New Orbital Constraints on Eye Rotation

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ABSTRACT

The familiar notion that extraocular muscle paths are little constrained except at origins and insertions was called into question by biomechanical modeling (Miller and Demer, 1992). Magnetic resonance imaging, having previously shown that the paths of rectus muscle bellies remain fixed in the orbit during large ocular rotations (Miller, 1989), was then used to show that they remained fixed across large surgical transpositions of their insertions (Miller *et al.*, 1993), confirming that pulleys near the globe equator couple muscle paths to the orbital wall. Autopsy and immunohistochemical studies showed that these *soft rectus muscle pulleys* were sleeves composed of dense bands of collagen, elastin and smooth muscle (Demer *et al.*, 1995a), suspended from the orbit and adjacent extraocular muscle sleeves by bands of similar composition. Evidence has been found of sympathetic, parasympathetic, and nitroxidergic neurotransmission, and innervation has been traced to the superior cervical ganglion in monkey (Demer *et al.*, 1995b).

Muscle actions under a pulley model (Miller *et al.*, 1995) are different from those under traditional models (Miller and Robinson, 1984; Robinson, 1975), therefore different control signals are required. The pulleys and associated tissues act, we believe, as a mid-orbital suspension, passively constraining the globe's rotational freedom to approximate Listing's Law. Tonic innervation of pulley smooth muscle stiffens musculo-orbital coupling, and perhaps pulley innervation is modulated to refine binocular coordination or move Listing's Plane.

INTRODUCTION

Identification of the midorbital constraints on extraocular muscle (EOM) paths that we have called *soft rectus muscle pulleys* (or just *muscle pulleys*) emerged from attempts to use biomechanical models (Miller and Robinson, 1984; Miller and Shamaeva, 1993; Miller *et al.*, 1995; Robinson, 1975) to predict outcomes of eye muscle surgery to correct the alignment disorders called strabismus.

Since at least 1845, scientists and physicians have created models to help understand how the 12 EOMs rotate the eyes with the precise coordination that maintains binocular

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alignment, how various disorders disturb alignment, and how disturbances can be treated. In 1857, for instance, Ruete constructed a device in which strings representing eye muscles pulled spheres representing the globes against bearings that permitted rotation about any axis (Ruete, 1857). With such devices, however, it is difficult to model much more than the geometric arrangement of orbital tissues.

The first biomechanical model to represent tissue properties was created by Robinson (1975), and elaborated by Miller & Robinson (1984). Related models have been developed by Kusel and Haase (1977), Haase and Kusel (1978), Günther, Kusel and Rassow (1986), and Simonsz (1990). These computer-based models aim to be homeomorphic, that is, representative of the parts of the eye positioning system and their interactions. Examples of non-homeomorphic models are: statistical models, which are models of data, and expert systems, which are psychological models (Collins *et al.*, 1985).

The early biomechanical eye positioning models were able to represent many strabismic disorders, and could accurately predict many surgical outcomes. But in some cases — notably muscle transposition surgery — they failed badly. A characteristic feature of homeomorphic models is that they can point to the physiologic studies that might explain their failures. Here, it was clear that we needed to know more about orbital connective tissues and their effects on muscle paths and globe rotation.

MUSCLE PATH MECHANICS

Despite the work of Koornneef (e.g. 1974, 1991) EOMs were thought to be little constrained, except at their origins and insertions. It was, of course, recognized that something had to prevent the recti from slipping wildly around the globe, and various *ad hoc* schemes were proposed (e.g. Robinson, 1975; Miller and Robinson, 1984), but could not be evaluated because the actual muscle paths during voluntary gaze were not known.

When the speed, resolution and safety of tomographic imaging had improved enough to provide these data, some were collected by Simonsz using X-ray CT (Simonsz *et al.*, 1985). Figure 1A shows the data we collected with MR imaging (Miller, 1989). Rectus muscle paths are remarkably stable with respect to the orbit as the globe rotates through its full range of gaze.

