Head Position–Dependent Changes in Ocular Torsion and Vertical Misalignment in Skew Deviation

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Objectives: To investigate whether ocular torsion and vertical misalignment differ in the upright vs supine position in skew deviation and to compare these findings with those in trochlear nerve palsy.

Methods: Ten patients with skew deviation, 14 patients with unilateral peripheral trochlear nerve palsy, and 12 healthy subjects were prospectively recruited. With subjects first in the upright position and then in the supine position, ocular torsion was measured by double Maddox rods and vertical misalignment was measured by the prism and alternate cover test.

Results: In patients with skew deviation, the abnormal torsion and vertical misalignment in the upright position decreased substantially with change to the supine position, whereas in patients with trochlear nerve palsy, it changed little between positions. Torsion was decreased by 83% in patients with skew deviation, 2% in patients with trochlear nerve palsy, and 6% in healthy subjects (P<.001). Similarly, vertical misalignment was decreased by 74% in patients with skew deviation and increased by 5% in patients with trochlear nerve palsy and 6% in healthy subjects (P<.001).

Conclusions: Our findings provide the basis for additional clinical tests to support the classic 3-step test: ocular torsion and vertical misalignment that decrease from the upright position to the supine position indicate skew deviation, whereas torsion and vertical misalignment that do not change significantly between positions indicate trochlear nerve palsy.

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Skew deviation is a vertical strabismus caused by supranuclear lesions and is often associated with ocular torsion and head tilt, constituting the ocular tilt reaction. It is typically caused by damage to the brainstem tegmentum or cerebellum or by acute peripheral vestibulopathy. Skew deviation has been attributed to an imbalance of the vestibulo-ocular reflex projections from the utricles in the inner ears to ocular motoneurons (i.e., the utriculo-ocular reflex); however, direct evidence for this is lacking. The utricles lie roughly in the horizontal plane, and they normally detect static positions (tilts) of the head. We postulate that if skew deviation is caused by an imbalance of the utriculo-ocular reflex, the abnormal torsion and vertical misalignment might be head position dependent. The purposes of this study were to investigate whether ocular torsion and vertical misalignment differ in the upright vs supine position in patients with skew deviation and to compare these findings with those in patients with unilateral peripheral trochlear nerve palsy.

Methods

Ten patients with skew deviation and 14 with unilateral peripheral trochlear nerve palsy were recruited. A complete history was taken and detailed ophthalmic and neurologic examinations were performed. When indicated, appropriate tests were performed to rule out myasthenia gravis, thyroid ophthalmopathy, or other orbital diseases. Magnetic resonance images with gadolinium enhancement and slice thickness of at least 5 mm were obtained in all of the patients.

In this investigation, skew deviation was diagnosed as follows: (1) a vertical misalignment (with or without head tilt or fundus torsion), the pattern of which is inconsistent with that found in palsy of 1 or more cyclovertical muscles; (2) lesions in the posterior fossa detected by magnetic resonance imaging; and (3) neurologic symptoms and signs (al-
though in our standard practice, neurologic findings are not necessary diagnostic criteria). Patients with acute peripheral vestibulopathy were not included because we do not encounter these patients in our neuro-ophthalmology practice.

Unilateral peripheral trochlear nerve palsy was diagnosed as follows11-13: (1) deficient depression of the hypertropic eye in adduction; (2) incomitant hypertropia that increased with adduction of the hypertropic eye and with head tilt toward the hypertropic eye; (3) presence of objective or subjective exocyclo deviation, ie, toroidal diplopia; (4) absence of any neurologic symptoms and signs suggestive of lesions in the trochlear nucleus or fascicle; and (5) negative magnetic resonance imaging results. Exclusion criteria were the following: (1) history of diplopia or strabismus dating to infancy or early childhood; (2) prior strabismus surgery; or (3) history of head trauma that could lead to skew deviation, trochlear nerve palsy, or both.

