Ocular Torsion According to Trochlear Nerve Absence in Unilateral Superior Oblique Palsy

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PURPOSE. To investigate the relationship between objective torsion and the presence or absence of the trochlear nerve in subjects with unilateral superior oblique palsy (SOP).

METHODS. A total of 159 subjects with congenital and acquired unilateral SOP were reviewed. Eighty-four subjects who had a normal trochlear nerve (present group) and 75 subjects without a trochlear nerve (absent group) were included. Cyclovertical motility parameters and objective ocular torsion were compared between groups, and factors related to ocular torsion were evaluated.

RESULTS. The degree of “net” excyclotorsion in the paretic eye was larger in the absent group compared to the present group (P = 0.002). The proportion of net excyclotorsion in the paretic eye was greater in the absent group (11% vs. 37%), while net incyclotorsion was greater in the present group (41% vs. 23%) (P < 0.001). Net excyclotorsion of the paretic eye was associated with absence of the trochlear nerve (P < 0.001) and smaller size of the paretic SO (P < 0.001). Net incyclotorsion of the paretic eye was related with a normal trochlear nerve (P = 0.005), larger size of the paretic SO (P = 0.002), and greater hypertropia during ipsilateral gaze (P = 0.024).

CONCLUSIONS. The status of the trochlear nerve, paretic SO size, and hypertropia during ipsilateral gaze which reflects the tensile strength of the ipsilateral superior rectus, significantly contribute to ocular torsion in unilateral SOP.

Keywords: superior oblique palsy, trochlear nerve, ocular torsion

Recent investigations based on advanced imaging modalities and functional anatomy have offered novel approaches to understand the etiology and pathophysiology of superior oblique palsy (SOP). Absence of the trochlear nerve has been well recognized as one of the major pathologic etiologies of SOP. In our earlier study of congenital SOP, 73% showed ipsilateral trochlear nerve absence and a variable extent of SO hypoplasia, whereas the remainder had a normal-appearing SO and trochlear nerve on both sides. The relevance of ocular torsion in the diagnosis of SOP is well recognized. Identification of bilateral excyclotorsion provides essential information in diagnosing bilateral SOP and incyclotorsion of the hypertropic eye suggests skew deviation. However, torsional patterns in unilateral SOP have shown inconsistent results, and little is known about the torsional changes in SOP according to its pathogenic etiology. To date, there are only a few studies investigating subjective and objective torsion in SOP according to its major etiologies. In our previous report, objective ocular torsion using fundus photographs with an internal fixator did not show any differences according to the presence of the trochlear nerve; however, the investigation was conducted only in congenital SOP whose diagnosis was based on clinical grounds, and in a relatively small number of subjects.

In this study, we sought to investigate ocular torsion in conjunction with cyclovertical motility parameters in subjects with unilateral SOP regardless of the clinical presentation. We determined if unilateral absence of the trochlear nerve is associated with changes of cyclovertical motility parameters and defined factors related to objective ocular torsion.

METHODS

Approval to conduct this study was obtained from the Institutional Review Board of Seoul National University Bundang Hospital. All aspects of the research protocol and clinical investigation were conducted according to the principles expressed in the Declaration of Helsinki. Informed consent was not given, as subject records and information were anonymized and de-identified prior to analysis.

Subjects

The medical records were reviewed retrospectively for 159 consecutive subjects who were diagnosed with unilateral SOP.
and had undergone high-resolution thin-section magnetic resonance imaging (MRI) and fundus photography at Seoul National University Bundang Hospital between January 2012 and August 2015.

Diagnosis of unilateral SOP was made by the following criteria: (1) hyperdeviation in the primary position; (2) unilateral underdepression in adduction with or without overrelevation in adduction; (3) the absence of reversal of the hypertropia on the diagnostic fields of gaze or head tilt and absence of cyclotorsional features suggesting bilateral SOP; and (4) lack of evidence of other ocular motility disorders causing vertical deviation, including contracture of the vertical rectus muscle except secondary contracture of superior rectus (SR) muscle associated with SOP paresis of multiple vertical muscles, previous muscle surgery, skew deviation, myasthenia gravis, and vertical deviation-related horizontal strabismus as well as structural abnormalities such as muscle pulley heterotopy or craniosynostosis. The etiology was defined as congenital based on clinical grounds with photographic evidence or reliable historical documentation of long-standing strabismus or torticolis since infancy, large fusional amplitudes of vertical deviation, and absence of torsional diplopia. Acquired cases were clinically diagnosed by an absence of the foregoing occurrence, normal vertical fusional amplitudes, presence of torsional diplopia, and suspicious history of a preceding event typically related to the onset of symptoms. Symptom duration was defined as the interval between the first time the patient was noticed with head tilt or strabismus and the time of initial examination at our institution.

