Author Response: Letter to the Editor of IOVS From Joseph L. Demer and Robert A. Clark Regarding Joel M. Miller, "EOM Pulleys and Sequelae: A Critical Review"

The Active Pulley Hypothesis, as I use the term, and as Demer and colleagues normally do, was described in their article, "Evidence for Active Control of Rectus Extraocular Muscle Pulleys,"[1] which proposed that each rectus muscle was functionally two independent muscles, one of which (the global layer [GL]) was inserted in the sclera to rotate the globe, and the other (the orbital layer [OL]) was inserted in and translated the pulley to alter the oculorotary action of the GL passing through it. The diagrammatic representation from that paper[1] (top half of Fig. 10), which has appeared in many versions since, is reproduced here (Figure). The APH is a *functional* hypothesis, not merely a statement about anatomy, and it proposes both mechanical and innervational independence of OL and GL. To claim otherwise, as Demer and Clark do in the main argument of their letter,[2] is to mislead.

One finding the APH sought to explain was the non-Listing "quarter angle" kinematics of the vestibulo-ocular reflex (VOR). Implausible relative laminar movements in the order of a half centimeter were proposed, but only when it was shown mathematically that no differential pulley movements could account for VOR kinematics,[3] did we get the narrowly drawn admission that the APH did not explain "steady state VOR during low frequency head rotation."[4] The original APH concept has otherwise been maintained across dozens of publications, for example:

- "The APH proposes that OL and GL fibers are under at least partially differential central neural control and have distinct mechanical actions."[5]
- "The APH suggests that pulleys, comprised of connective tissue rings encircling rectus EOMs, are translated by the EOMs' fibers while global layer fibers insert on the eye to rotate it. Anteroposterior locations of rectus pulleys are thus neurally controlled."[6]
- "If substantial coupling were demonstrated between EOM compartments during active contraction, the biomechanical basis of the APH . . . would be undermined."[7]

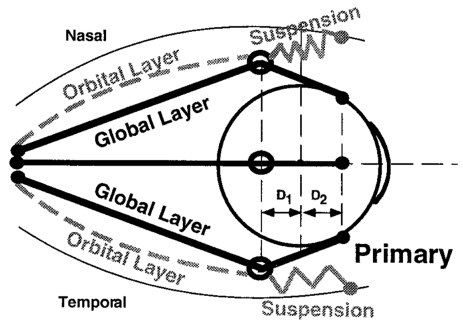

Figure. Reprinted with permission from Demer JL, Oh SY, Poukens V. Evidence for active control of rectus extraocular muscle pulleys. *Invest Ophthalmol Vis Sci.* 2000;41:1280-1290. © 2000 ARVO

The APH must entail laminar shear in the order of millimeters if the OL-controlled pulley is to significantly modify GL actions, but experimental surgical manipulations, connective tissue studies, and common sense suggest that this is unlikely, and, indeed, such relative movements are not seen. Although in vitro studies of bovine EOM claim near-complete fiber independence, researchers from other laboratories consider those findings to be experimental artifacts. It has long been known that many motoneurons innervate both OL and GL, and the recent failure to find separate nerve branches to OL and GL of any muscle[5] imply that independent control is impossible.

In an earlier review[8] I argued that anatomic findings from the Demer laboratory,[1,9,10] which had come under attack because of their association with the APH, could be accepted regardless of whether there was differential OL-GL movement. To make the point, I defined "Coordinated Active Pulleys" as the *null version* of Demer's hypothesis, in which different fiber types were innervated to contract as a unified whole, as in any heterogeneous muscle. If Demer and Clark now wish to claim that this is what they mean by "APH," they must admit there is nothing distinctively "active" about it, that their many efforts to demonstrate mechanical and innervational independence were unmotivated, and that the APH is a theory empty of content. Identifying the APH with its null version is simply a backhanded way to admit that it has been effectively disproven.

To forestall further confusion and obfuscation, I've urged that the fundamental and well-supported EOM pulley concept be referred to as "longitudinally-dragged pulleys" to highlight its passive mechanics, or "M-D pulleys," to reference its developers.[11]

PPV Does Not Measure Muscle Contraction

The Demer laboratory infers muscle contraction from MRI data. Muscle volume in a region of interest (ROI) centered on the point of maximum cross-section (MaxCS) in such images would be a reasonable measure of muscle contraction,[11] but the method they use, posterior partial volume (PPV), being both complexly contaminated and vulnerable to bias, is not as follows:

- PPV has no basis as a measure of muscle contraction apart from its correlation with duction, and duction has a nontrivial relationship to muscle contraction.[11]
- Instead of measuring the muscle thickening that's closely related to contraction, PPV admittedly[12] is contaminated by contraction-related movement of muscle tissue that causes different parts of a muscle to be measured in different contractile states. Failure to track MaxCS also makes PPV highly sensitive to choice of ROI, and so, vulnerable to bias[11] (Fig. 1).
- Additionally, the ROI used to compute PPV is referenced to the globe-optic nerve junction, which moves with gaze so that comparisons of muscle cross-sections in different gazes are actually compar-

iovs.arvojournals.org | ISSN: 1552-5783

Investigative Ophthalmology & Visual Science

isons of different MRI slices imaging different parts of the orbit[11] (Fig. 2).

