Multiple Mechanisms of Extraocular Muscle “Overaction”

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Objective: To assign more specific pathophysiologic processes to the protean patterns of extraocular muscle “overaction” that we see in clinical practice.

Methods: By extrapolating from known principles of striated muscle physiology, a cohesive theory about extraocular muscle behavior is derived.

Results: The key to understanding apparent extraocular muscle overaction is to differentiate between a muscle that has decreased elasticity and one that is strengthened. Primary inferior oblique muscle overaction has the characteristics of a muscle that primarily has decreased elasticity, the superior rectus overaction/contraction syndrome appears to represent a muscle that is strengthened, and inferior oblique overaction secondary to ipsilateral superior oblique palsy has elements of both decreased elasticity and strengthening. Many motility patterns that appear to be due to an overacting muscle may in fact be caused by other muscles than the suspected one.

Conclusion: Apparent extraocular muscle overaction can be caused by many different factors.


When an eye moves excessively into the field of action of an extraocular muscle on version testing, that muscle is typically described as being overacting. Because terminology influences understanding, the use of the term overacting can be misleading for several reasons. In many circumstances, an excessive movement of an eye may in fact be in the field of action of a muscle that is not actually responsible for the abnormal movement. For example, overelevation in adduction can be due to one of multiple different causes, many of which are not related to the inferior oblique (IO) muscle in the adducting eye. However, the aforementioned definition would categorize this as IO overaction. Common examples of clinical scenarios that all might be incorrectly thought of as being due to an overacting IO are described in the Table. They include the following: Duane syndrome,

1, 2 dissociated vertical divergence, 3 craniofacial syndromes, 4, 5 the antielevation syndrome that can occur after anterior transposition of the IO, 6 mechanical restriction of the contralateral inferior rectus (IR), 7 pseudo IO overaction associated with a Y or V pattern, 8 and pulley heterotopia or instability (according to Oh et al 9 and Demer 10).

There are numerous other clinical situations in which an excessive movement of an eye is in fact caused by the muscle in whose field of action the movement occurs. Common examples include primary inferior oblique muscle overaction (IO-OA) that often accompanies horizontal strabismus, 11 overaction of the IO that is secondary to ipsilateral superior oblique (SO) palsy, 12, 13 and the superior rectus (SR) overaction/contracture syndrome of Jampolsky that can occur with ipsilateral SO palsy. 14-20 Even in these circumstances, the term overaction is inadequate because many different situations can result in an increase in a muscle’s force. As is described later in this article, an increase in a muscle’s contractile or elastic force may cause an eye to rotate excessively into its field of action on version testing, yet these represent very different pathophysiologic processes. In addition, multiple different scenarios can lead to an increase in contractile force. These include an increase in innervation, increase in muscle bulk (cross-sectional area), and changes in the types of muscle fibers within the muscle. Consequently, the use of the term overaction to describe heterogeneous situations may be misleading and can confuse our understanding of why particular motility patterns develop in different strabismic disorders because it im-
the application of those principles to accepted observations of established principles of striated muscle physiology and clinical observations with known concepts. It consists of a review apparent extraocular muscle overaction that reconciles clinical action of the ipsilateral IR. In the SR overaction/ contraction syndrome of Jampolsky, the Bielschowsky head tilt test is typically positive, yet often the forced ductions feel normal. However, primary IO-OA, which looks clinically identical on version testing to secondary IO-OA, does not have a positive head tilt test. Theoretically, the hypertropia should increase with head tilt toward the contralateral side because the overacting IO, if it is truly strengthened, should overpower the vertical action of the ipsilateral IR. In the SR overaction/contraction syndrome of Jampolsky, the Bielschowsky head tilt test is typically positive, yet often the forced ductions feel normal. Kono and Demer recently reported that overacting IOs secondary to SO palsy appear to have normal size on orbital imaging, yet our concept of an overacting muscle as being strengthened suggests that perhaps they should be hypertrophied. Putting it succinctly, the term overaction is misleading because it assumes that clinical observation implies etiology.