**Clinical Measurement**

Clinical characteristics were collected and all study subjects underwent complete ophthalmologic examinations. Examinations included prism and alternate cover measurements in the six diagnostic positions of gaze; primary position at distance and near, up, down, right, and left gazes, as well as right and left head tilt positions. Ocular motility assessment for the oblique muscles was graded based on a subjective scale (0–4) of underaction (−) or overaction (+). SR overaction or contracture was defined by clinical criteria previously published as follows: a vertical deviation of 15 prism diopters (PD) or more in the primary position, equal or larger hypertropia with ipsilateral head tilt than with the eyes looking straight ahead, more than 5 PD hypertropia of the affected eye in gaze to the side of the SO palsy, hypertropia in all upgazes, and overaction of the contralateral SO muscle of +1 or more. The "net" hypertropia in ipsilateral gaze was defined as the difference between hypertropia in ipsilateral gaze and the primary position, which represented the tensile strength of the ipsilateral SR. Laterality of the paretic eye, fixation dominance, dissociated vertical deviation, and associated horizontal strabismus were also noted. Subjective torsion in the primary gaze was assessed with double Maddox rods. Objective ocular torsion was evaluated by fundus photographs obtained using KOWA VX-10 and TRC-50IA fundus cameras using internal fixation. Based on the methods described by Kushner and Hariraham, the direction of torsion and the number of degrees of rotation from horizontal plane were recorded. For analysis of torsion, we encountered objective torsion by measuring the relative position of the disc and fovea on fundus photographs. Inborn variation of the anatomic position of the disc and fovea was adjusted to determine the net angle of torsion in the paretic eye, which was measured by subtracting the fovea-disc angle of the contralateral eye. As the intereye difference of the fovea-disc angle in normal participants was observed in a range of 0.0° to 4.4° based on fundus photographs by Bixenman and von Noorden, an intereye difference beyond this range was defined as net excyclotorsion or incyclotorsion. Quantification of compensatory head tilt posture was evaluated using clinical and photographic methods. The presence of facial asymmetry was graded subjectively by two independent observers on full-face frontal photographs obtained while the subject fixated on a distant target at the primary position.

**Magnetic Resonance Imaging: Trochlear Nerve and Superior Oblique Muscle**

MRI was performed by using a 3T system (Intera Achieva; Philips Healthcare, Best, The Netherlands) with an 8-channel sensitivity encoding head coil, and general aspects of the MRI protocol were in accordance with our previous description. Children younger than 6 years were sedated by chloral hydrate. We measured the areas of the SO manually using Picture Archiving and Communication System (PACS) software (INFINITT, Seoul, Korea), which provides automatic acquisition for area. The optic nerve–globe junction was defined as the standard point, and SO areas were measured in the coronal section at the point. Recent research data support that a ratio of paretic/nonparetic (P/N) side SO area ≤ 0.75 at the optic nerve–globe junction demonstrated high predictability for trochlear nerve absence. Thus, the ratio of SO area (P/N) of ≤ 0.75 was adapted as the cutoff value indicating clinically significant SO atrophy in the present study.

**Statistical Analyses**

Statistical analyses were performed with SPSS software version 20 (SPSS, Inc., Chicago, IL, USA). We compared groups using the independent t-test for continuous variables, Pearson’s r² test, Fisher’s exact test and likelihood ratio test for trend for categorical data. Pearson’s r² test was selected when the sample size was sufficiently large and all the expected cell counts were 5 or more. Fisher’s exact test was used when any expected frequency was less than 1 or 20% of expected frequencies were less than 5. Univariate and multivariate analyses by linear logistic regression were performed to identify significant relevant factors affecting the laterality of excyclotorsion, including absence of the trochlear nerve, symptom duration, symptom duration of less than 1 year, head tilt angle, hypertropia in ipsilateral gaze, net hypertropia in ipsilateral gaze, hypertropia in ipsilateral tilt, SR overaction/contracture, paretic eye fixation, and paretic and nonparetic SO size. A P value of < 0.05 was considered statistically significant.

**RESULTS**

A total of 159 subjects met the inclusion criteria and among them, 75 (47%) subjects were in the absent group. All subjects in the absent group had an ipsilateral absent trochlear nerve and variable degree of SO muscle hypoplasia, while the fellow eye had an intact trochlear nerve and normal-sized SO muscle, which was consistent with our previous study. The present group had normal anatomic features of the trochlear nerve on both sides.

