

# Ocular Torsion Reveals the Mechanisms of Cyclovertical Strabismus

## The Weisenfeld Lecture

David L. Guyton

In the mid 1970s, during my ophthalmology training at Johns Hopkins, the mechanisms involved in the common horizontal misalignments of the eyes (horizontal strabismus) were reasonably well understood. At least the muscles involved were known. But even the common forms of cyclovertical strabismus were poorly understood: overacting /underacting oblique muscles, “A” and “V” patterns, dissociated vertical deviation, and congenital superior oblique paresis. Over the course of my career, the key to understanding the mechanisms involved in these forms of cyclovertical strabismus has been ocular torsion. This is a chronologic story of how I came to appreciate ocular torsion, learned how to measure it, and with a succession of colleagues have been able to use the torsional positions and torsional movements of the eyes to gain useful insight into the mechanisms involved in these forms of cyclovertical strabismus.

Some of the “truths” that I believe we have discovered will seem very speculative to many—almost “leaps of faith.” As we continue to seek further evidence for the theories presented here, I frequently recall the “three stages of truth” attributed to the 19th-century philosopher Arthur Schopenhauer<sup>1</sup>: “All truth passes through three stages. First, it is ridiculed. Second, it is violently opposed. And third, it is accepted as being self-evident.” My hope is that there will prove to be something new and valuable in what I have to say, valuable enough to withstand the test of time.

### MEASUREMENT OF OCULAR TORSION

Ocular misalignment can be horizontal, vertical, and/or torsional, that is, twisted about the line of sight. It should be immediately obvious that we can see horizontal and vertical deviations externally, but there are no external landmarks to judge torsional deviations.

In the 1970s ocular torsion was measured in various ways, most commonly subjectively, with double Maddox rods or, rarely, with the Lancaster Red-Green Test.<sup>2</sup>

*Objectively*, there were additional measurement techniques: blind spot mapping, fundus photography, and estimation by indirect ophthalmoscopy.

But in the 1970s, fundus torsion was still rarely recognized. When an abnormal fovea/disc relationship was seen in fundus

photographs, it was called foveal ectopia, not recognized as abnormal torsion of the globe. Torsion was measured subjectively, and fundus torsion was basically ignored. For example, Dr. Marshall Parks stated in his 1975 text on strabismus<sup>3</sup> that the clinical condition known as primary inferior oblique overaction shows zero excyclodeviation, helping to distinguish it from secondary inferior oblique overaction where excyclodeviation is present. But he was measuring torsion only subjectively. After the recognition of fundus torsion, we now know that primary inferior oblique overaction shows up to 10° to 15° of extorsion, more than most cases of secondary inferior oblique overaction.<sup>4</sup>

My first investigation into ocular torsion was in 1976 as a clinical fellow with Gunter von Noorden. von Noorden was puzzled about why a torted eye does not right itself when the fellow eye is covered, and yet the torted image subjectively straightens to the patient. So we began to investigate ocular torsion.

To investigate subjective versus objective torsion, I compared careful double Maddox Rod measurements with fundus photographs. We discovered that there is significant subjective adaptation to fundus torsion. Young children adapt physiologically to show no subjective torsion, and adults adapt at least monocularly to perceive the world as straight even though the eye remains torted when the other eye is covered—a type of adaptation that we call psychologic for lack of a better word.

It turned out that primary inferior oblique overaction that develops in early childhood shows large amounts of fundus extorsion, but shows zero subjective extorsion on double Maddox rod or Lancaster Red-Green tests, because of complete sensory adaptation.<sup>5,6</sup>

In my early practice of strabismus, I needed a practical assessment of fundus torsion so that I could correlate the amount of abnormal ocular torsion with other aspects of strabismus. It was not practical to do careful blind spot mapping or take frequent fundus photographs. It was practical, though, to use indirect ophthalmoscopy, because we already used this for fundus exams. But I reasoned that this would only work if I could learn to think in terms of the inverted and reversed view.

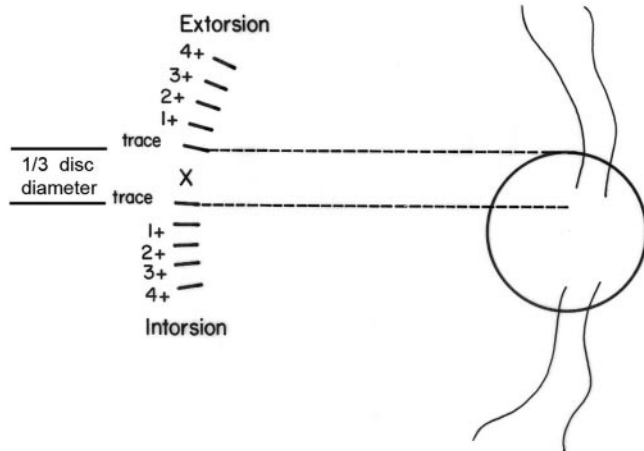
Therefore I devised a scheme for grading the amount of abnormal fundus torsion as viewed with the indirect ophthalmoscope (Fig. 1).<sup>7</sup> I began to *think* in terms of, *teach* in terms of, and even *publish* in terms of, the inverted and reversed fundus image, which greatly eased the mental gymnastics needed to judge the direction and amount of abnormal torsion. After teaching this scheme to my residents and fellows, and after having them commit themselves on a scrap of paper regarding the type and amount of fundus torsion that they saw in patients we examined together, the subjective grading of fundus torsion soon became automatic and reasonably repeatable.

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Corresponding author: David L. Guyton, The Wilmer Institute 233, Johns Hopkins Hospital, 600 N. Wolfe Street, Baltimore, MD 21287-9028; dguyton@jhmi.edu.



**FIGURE 1.** Grading system for estimating abnormal ocular torsion by indirect ophthalmoscopy. An indirect ophthalmoscopic view of the left fundus is illustrated. The normal range for the fovea is within the upper third of the optic disc in this view. Modified with permission from Guyton DL. Clinical assessment of ocular torsion. *Am Orthopt J.* 1983;33:7-15. © 1983, The University of Wisconsin Press.

### OBLIQUE MUSCLE OVERACTION/UNDERACTION AND “A” AND “V” PATTERNS

I began to correlate fundus *extorsion* with “V” patterns and with what we called overacting inferior oblique muscles (Fig. 2), and fundus *intorsion* with “A” patterns and overacting superior oblique muscles. Others, without being aware of the abnormal fundus torsion, were noting the strong correlation between overacting inferior oblique muscles and “V” patterns and between overacting superior oblique muscles and “A” patterns.<sup>8</sup>

It soon became evident to me that the abnormal fundus torsion that I was seeing in these patients was in the right direction to actually explain the oblique overaction and associated “A” or “V” pattern simply by rotation of the planes of action of the rectus muscles (Fig. 3). I discovered that Dr. Jean-Bernard Weiss in France, in 1966, had proposed exactly this mechanism.<sup>9</sup>

We mapped the eye movement patterns of a number of our patients with fundus torsion and found remarkably good correlation between the amount of abnormal fundus torsion and the relative rotation of the eye movement patterns (Figs. 4A and 4B).<sup>10</sup>

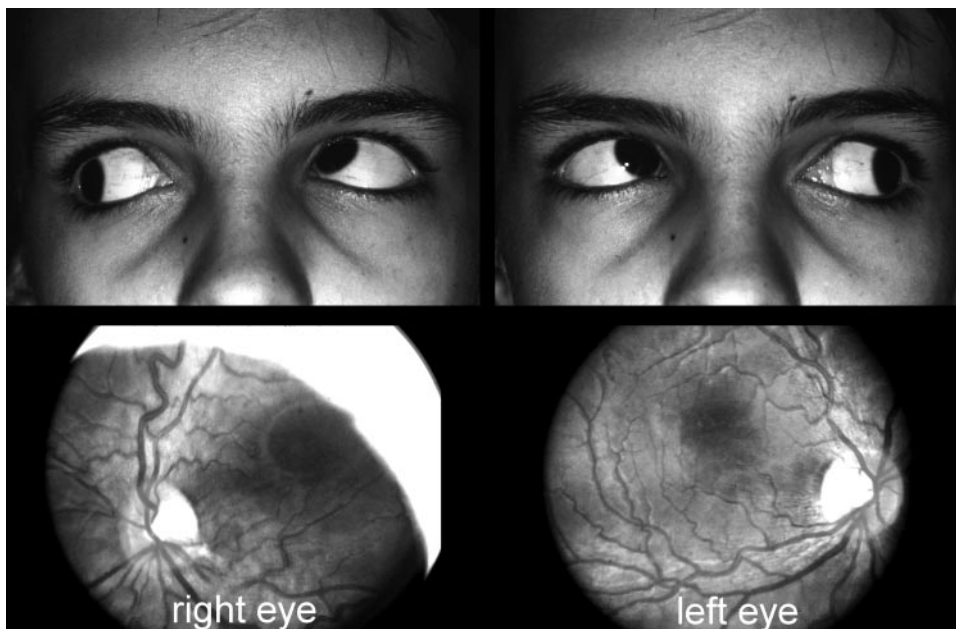
But what maintains the abnormal torsion? It seemed clear to me that the rectus extraocular muscles would oppose abnormal torsion and would tend to right the eye. So *extorsion*, for example, must arise and be maintained either by increased neurologic tonus to the inferior oblique muscle, or by a physically shortened inferior oblique muscle along with a lengthened superior oblique muscle—a mechanical effect. The obvious question was whether this oblique muscle effect was neurologic or mechanical, or some of both. And furthermore, how did it develop in the first place? This led me to theorize about how changes in strabismus occur over time.

