Does Infantile Esotropia Arise From a Dissociated Deviation?

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Tonus refers to the effects of baseline innervation on musculature in the awake, alert state. Since the normal anatomical resting position of the eyes is one of exodeviation, extraocular muscle tonus plays a vital physiologic role in establishing ocular alignment. Under normal conditions, binocular esotonus is superimposed on the baseline anatomical position of rest to maintain approximate ocular alignment, save for a minimal exophoria that is easily overcome by active convergence. When binocular visual input is preempted early in life, monocular fixation may give rise to a larger dissociated esotonus that gradually drives the 2 eyes into a “convergent” position, resulting in infantile esotropia.

In our companion article, we examine clinical and evolutionary evidence for the proposition that dissociated horizontal deviation is a clinical expression of dissociated esotonus. When superimposed on a baseline orthoposition, dissociated esotonus manifests as an intermittent esotropia that is asymmetrical or unilateral. More commonly, dissociated esotonus is superimposed on a baseline exodeviation, producing an intermittent esodeviation that is asymmetrical, unilateral, or associated with a paradoxical exodeviation when the nonpreferred eye is used for fixation.

Contrary to the stereotype of “congenital” esotropia as a large-angle deviation that is present at birth, most cases are acquired (ie, “infantile” in origin). Furthermore, the eyes do not simply snap in to their final esotropic position. Before 12 weeks of age, nascent infantile esotropia is an intermittent, variable esodeviation that gradually becomes constant after building in intensity to a large fixed angle of horizontal misalignment. Ing has noted that 50% of patients with infantile esotropia show an increase in the mea-
sured angle between the time of first examination and the date of surgery. Clearly, unequal visual input in infancy must produce a gradual and progressive increase in the angle of esotropia. That this esodeviation appears during the early period when stereopsis is developing, but before macular anatomy has matured sufficiently to provide high-resolution acuity, suggests that it is actively driven primarily by an imbalance in peripheral visual input.

In a recent hypothesis, Guyton has invoked vergence adaptation and muscle length adaptation to explain how a small innervational bias (such as the convergence produced by increased accommodative effort in the presbyope) can build slowly over time into a large constant deviation. Vergence adaptation refers to the tonic levels that normally operate to maintain a baseline ocular alignment and thereby minimize retinal image disparity. According to Guyton, vergence adaptation can allow primitive ocular motor biases to gradually amplify and create strabismic deviations under pathological conditions. Muscle length adaptation refers to the change in extracocular muscle length due to gain or loss of sarcomeres. Muscle length adaptation is driven in part by the physiologic effects of vergence adaptation.

Our results suggest that dissociated esotonus could provide the sensorimotor substrate for vergence adaptation when binocular cortical control mechanisms fail to take hold. The finding of a positive Bielschowsky phenomenon in dissociated horizontal deviation shows that peripheral lumino- reflexes are retained, as in dissociated vertical divergence. In this setting, both peripheral (lumino- and optokinetic) and central (fixational) reflexes augment dissociated esotonus and lead over time to infantile esotropia. Subcortical visual reflexes would provide the default system through which dissociated esotonus operates to reestablish the baseline horizontal eye position. This process can ultimately lead to loss of sarcomeres and secondary shortening of the medial rectus muscles. The fact that the eyes straighten to an almost normal baseline position under general anesthesia, however, suggests that esotonus is the driving force for infantile esotropia and that mechanical effects play a secondary role in its pathogenesis. It is therefore possible that the stable large-angle esodeviation that we recognize as infantile esotropia simply represents the final stage of dissociated esotonus. As with many other forms of ocular misalignment, the constant esodeviation that develops over time may eventually obscure the pathogenesis.

Early monocular visual loss is known to generate esotonus and reproduce the same constellation of dissociated eye movements that accompany infantile esotropia. Patients with unilateral congenital cataract often develop large-angle esotropia, latent nystagmus, dissociated vertical divergence, and a head turn to fixate in adduction with the preferred eye. By contrast, early infantile esotropia is often characterized by similar visual acuity in the 2 eyes, with alternating suppression of the nonfixating eye. So perhaps dissociated horizontal deviation is not an epiphenomenon of infantile esotropia but a “footprint in the snow” of the dissociated esotonus that is responsible for its inception.

There remains the unfortunate tendency in the strabismus literature to conflate esotonus of the eyes as a baseline innervation with convergence of the eyes as an active function. Jampolsky has emphasized the mechanistic importance of distinguishing between convergence as an active binocular function and esotonus as a baseline innervational state that is centrally driven by unequal visual input to the 2 eyes. The importance of this distinction lies in understanding that convergence implies a deviation from baseline under normal conditions of sensory input, whereas esotonus implies a return to baseline under altered conditions of sensory input. The distinction between convergence (the effect) and monocular esotonus (the cause) lies at the heart of understanding infantile esotropia. Horwood and colleagues have recently shown that normal infants display fleeting large-angle convergence eye movements during the first 2 months of life and that these spontaneous convergence movements are ultimately predictive of normal binocular alignment. By contrast, infantile esotropia tends to increase over the period when this excessive convergence is disappearing in normal infants. This time course challenges the dubious assumption that infantile esotropia arises from excessive convergence output. The evidence for dissociated esotonus suggests that we retain a primitive tonus system, independent of convergence output, that can operate under conditions of unequal visual input to reset eye position to a new baseline “convergent” position. This mechanism would explain why infantile esotropia is so much more common than infantile exotropia.