The purpose of this article is to assign more specific pathophysiologic processes to the protean patterns of extraocular muscle overaction that we see in clinical practice.

### Methods

This article is a derivation of a unifying hypothesis to explain many of the different mechanisms responsible for apparent extraocular muscle overaction that reconciles clinical observations with known concepts. It consists of a review of established principles of striated muscle physiology and the application of those principles to accepted observations about various abnormal patterns of ocular motility.

### Basic Striated Muscle Physiology

A muscle is made up of multinucleated cells called muscle fibers, each of which contains many myofibrils that run longitudinally within the muscle. The basic contractile unit within the myofibrils is the sarcomere. It consists of overlapping thin filaments (actin) and thicker filaments (myosin) as shown in Figure 1A. The actin filaments insert on an electron dense structure called the Z line, which delineates the end of the sarcomere. The myosin filaments lie between parallel filaments of actin and bridge the gap between actin filaments that are adjacent serially (end to end). Myosin filaments have knob-like heads that interact chemically with actin filaments, causing them to move along the adjacent actin filament resulting in muscle contraction (Figure 1B). The increase in force that results from this active contraction is referred to as the muscle’s active (contractile) force generation. If a muscle is given a single maximum stimulation, the resultant contractile force is called the muscle’s twitch. The magnitude of the twitch that a muscle can generate is proportional to the sum of the contractile force of each of the parallel contractile elements (sarcomeres) in the muscle. Thus, a muscle with a stronger twitch than normal may have a somewhat larger cross-sectional diameter because it may have more sarcomeres in parallel. This increase in muscle strength can be due to each muscle fiber having a larger diameter (muscle hypertrophy) or due to a greater total number of parallel fibers (muscle hyperplasia).

A muscle’s tetanic tension is that force it develops in response to a constant stimulus. A muscle with a higher peak tetanic tension may have a greater cross-sectional diameter than one with a lower tetanic tension if hyperplasia or hypertrophy were responsible for the increased tetanic tension. Conversely, a muscle that has lost elasticity but has not developed a change in its twitch or tetanic tension (contractile force) has only undergone a change in the number of sarcomeres in series (end to end). Consequently it should have a normal cross-sectional diameter because there is no change in the number of sarcomeres in parallel. Muscles with either an increased twitch or tetanic tension can be thought of as being stronger than muscles with a lower twitch or tetanic tension. The number of sarcomeres in series (end to end) does not affect muscle contractile force, however, acute changes in muscle length do. If a muscle is stretched substantially beyond its resting length, there is insufficient overlap of the actin and myosin to generate as effective a contractile force (Figure 1C). If the muscle is passively shortened considerably, there is insufficient room for the myosin to move along the adjacent actin filament before it collides with the dense Z band (Figure 1B). In either circumstance, shortening or shortening from the optimum length will decrease the contractile force a muscle can generate. For skeletal muscles, the contractile force is at its peak when the length of the muscle provides optimum overlap of the actin and myo-