### CHANGES IN STRABISMUS OVER TIME

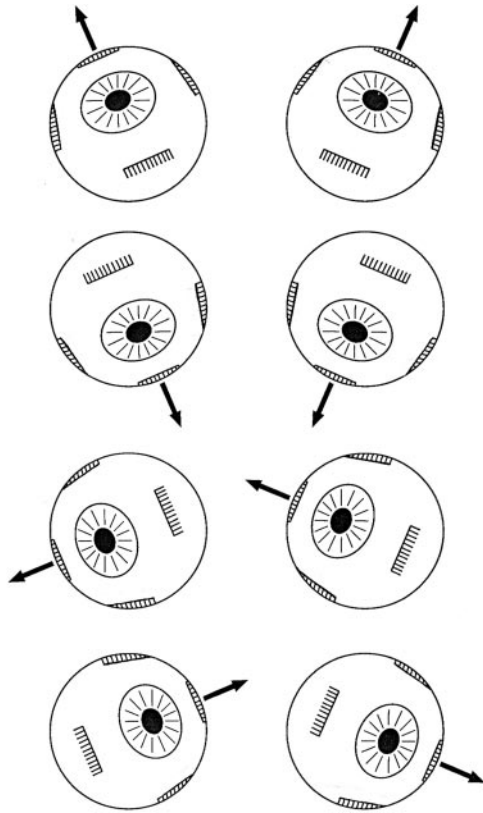
One of the most informative deviations of the eyes is the condition we call sensory exotropia. When vision is lost in one eye from injury or eye disease, that eye typically turns outward slowly over time. But this process does not require loss of vision per se; it is the loss of binocular fusion that is the operative factor. With the loss of sensory input from one eye, fusion can no longer occur, and it is fusion that holds the eyes straight over time.

But fusion does not occur only horizontally; it occurs vertically and torsionally as well. With loss of fusion, therefore, the eyes can become misaligned horizontally, with what we call sensory exotropia (or in some situations sensory esotropia), misaligned vertically, which we may call sensory hypertropia, or misaligned torsionally, which I have dubbed “sensory torsion.”<sup>10</sup> But is this misalignment due to changes in the neurologic signals to the eye muscles, that is, changes in so-called neurologic tonus, or due to actual muscle length changes?

In the 1970s and 1980s, muscle physiologists in France and England investigated the phenomenon of muscle length adaptation.<sup>11-13</sup> Skeletal muscles adapt their lengths throughout life by the addition or subtraction of sarcomeres for optimal function over the range that they are used.<sup>14</sup> The half-life of the contractile protein in the skeletal muscles is only 7 to 15 days.<sup>11</sup>



**FIGURE 2.** Striking “clinical overaction of the inferior oblique muscles,” (top) correlated with 4+ extorsion of both eyes as seen in the indirect ophthalmoscope view.



**FIGURE 3.** Extorsion of the globes causes rotation of the planes of action of the vertical and horizontal rectus muscles. Activation of the vertical rectus muscles (*upper drawings*) produces a “V” pattern, while activation of the horizontal rectus muscles to either side (*lower drawings*) produces upshoot in adduction (apparent “overaction of the inferior oblique muscles”). Reprinted with permission from Guyton DL, Weingarten PE. Sensory torsion as the cause of primary oblique muscle overaction/underaction and A- and V-pattern strabismus. *Binoctul Vis Eye Muscle Surg Q.* 1994;9(3)215. © 1994 Dillon, CO: Binoculus.

There are several stimuli that induce muscle length adaptation, including tension or the lack thereof, mechanical stretch or the lack thereof, and neurologic stimulation or the lack thereof. Of particular relevance to the eye muscles is the presumed responsiveness of sarcomere adaptation to neurologic stimulation. If the extraocular muscles behave as other skeletal muscles, increased stimulation will shorten them via loss of sarcomeres, and decreased stimulation will allow them to lengthen via gain of sarcomeres.

With this critical information, we can complete a hypothetical model of the dynamic feedback system for maintenance of long-term ocular alignment.

### Modeling the Ocular Alignment Control System

The basic components are now in place to model the ocular alignment control system (Fig. 5). The model begins with the existing basic muscle lengths of each muscle, determined by the number of sarcomeres. Each muscle receives a resting level of stimulation (vergence tonus) to result in the functional muscle length to yield aligned eyes.

But then along comes a perturbation, such as a hormonal growth spurt with a change in the divergence of the orbits, or simply a new pair of glasses with slight optical differences from the old pair. Such a perturbation requires different eye alignment and will thus result in misaligned eyes for new tasks if no compensation is made. But misaligned eyes cause retinal image disparity, with double vision, which the brain does not like. So

the brain responds with fast fusional vergence, changing the stimulation levels to the muscles. This yields new functional muscle lengths in the proper direction to compensate for the original perturbation and realigns the eyes.

Something else now happens. Sustained fast fusional vergence leads to vergence adaptation, which adjusts the basic level of vergence tonus to ease the burden on fast fusional vergence, freeing it to be able to respond to the next perturbation.

But there is a limit to the amount of vergence adaptation that can be sustained, so something further happens. In response to the overall vergence tonus, the muscle lengths slowly adapt to new basic lengths in the proper direction to reduce the original image disparity. Once the basic muscle lengths have adapted, the neurologic feedback mechanisms that the original perturbation brought into play can subside, with the eyes aligned once again. And the neurologic mechanisms can now be maximally responsive to the next perturbation.

This is my model of the normal functioning of the long-term ocular alignment control system. This is the feedback scheme that I believe keeps the eyes aligned during the growth of the skull in early life, throughout the development of hand-eye coordination in oblique directions of gaze, and throughout the development of presbyopia, which would otherwise cause a significant disruption of near versus distance alignment.