Twelve healthy subjects served as control subjects (mean [SD] age, 31 [7] years; median age, 29 years; age range, 20-45 years; 8 women). The research protocol was approved by the Research Ethics Boards of The Hospital for Sick Children and University Health Network. Informed consent was obtained from all of the subjects.

MEASUREMENT OF OCULAR TORSION

Ocular torsion was quantitatively measured using double Maddox rods. While wearing a trial frame, a red Maddox rod lens was placed in front of each eye. The direction of the glass rods was aligned with the 90° marks of the trial frame. The subject was instructed to fixate on a small white penlight located 1 m away in the midsagittal plane at eye level. This distance was chosen so that a standardized target could be used in both the upright and supine positions. Through the Maddox rods, the images of the penlight appeared as 2 red horizontal streaks. If one or both horizontal streaks were perceived as slanted, the subject was instructed to rotate the lens(es) until the streak(s) became perfectly horizontal. Three trials were performed while the subject sat in an upright position (ie, subjects were not allowed to adopt their usual abnormal head posture, if present), and the trials were repeated while the subject lay in a supine position with the head maintained in the neutral position. The mean value of the final position of the lenses from the 3 trials was used for analysis. The mean within-subject variability was 0.20° in patients with skew deviation and 0.21° in patients with trochlear nerve palsy.

MEASUREMENT OF VERTICAL MISALIGNMENT

The magnitude of vertical strabismus was measured by the prism and alternate cover test. While sitting upright with the head erect (ie, subjects were not allowed to adopt their usual abnormal head posture, if present), the subject fixated on a single letter c of optotype size 3/32 inch (12-point font size) located 1 m away in the midsagittal plane at eye level. Prisms of increasing power were placed over the deviated eye while the cover alternated between the eyes. The highest prism strength when no refixation movement occurred was recorded. The test was repeated with the subject lying in a supine position.

DATA ANALYSIS

To compare torsion between the upright and supine positions, a torsion change index (TCI) score, defined as $(T_{up} - T_{supine}) / (T_{up} + T_{supine})$, was calculated, where $T_{up}$ is torsion in the upright position and $T_{supine}$ is torsion in the supine position. A TCI score of 1.0 indicates complete disappearance of torsion when changing from the upright position to the supine position, whereas a TCI score of 0.0 indicates no change between positions. Similarly, a vertical change index (VCI) score, defined as $(V_{up} - V_{supine}) / (V_{up} + V_{supine})$, was calculated, where $V_{up}$ is vertical misalignment in the upright position and $V_{supine}$ is vertical misalignment in the supine position. The TCI scores were analyzed using a 3 (between) × 2 (within) nested repeated-measures analysis of variance. The between-subjects factor was the diagnosis (skew deviation, trochlear nerve palsy, and healthy) and the within-subjects factors were the hypertropic and hypotropic eyes. The VCI scores were analyzed using analysis of variance. If significant ($P < .05$), the specific effects of each factor were analyzed further with post hoc Tukey tests.

For patients with skew deviation (n = 10), the mean (SD) age was 25 (18) years (age range, 9-63 years) (Table 1). Seven were women. The mean (SD) duration of symptoms was 48 (42) months (range, 15-145 months). Four patients had lesions affecting both the cerebellum and medulla, 3 had primarily cerebellar lesions, and 2 had primarily brainstem lesions (Table 2). In a 10th patient with a history of acute lymphoblastic lymphoma, leptomeningeal enhancement was evident on magnetic resonance imaging. All of the 10 patients had abnormal ocular torsion in 1 or both eyes (see later). Of the 10 patients, 6 (60%) had abnormal head tilt toward the side of the hypotropic eye; the other 4 had no head tilt. Thus, the complete ocular tilt reaction was present in 60% of patients. Five patients had bilateral lesions in the posterior fossa, 3 had unilateral lesions in the medulla and/or cerebellum with contralesional hypertropia, and 2 had unilateral pontomesencephalic lesions with ipsilesional hypertropia. The vertical strabismus was comitant in 8 patients, incomitant in 1, and alternating in 1. Five patients had no spontaneous nystagmus, 1 had an upbeat nystagmus in the primary position, and 4 had gaze-evoked nystagmus. There were no difficulties measuring torsion and vertical strabismus in the upright and supine positions in any patients, with or without nystagmus.

