilis 1991; Frens et al. 1998; Haslwanter et al. 1992; Hess and Angelaki 2003; Suzuki et al. 1997). This mechanical configuration depicted in Fig. 8 during counter-rolling appears consistent with LL half angle behavior if one assumes a simple torsional offset of Listing’s plane equal to ocular torsion. However, failure of premotor saccadic circuits to account
for quarter angle dependence of ocular rotational axis on torsional eye position might be the muscular effect proposed by Klier et al. to account for errors in visually guided saccade direction (Klier and Crawford 1998) associated with OCR (Klier and Crawford 1998), and pathologic ocular torsion induced by riMLF lesion (Crawford and Vilis 1992).

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 the 50% rotation required by LL. Recent experiments in humans undergoing transient whole-body yaw at high acceleration in darkness has supported a quarter angle dependence of VOR velocity axis on vertical eye position (Crane et al. 2005). The pulley array torsion depicted in Fig. 8 is consistent with the known quarter angle dependence of the VOR on torsional eye position. The arrangement in Fig. 8 does not account, however, for the known quarter angle dependence of VOR velocity axis on horizontal and vertical eye position. Although the proposed arrangement in Fig. 8 partially accounts for quarter angle behavior on a mechanical basis, if this were the only mechanical factor the dependence of ocular torsion on horizontal and vertical eye position during the yaw and pitch VOR would still require explicit neural commands to the oblique EOMs. It is therefore perplexing that recordings of cyclovertical motoneurons in monkeys have not demonstrated evidence of such quarter angle commands, instead showing similar behavior during the yaw VOR as during horizontal pursuit, and similar behavior during the pitch VOR as during vertical pursuit (Ghasia and Angelaki 2005). This paradox suggests that the EOMs have additional mechanical features yet to be discovered.

While the static torsional VOR maintains torsional eye position of only a few percent of head tilt, the dynamic torsional VOR has a much higher gain in the velocity domain (Schmid-Priscoveanu et al. 2000), even approaching 100% of head velocity under some conditions such as visual enhancement of the VOR (Misslisch and Hess 2002). Non-Listing VOR kinematics cannot be explained by anteroposterior shifts in rectus pulley locations (Misslisch and Tweed 2001). It is attractive to suspect that coordinated torsional shifts of rectus pulleys proposed here for the static
torsional VOR might also occur during the dynamic torsional VOR, and be reflected in the 3-D neural commands necessary to evoke that VOR.

**Implications for Neural Control.** Of course, central neural signals correlated with all types of eye movements would be expected to reflect effects of torsional reconfiguration of rectus pulleys during the VOR. Recordings from burst neurons in monkeys are compatible with torsional shift of rectus pulleys transverse to the EOM axes in the direction of OCR induced by static head tilt (Scherberger et al. 2001). 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 2003), and such shifts may be dynamic during semicircular canal stimulation (Hess and Angelaki 1997a, b). The suggestion of Hess and Angelaki that shift in LP is mediated by the otolith input to the 3-D neural integrator (Hess and Angelaki 2003) may be reconciled with the observation that lesion of the integrator in the riMLF also abolishes the torsional shift in LP associated with OCR (Crawford et al. 2003b) if the torsional shift of pulleys is also mediated by the 3-D neural integrator. It would then be predicted that lesion of the neural integrator would abolish counter-roll of the pulley system during static and dynamic vestibular stimulation, by blocking polysynaptic vestibular input to the oblique EOMs whose tonic activity also maintains torsional pulley array orientation.

In monkeys, the preferred directions of saccadic neurons in the superior colliculus shift in the opposite direction, and by slightly more than half the amount, of static head tilt (Frens et al. 1998). Based on simultaneous measurements of OCR and changes in preferred directions of superior collicular neurons, Frens et al. found that the changes in the horizontal and vertical pulling directions of the EOMs during OCR are probably about two-thirds of the angle of counter-rolling (Frens et al. 1998). Assuming as they did that collicular output is retinotopic and that the projection of the visual world onto the colliculus is thus shifted torsionally as OCR shifts the retina, Frens et al. concluded that a neural signal downstream from the superior colliculus is responsible for the remaining change in preferred directions of collicular neurons. That
interpretation is compatible with the current findings that counter-rolling of the rectus pulley array is less than OCR.

Regardless of the ocular motor subsystem involved, the torsional pulley shifts observed here during OCR would not void the advantage of apparent commutativity, the “linear plant” behavior, of the peripheral ocular motor apparatus for concurrent saccades and pursuit movements. This commutativity would be valuable in processing higher-level sensorimotor transformations that must account for 3-D geometrical effects of eye and head orientation (Crawford et al. 2003a; Frens et al. 1998; Klier and Crawford 1998; Van Opstal et al. 1991), and is incorporated in some modern models of ocular motor control (Crawford et al. 2003a; Crawford et al. 2003b; Glasauer et al. 2001; Quaia and Optican 1998; Raphan 1998). Neural processing for the VOR must be generated in 3-D, based on transduction of head motion in three degrees of freedom, and on 3-D eye orientation in the head.

A modeling study has suggested that time-dependent variations in the eye position dependence of the velocity axis of the transient yaw VOR may be explainable by half angle pulley behavior, with time-dependent roll gain (Thurtell et al. 2000). This model assumed homogeneous behavior of all orbital pulleys and did not consider the possible quarter angle behavior of the rectus pulley array in response to ocular torsion suggested here. Nevertheless, it does emphasize other suggestions that neural control of the roll component of the VOR is probably key for understanding its non-LL kinematics (Misslisch and Tweed 2001).

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