One way to explain this finding is that a balance between muscle tension, which tends to slip the muscle sideways to take the shortest path across the globe, and intermuscular fascia, which tend to stabilize the muscle with respect to the globe, results in stability with respect to the orbit. Another explanation is that some midorbital connective tissues are suitably arranged and sufficiently stiff to couple the muscles, pulley-like, to the orbital wall. But if such pulleys exist, why are they not apparent during eye muscle surgery? Perhaps, we hypothesized, the requisite stiffness of the pulleys is provided by smooth muscle, which is relaxed by surgical anesthesia.

Either explanation can account for observed muscle paths. The mechanics, however, differ in important ways. According to the first, *conventional model*, a muscle rotates the globe about an axis determined by the globe's center of rotation, the muscle's anatomic origin, and its point of tangency with the globe, whereas, according to the second, *pulley model*, the axis of rotation is determined by the globe's center of rotation, the pulley, and

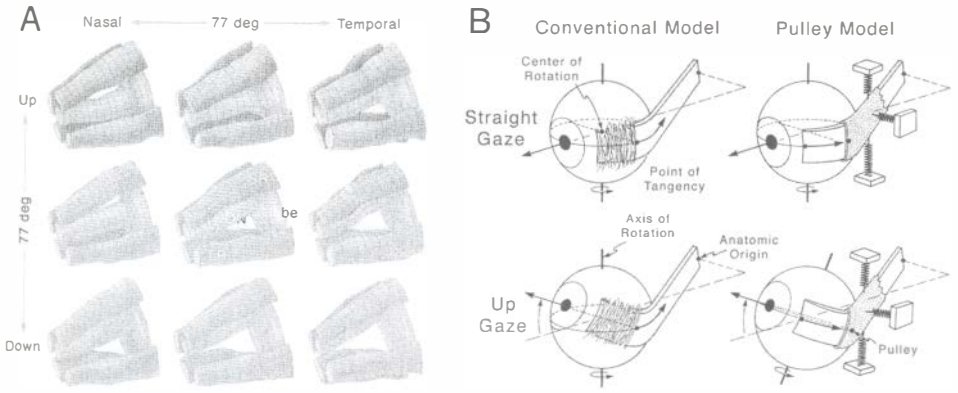

Figure 1 (A). Reconstructions based on MR images of four normal humans holding gaze along the orbital axis (center panel), and at eightpoints 38° eccentric. (B). Conventional and pulley models may give similar muscle paths, but have different mechanics and give different axes of rotation.

the muscle's insertion in the globe (Figure 1B). These two mechanisms require different control signals. The conventional model, for instance, simplifies the vestibulo-ocular reflex, since a muscle's axis of rotation remains head-fixed, whereas the pulley model simplifies visual tracking, since a muscle's axis of rotation remains globe-fixed (Figure 1B).

Transposition surgery, which severs all anterior attachments and relocates muscle insertions, provides a test. If lateral rectus (LR) muscle function is lost, eye alignment can be improved by disinserting the superior rectus (SR) and inferior rectus (IR), and reinserting them at the margins of the paralyzed LR. The conventional model predicts that the paths of transposed muscles would follow their insertions (Figure 2A, top), whereas the pulley model predicts that only segments anterior to the pulleys would move (Figure 2B, top). (Surgeons do not sever midorbital connective tissues to avoid releasing posterior orbital fat).

Results were clear: only the anterior segments of transposed muscles moved significantly; middle and posterior segments were little affected by the surgery (compare Figure 2C with 2D). A biomechanical model incorporating rectus pulleys (Figure 2B, top; Miller *et al.*, 1995) closely matched the post-operative superior and inferior rectus muscle paths observed by MRI (Figure 2C), and was able to predict the pattern of post-operative binocular alignment (Figure 2B, bottom). Without pulleys, the model predicted unphysiologic muscle paths, and a pattern of post-operative misalignment that is never observed (Figure 2A; Miller, Demer and Rosenbaum, 1993; Demer, Miller and Poukens, 1996).