### Breakdown of the Ocular Alignment Control System

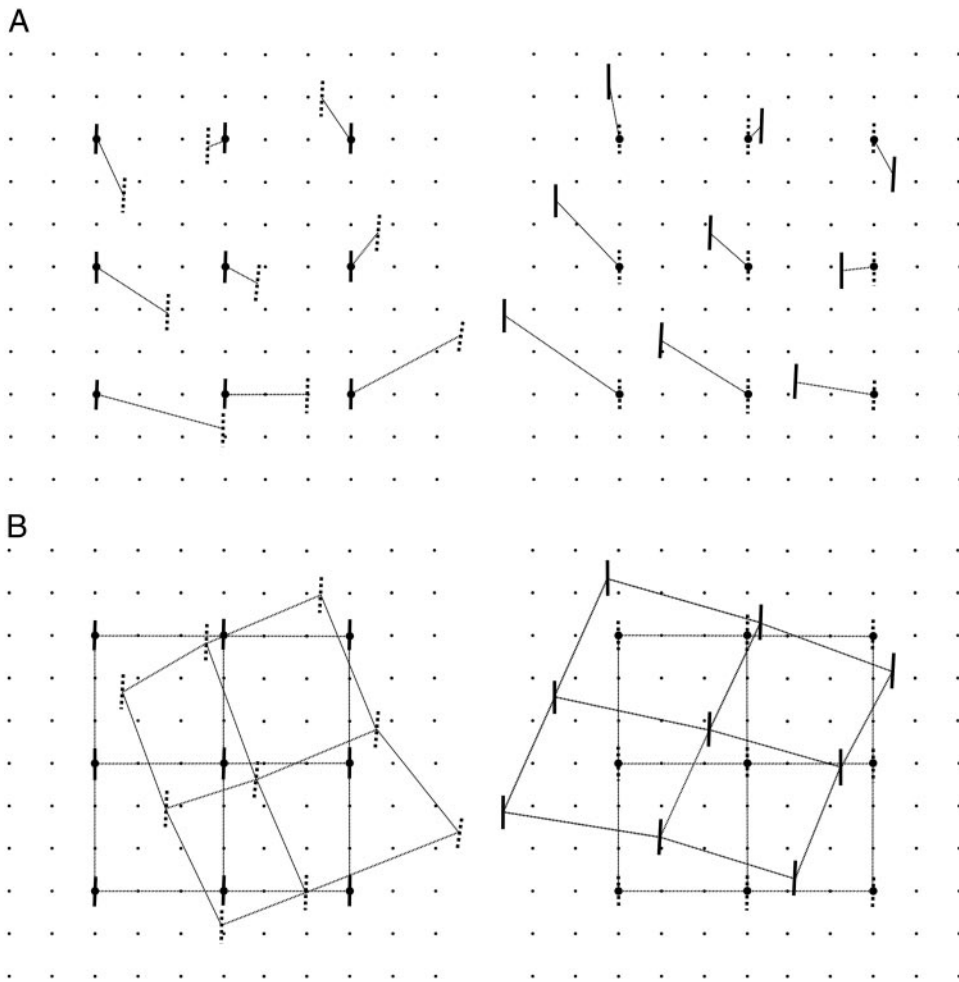
But what happens when something malfunctions in this feedback system? I cannot emphasize strongly enough that abnormalities can be present, or can develop, at various levels within this system, any of which will lead to misalignment of the eyes. But the most common abnormality is probably the absence of, or loss of, fast fusional vergence, which I shall refer to simply as fusion. Fusion is at a most critical position in this feedback pathway system.

If fusion does not occur in response to retinal image disparity, stimulation levels do not change appropriately, and the entire system breaks down. With loss of input from the fast fusional vergence system, the longer-term mechanisms for ocular alignment, vergence adaptation and muscle length adaptation, become free-wheeling—in other words, without guidance.

But neurologic feedback mechanisms do not necessarily shut off when their input disappears. They often continue to function at a basal level, with a low level of output being generated. This basal output level can be biased, though, in one direction or the other, and therefore in this case can continue to drive the muscle length adaptation mechanism slowly in one direction or the other, producing strabismus that was not there in the first place, or causing progressive misalignment if strabismus was already present.

A prime example of this mechanism is the phenomenon of sensory exotropia. With loss of vision in one eye, fusion is lost, and, as we have assumed in the past, the eye simply drifts outward over time. From the feedback model, though, we can begin to understand that if poor vision develops in one eye and therefore if the eyes do not have any need for convergence, the average vergence stimulation to the extraocular muscles will shift slightly toward less convergence. The previous balance of vergence stimulation was holding the eyes straight, so the imbalance caused by less convergence actively drives the eyes outward into a position of exotropia. This resulting “sensory” exotropia can thus be seen to be not a passive process after all, but an active driving of the eyes outward by the otherwise *normal* alignment mechanisms that have become imbalanced by the loss of proper guidance.

When we apply this scenario to the cyclofusion mechanism, when fusion is faulty or is lost, it is easy to see how progressive



**FIGURE 4.** (A) Lancaster red-green plots from an adult with overacting inferior oblique muscles and a large “V” pattern since childhood. *Pairs of lines*: projection of the two eyes’ subjective vertical meridians onto the wall 1 m away: *solid lines*, right eye; *dashed lines*, left eye. The horizontal and vertical separation between adjacent dots in the grid represents 15 prism diopters of deviation. The right eye is fixing at the standard grid coordinates in the plot on the *left*, and the left eye is fixing on those same coordinates in the plot on the *right*. The patient also has esotropia (crossed eyes), with the projections crossing over one another to strike the wall, crossing more in down gaze than in up gaze, documenting the “V” pattern. Note that there is no sensory extorsion in any gaze position—the individual pairs of streaks are parallel. (B) When the right eye projections and left eye projections in Figure 4A are connected with each other respectively, significant rotation of one eye movement pattern with respect to the other is evident, consistent with more than 20° of objective net fundus extorsion between the two eyes on fundus photographs.

torsional misalignment can develop. Abnormal torsional misalignment produces “A” or “V” patterns when the vertical rectus muscles act, and clinical “overaction” or “underaction” of the oblique muscles on side gazes.

Seeking evidence to support this mechanism, we did a retrospective study of 21 patients with intermittent exotropia, intermittently fusing, who lost fusion for at least one month via overcorrection from strabismus surgery.<sup>15</sup> In 43% of them, a significant “A” or “V” pattern developed. This finding was in comparison with a control group of 21 similar patients, all of whom maintained fusion after surgery, with a pattern developing in only one of them, years later (Fig. 6).

Thus at the beginning of the list of cyclovertical deviations, in my mind, I felt that I understood primary oblique muscle overaction or underaction, and “A” and “V” patterns.

## DISSOCIATED VERTICAL DEVIATION

Next was dissociated vertical deviation. What was the mechanism, and which extraocular muscles were involved? The drifting upward of one or the other eye is now known as “DVD,” or with its torsional and horizontal components, as the “dissociated strabismus complex.” This phenomenon had eluded explanation since it was first described by George Stevens in 1895. It appears to violate Hering’s Law of equal innervation of yoke muscles.

DVD can be latent, intermittent, or constant (Fig. 7). Because patients with DVD appear “spaced out,” it is commonly assumed that the onset of manifest DVD is indicative of day-

dreaming. But we have evidence, that I shall present later, to suggest that it usually occurs to help them see more clearly.<sup>16</sup>

DVD is known to be strongly associated with early strabismus and with latent nystagmus, especially latent nystagmus with a torsional component. Many patients with DVD have anomalous head postures.<sup>17</sup> But what is the mechanism?

A major stumbling block to understanding has been the teaching that DVD serves no obvious purpose. Indeed in 1938, Marlow wrote, “Divergence from parallelism is quite purposeless. Any useful purpose served by it is unthinkable.”<sup>18</sup>

Marlow suggested that “[Dissociated vertical deviation] may be . . . a vestige or rudiment of an earlier stage when the eyes could be used simultaneously in the interest of circumferential vision.” Michael Brodsky has advanced a similar theory more recently—that DVD represents a vestigial, primitive righting reflex, with no active purpose in humans.<sup>19</sup>

But others have questioned these opinions. In 1981, Joyce Mein, a British orthoptist, observed the natural history of latent nystagmus. It decreased as DVD developed, and she suggested that DVD occurs to damp latent nystagmus, improving vision in the fixing eye.<sup>20</sup> A similar suggestion was made to me by a fellow applicant, Scott McClatchy, in 1992, and then independently by my clinical fellow Ed Cheeseman in 1997.

With the help of David Zee and his laboratory, we set out to investigate. Using bilateral scleral search coils, we obtained simultaneous horizontal, vertical, and torsional eye movement recordings of six young adult patients with DVD. We found that all of the patients showed latent nystagmus that appeared or worsened when one eye was covered and became damped as DVD developed.<sup>21</sup> Figure 8 shows an example of the recordings.

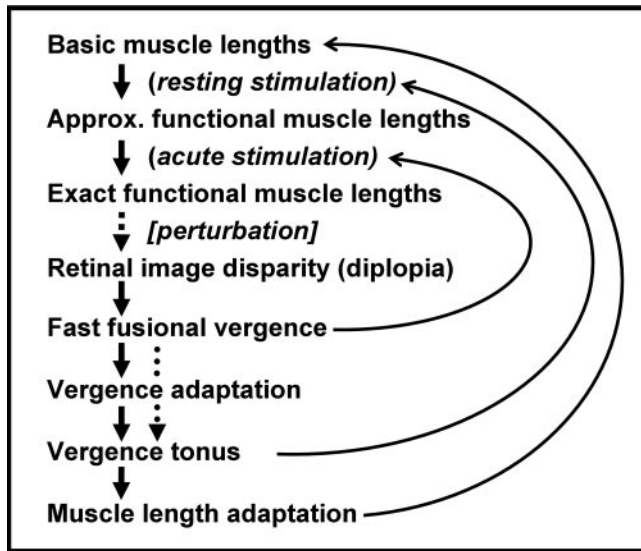


FIGURE 5. Retinal image disparity (center) elicits fast fusional vergence, which leads in the short term to vergence adaptation, which changes vergence tonus. Vergence tonus stimulates muscle length adaptation over a longer term, all of which reduce the retinal image disparity. Each level of this marvelous three-stage feedback process works in the direction to ease the burden on the process that precedes it. Vergence adaptation frees up fast fusional vergence to be able to respond accurately to rapid changes in retinal image disparity. Muscle length adaptation relieves vergence adaptation of excessive demands which would otherwise saturate neurologic firing rates, and thereby effectively resets vergence adaptation so that it can continue to function optimally in response to input from fast fusional vergence. Modified with permission from Guyton DL. Changes in strabismus over time: the roles of vergence tonus and muscle length adaptation. The 10th Bielschowsky Lecture. *Binocul Vis Strabismus Q.* 2006;21(2):83. © 2006 Dillon, CO: Binoculus.