### Table. Conditions Causing Overelevation in Adduction Not Related to the Inferior Oblique in the Adducting Eye

<table>
<thead>
<tr>
<th>Clinical Condition</th>
<th>Comment</th>
</tr>
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<tbody>
<tr>
<td>Duane syndrome 1-2</td>
<td>Elevation in adduction caused by cocontraction of lateral rectus</td>
</tr>
<tr>
<td>Dissociated vertical divergence 1</td>
<td>Dissociation by the nose can bring out a manifest dissociated vertical divergence in adduction</td>
</tr>
<tr>
<td>Craniofacial syndromes 4-6</td>
<td>Eycliclorotation of all the rectus muscles can cause elevation in adduction</td>
</tr>
<tr>
<td>Antielevation syndrome after IO anterior transposition 2</td>
<td>The antielevating effect of the IO anterior transposition restricts elevation in abduction, causing fixation duress to the contralateral eye and resulting in overelevation</td>
</tr>
<tr>
<td>Mechanical restriction of the inferior rectus 2</td>
<td>Restriction of elevation in abduction causes fixation duress to the contralateral eye, resulting in overelevation</td>
</tr>
<tr>
<td>Pseudo IO overaction with Y or V pattern 8</td>
<td>Cocontraction of the lateral rectus on attempted upgaze mimics IO overaction</td>
</tr>
<tr>
<td>Pulley heterotopia 9-12</td>
<td>Abnormal position of one or more of the rectus muscle pulleys can cause overelevation in adduction</td>
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Abbreviation: IO, inferior oblique.
than normal and with a shorter than normal tether length) as which the muscle will tear. Throughout this article, I refer to a beyond its slack length, the elastic tension rises rapidly said to be at its primary length. As a muscle is passively stretched is in the primary position. In this latter position, the muscle is this is typically shorter than the muscle’s length when the eye bers within the muscle (eg, twitch or singly innervated fibers nervation, a change in the proportion of different types of fi- of the sarcomere. This same anatomic relationship would be seen if the muscle was passively shortened. If a muscle is passively shortened, there is decreased contractile efficiency. If a muscle is passively stretched, there is less room for active contraction to occur before the myosin filament collides with the dense Z band. Consequently, a passively shortened muscle has less overlap of the actin and myosin filaments (C). This results in less area over which the Z filaments can interact, also decreasing contractile efficiency.

sin filaments. For most skeletal muscles, this is typically around its resting length (Figure 2). Other factors that can increase the contractile force of a muscle include an increase in its in-ervation, a change in the proportion of different types of fibers within the muscle (eg, twitch or singly innervated fibers vs nonwitch or multiply innervated fibers; or high oxidative vs low oxidative fast twitch fibers).20-34

In addition to a muscle’s force that results from active con- traction, a muscle has an elastic resistance to stretch much like a rubber band or spring. Each myosin filament is anchored to the adjacent Z line by an elastic protein called titan, which is responsible for most of the muscle’s elastic resistance to stretch (Figure 1A). A muscle’s slack length is that length below which the muscle exerts no elastic force.35 For an extracocular muscle, this is typically shorter than the muscle’s length when the eye is in the primary position. In this latter position, the muscle is said to be at its primary length. As a muscle is passively stretched beyond its slack length, the elastic tension rises rapidly (Figure 2). The tether length of a muscle is the length beyond which the muscle will tear. Throughout this article, I refer to a muscle that has increased resistance to passive stretch (is stiffer than normal and with a shorter than normal tether length) as having decreased elasticity or being (relatively) inelastic. I refer to a muscle that generates a greater twitch (active contraction to a single maximum stimulus) or tetanic tension as being stronger than normal or strengthened.

The total force of a muscle is the sum of the contractile force it can generate and the elastic forces. Because both contractile and elastic forces are a function of a muscle’s length, the relationship between muscle length and total force (contractile plus elastic) is biphasic as depicted in Figure 2.

MUSCLE PHYSIOLOGY
IN ABNORMAL SITUATIONS

Studies of animal skeletal muscles have shown great plasticity in muscle structure as a response to chronic stretching or short-ening.27,30-38 If a muscle is passively stretched, the length of each sarcomere initially increases, putting the actin and myosin fila-ments in a disadvantaged relationship with respect to contractility as shown in Figure 1C. However, if that stretch is main-tained for a period of several weeks, new sarcomeres are laid down in series (end to end), thus allowing each sarcomere to return to its initial optimum length (Figure 3). If a muscle is passively shortened, each sarcomere is initially shortened as shown in Figure 1B, also resulting in a suboptimal actin-myosin relationship. However, if the shortened position of the muscle is maintained for several weeks, sarcomeres drop out serially (end to end). When the muscle loses sarcomeres in this manner, the remaining sarcomeres are able to resume their original optimum length (Figure 4). A muscle taking up its slack in this manner is the physiologic basis for a muscle losing elasticity, which results in increased stiffness. This is also de-scribed as a muscle being contractured. When a muscle loses elasticity in this manner, there typically is not an increase in its cross-sectional area. There is substantial evidence these obser-vations hold true for extracocular muscles.30-43 Muscles can also lose elasticity secondary to infiltration by or addition of stiffer tissue as in Graves orbitopathy44 or congenital extracocular muscle fibrosis.45 In addition, surgical resection or advance-ment of an extracocular muscle will cause a temporary loss of elasticity until sarcomere remodeling occurs.