PULLEY COMPOSITION & INNERVATION

Next, we looked for midorbital connective tissues suitable to function as pulleys. Whole 10 mm-thick sections of cadaveric human orbits were cut in the coronal plane through

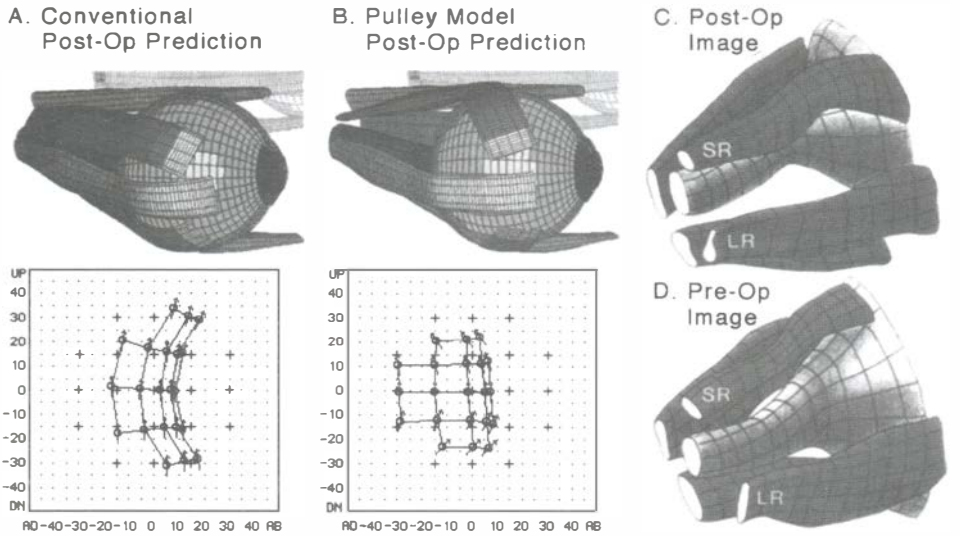

Figure 2 (A). Post-op predictions of conventional (no pulleys) model. Transposing the SR and IR insertions causes the SR and IR muscle paths to approximate that of the LR (top), which results in an unusual pattern of binocular misalignment (bottom). (B). Post-op predictions of pulley model. SR and IR paths posterior to the pulleys are little affected by transposition of their insertions (top), which results in the expected post-operative alignment. (C). Post-op MR image shows that SR path is best predicted by pulley model (this is true for IR path, too). (D). Comparison with a Pre-op image of the same patient shows that the belly of the transposed SR hardly moved at all.

the equatorial region of the globe. Contiguous sections were stained with Masson's trichrome, van Gieson's elastin stain, and a monoclonal stain for smooth muscle α-actin, respectively.

Figure 3 shows sample results for all three stains (collagen and muscle, distinguished by Mason's trichrome, are digitally separated in panels B and C). Examination of these sections shows that each rectus muscle has a specialized sleeve of connective tissue near the equator of the globe. Most anteriorly, the sleeves loose their global aspects, forming *slings*, which extend from the orbital wall around the orbital surface of each muscle, concave to the globe. In the middle of the anteroposterior extent of each sleeve, collagen completely encircles the EOM, and is stiffened by abundant elastin, particularly on the orbital side (Figure 3D). Extending from the anterior sling, the central sleeve and its elastin mass are bands that contain collagen, elastin, and cells immunoreactive for smooth muscle α-actin (Figure 3E). Fibroelastic bands were found to extend between adjacent rectus EOMs, from the SR to the superior oblique trochlea, and from the IR to the inferior oblique muscle. Posteriorly, the pulleys again become slings, but here they extend from the orbit to the global side of the EOM, concave to the orbital wall. Smooth muscle was not found in the posterior pulley slings. The anteroposterior extent (including slings) of the pulleys ranged from 13 mm for inferior rectus to 19 mm for medial rectus. The medial rectus pulley contained the greatest amount of fibroelastic tissue, and the superior rectus pulley the least. Posterior to the globe, EOMs were encapsulated thinly or not at all. Little collagen was found, and no elastin or smooth muscle.