In some cases the latent nystagmus was very transient, and it was not always visible clinically. But it was always present on the scleral search coil recordings. Thus, our observation that latent nystagmus was always present and became damped when DVD developed was at least consistent with our thesis that DVD has a purpose after all—to damp latent nystagmus to improve vision in the fixing eye. Perhaps this unthinkable divergence from parallelism was thinkable after all.

Subsequent scleral search coil recordings gave additional evidence that DVD damps latent nystagmus, for example by the fact that latent nystagmus began to reappear in some cases

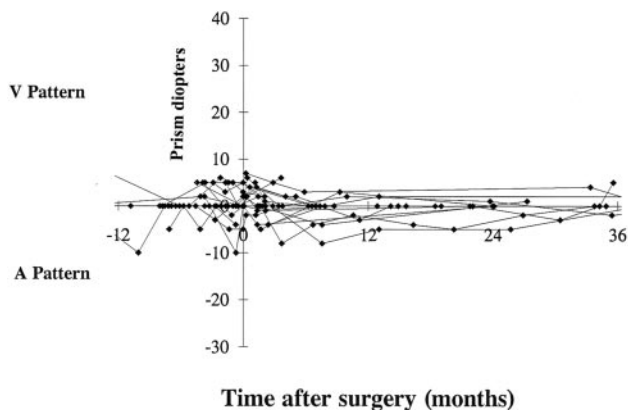


FIGURE 6. “A” or “V” patterns developing in patients after surgery for intermittent exotropia. A control group of 21 patients maintained fusion post-operatively (left) and did not develop significant “A” or “V” patterns. But of 21 patients who lost fusion post-operatively because of surgical overcorrection (right), 43% developed a significant “A” or “V” pattern. Modified with permission from Miller MM, Guyton DL. Loss of fusion and the development of A or V patterns. *J Pediatr Ophthalmol Strabismus.* 1994;31:220–224. © 1994 Thorofare, NJ: Slack.

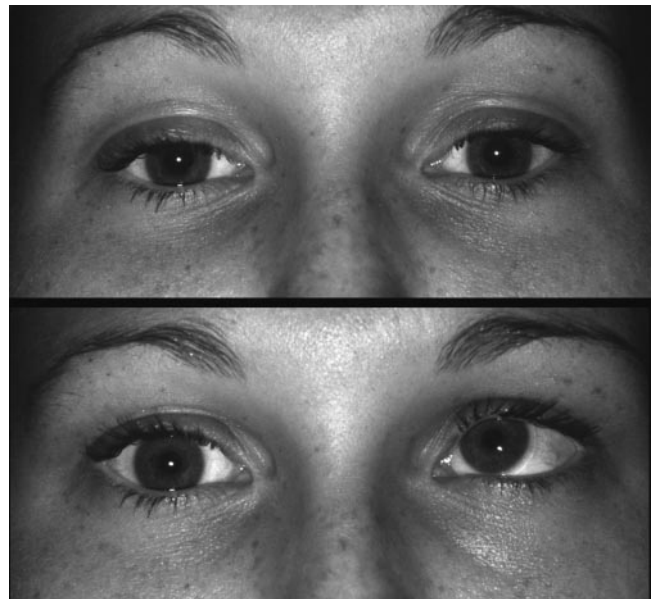
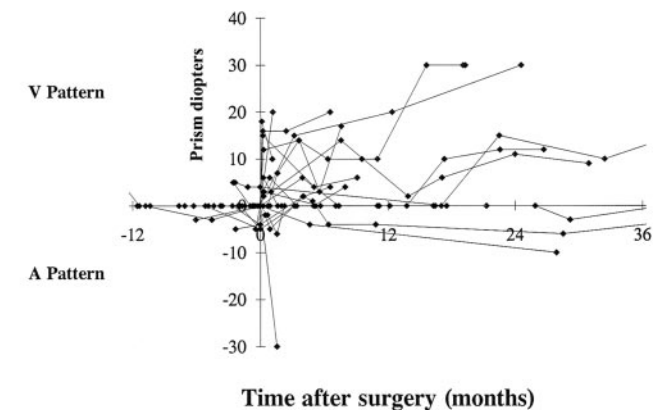


FIGURE 7. Patient with intermittent DVD, fusing above and showing left DVD with an accompanying esodeviation below.

as the DVD diminished, consistent with decreasing effort being exerted to damp the nystagmus (Fig. 9).<sup>16</sup>

In addition, some patients had learned what it felt like to fix with one eye or the other and, in two cases, what it felt like to fuse. They described it as similar to raising one hand or the other; they simply willed it to happen. They could even will “fixation” with either eye in total darkness, and in addition the two patients could will “fusing” with both eyes in total darkness. So we did scleral search coil recordings in the dark. We documented that when “willing” a “switch of fixation” from one eye to the other in the dark, or when “willing” a switch from “fusing” to “fixing with one eye” in the dark, the patients developed the appropriate direction of latent nystagmus, DVD developed, and the latent nystagmus became damped when the DVD developed.<sup>16</sup>

While many others still believe that latent nystagmus and DVD simply coexist and do not influence one another, it is my clear impression, strengthened by the results from these recordings in the dark, that via repeated recruitment to damp latent nystagmus to improve vision, DVD can become a learned, anticipatory response that is initiated automatically



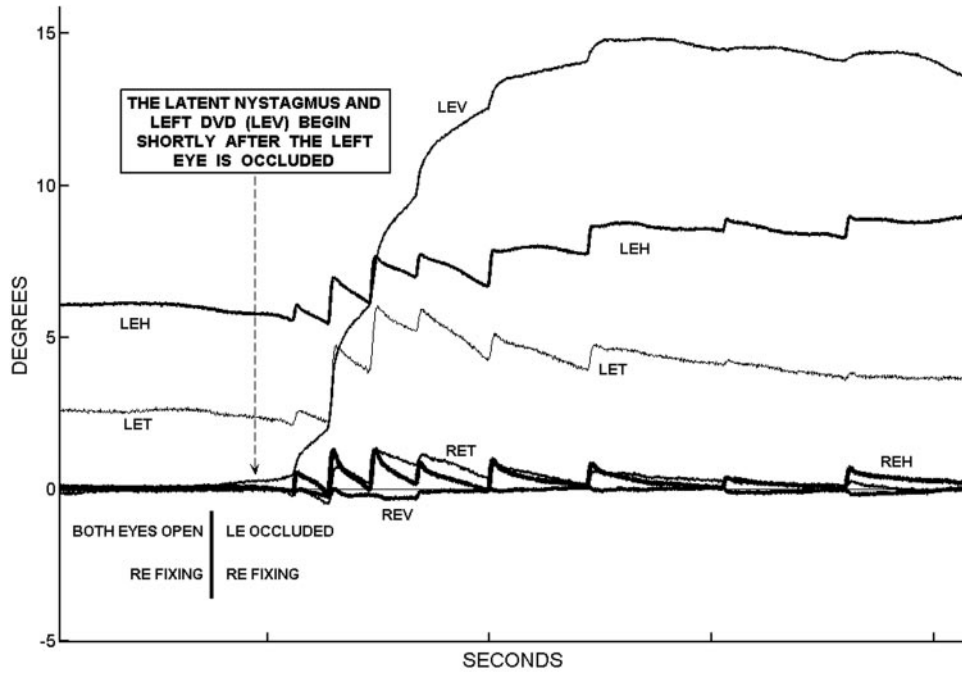


FIGURE 8. DVD developing (LEV increasing markedly) when the left eye is covered. Eye movement directions are from the patient's perspective looking forward. For vertical movement of the right eye (REV) and of the left eye (LEV), the recording of an upward deflection signifies upward movement. For horizontal movement of the right eye (REH) and of the left eye (LEH), recording of an upward deflection signifies movement to the patient's right. And for torsional movement of the right eye (RET) and left eye (LET), the recording of an upward deflection signifies clockwise rotation about the line of sight. Here strong latent nystagmus develops as soon as the left eye is covered, with horizontal, vertical, and torsional components. All three components of the suddenly induced latent nystagmus become significantly damped (best judged by decreased slopes of the slow phases) as the DVD develops. Modified with permission from Guyton DL. Dissociated vertical deviation: An acquired nystagmus blockage phenomenon. Richard G. Scobee Memorial Lecture. *Am Orthopt J.* 2004;54:77-87; © 2004, The University of Wisconsin Press.

when switching fixation to one eye, even in the dark. There is a familiar precedent for such an anticipatory eye movement—the “rebound” or “bounce” phenomenon that often occurs when strabismus is measured with the prism and alternating cover test.