For patients with unilateral peripheral trochlear nerve palsy (n = 14), the mean (SD) age was 36 (14) years (age range, 14-63 years) (Table 1). Six were women. The mean (SD) duration of symptoms was 34 (36) months (range, 3-145 months). Of the 14 patients, 9 (64%) exhibited an abnormal head tilt toward the hypotropic eye; the other 5 had no head tilt. No patients had any neurologic findings.

In the upright position, all of the 10 patients with skew deviation had abnormal ocular torsion (Figure 1A), defined as torsion higher than the 95% confidence interval in healthy subjects (ie, $> 2.4^\circ$; see later). Abnormal torsion was found in both eyes in 3 patients (30%; patients S3, S6, and S10), in the hypotropic eye only in 5 (50%; patients S1, S2, S4, S5, and S9), and in the hypertropic eye only in 2 (20%; patients S7 and S8). When torsion was observed, an excyclodeviation was always measured in the hypotropic eye (n = 8) and an incyclodeviation in the hypertropic eye (n = 5). In the 6 patients with ocular tilt reaction, 5 had conjugate torsion of both fundi (patients S2, S3, S5, S6, and S10). The abnormal torsion either decreased substantially or disappeared com-
pletely in the supine position with the head in its neutral position (Figure 1A) in all of the patients. For example, in patient S9, the 10° of excyclodeviation of the hypotropic right eye in the upright position decreased to 2° of excyclodeviation in the supine position using the double Maddox rods test (no torsion was found in the hypertropic left eye). Consistent with this subjective finding, fundus photography (RetCam; Massie Laboratories, Inc, Pleasanton, California) of the hypotropic right eye revealed a reduction from 12° (upright) to 2° (supine) of excyclodeviation (Figure 2).

Excyclodeviation was found in the hypertropic eye in 10 of 14 patients with unilateral peripheral trochlear nerve palsy in the upright position (71%; patients T1-T9 and T11) (Figure 1B). It was abnormal (ie, > 2.4°) in 8 of these 10 patients (patients T2-T9). In contrast to patients with skew deviation, the abnormal torsion in patients with trochlear nerve palsy did not change significantly between positions. For example, in patient T4, the hypertropic right eye exhibited 10° of excyclodeviation in the upright position, which increased slightly to 11° of excyclodeviation in the supine position (no torsion was found in the hypotropic left eye).

Figure 1C shows that in healthy subjects, up to 6° of cyclodeviation was present; however, this cyclodeviation did not exhibit any significant difference between head positions. The mean (SD) torsion in healthy subjects was 1.2° (2.1°) (95% confidence interval, 0.0°-2.4°).

### Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Patient No./Sex/ Age, y</th>
<th>Symptom Duration, mo</th>
<th>Visual Acuity OD</th>
<th>Visual Acuity OS</th>
<th>Refractive Error, Spherical Equivalents OD</th>
<th>Refractive Error, Spherical Equivalents OS</th>
<th>Side (Comitance) of Hypertropia</th>
<th>Side of Head Tilt</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1/F/18</td>
<td>60</td>
<td>20/30 20/25</td>
<td>-0.25 +0.25</td>
<td>Left (comitant)</td>
<td>Right (alternating)</td>
<td>Right</td>
<td>Left</td>
</tr>
<tr>
<td>S2/M/18</td>
<td>30</td>
<td>20/25 20/25</td>
<td>Plano Plano</td>
<td>Left (alternating)</td>
<td>Right</td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>S3/F/17</td>
<td>22</td>
<td>20/15 20/20</td>
<td>Plano Plano</td>
<td>Right (comitant)</td>
<td>Left</td>
<td>None</td>
<td>Right</td>
</tr>
<tr>
<td>S4/F/23</td>
<td>26</td>
<td>20/25 20/20</td>
<td>-1.00 -1.00</td>
<td>Left (comitant)</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>S5/M/11</td>
<td>24</td>
<td>20/30 20/30</td>
<td>Plano Plano</td>
<td>Left (comitant)</td>
<td>Right</td>
<td>Right</td>
<td>Left</td>
</tr>
<tr>
<td>S6/F/20</td>
<td>32</td>
<td>20/30 20/40</td>
<td>Plano Plano</td>
<td>Left (comitant)</td>
<td>None</td>
<td>None</td>
<td>None</td>
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<tr>
<td>S7/M/63</td>
<td>145</td>
<td>20/40 20/20</td>
<td>Plano Plano</td>
<td>Right (comitant)</td>
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<td>None</td>
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<td>S8/F/23</td>
<td>96</td>
<td>20/25 20/25</td>
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<td>None</td>
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<td>S9/F/52</td>
<td>26</td>
<td>20/30 20/20</td>
<td>Plano Plano</td>
<td>Left (comitant)</td>
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<td>None</td>
<td>None</td>
</tr>
<tr>
<td>S10/F/9</td>
<td>15</td>
<td>20/20 20/20</td>
<td>+0.25 +0.25</td>
<td>Right (comitant)</td>
<td>Left</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

### Table 2. Neurologic and Magnetic Resonance Imaging Findings in Patients With Skew Deviation

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Magnetic Resonance Imaging Findings</th>
<th>Clinical Features in Addition to Skew Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1</td>
<td>Medulloblastoma involving the cerebellum and medulla bilaterally</td>
<td>Facial nerve palsy, ataxia</td>
</tr>
<tr>
<td>S2</td>
<td>Pilocytic astrocytoma involving the cerebellum and medulla bilaterally</td>
<td>Gaze-evoked nystagmus, facial nerve palsy, ataxia</td>
</tr>
<tr>
<td>S3</td>
<td>Left cerebellar hemorrhage from arteriovenous malformation</td>
<td>Gaze-evoked nystagmus, ataxia</td>
</tr>
<tr>
<td>S4</td>
<td>Left clival chordoma</td>
<td>Right-sided weakness and spasticity, ataxia</td>
</tr>
<tr>
<td>S5</td>
<td>Acute lymphoblastic lymphoma with leptomeningeal enhancement bilaterally</td>
<td>Ataxia, facial nerve palsy</td>
</tr>
<tr>
<td>S6</td>
<td>Bilateral cerebellar hypoplasia</td>
<td>Upbeat nystagmus, ataxia</td>
</tr>
<tr>
<td>S7</td>
<td>Acute disseminating encephalomyelitis involving the cerebellar peduncles</td>
<td>Gaze-evoked nystagmus, ataxia</td>
</tr>
<tr>
<td>S8</td>
<td>Left cerebellar hemispheric hemorrhage extending into the mesial aspect of the right cerebellar hemisphere</td>
<td>Hypometric saccades, saccadic pursuit, gaze-evoked nystagmus, head tremor, ataxia</td>
</tr>
<tr>
<td>S9</td>
<td>Hemosiderin deposits in the left pons</td>
<td>Left internuclear ophthalmoplegia</td>
</tr>
<tr>
<td>S10</td>
<td>Astrocytoma involving the left medulla and left middle cerebellar peduncle</td>
<td>Ataxia</td>
</tr>
</tbody>
</table>
In patients with skew deviation, the mean (SD) TCI score was 0.85 (0.27) in the hypertropic eye and 0.81 (0.20) in the hypotropic eye (Figure 3); these scores were significantly higher than those in patients with unilateral peripheral trochlear nerve palsy (mean [SD] TCI score: hypertropic eye, 0.01 [0.09]; hypotropic eye, 0.07 [0.15]) and in healthy subjects (mean [SD] TCI score: right eye, 0.08 [0.11]; left eye, 0.01 [0.01]) (P < .001).