**Subject Characteristics**

The clinical characteristics of both groups are presented in Table 1. The etiology was congenital in 46% (39/84) of the
present group and 100% (75/75) of the absent group. There was no significant difference in symptom duration between the absent group and present group (P = 0.359). However, the proportion of subjects with very short symptom duration (less than 1 year) was higher in the present group (P = 0.025). Compensatory head tilt and facial asymmetry were more frequent in the absent group (P = 0.001, 0.002, respectively). According to the Knapp classification, the most frequent pattern was class I in the present group (48%) and class III in the absent group (43%). The rate of paretic eye fixation was similar in both groups (18% in the present group versus 15% in the absent group) (P = 0.587).

Cyclovertical Motility, Ocular Torsion, and Superior Oblique Muscle Area

Table 2 presents the cyclovertical motility components, ocular torsion, and MRI features including SO muscle area according to the existence of the trochlear nerve. The absent group presented greater hypertropia during ipsilateral gaze and ipsilateral tilt.

The absent group more frequently showed excyclotorsion in the paretic eye on fundus photographs using the methods by Kushner and Hariharan (30% vs. 52%; P = 0.004), and a larger degree of excyclotorsion (−0.9 ± 4.5° vs. 1.5 ± 5.2°; P = 0.002). The net torsional angle of the paretic eye consistently showed more excyclotorsion in the absent group compared with the present group (P = 0.002). The proportion of net excyclotorsion in the paretic eye was greater in the absent group (11% vs. 37%), while net incyclotorsion was greater in the present group (41% vs. 25%) (P < 0.001). As the mean torsional angle of the net incyclotorsion group (n = 51) was −2.9 ± 3.2 (range, −10.0 to 0.0)° in the paretic eye and 5.2 ± 3.5 (range, −3.6 to 11.1)° in the nonparetic eye, net incyclotorsion of the paretic eye was more likely to be net excyclotorsion of the nonparetic eye.

Regarding SO muscle area, the ratio of SO area (P/N) at the optic nerve-globe junction was significantly smaller in the absent group (0.96 ± 0.11 vs. 0.45 ± 0.17) (P < 0.001). The ratio of SO area (P/N) was 0.75 or less in all subjects of the absent group, while only 4% (3/84) of the present group were in this range (P < 0.001).

Factors Associated With Net Cyclotorsion of the Paretic Eye

Table 3 shows factors related to net excyclotorsion or incyclotorsion of the paretic eye by multivariate logistic regression analysis. Net excyclotorsion was strongly associated with absence of the trochlear nerve (β = 5.69; P < 0.001) and smaller paretic SO size (β = 0.64; P < 0.001). Net hypertropia in ipsilateral gaze was negatively correlated with net excyclotorsion (β = 0.90; P = 0.024).

Net incyclotorsion of the paretic eye was inversely related with absence of the trochlear nerve (β = 0.33; P = 0.005). Larger paretic SO size (β = 1.33; P = 0.002) showed significant association with net incyclotorsion of the paretic eye. The amount of hypertropia during ipsilateral gaze showed a positive correlation (β = 1.08; P = 0.024).

We performed a subgroup analysis in patients with an absent trochlear nerve to determine factors related to net incyclotorsion in the absent group, who are a particularly interesting group. Greater amount of hypertropia during ipsilateral gaze (β = 1.20; P = 0.005) and larger paretic SO size (β = 2.94; P = 0.005) were identified as significant variables related to net incyclotorsion in the absent group.
Hypertropia in IL gaze, PD 1.08 ± 0.04 ± 0.024
Net hypertropia‡ in IL gaze, PD 0.90 ± 0.05 ± 0.024
SO area† ratio, P/N 0.12 ± 0.70 0.002 5.24 ± 0.66 ± 0.013
SO area†, P 0.64 ± 0.17
Absence of trochlear nerve 5.59 ± 0.49

Subjects With a Trochlear Nerve (Present Group) Versus Those Without a Trochlear Nerve (Absent Group)

TABLE 3. Logistic Regression Analysis for Factors Related to the Presence of Net* Excyclotorsion and Incyclotorsion of the Paretic Eye

<table>
<thead>
<tr>
<th>Variables</th>
<th>Net* Excyclotorsion of the Paretic Eye</th>
<th>Net* Incyclotorsion of the Paretic Eye</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β</td>
<td>Standard Deviation</td>
</tr>
<tr>
<td>Absence of trochlear nerve</td>
<td>5.69</td>
<td>0.49</td>
</tr>
<tr>
<td>SO area†, P</td>
<td>0.64</td>
<td>0.17</td>
</tr>
<tr>
<td>SO area†, P/N</td>
<td>0.12</td>
<td>0.70</td>
</tr>
<tr>
<td>Net hypertropia‡ in IL gaze, PD</td>
<td>0.90</td>
<td>0.05</td>
</tr>
<tr>
<td>Hypertropia in IL gaze, PD</td>
<td>0.90</td>
<td>0.05</td>
</tr>
</tbody>
</table>

P, paretic side; N, nonparetic side; IL, ipsilateral.