But which extraocular muscles are primarily involved in the DVD response? After all, as strabismus surgeons, we were anxious to improve the results of surgery for DVD, which up to that point was empiric and not overly successful.

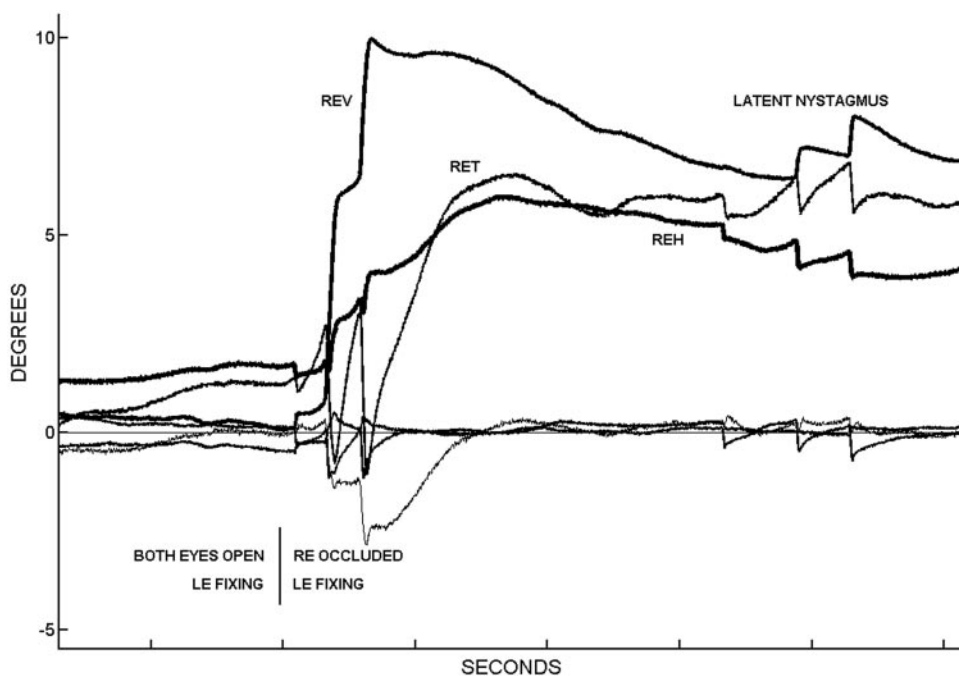


FIGURE 9. DVD develops when the right eye is covered (REV), but then begins to diminish as the left eye continues to fix along the baseline. As the DVD diminishes, latent nystagmus begins to appear. (Same labeling as in Fig. 8.) Reprinted with permission from Guyton DL. Dissociated vertical deviation: An acquired nystagmus blockage phenomenon. Richard G. Scobee Memorial Lecture. *Am Orthopt J.* 2004;54:77-87; © 2004, The University of Wisconsin Press.

Here is where the analysis of torsional eye movements proved indispensable. This analysis<sup>21</sup> is far beyond the scope of this presentation, but was based on the key concept that if an eye is rotating downward and simultaneously intorting, the superior oblique muscle must be playing a major role, and if it is moving downward and simultaneously extorting, the inferior rectus muscle is playing a major role. Using this simple but powerful qualitative analysis, DVD could be decomposed into vergence and version eye movements. And, each vergence and version eye movement obeyed Hering's Law.

As it turned out, several eye movements participate in the dissociated strabismus response. If there is a significant horizontal component of the latent nystagmus, an exaggerated convergence usually occurs to damp this component, as seen clearly in our recordings. The cyclovertical component of the latent nystagmus is damped by a vertical vergence. This vertical vergence, which is responsible for the elevation of the eye behind the cover, largely involves the oblique muscles. The movement is an exaggeration of a cyclovergence/vertical vergence particularly involving the oblique muscles that appears from our recordings to be normally involved in the vertical fusion response (see Fig. 13, later). The involvement of the oblique muscles in vertical fusion was first investigated in 1992 by Enright,<sup>22</sup> using video oculography. Hence our title in 1998: "Dissociated vertical deviation: An exaggerated *normal* eye movement used to damp cyclovertical latent nystagmus."<sup>23</sup>

Head tilts are often used as an alternative or adjunctive method of damping the cyclovertical component of latent nystagmus. When the head is tilted to a nonfavored position, DVD has to be used to damp the nystagmus. Because the DVD lessens or disappears when the head is tilted back toward the favored position, it has often been assumed by clinicians that the head tilt is being used to decrease the DVD. It is actually the latent nystagmus that the head tilt is decreasing, and with the latent nystagmus damped, the DVD decreases because it does not have to be used.

Especially valuable were the comments of one 20-year-old patient with DVD and a small customary left head tilt.<sup>16</sup> She could fuse or fix with either eye voluntarily, with or without head tilt. We recorded moderate manifest latent nystagmus when she was fusing with her head straight, less with her customary head tilt, and least when she broke fusion and displayed DVD. She volunteered (as have other patients) that she preferred to fuse when looking in the distance, but that when she wanted to see most clearly, she voluntarily broke fusion and let one eye go up. She indeed read several letters better on the 20/20 line when the DVD was manifest, as consistently measured with the ATS3 automated staircase visual acuity test,<sup>16</sup> at a distance of 3 m with single letters with surround bars.

Other patients have also shown the onset or worsening of DVD when trying to read smaller and smaller letters, as illus-

trated in Figure 10 in the form of three movies for online viewing, <http://www.iovs.org/cgi/content/full/49/3/847/DC1>.

But DVD occurs not only with increased attention, it can indeed occur with tiredness or daydreaming. This typically happens, though, from my observations, in patients with DVD who can fuse. When they tire or daydream and no longer maintain the effort to fuse, monocular fixation appears, along with the accompanying, anticipatory DVD movement.

Thus, to my satisfaction, despite other theories to the contrary, the mechanism and purpose of DVD were explained, as documented by our eye movement and video recordings, and could await future confirmation by others.

## CONGENITAL SUPERIOR OBLIQUE PARESIS

The last common cyclovertical deviation to explain was congenital superior oblique palsy. Head trauma or certain neurosurgical procedures can damage the fourth cranial nerve, causing a characteristic ocular motility pattern, complete with extorsion of the involved eye and a compensatory head posture, that we call acquired fourth nerve palsy. The fourth cranial nerve innervates only the superior oblique muscle, and so this condition is often called acquired superior oblique palsy.

But a very similar ocular motility pattern, with the same compensatory head posture and the same extorsion of the involved eye, can arise in any decade of life, more commonly in the early decades, and is of unknown cause. We have always assumed that this pattern also represents superior oblique palsy, or simply superior oblique paresis (weakness), that the patient was always able to control in younger life, but which finally decompensated. Therefore, this disorder has been termed congenital superior oblique paresis, a presumed inborn weakness of the superior oblique muscle not manifest until later in life.

With the exception of the cyclovertical deviations I have already mentioned and with the exception of a few restrictive and third cranial nerve syndromes, superior oblique paresis, in its acquired and congenital forms, is the most common cyclovertical deviation that we see in clinical practice. In other words, most cyclovertical deviations of the eyes are attributed to superior oblique palsy or paresis.

But this is very strange, especially if we try to draw an analogy to horizontal deviations. We divide the various types of horizontal deviations of the eyes into parietic types and nonparietic types. For example, a few cases of esotropia (crossed eyes) are due to sixth cranial nerve palsy, but most cases of esotropia are due to nonparietic mechanisms.