Collins and Jampolsky46 have observed that when human rectus muscles lose elasticity as a result of maintaining a chronically shortened length, their length-elastic tension
curve retains its normal shape; however, the curve is merely shifted to the left on the length axis (Figure 5). The slack length is shorter, and elastic forces begin to develop at a shorter length than in a normal muscle. However, they found the active contractile force to be unchanged in muscles with decreased elasticity. This would mean that the total force produced by stimulation of a relatively inelastic muscle at any given length (as long as it exceeds its slack length) would be greater than normal because the total force is the sum of the contractile and elastic forces. Only the elastic force, however, would be responsible for the increase seen in total force. Below the slack length there would be no

Figure 3. At resting length, actin and myosin have the optimum relationship (A). If a muscle is stretched, the sarcomeres initially lengthen and actin and myosin have a less efficient relationship (B). With time, sarcomeres are added serially (end-to-end) (C). This allows the sarcomeres to shorten. Actin and myosin return to their initial optimum length despite the overall elongation of the muscle length.

Figure 4. At resting length, actin and myosin have the optimum relationship (A). If a muscle is shortened, the sarcomeres initially shorten, and actin and myosin have a less efficient relationship (B). With time, sarcomeres drop out serially (end-to-end) (C). This allows the remaining sarcomeres to lengthen (D). Actin and myosin return to their initial optimum relationship despite the overall shortening of the muscle length.
contribution from contractile forces by definition, and consequently this statement would not hold true.

The main factor responsible for increasing a muscle’s contractile strength (increased twitch and/or tetanic force) is a chronic increased innervation of a muscle to contract that exceeds the normal resting innervation. This can either result in an isometric contraction (eg, one that is not accompanied by a change in muscle length) or an isotonic contraction (eg, one that is accompanied by muscle movement). Studies done on animal skeletal muscle show that increased innervation is often accompanied by a change of many of the fast twitch fibers to slow twitch; however, this has not been observed in humans.26 Although both isometric and isotonic exercise result in an increase in muscle strength, an increase in the cross-sectional area of the muscle fibers depends on the nature and duration of the exercise and has not been described as occurring in human extraocular muscles. Results in other species have been conflicting.29 These types of exercise can also be associated with a slight increase in resistance to passive stretch but not nearly to the degree that occurs with chronic shortening.26

There are 6 important principles for understanding why human extraocular muscles may appear to overact. Five relate to general principals of muscle physiology and one involves understanding Hering’s law.26 (1) Chronic shortening, either passive or secondary to increased stimulation, causes loss of elasticity (contractile). (2) A chronic increase in stimulation, either without muscle shortening (isometric) or with muscle shortening, is necessary for strengthening to occur. This may not necessarily result in an increase in cross-sectional area, depending on the type of cellular changes that occur. (3) Chronic isometric stimulation, therefore not associated with muscle shortening, will result in strengthening but not substantial decrease in elasticity. (4) Chronic increased stimulation associated with chronic shortening may result in both strengthening and loss of elasticity. (5) It follows that extraocular muscle overaction can result from a temporal sequence in which increased stimulation can lead to contracture. (6) With head tilt to the right or left, the innervation to the vertical muscles must be proportional to the adjacent rectus and oblique muscle to maintain vertical alignment and hence must be greater in absolute value to the oblique muscle. The importance of this is outlined later in the article; however, the reasoning can be understood by considering the right eye of a normal subject tilting his head to the right. It is classically held that there would be stimulation to the right SR and right SO muscles to provide some degree of static countertorsion.23 Because the SR muscle is an elevator and the SO muscle is a depressor, their vertical actions cancel one another, resulting in no change in vertical alignment. However, the SR muscle can normally create a much greater vertical force vector in the primary position than can the SO muscle.20,24,47,48 If the net vertical forces from stimulating these 2 muscles in fact cancel each other, there must be greater stimulation of the SO muscle in absolute terms.