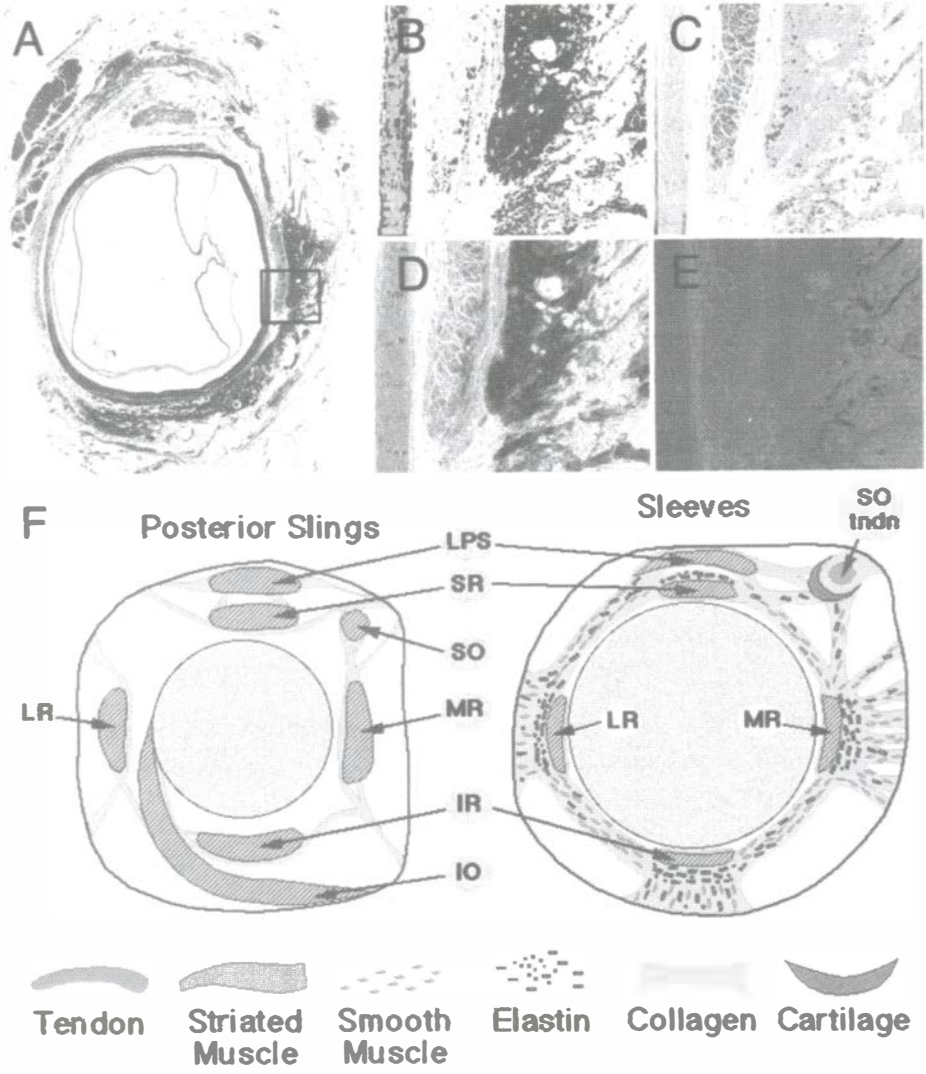

Figure 3 (A). Section of a human orbit near the globe equator. Boxed neighborhood of inferior MR is further examined. (B). Collagen is highlighted. (C). Muscle. (D). Elastin. (E). Smooth muscle. (F). Schematic of midorbital connective tissues, based on autopsy, histochemical and immunohistochemical studies.