We know that some cases of cyclovertical deviations are definitely due to fourth cranial nerve palsy, but where is the analogous group of nonparietic cyclovertical deviations? We do not recognize such a group! Is there not an analog of basic esotropia in the cyclovertical "plane"? I have long suspected



**FIGURE 10.** *Left:* 22-year-old female consistently broke fusion and developed right DVD and esotropia when reading down the eye chart and encountering the 20/40 line of letters (Movie 1). *Middle:* 6-year-old female consistently developed left DVD when reading across the 20/30 line of letters (Movie 2). *Right:* 6-year-old myopic female developed right DVD when the right eye was occluded, and the DVD worsened when she then tried to read the letters at the threshold of her uncorrected visual acuity (Movie 3). Movies are online at <http://www.iovs.org/cgi/content/full/49/3/847/DC1>.

that many cases of what we call congenital superior oblique paresis are not the result of paresis after all, but rather represent in the cyclovertical “plane” the analog of basic esotropia in the horizontal plane. This thought festered in my mind for years, but I could not think of a way to investigate it.

Recent studies have shown that many patients with apparent superior oblique paresis have superior oblique muscles with normal cross-sectional area and normal contractility. Demer et al.<sup>24</sup> wrote in 1995, “Of 19 SO muscles diagnosed to be palsied based on clinical criteria, MRI demonstrated that about half exhibited normal cross-sectional size and contractile characteristics.” Might these patients simply have “basic cyclovertical deviations,” with no paresis?

Finally, on thinking more about what causes strabismus to change over time, and by making a critical observation in many of my patients, I came up with a way to investigate the mechanism that may be involved in a hypothetical “basic cyclovertical deviation” that masquerades as a true congenital superior oblique paresis.

The critical observation was that changes in strabismus are almost always bilateral,<sup>25</sup> as evidenced by the patients in Figures 11 and 12. This observation leads to the realization that extraocular muscles must behave differently from the other skeletal muscles throughout the body. I developed the hypothesis that extraocular muscles generally do *not* adapt their lengths to the position in which they are held neurologically.

There are two basic types of extraocular muscle stimulation. *Version* stimulation aims the eyes in given directions, moving the eyes from one gaze position to another. The other type of stimulation is *vergence* stimulation, such as convergence, divergence, or vertical vergence, which aligns the eyes with one another. I hypothesize that the extraocular muscles do not ordinarily adapt their lengths in response to version



**FIGURE 11.** An 80-year-old woman with dense amblyopia in her left eye since childhood, fixing with her right eye only, all her life. Note the left “sensory” exotropia (*top*)—the poorly seeing left eye drifted out over the years because the vision was not good enough for sensory fusion with the other eye. But under general anesthesia, when the eyes reached their stable, deep-anesthesia state (*bottom*), both eyes turned out, equally, and significantly farther than the usual divergence seen under general anesthesia (in 110 patients with exotropia, Apt and Isenberg<sup>26</sup> documented an increased divergence under general anesthesia of only 11.9 prism diopters). Both lateral rectus muscles were equally and abnormally tight when operated. The strabismus had occurred bilaterally. Reprinted with permission from Guyton DL. Changes in strabismus over time: the roles of vergence tonus and muscle length adaptation. The 10th Bielschowsky Lecture. *Binocul Vis Strabismus Q.* 2006;21(2):85. © 2006, Dillon, CO: Binoculus.



**FIGURE 12.** A particularly telling patient, a 33-year-old woman with esotropia (crossed eyes) since birth. Her right eye, only, was operated for the esotropia at age 2½, but the esotropia recurred (*top*). The right eye turned in again—or did it? She had fixed with her left eye only, as long as she could remember, because of mild hyperopia and amblyopia in her right eye. But the extraocular muscles of the two eyes had not adapted to these positions, because when she was placed under deep anesthesia (*bottom*), both eyes deviated rightward—the right eye because of the original surgery turning it outward, and the left eye because of the original esotropia, with still further esotropia developing later. When awake, her muscles were stimulated neurologically to hold her eyes so that she could fix with her better eye—her left eye, but the muscle lengths had not adapted long-term to this type of stimulation. Reprinted from Guyton DL. Changes in strabismus over time: the roles of vergence tonus and muscle length adaptation. The 10th Bielschowsky Lecture. *Binocul Vis Strabismus Q.* 2006;21(2):87. © 2006, Dillon, CO: Binoculus.

stimulation, but rather that they *do* adapt bilaterally in response to vergence stimulation. This notion makes sense to me, because it is vergence stimulation that normally neurologically keeps the eyes aligned with each other, and vergence stimulation is therefore the most logical candidate to fine-tune this alignment over time via bilateral muscle length adaptation.

The only problem with this analysis is that most neurophysiologists have long believed that version and vergence stimulation, while arising in different centers in the brain stem, are combined into a “final common pathway” at the motoneurons whose axons are the motor nerves to the extraocular muscles.<sup>27,28</sup> In other words, it has been believed that version and vergence stimulation are indistinguishable by the time the impulses reach the extraocular muscles. If that were the case, there could be no preferential muscle length adaptation to vergence stimulation.

But recent evidence suggests that there are different populations of motoneurons in the motor nerves,<sup>29</sup> that a certain type of motoneuron may be involved in slow eye movements such as vergence,<sup>30</sup> and that there cannot be a strict final common pathway because of anomalies in muscle force observed during asymmetric vergence.<sup>31</sup> It is tempting to speculate that certain fiber types receiving vergence stimulation are those primarily responsible for muscle length adaptation, but such details have not yet been worked out.

I believe that many changes in *horizontal* strabismus over time can be explained by bilateral muscle length adaptation to chronic low-grade vergence stimulation in the absence of fusion. For example, some young children have significant hyperopia (farsightedness). They learn to accommodate to overcome the hyperopia to see clearly up close, but they

overconverge along with this accommodation, and what we call accommodative esotropia develops. Their eyes cross, initially only when they look up close. It is my hypothesis that as this overconvergence continues, the medial rectus muscles shorten via unintended muscle length adaptation, and then the eyes cross even without accommodation.

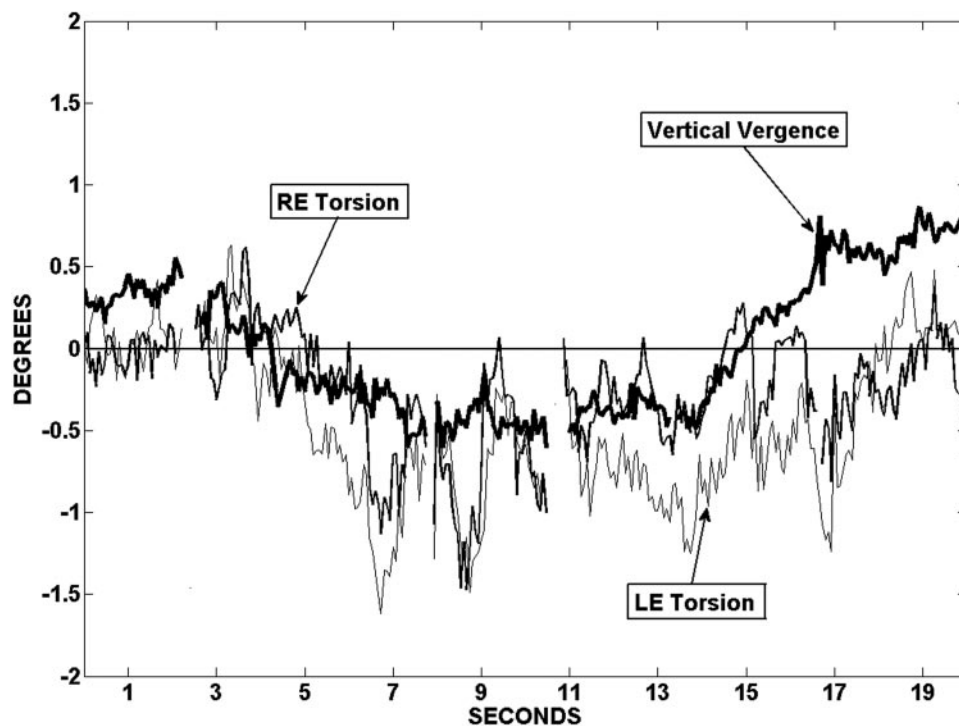
There is another example of horizontal strabismus that may be due to this mechanism. Adults who have had eye muscle surgery for crossed eyes as children, and who have poor fusion abilities, can experience a redevelopment of that crossing in their 30s and 40s as they lose accommodation. They expend increasing effort to see up close, but this causes increased convergence tonus, which we believe leads to shortening of the medial rectus muscles over time, causing a recurrence of the esotropia.<sup>32</sup>

Now, in the cyclovertical "plane," there should be normal forms of vergence that can produce progressive cyclovertical deviations if fusion is faulty, via muscle length adaptation of the cyclovertical muscles. In fact, this is probably the cause of my hypothesized "basic cyclovertical deviation" that masquerades as congenital superior oblique paresis. Recall from our study of DVD (and as later illustrated in Fig. 13) the cycloverision/vertical vergence particularly involving the oblique muscles that we believe is normally involved in vertical fusion. A chronic low level of this type of vergence stimulation, in the presence of faulty fusion, may indeed drive the eyes into a basic cyclovertical deviation, one involving both the vertical rectus muscles and the oblique muscles.