APPLICATIONS OF BASIC MUSCLE PHYSIOLOGY TO OCULAR MOTILITY DISORDERS

I propose that the previously described inconsistencies that derive from our use of the term muscle overaction can be reconciled if one differentiates between a relatively inelastic muscle and a muscle that is actually stronger than normal and if one pays attention to the effects of the Law of Yoke Muscles (Hering’s law) and the Law of Reciprocal Innervation (Sherrington’s law).46 The former states that there is proportional innervation to yoke muscles, and the latter states that there is inhibition of the muscle that is the antagonist of a stimulated muscle. In brief, my hypothesis states that strengthened extraocular muscles overact and inelastic extraocular muscles represent a form of pseudo-overaction.

PRIMARY IO MUSCLE OVERACTION

A key observation for understanding primary IO-OA is that objective fundus extorsion typically precedes the development of the clinical picture of IO-OA (eg, overrelevation in adduction), often by many months to several years. I reported this observation in my discussion of the article by Guyton and Weingarten29 on sensory torsion at the 21st Annual Scientific Meeting of the American Association for Pediatric Ophthalmology and Strabismus (unpublished oral presentation, 1993), and I have found it to be valid for more than 20 years. Subsequently, Eustis and Nussdorf20 confirmed this observation in a prospective study. They found that the presence of objective fundus extorsion in children with infantile esotropia had a 100% positive predictive value for the subsequent development of IO-OA. Guyton and Weingarten29 postulated that this torsion occurs because of a “free-wheeling” torsional drift of the eyes resulting from a loss of fusion. Any substantial extorsional drift must either come from increased stimulation to the IOs or decreased stimulation to the SOs because the vertical rectus muscles have weak torsional vectors. It is unlikely to be due to decreased stimulation to the SOs because if it were, the Bielchowsky head tilt test should be positive; in fact, it is negative in primary IO-OA.11,24 Therefore, the extorsion is probably caused by increased stimulation to the IOs. A long-standing extorsional rotation of the globe will result in a chronic shortening of the IO because the insertion of the IO would be rotated closer to its origin. That, combined with a chronic mildly increased stimulation to the IO will result in loss of elasticity. Depending on the amount by which the stimulation to the IO is increased and how long it lasts, there may be some strengthening of the IO. However, because one typically can observe fundus extorsion prior to the appearance of IO-OA, there is probably only a slight increase in IO stimulation initially. Consequently, the predominant change in the
IO is loss of elasticity and only a relatively small degree of strengthening. Similarly, the SO muscle will be stretched, which will initially increase its passive tension. Subsequently, new sarcomeres should be created, which returns the SO muscle to its original length-tension curve. The lengthened muscle, however, will be relatively lax if the eye is put in the normal position torsionally.