If the dissociated esotonus that manifests as dissociated horizontal deviation gives rise to infantile esotropia, why does dissociated horizontal deviation manifest as an intermittent exotropia? Although we use the term intermittent exotropia diagnostically, it is ultimately a descriptive term comprising a variety of conditions with different diagnostic implications. The intermittent exodeviation caused by dissociated horizontal deviation simply constitutes one distinct form of intermittent exotropia with its own unique pathophysiology.

Many clinicians apply the hybrid term intermittent exotropia/dissociated horizontal deviation, implying that the 2 conditions often coexist, and perhaps acknowledging some diagnostic ambiguity. So what are the innervational substrates for these distinct but overlapping categories of intermittent exotropia? Although Burian believed intermittent exotropia to be caused by an active divergence mechanism, independent studies have found that these patients are approximately 30 prism diopters more exotropic when deeply anesthetized than in the awake state, suggesting that intermittent exotropia actually results from intermittent fusional control of a large baseline exodeviation.

When intermittent exotropia is associated with dissociated horizontal deviation, fixation with either eye...
superimposes dissociated esotonus on the baseline exodeviation to produce a variable intermittent exodeviation.\textsuperscript{2} The distinction between nondissociated intermittent exotropia and dissociated horizontal deviation lies primarily in the relative activation of binocular fusion (which behaves as an all-or-nothing phenomenon in most forms of intermittent exotropia) vs dissociated esotonus (which functions as an open-loop process without reference to ultimate binocular alignment in dissociated horizontal deviation). Because fixation with the nonpreferred eye exerts greater esotonus,\textsuperscript{2} the baseline exodeviation can be unilateral, asymmetrical, or associated with a paradoxical esotropia when the nonpreferred eye is used for fixation.

Infantile esotropia and intermittent exotropia are universally regarded as distinct forms of strabismus that occupy opposite points on a clinical spectrum. In contrast to infantile esotropia, intermittent exotropia usually has a later onset and is rarely associated with prominent dissociated eye movements (although small degrees of dissociated vertical divergence can be detected).\textsuperscript{39} At first glance, it is difficult to imagine how these diametrical forms of horizontal misalignment are not mutually exclusive.

The beauty of dissociated horizontal deviation is that it allows us to recast horizontal strabismus as the relative balance of mechanical and innervational forces, without regard to final eye position. Dissociated esotonus can still be expressed from an exodeviated position, because it is generated by unbalanced binocular input that exerts its influence on any baseline deviation. Consequently, intermittent esotropia is a common clinical manifestation of dissociated esotonus. Mechanically, there is nothing sacred about orthotropia as a clinical demarcation and nothing signatory about the direction of horizontal misalignment.

In this light, dissociated horizontal deviation is transformed from a clinical curiosity to a fundamental piece of the puzzle for understanding horizontal strabismus. The exotropic form of dissociated horizontal deviation uniquely embodies the coexistence of the mechanical exodeviating forces that give rise to intermittent exotropia and the dissociated esotonus that may give rise to infantile esotropia. For example, infantile exotropia is often accompanied by dissociated eye movements such as latent nystagmus and dissociated vertical divergence.\textsuperscript{36,37} Some infants exhibit an intermittent form of exotropia with other dissociated eye movements,\textsuperscript{38} suggesting a component of dissociated horizontal deviation. Patients with primary dissociated horizontal deviation also display an intermittent exodeviation of one or both eyes with other signs of dissociation.\textsuperscript{9}

All of these conditions share a common pathophysiology wherein dissociated esotonus is superimposed on a baseline exodeviation to produce an intermittent exodeviation that varies in size depending on which eye is used for fixation. In patients without binocular fusion, dissociated esotonus can cause a constant exodeviation to appear intermittent. In patients who retain binocular fusion, it can produce a combined clinical picture of intermittent exotropia (with intermittent fusion), an asymmetrical exodeviation of the 2 eyes, or an exodeviation of the nonpreferred eye with a paradoxical esodeviation of the preferred eye. In classifying these disorders pathogenetically, it is critically important to distinguish sensorimotor factors from the different forms of ocular misalignment that they ultimately produce. Dissociated horizontal deviation shows us how it is only the resultant horizontal deviations, and not the underlying conditions, that are diametrically opposed.

In conclusion, our findings raise the intriguing possibility that dissociated esotonus, an unrecognized dissociated eye movement, may be the cause, rather than the effect, of infantile esotropia. If this proves to be the case, then the prevailing concept of infantile esotropia as the proximate cause of dissociated deviations may need to be revised.

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