We reasoned that we might be able to investigate this with adaptation experiments in normal subjects.<sup>25</sup> By adapting normal subjects to fuse a vertical disparity over 30 minutes, we could then take careful eye movement recordings to determine the motility patterns involved in vertical fusion and in responding to forced head tilt. We could then compare these adapted normal subjects with patients with acquired and congenital superior oblique paresis. If we found similar eye movement patterns occurring, then we would have created a model in normal subjects helping to explain the basic cyclovertical deviation masquerading as congenital superior oblique paresis—a model not involving primary paresis at all.

We constructed a special haploscope from an old arc perimeter that allows adaptation to increasing vertical, torsional, or horizontal disparities, with near fixation, and with fields of view of more than 50°, using video-oculography for recording. The entire apparatus can tilt, up to 45°, to the right or to the left (Ramey NA, Ying HS, Irsch K, et al. A novel haploscopic viewing apparatus with a three-axis eye tracker. Manuscript submitted). Investigations with human subjects followed the tenets of the Declaration of Helsinki.

First, we investigated cyclovertical eye movements during fusion of induced vertical disparity. The same patterns of eye movements (Fig. 13) were documented in three subjects, showing that both eyes torted in the same direction as vertical vergence occurred, strongly suggesting participation of the oblique muscles in vertical fusional movements.



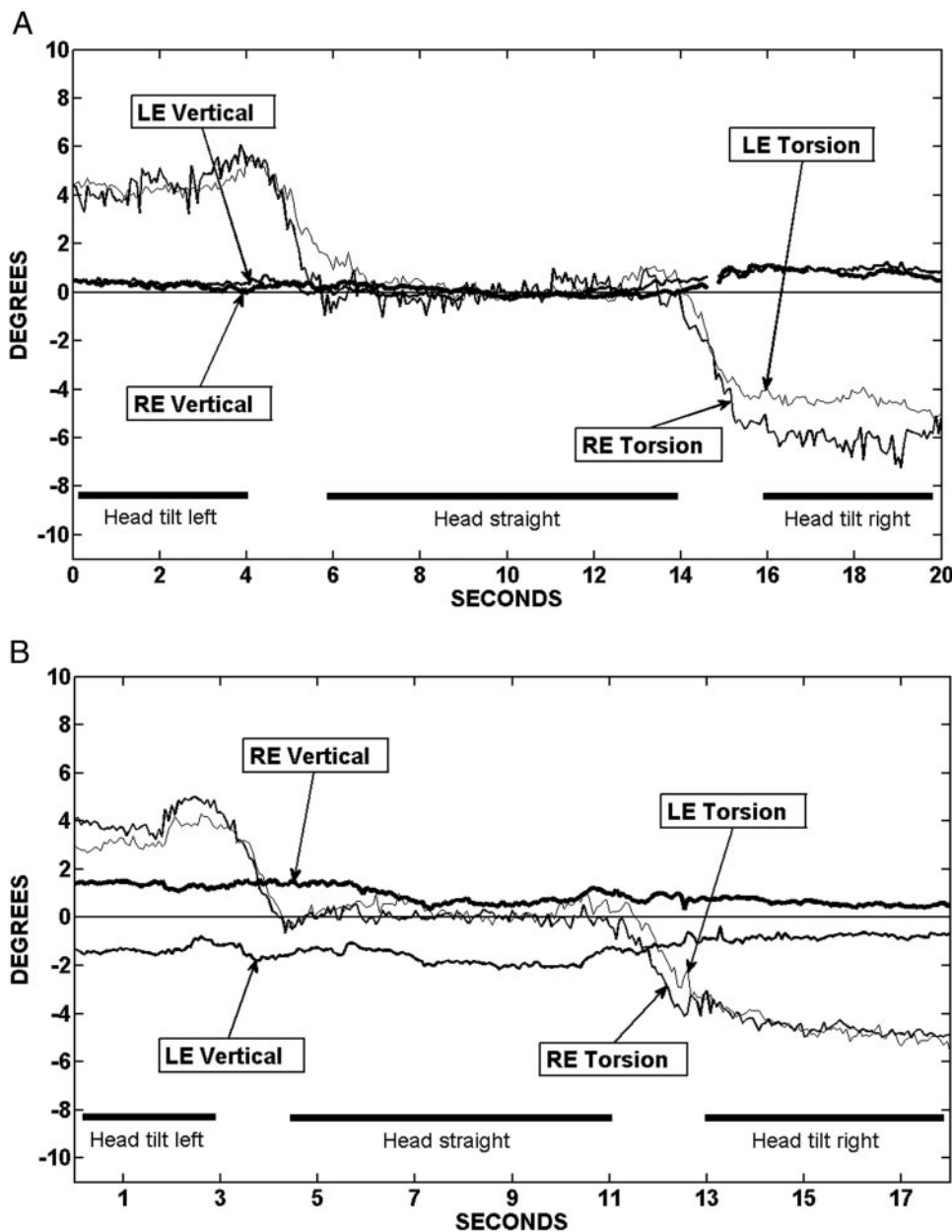
**FIGURE 13.** Approximately every 15 seconds, over a 30-minute period, a normal subject smoothly moved a lever to alternate the positions of the two eyes' targets between right and left vertical disparities, building up to as much vertical disparity as could be alternately fused in each direction. The targets were concentric circles, providing no torsional disparity. Eye movements were recorded as this task continued. Here vertical vergence (bold) has been calculated and plotted as the vertical position of the right eye minus that of the left eye, with positive representing the right eye higher than the left. As the initial right hyperdeviation changed to a right hypodeviation as the subject continued fusing the moving targets, and then back again, both eyes first torted in the minus direction (counter-clockwise from the subject's perspective looking forward) and then torted back clockwise. Two blink artifacts have been removed from the tracings (at the gaps). The right eye thus initially moved downward and intorted, while the left eye moved upward and extorted, only possible mechanically via involvement of the oblique extraocular muscles. These results thus provide evidence that the oblique muscles play a significant role in the fusional response to induced vertical disparity.

Second, we adapted normal subjects to vertical disparities increasing up to  $6^\circ$  for 30 to 45 minutes. Again, with adaptation, we expected to find that the hyperdeviations induced would be accompanied by torsional changes and that the results, especially with forced head tilting, would help us explain the patterns we have heretofore associated with what we call congenital superior oblique paresis. Figures 14A and 14B are examples of typical vertical changes that we recorded with pre- and post-adaptation head tilting.

Five other subjects showed similar responses. Full explanation of the mechanisms of the changes recorded awaits further experimentation. We hypothesize, however, that it is largely the oblique extraocular muscle tonus that is temporarily altered by the vertical vergence adaptation, and less so the tonus of the vertical rectus muscles. If this is true, and if increased tonus results in an increased response to head tilting, then head tilting would be expected to affect the oblique muscle forces more than the rectus muscles forces, creating the changes in hyperdeviation that we are recording.

Although we cannot create an actual superior oblique muscle paresis with these adaptation experiments, simply the demonstration of head-tilt changes accompanying induced cyclovertical deviations suggests that changes in vertical misalignment with head tilting are not pathognomonic of superior oblique paresis. "Basic cyclovertical deviations" of the eyes can show changes with head tilting that we hypothesize can mimic, and thus be confused with, true superior oblique paresis. To explore this thesis, we plan to use these adaptation techniques to study not only normal subjects but also patients with congenital and acquired forms of apparent superior oblique paresis.

We cannot yet confirm our suspected mechanism for the basic cyclovertical deviation that masquerades as congenital superior oblique paresis, the last of the obscure cyclovertical deviations, but we are coming closer. We have come a very long way since the 1970s when ocular torsion was more of a curiosity. It is now a powerful tool that we are learning to put to good use.