Electron microscopy has revealed an ultrastructure specialized for strength (Porter *et al.*, 1996). The fine structure of the pulleys is a dense collagen matrix with alternating, crossed bands of collagen, apparently optimized for high tensile strength over a range of pulling directions. Elastin fibrils were interspersed in the collagen matrix. Smooth muscle was distributed in discrete bundles, usually 30–150 μm in diameter, which were encased in collagen and anchored in the dense portion of the pulley tissue. This arrange-

ment contrasts, for instance, with the thin, wide sheets of smooth muscle fibers loosely encased in connective tissue that compose Müller's muscle.

The overall arrangement of tissues is schematized in Figure 3F. Koornneef described much of this connective tissue structure, but lacking direction from a biomechanical model and our sensitive immunohistochemical method for detecting smooth muscle, did not identify the pulleys.

Next, we sought to characterize smooth muscle innervation with histo- and immunohistochemical studies of rhesus monkey and human orbital tissues (Demer *et al.*, 1995b; Demer *et al.*, 1995c). Both superior cervical ganglia of a monkey were injected with the lectin anterograde tracer PHA-L, prior to immunohistochemical study.

Rich innervation was found in human and monkey pulley smooth muscle. Numerous axons terminating in motor endplates in smooth muscle bundles were immunoreactive to tyrosine hydroxylase, indicating catecholamine synthesis; to dopamine β-hydroxylase, specifying norepinephrine synthesis; and to PHA-L (in the monkey), demonstrating a projection from the superior cervical ganglion. There was no immunoreactivity to catechol-O-methyltransferase, indicating that the norepinephrine was not converted to epinephrine. Smaller axons and motor endplates were also demonstrated by immunoreactivity to nitric oxide synthase and the histochemical reaction for NADPH diaphorase, indicating nitroxidergic transmission; and to acetylcholinesterase, presumably indicating parasympathetic transmission by acetylcholine. The pterygopalatine ganglion, and to a lesser extent, the ciliary ganglia, had cells with immunoreactivity indicating nitroxidergic transmission. Although large orbital nerves were immunoreactive for myelin basic protein, none was found in nerves within pulley smooth muscle.

We conclude that the smooth muscle suspension of monkey and human rectus pulleys has a sympathetic projection employing norepinephrine from the superior cervical ganglion, a nitroxidergic projection, possibly from the pterygopalatine ganglion, and a cholinergic parasympathetic projection. These multiple projections suggest excitatory and inhibitory control of rectus pulley smooth muscle, possibly subserving dynamic regulation of ocular motility in addition to the tonic stiffening originally hypothesized. We have begun electrical stimulation and lesioning experiments in monkey to determine how innervation affects muscle force and eye position.

LISTING'S LAW

If the globe were suspended trampoline-like from the orbital wall by connective tissues at its equator, it would obey Listing's Law, unless the EOMs interfered. The tissues diagrammed in Figure 3, and the paucity of similar tissues in anterior and posterior regions, appear to approximate the required suspension.

Current thought, however, supposes that Listing's Law is enforced solely by brainstem innervations to the striated EOMs. Two ideas, we think, underlie this presumption: (1) there is nothing in the orbit that could provide a mechanical substrate, and (2) the many predictable violations of Listing's Law result from characteristic failures of, or variations, in its active control.

The first idea could be maintained by minimizing the mechanical significance of extraocular connective tissues, such as described by Koornneef (1974, 1991). However, with the findings of the previous section, this idea has become less tenable.