After the IO is chronically shortened in this manner, its elastic force is increased (and hence total force is also increased), resulting in the elevation in adduction and a V pattern that is typically associated with IO-OA. If the IO is indeed less elastic, it will resist stretching out the normal amount as the eye moves into adduction, which would force the eye to elevate. This is perhaps accentuated by the antagonist SO having a weaker than normal resistance to stretch due to sarcomere remodeling. Theoretically, the extorsion alone might explain the elevation in adduction and a V pattern seen with IO-OA. With an exocyclopia, all the rectus muscle insertions should be rotated (counterclockwise in the right eye and clockwise in the left eye). The elevation of the medial rectus insertion and lowering of the lateral rectus insertion would create a vertical vector that should result in elevation in adduction. The nasal displacement of the IR insertion and temporal displacement of the SR insertion would create horizontal vectors that should result in a V pattern. There are 3 compelling reasons, however, that suggest that these force vector changes are not the primary explanation for the elevation in adduction or the V pattern. First, the aforementioned observation that fundus extorsion typically precedes the elevation in adduction, often by many months to several years, should not be found if the pattern and version abnormality was primarily caused by the torsion. Second, if the change in force vector of the rectus muscles caused the torsion, the rise of the eye should be linear as the eye moves from primary into adduction. If fact, the eye typically seems to rise exponentially. Third, transposition procedures that are successful in treating A or V patterns should actually worsen the accompanying torsion. For example, a V-pattern esotropia can be successfully treated with recession and infraposition of the medial rectus muscles. However, that surgical procedure should increase extorsion. If the elevation in adduction and V pattern were directly caused by the extorsion, that surgical procedure should be ineffective. Fourth, I have observed that sometimes fundus extorsion may persist to a substantial degree after surgical weakening of the IOs, yet the elevation in adduction and V pattern may be completely eliminated. Finally, I have observed that patients with bilateral fourth nerve palsy often have larger amounts of extorsion in each eye than one typically sees in patients with unilateral fourth nerve palsy. In spite of this, they usually have relatively small degrees of elevation in adduction. If extorsion was primarily responsible for elevation in adduction, they would be expected to manifest large upshoots on adduction.

If this reasoning is correct, it follows that an IO that is primarily overacting should behave predominantly like an inelastic muscle and less like one that has increased contractile force; however, both can coexist. Inferior oblique inelasticity should be characterized by a palpably stiff muscle on exaggerated forced duction testing. However, because the IO is not substantially stronger than normal, it should not develop an increased active generated force when stimulated, irrespective of there being a slight increased resting innervation to the muscle, as postulated earlier in the article. One would therefore not expect the Bielschowsky head tilt test to be positive as only the normal increase in contractile force would occur with head tilt. In fact, primary IO-OA is not characterized by a positive Bielschowsky head tilt test and typically is characterized by a palpable stiffness. Guyton reported that stiffness of the oblique muscles as determined by the exaggerated traction test correlated reasonably well with the clinical picture of muscle overaction, and he did not report different findings with primary or secondary IO-OA. This is consistent with my own unpublished experience with that test over the past 15 years. More recently Guyton indicated that the stiffness of the IO as felt with the exaggerated traction test correlates even more strongly with the amount of extorsion than with the degree of elevation in adduction (written communication, January 2005). This is to be expected if my hypothesis is correct, and IO inelasticity is a direct result of extorsion.

INFERIOR OBLIQUE “OVERACTION” SECONDARY TO SO PALSY

Inferior oblique overaction that is secondary to ipsilateral SO palsy represents a somewhat different scenario. In this situation, there is still shortening of the muscle due to the exocyclopia that occurs in SO palsy, and consequently there is loss of the IO elasticity. However, other factors are operative. Consider a hypothetical person with a left SO palsy. The person will habitually assume a compensatory right head tilt to facilitate fusion. With the head tilted to the right, there is chronic stimulation to the left IO as depicted in Figure 6. Because the eye is maintained in the primary position due to the compensatory head posture, this chronic innervation to the left IO causes an isometric contraction and should be accompanied by the microstructural changes that result from isometric exercise. In addition, the left IO is undergoing intermittent but frequent active shortening when the left hypertropia becomes manifest due to inattention or fatigue, during sleep, or with other factors that exceed the fusional vergences. Thus, the left IO would be relatively inelastic and also would develop a somewhat increased contractile force. There is evidence that an IO that is overacting secondary to SO palsy is in fact a strengthened muscle. I have found that the anticompenatory extorsional saccades that occur during the dynamic phase of ipsilateral head tilting (eg, extorsion of left eye on tilting left) are longer and faster in patients with SO palsy than in normal subjects.