Similar to the patterns of torsional change, the vertical misalignment decreased substantially or disappeared completely in patients with skew deviation.

Figure 1. Changes in torsion between the upright and supine positions. A, Patients with skew deviation. The abscissa specifies the patient number (S1-S10), whereas the ordinate specifies degree of torsion, with excyclodeviation being positive and incyclodeviation negative. When torsion was present, excyclodeviation was always found in the hypotropic eye and incyclodeviation in the hypertropic eye. Circles indicate torsion in the upright position; lines, torsion in the supine position; and arrows, the direction of torsional changes from the upright position to the supine position. For example, patient S1 had 5° of excyclodeviation in the hypotropic eye in the upright position, which decreased to 0° in the supine position. No torsion was reported in the hypertropic eye. In each of 10 patients with skew deviation, the abnormal torsion decreased substantially or disappeared completely in the supine position. B, Patients with unilateral peripheral trochlear nerve palsy. When torsion was present, excyclodeviation was always found in the hypertropic eye, with minimal incyclodeviation or excyclodeviation in the hypotropic eye. The abnormal torsion seen in patients with unilateral peripheral trochlear nerve palsy did not change significantly from the upright position to the supine position. The patient numbers are indicated (T1-T14). C, Healthy control subjects. Up to 6° of cyclodeviation could be observed; however, this cyclodeviation did not exhibit any significant difference between the upright and supine positions in each of 12 healthy subjects. The subject numbers are indicated (H1-H12).

Figure 2. Fundus photographs of patient S9 with skew deviation and abnormal torsion in the right eye but no abnormal head tilt. The hypotropic right eye exhibited 12° of excyclodeviation in the upright position and 2° of excyclodeviation in the supine position. The RetCam camera (Massie Laboratories, Inc, Pleasanton, California) was positioned, in both the upright and supine positions, by aligning a specific mark on the RetCam with a premarked dot that was located above the midpupil of each eye on the forehead.

Figure 3. Mean torsion change index (TCI) scores in patients with skew deviation, patients with trochlear nerve palsy, and healthy control subjects. The TCI scores in patients with skew deviation were significantly higher than those in patients with trochlear nerve palsy and healthy control subjects. High eye indicates hypertropic eye; low eye, hypotropic eye; and error bars, standard deviation.
The principal finding in this investigation is that the abnormal torsion and vertical misalignment in patients with skew deviation are head position dependent—they decrease substantially or disappear completely when the head changes from an upright erect position to a supine position. This head position–dependent reduction in torsion and vertical misalignment was present whether the patients had isolated cerebellar lesions, isolated brainstem lesions, or combined lesions. In contrast, in unilateral peripheral trochlear nerve palsy, there are little or no changes in torsion or vertical deviation in different head positions.

In healthy humans, static lateral head tilt activates the utricles, which results in sustained conjugate low-amplitude counterroll of the eyes and a small vertical deviation. Head rotation toward the right shoulder is accompanied by counterrolling of both eyes combined with slight upward movement of the right eye and downward movement of the left eye. This reflexive vertical divergence is minimally compensatory to downward displacement of the right eye and upward displacement of the left eye relative to the earth-horizontal plane due to the head tilt.

The ocular tilt reaction is a pathological synkinetic triad of skew deviation, ocular torsion, and head tilt. It has been attributed to lesions in the vestibular organ and its nerve as well as central connections within the brainstem or cerebellum that asymmetrically disrupt the utriculo-ocular pathway. Brandt and Dieterich reviewed 56 patients with skew deviation. They found abnormal ocular torsion in all of the patients, with both eyes affected in 19%, only the hypotropic eye affected in 31%, and only the hypertropic eye incyclodeviated.9 The clinical characteristics of our patients with skew deviation are in close agreement with those described by Brandt and Dieterich.