* Difference of the torsional angle between fellow eyes (paretic eye – nonparetic eye) on fundus photographs; a positive value over the normal range of 4.4° indicates net excyclotorsion and a negative value under the normal range of –4.4° indicates net incyclotorsion of the paretic eye. 19
† Degree of rotation on fundus photographs. 17
‡ Difference of hypertropia in IL gaze and the primary position.

which was higher than our observations. This discrepancy might result from the methodologic and/or etiologic differences in subjects among studies. Na et al. 16 included a relatively small number of acquired SOP subjects compared to congenital SOP and applied Bixenman and von Noorden’s method 19 to estimate fundus torsion. Olivier and von Noorden 25 explored fundus torsion only in SOP subjects who had subjective torsion by the double Maddox rod test. Lee et al. 24 assessed fundus torsion only in subjects with acquired SOP via “tangential value”.

In our study, a high association between trochlear nerve absence and net excyclotorsion (β = 5.69; P < 0.001) was found. This is consistent with the significantly smaller SO area in the net excyclotorsion group compared to the net incyclotorsion group. The smaller ratio of the P/N side SO area at the optic nerve-globe junction demonstrates excellent

TABLE 2. Ocular Motility, Ocular Torsion, and Superior Oblique Muscle Area in Subjects With Unilateral Superior Oblique Palsy Compared Between Subjects With a Trochlear Nerve (Present Group) Versus Those Without a Trochlear Nerve (Absent Group)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Present Group, n = 84</th>
<th>Absent Group, n = 75</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertropia in primary gaze, PD</td>
<td>15.9 ± 9.2 (3 to 35)</td>
<td>17.7 ± 8.6 (3 to 40)</td>
<td>0.154</td>
</tr>
<tr>
<td>Hypertropia in IL gaze, PD</td>
<td>8.4 ± 7.1 (0 to 30)</td>
<td>11.1 ± 8.0 (0 to 30)</td>
<td>0.025</td>
</tr>
<tr>
<td>Hypertropia in CL gaze, PD</td>
<td>15.0 ± 9.4 (0 to 45)</td>
<td>17.4 ± 8.9 (0 to 35)</td>
<td>0.121</td>
</tr>
<tr>
<td>Hypertropia in IL tilt, PD</td>
<td>17.5 ± 9.2 (0 to 40)</td>
<td>22.8 ± 10.3 (2 to 50)</td>
<td>0.001</td>
</tr>
<tr>
<td>Hypertropia in CL tilt, PD</td>
<td>6.3 ± 6.5 (0 to 30)</td>
<td>6.0 ± 7.1 (0 to 30)</td>
<td>0.910</td>
</tr>
<tr>
<td>SO overaction/contracture*</td>
<td>6/84 (7)</td>
<td>157/75 (20)</td>
<td></td>
</tr>
<tr>
<td>Fundus excyclotorsion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paretic eye</td>
<td>25/84 (30)</td>
<td>39/75 (52)</td>
<td>0.004</td>
</tr>
<tr>
<td>Fellow eye</td>
<td>52/84 (38)</td>
<td>19/75 (26)</td>
<td>0.085</td>
</tr>
<tr>
<td>Torsional angle†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipsilateral, °</td>
<td>–0.9 ± 4.3 (–9.0 to 12.7)</td>
<td>1.5 ± 5.2 (–9.0 to 14.6)</td>
<td>0.002</td>
</tr>
<tr>
<td>Contralateral, °</td>
<td>1.5 ± 4.6 (–9.0 to 11.1)</td>
<td>0.8 ± 5.0 (–8.9 to 14.9)</td>
<td>0.385</td>
</tr>
<tr>
<td>Net angle between eyes‡,  °</td>
<td>–2.3 ± 5.3 (–12.7 to 8.9)</td>
<td>1.1 ± 7.6 (–20.1 to 17.2)</td>
<td>0.002</td>
</tr>
<tr>
<td>Net excyclotorsion§</td>
<td>9/84 (11)</td>
<td>28/75 (37)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Net incyclotorsion§</td>
<td>34/84 (41)</td>
<td>17/75 (23)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Subjective excyclotorsion§, n = 100</td>
<td>10/55 (18)</td>
<td>11/45 (24)</td>
<td>0.444</td>
</tr>
<tr>
<td>SO area† ratio, P/N</td>
<td>0.96 ± 0.11 (0.39 to 1.15)</td>
<td>0.45 ± 0.17 (0.03 to 0.75)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data are mean ± standard deviation (range) or n (%). IL, ipsilateral; CL, contralateral; P, paretic side; N, nonparetic side.