It should be noted that the left IR muscle should also be receiving chronic isometric stimulation with a chronic right head tilt in the hypothetical example of a left SO palsy as described earlier in the article. However, the actual amount of innervation to the left IR muscle must be substantially less than that to the left IO for the reasons described earlier. Also, the IR muscle is not undergoing the same increase in active shortening that occurs in the IO when the hypertropia becomes manifest. Consequently, there is no substantial increase in the active generated force of
the IR muscle with ipsilateral SO palsy, nor does it become relatively inelastic. In addition, the contralateral (right) SO will be receiving chronic stimulation with the head tilted to the right. The significance of this will be discussed later in this article.

Patients with bilateral SO palsy typically have a lesser degree of IO-OA as well as a smaller Bielschowsky head tilt difference than patients with unilateral SO palsy. This is not surprising. The aforementioned mechanisms that contribute to the increased contractile strength of the ipsilateral IO in patients with unilateral SO palsy would not be occurring if the problem was bilateral. Patients with bilateral SO palsy tend to compensate with a chin-down head posture rather than a head tilt. Also, with a persistent chin-down head posture, both the IOs and SRs are chronically shortened and are receiving an increased degree of innervation. This should lead to some degree of inelasticity as well as strengthening of both sets of muscles. Because the SRs primarily have an elevating vector, the changes occurring in the SRs would tend to cause an elevation in abduction, which will tend to diminish the appearance of overaction of the IO in the other eye on version testing. On the other hand, the IOs primarily have a torsional vector. The changes occurring in the IOs would have the primary effect of substantially increasing the excyclotropia. This may be the reason that there tends to be less elevation in adduction in bilateral fourth nerve palsy despite there being large amounts of extorsion.

**SR MUSCLE OVERACTION/CONTRACTURE**

The SR overaction/contracture syndrome as described by Jampolsky usually occurs secondary to ipsilateral SO palsy; however, it can occur idiopathically or after periocular anesthetic injection. It can have a variable presentation; however, in many cases it is characterized by a hypertropia of the affected eye that increases in upgaze rather than downgaze, a positive Bielschowsky head tilt test, and relatively normal forced ductions. This constellation of findings is most consistent with a muscle that has an increased active generated force but does not actually have decreased elasticity. In some patients with this syndrome, the hypertropia of the affected eye does increase in downgaze; however, forced ductions are still normal or only slightly increased. This is what one should expect. The critical ingredient for development of muscle inelasticity (eg, loss of sarcomeres in series with a shorter slack length) is the maintenance of the muscle in a chronically shortened position. This does not occur in the most common settings of the SR overaction/contracture syndrome, specifically when it is secondary to ipsilateral SO palsy. Because the affected eye is usually in the primary position, perhaps as a result of a compensatory head posture, the SR is not chronically shortened. However, the muscle is in fact repeatedly “exercised” as it makes frequent contractions to elevate the eye during sleep and when fusion is broken, and a hypertropia of the affected eye becomes manifest. These events occur even though the SR is chronically inhibited somewhat because of the inhibition that occurs to the superior muscles with chronic head tilt toward the opposite side. However, the amount of inhibition of the SR with head tilt to the opposite side must be relatively small for reasons that are analogous to the aforementioned discussion of the relative stimulation that occurs to the 2 inferior muscles with head tilt to the opposite side. It appears the inhibition of the SR resulting from chronic head tilt to the opposite side is not sufficient to prevent muscle strengthening from occurring.