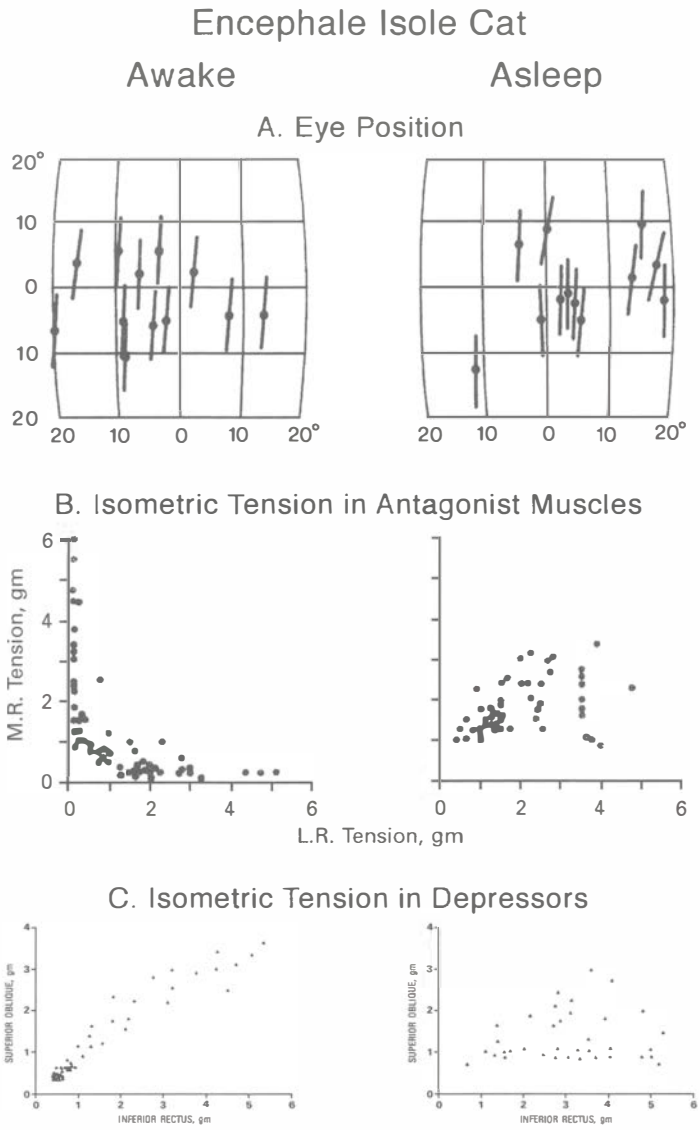

Figure 4 (A). 3-D gaze in an *encephale isole* cat. Torsion becomes slightly disordered in sleep. (B). The expected "reciprocal" relationship between LR tension and MR tension is lost in sleep. (C). The positive correlation between ipsilateral depressors is lost in sleep (adapted from Nakayama, 1975).

Nakayama presented interesting evidence for the second idea from studies of 3D eye alignment and muscle forces in the *encephale isole* cat (Nakayama, 1975). His argument began with the observation that eye torsion, which has an orderly relationship to gaze angle when the animal is awake, became disordered in sleep (Figure 4A). Then he noted that the reciprocal tensions in antagonistic muscles (Figure 4B), and the positive correlation of tensions in ipsilateral depressors (Figure 4C) and elevators also became disor-

dered in sleep. Having found that disordered innervations caused disordered torsion, Nakayama concluded that coordinated innervations were responsible for Listing's Law. However, even these data suggest more complex causation: near total destruction of innervational coordination (Figures 4B & C) caused only minor torsional errors (Figure 4A).

Thus, we suggest that the rectus muscle pulleys and related tissues define Listing's plane. Mostly, innervations are coordinated to avoid rotations about the plane's normal axis, minimizing stretching of the suspensory tissues. However, to serve some purpose (e.g. utricular counterrolling), or as a side-effect (violations in sleep), the powerful striated EOMs may strain against the eye's orbital suspension.

Other interactions are suggested by our findings concerning pulley innervation. We originally looked for smooth muscle to augment tonic pulley stiffness in the awake state, but perhaps, pulley stiffness and position are also modulated to refine binocular coordination, assist convergence, permit axial rotation, or move Listing's Plane. From this perspective, disordered torsion in sleep would be due to relaxation of pulley tissues, as well as disordered EOM innervations.

Why does the eye tend to obey Listing's Law? Our studies of extraocular biomechanics suggest an answer in the predominantly equatorial suspension of the globe and muscles, which the EOMs simply avoid straining. Had evolution instead provided extraocular gimbals and bearings, we might instead be suggesting the basis of Helmholtz's or Fick's Law.

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