None of these issues are substantively addressed in Demer and Clark's letter.[2]

Force and Movement

Isometric muscle contraction, in which tension increases but length is fixed, is commonly distinguished from isotonic contraction, in which a muscle shortens under constant tension. Given the implausibility of intramuscular *shearing movements* in the order of millimeters required by the APH (the pulley is supposed to move sufficiently to alter the pulling direction of the GL passing through it), it is helpful to notice that the EOM compartments hypothesis requires only a *force gradient* across a muscle's width, which might be balanced isometrically by opposing forces, such as those of an antagonist muscle. This distinction (force gradients verses movement gradients) is one reason the theory of EOM compartments remains viable and the APH does not.[11]

Biased MRI Quantification

Demer and Clark[2] did not comment on our critique of their MRI methodology, the poor quality of which is surprising, given its centrality to their work:

- Their measurements have unstable referents—the globe-optic nerve junction and the interhemispheric sulcus—that introduce systematic errors by their movements under experimental manipulations.[11]
- Simply stacking MRI slabs is a poor way to estimate volumes. Better methods are readily available[11] (Fig. 3).
- Biased analyses, clearly evident in published images, raise general concerns about the reliability of their data[11] (Figs. 4 and 5).[13]

Cause or Effect?

Demer and Clark[2] did not comment on our suggestion that changes in the shape of a muscle's cross-section were better explained by bending around its pulley than by differential compartmental contraction.

Scientific Validity

Demer and Clark suggest that conceptual confusion, invalid statistics, biased image interpretation, generally poor methodology, and absence of independent confirmation are quibbles that don't apply to their "exploratory basic science." All shortcomings, they suggest, are offset by voluminous publication. But articles from the Demer laboratory are unusually abstruse, and readers likely skim them uncritically, supposing they must be true because of their complexity, apparent thoroughness, and the authority of the investigators, failing to see that beneath the surface, they are broadly defective.

Joel M. Miller

Eidactics, San Francisco, California, United States.
E-mail: jmm@eidactics.com.

References

1. Demer JL, Oh S, Poukens V. Evidence for active control of rectus extraocular muscle pulleys. *Invest Ophthalmol Vis Sci*. 2000;41:1280–1290.
2. Demer JL, Clark RA. Re: Joel M. Miller, EOM pulleys and sequelae—a critical review. *Invest Ophthalmol*. 2020;61(6):10.
3. Misslisch H, Tweed D. Neural and mechanical factors in eye control. *J Neurophysiol*. 2001;86:1877–1883.
4. Kono R, Clark RA, Demer JL. Active pulleys: magnetic resonance imaging of rectus muscle paths in tertiary gazes. *Invest Ophthalmol Vis Sci*. 2002;43:2179–2188.
5. Peng M, Poukens V, da Silva Costa R, Yoo L, Tychsen L, Demer JL. Compartmentalized innervation of primate lateral rectus muscle. *Invest Ophthalmol Vis Sci*. 2010;51:4612–4617.
6. Demer JL, Clark RA, da Silva Costa RM, Kung J, Yoo L. Expanding repertoire in the oculomotor periphery: selective compartmental function in rectus extraocular muscles. *Ann N Y Acad Sci*. 2011;1233:8–16.
7. Shin A, Yoo L, Demer JL. Independent active contraction of extraocular muscle compartments. *Invest Ophthalmol Vis Sci*. 2015;56:199–206.
8. Miller JM. Understanding and misunderstanding extraocular muscle pulleys. *J Vis*. 2007;7:10 11–15.
9. Oh S, Poukens V, Demer JL. Quantitative analysis of rectus extraocular muscle layers in monkey and humans. *Invest Ophthalmol Vis Sci*. 2001;42:10–16.
10. Lim KH, Poukens V, Demer JL. Fascicular specialization in human and monkey rectus muscles: evidence for anatomic independence of global and orbital layers. *Invest Ophthalmol Vis Sci*. 2007;48:3089–3097.
11. Miller JM. EOM Pulleys and Sequelae: A Critical Review. *Investigative Ophthalmology & Visual Science*. 2019;60:5052–5058.
12. Clark RA, Demer JL. Functional morphometry of horizontal rectus extraocular muscles during horizontal ocular duction. *Invest Ophthalmol Vis Sci*. 2012;53:7375–7379.
13. Miller JM, Scott AB. Re: Clark et al.: The globe's eccentric rotational axis: why medial rectus surgery is more potent than lateral rectus surgery (Ophthalmology. 2018;125:1234-1238). *Ophthalmology*. 2019;126:e8–e9.

Citation: *Invest Ophthalmol Vis Sci*. 2020;61(6):9.
https://doi.org/10.1167/iovs.61.6.9