**COMMENT**

Understanding what is commonly called muscle overaction requires recognition that multiple factors can cause an eye to move excessively in the field of action of a muscle. Some of these factors are caused by pathophysiologic features that are unrelated to the suspected offending muscle. It also requires differentiating between muscles that have decreased elasticity and muscles with increased contractile force as well consideration of the effect of Hering’s law and Sherrington’s law.

Pulley heterotopia can result in incomitant strabismus that may mimic an overacting IO. This mechanism, however, cannot explain the tightness of the IO that can be felt with exaggerated forced ductions, the fact that objective extorsion frequently precedes the elevation seen in adduction, and the typical normalization of versions after IO recession, all of which are characteristics of the entity commonly referred to as IO-OA. Probably pulley heterotopia only accounts for some patients who show elevation in adduction; in many the problem may be due to a loss of elasticity of the IO.

Kono and Demer compared the size and contractility of the IO in normal subjects with those with known SO palsy using dynamic orbital imaging and found essentially no difference between the 2 groups. They concluded the overelevation in adduction seen in patients with SO palsy must come from some mechanism other than muscle hypertrophy and attributed it to pulley dysfunction. They did not discuss the possibility that relative inelasticity of the IO could be responsible, which would still be consistent with their radiographic findings. Interestingly, they also found that the IO on the contralateral side showed hypertrophy as compared with normal controls. This is what one should expect given the chronic isometric contraction occurring in that muscle if the patient assumes a compensatory head tilt to control the hypertropia (Figure 6). This may result in an increase in the hypertropia of the eye with the SO palsy when it is in abduction, which could mimic SR overaction/contraction on that side. It would also cause an increase in the Bielschowsky head tilt difference because the hypertrophied contralateral SO would cause a greater downward force with head tilt toward the side of the paretic SO.

Brodsky and Donahue offered a theory on the cause of IO-OA based on evolutionary and teleological reasoning. Their theory would not account for the fact that fundus extorsion precedes the clinical picture of IO-OA. Nevertheless, their theory is completely compatible with and complementary to the ideas set forth in this article.

A serious obstacle to our understanding of eye muscle pathology in these different clinical circumstances is the lack of a practical way to obtain tissue samples of the entire muscle in humans with strabismus. It should be stated, however, that there are some known differences between the extraocular muscles and other striated muscles. The muscle fibers that make up the extraocular muscles are unique in that they do not follow any traditional skeletal muscle fiber classification schemes and have a smaller muscle fiber diameter than most other skeletal muscles. Eighty percent of the orbital layer muscle fibers are fast twitch, singly innervated, and resistant to fatigue. Also, they have the smallest ratio of muscle fibers to motor neurons of any muscles in the body. Skeletal muscles usually have a heterogeneous cross-
sectional structure with a layered or compartmentalized arrangement. This is also the case with the extraocular muscles; however, the rectus and oblique muscles characteristically differ from one another. In the oblique muscles, the orbital layer often completely surrounds the global layer whereas in the rectus muscles the orbital layer is C-shaped in cross-section and does not completely surround the global layer. Oblique and rectus muscles differ primarily with respect to the total number of fibers within the orbital but not the global layers. Furthermore, the orbital and global layers differ with respect to fiber type and speed of contraction with the orbital layer being slower.

Because of all of these unique qualities of extraocular muscles, some conclusions about the extraocular muscles that are extrapolated from the behavior of other striated muscles may be flawed. In addition, my theory predicts there should be a shorter slack length in IO muscles that are either primarily or secondarily overacting than in normal muscles. Because it is not currently practical to obtain such measurements in normal subjects, confirmation of this hypothesis must await new technology for obtaining this information. Nevertheless, a confluence of clinical signs conspire to suggest that overlapping pathophysiologic features can lead to different forms of extraocular muscle overaction and correlate with different clinical disorders.

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REFERENCES

42. Christiansen SP, Soulsby ME, Seifen EE. Type-specific changes in fiber morphometry following denervation of canine extraocular muscle. Exp Mol Pathol. 1992;56:87-95.