**FIGURE 14.** (A) Video-oculographic eye movement recordings from a normal 63-year-old subject before any vergence adaptation. Upward deflections of the vertical tracings represent upward eye movements, and upward deflections of the torsional tracings represent clockwise eye movements from the subject's perspective looking forward. With the head initially tilted  $45^\circ$  to the left, and with the subject fusing the concentric circle targets straight ahead, normal ocular counter-roll was seen in the clockwise direction. The counter-roll later changed to the counter-clockwise direction with head tilt to the right. No significant vertical misalignment was recorded at any point. (B) Recordings from the same subject in Figure 14A after being slowly adapted over 30 minutes, while maintaining fusion with head straight, to a right-over-left vertical disparity increasing to  $6^\circ$ . After adaptation, the relative positions of the eyes were recorded in the fusion-free, dissociated state. The eyes had partially adapted to the stimulus by developing a measured right hyperdeviation of approximately  $3^\circ$  with one target blanked, and this misalignment persisted at least several minutes under these dissociated conditions. Note in the tracings that the hyperdeviation (RE vertical minus LE vertical) was slightly over  $3^\circ$  with left head tilt, was approximately  $3^\circ$  with head straight, and decreased to approximately  $1.5^\circ$  with right head tilt. When recording began with a right head tilt, the hyperdeviation increased with subsequent tilt to the left (not shown). Again, it is the simultaneous directions of the movements of each eye, both torsional and vertical, that will help us determine which cyclovertical muscles are predominantly acting in these various situations.

## SUMMARY

From this investigation, we believe that a basic three-level feedback control system exists for the maintenance of ocular alignment. Central to this theory is our hypothesis that extraocular muscle lengths are primarily regulated by vergence stimulation, as opposed to version stimulation.

Even though we have treated the mechanisms involving ocular torsion in a black-box fashion in the beginning, we have been able to use the resulting interactions and consequences to hypothesize plausible explanations for previously enigmatic phenomena such as so-called primary overaction/underaction of the oblique extraocular muscles and the development of "A" and "V" patterns. Dissociated vertical deviation can be explained using these hypotheses, strengthening our belief that it serves a purpose after all. And we are beginning to appreciate previously unexplained patterns of misalignment such as the basic cyclovertical deviation that we believe masquerades as congenital superior oblique paresis.

There are still a host of unanswered questions, and some of the mechanisms I have proposed are quite speculative. But such speculation leads to candidate models that can help guide both our clinical observations and further research. We hope to understand eventually not only how strabismus changes over time, but also the causes of the many forms of strabismus. This will foster the development of better and longer-lasting treatment methods for the future.

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## References

- Haselhurst G, Howie KJ. *Philosophical Sketches*. <http://www.spaceandmotion.com/books/online-book-publishing.htm>; Space and Motion Online Book Publishing; 2005.
- Christoff A, Guyton DL. The Lancaster red-green test. *Am Orthopt J*. 2006;56:157-165.
- Parks MM. *Ocular Motility and Strabismus*. Hagerstown, MD: Harper & Row; 1975:143.
- Kushner BJ. The role of ocular torsion on the etiology of A and V patterns. *J Pediatr Ophthalmol Strabismus*. 1985;22(5):171-179.
- Guyton DL, von Noorden GK. Sensory adaptations to cyclodeviations. In: Reinecke RD ed. *Strabismus: Proceedings of the Third Meeting of the International Strabismological Association, May, 1978, Kyoto, Japan*. New York: Grune & Stratton; 1978:399-403.
- Guyton DL. Ocular torsion: sensorimotor principles. *Am Orthopt J*. 1987;37:13-21.
- Guyton DL. Clinical assessment of ocular torsion. *Am Orthopt J*. 1983;33:7-15.
- Ciancia AO, Oliveri NC, Zabalo S. Oblique muscle overaction and anisotropia in infantile esotropia with abduction nystagmus. *Am Orthopt J*. 1992;42:3-7.
- Weiss JB. Ectopies et pseudoectopies maculaires par rotation. *Bull Mém Soc Fr Ophtal*. 1966;79:329-349.
- Guyton DL, Weingarten PE. Sensory torsion as the cause of primary oblique muscle overaction/underaction and A- and V-pattern strabismus. *Binocul Vis Eye Muscle Surg Q*. 1994;9(3):209-236.
- Goldspink G, Williams P. Cellular mechanisms involved in the determination of muscle length and mass during growth; problems arising from imbalance between antagonists muscle groups. In: Scott AB, ed. *Proceedings of the Mechanics of Strabismus Symposium*. San Francisco, CA: The Smith-Kettlewell Eye Research Institute; 1992:195-206.
- Tabary J-C, Tardieu C, Tardieu G, Tabary C. Experimental rapid sarcomere loss with concomitant hypoextensibility. *Muscle Nerve*. 1981;4(3):198-203.
- Williams PE, Catanese T, Lucey EG, Goldspink G. The importance of stretch and contractile activity in the prevention of connective tissue accumulation in muscle. *J Anat*. 1988;158:109-114.
- Goldspink G, Williams P, Simpson H. Gene expression in response to muscle stretch (review). *Clin Orthop Relat Res*. 2002(Suppl):S146-152.
- Miller MM, Guyton DL. Loss of fusion and the development of A or V patterns. *J Pediatr Ophthalmol Strabismus*. 1994;31(4):220-224.
- Guyton DL. Dissociated vertical deviation: an acquired nystagmus blockage phenomenon. Richard G. Scobee Memorial Lecture. *Am Orthopt J*. 2004;54:77-87.
- Bechtel RT, Kushner BJ, Morton GV. The relationship between dissociated vertical divergence (DVD) and head tilts. *J Pediatr Ophthalmol Strabismus*. 1996;33(6):303-306.
- Marlow FW. A tentative interpretation of the findings of the prolonged occlusion test on an evolutionary basis. *Arch Ophthalmol*. 1938;19(2):194-204.
- Brodsky MC. Dissociated vertical divergence: a righting reflex gone wrong. *Arch Ophthalmol*. 1999;117(9):1216-1222.
- Mein J, Johnson F. Dissociated vertical divergence and its association with nystagmus. In: Mein J, Moore S, eds. *Orthoptics, Research and Practice*. London: Kimpton; 1981:14-16.
- Guyton DL. Dissociated vertical deviation: etiology, mechanism, and associated phenomena. Costenbader Lecture. *J AAPOS*. 2000;4(3):131-144.
- Enright JT. Unexpected role of the oblique muscles in the human vertical fusion reflex. *J Physiol*. 1992;451:279-293.
- Guyton DL, Cheeseman EW Jr., Ellis FJ, Straumann D, Zee DS. Dissociated vertical deviation: an exaggerated normal eye movement used to damp cyclovertical latent nystagmus. *Trans Am Ophthalmol Soc*. 1998;96:389-429.
- Demer JL, Miller JM, Koo EY, Rosenbaum AL, Bateman JB. True versus masquerading superior oblique palsies: Muscle mechanisms revealed by magnetic resonance imaging. In: Lennerstrand G, ed. *Update on Strabismus and Pediatric Ophthalmology*. Boca Raton, FL: CRC Press; 1995:303-306.
- Guyton DL. Changes in strabismus over time: the roles of vergence tonus and muscle length adaptation. The 10th Bielschowsky Lecture. *Binocul Vis Strabismus Q*. 2006;21(2):81-92.
- Apt L, Isenberg S. Eye position of strabismus patients under general anesthesia. *Am J Ophthalmol*. 1977;84(4):574-579.
- Keller EL, Robinson DA. Absence of a stretch reflex in extraocular muscles of the monkey. *J Neurophysiol*. 1971;34(5):908-919.
- Scott AB, Collins CC. Division of labor in human extraocular muscle. *Arch Ophthalmol*. 1973;90(4):319-322.
- Eberhorn AC, Büttner-Ennever JA, Horn AKE. Identification of motoneurons supplying multiply- or singly-innervated extraocular muscle fibers in the rat. *Neuroscience*. 2005;137(3):891-903.
- Ugolini G, Kalm F, Dans MD, et al. Horizontal eye movement networks in primates as revealed by retrograde transneuronal transfer of rabies virus: differences in monosynaptic input to "slow" and "fast" abducens motoneurons. *J Comp Neurol*. 2006;498:762-785.
- Miller JM. No oculomotor plant, no final common path. *Strabismus*. 2003;11(4):205-211.
- Wright WW, Gotzler KC, Guyton DL. Esotropia associated with early presbyopia: caused by inappropriate muscle length adaptation. *J AAPOS*. 2005;9(6):563-566.