As mentioned above, the righting reflex is elicited when the head changes from an upright position to a supine position. This head position–dependent reduction in torsion and vertical misalignment in skew deviation. Although the exact mechanism remains to be elucidated, our findings that torsion and vertical misalignment decrease when changing from an upright position to a supine position in patients with skew deviation are consistent with the currently accepted role of the utricles in detecting changes in head orientation and provide support that skew deviation is caused by disruption of the utriculo-ocular reflex.

In isolated unilateral peripheral trochlear nerve palsy, the utriculo-ocular pathway remains intact. Thus, the magnitude of vertical deviation and cycloversion in the hypertropic eye remains the same in different head positions. The contralateral head tilt commonly seen in unilateral trochlear nerve palsy is a compensatory mechanism that exploits the normal intact utriculo-ocular reflex to minimize the magnitude of vertical deviation and diplopia. Sydnor et al found that the head tilt in unilateral trochlear nerve palsy disappears in the supine position.


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Because there is no change in utricular input with roll tilts when supine, the utriculo-ocular reflex is no longer effective in reducing the vertical deviation in unilateral trochlear nerve palsy in the supine position; thus, the head tilt disappears.21

Trochlear nerve palsy is typically diagnosed with the clinical 3-step test.13 In contrast, the vertical misalignment in skew deviation does not follow any set patterns; it may be comitant or incomitant, or it may even be alternating with right hypertropia on right gaze and left hypertropia on left gaze.7,22,23 Some skew deviations are known to mimic trochlear nerve palsy during the 3-step test.24,25 Conversely, trochlear nerve palsy with spread of comitance may simulate a comitant skew deviation because in both conditions the head is usually tilted toward the side of the hypotropic eye. Because both skew deviation and trochlear nerve palsy may result from brain trauma or from lesions in the posterior fossa,26 differentiating these 2 conditions can be challenging. In this situation, indirect ophthalmoscopy is useful—the fundus is excyclodeviated in the hypertropic eye in patients with trochlear nerve palsy, but it is incyclodeviated in the hypertropic eye in patients with skew deviation (if torsion is present). In addition, the fundus of the hypotropic eye in patients with skew deviation may be excyclodeviated.9,27,28

The double Maddox rods test as well as the prism and alternate cover test are simple and quick. They also have the advantage of not requiring pupillary dilation or indirect ophthalmoscopy, which may not be readily available or feasible for nonophthalmologists, including neurologists and orthoptists. Although the magnitude (but not direction) of torsion estimated by double Maddox rods (subjective torsion) may differ from the measurement by fundus photography (objective torsion),29 our results provide the basis of additional tests that could be used clinically to differentiate skew deviation from trochlear nerve palsy: ocular torsion and vertical misalignment that de-
ce from the upright position to the supine position indicate skew deviation, whereas torsion and vertical misalignment do not change significantly between the upright and supine positions indicate troclear nerve palsy. Head position–dependent changes in torsion and vertical misalignment suggest skew deviation and warrant investigation for a lesion in the posterior fossa as the cause of vertical diplopia.

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REFERENCES


I n 1941, for the first time by means of the biomicroscope, aqueous humor was seen to stream thorough conjunctival and episcleral veins of the normal human eye. Vessels containing a clear fluid, sometimes mixed with varying amounts of blood, can be found in at least one third of all quiet human eyes with the use of the corneal microscope and slit lamp illumination. . . .

Many ophthalmologists have had difficulty in recognizing the aqueous veins, whereas others have confirmed their occurrence and significance. Photographs of recipient vessels have corroborated the presence of highly diluted blood in these vessels, as well as the influence of drugs on the elimination of intraocular fluid through the aqueous veins.