* Defined as the clinical criteria by Molinari et al.18
† Degree of rotation on fundus photographs. 17
‡ Difference of the torsional angle between fellow eyes (paretic eye – nonparetic eye) on fundus photographs; a positive value over the normal range of 4.4° indicates net excyclotorsion and a negative value under the normal range of –4.4° indicates net incyclotorsion of the paretic eye. 19
§ Subjective excyclotorsion ≥5° by the double Maddox rod test.
|| SO area measured at the reference plane of the optic nerve–globe junction on MRI.
# Independent t test.
** Pearson’s χ2 test.
†† Likelihood ratio test for trend.

DISCUSSION

This study presented several findings that have not been previously reported in the literature. Unilateral SOP subjects featured different patterns of cyclovertical motility and torsion according to trochlear nerve agenesis, SO hypoplasia, and the degree of hypertropia during ipsilateral gaze. Unilateral SOP subjects without a trochlear nerve and smaller SO area more frequently showed net excyclotorsion of the paretic eye on fundus photographs. Conversely, unilateral SOP subjects with a normal trochlear nerve, larger SO area, and greater hypertropia during ipsilateral gaze more frequently showed net incyclotorsion of the paretic eye, or excyclotorsion of the nonparetic eye.

In previous literature, excyclotorsion of the paretic eye was documented in 61% to 75% of unilateral SOP, 16,23,24 which was higher than our observations. This discrepancy might result from the methodologic and/or etiologic differences in subjects among studies. Na et al. 16 included a relatively small number of acquired SOP subjects compared to congenital SOP and applied Bixenman and von Noorden’s method 19 to estimate fundus torsion. Olivier and von Noorden 25 explored fundus torsion only in SOP subjects who had subjective torsion by the double Maddox rod test. Lee et al. 24 assessed fundus torsion only in subjects with acquired SOP via “tangential value”.

In our study, a high association between trochlear nerve absence and net excyclotorsion (β = 5.69; P < 0.001) was found. This is consistent with the significantly smaller SO area in the net excyclotorsion group compared to the net incyclotorsion group. The smaller ratio of the P/N side SO area at the optic nerve-globe junction demonstrates excellent

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predictability for trochlear nerve absence in congenital SOP.\textsuperscript{22} It is also known that SO contractility well correlates with its maximum cross-sectional area.\textsuperscript{23} Thus, it may be concluded that the status of the trochlear nerve and SO muscle hypoplasia substantially affect the pattern of ocular torsion in SOP.

In our study, 32\% (51/159) of subjects showed net incyclotorsion in the paretic eye of unilateral SOP. The lack of ipsilateral fundus excyclotorsion may be a clinical indication of a tight ipsilateral SR muscle, as this may negate the effect of excyclotorsion caused by SO palsy.\textsuperscript{17} In previous studies, 17\% to 46\% of patients with unilateral SOP had accompanying ipsilateral SR contracture.\textsuperscript{10,18,26} SR contracture mainly occurs when there is a large angle of longstanding strabismus regardless of fixation preference.\textsuperscript{10,18,26} However, the direct correlation of SR contracture with net incyclotorsion was not verified in our study due to the small number of subjects (13\%) satisfying the previously published criteria of SR contracture/overaction. Therefore, we evaluated the amount of hypertropia during ipsilateral gaze to assume indirect evidence of a tight SR.\textsuperscript{17} In the subset of patients with an absent trochlear nerve, a greater amount of hypertropia during ipsilateral gaze ($\beta = 1.20; P = 0.005$) and a larger paretic SO size ($\beta = 2.94; P = 0.005$) positively correlated with net incyclotorsion. This reflects the potential influence of a tight SR leading to net incyclotorsion of the paretic eye in SOP.

The present study proposed that the absence of trochlear nerve, SO hypoplasia, and the potential effect of SR could contribute to the alteration of net torsional positions in the paretic eye. These findings indicate that the relative cyclotorsion may be affected by complex cyclotorsional forces working on the paretic eye, substantially the tonus of the paretic SO and mechanical restriction of the ipsilateral SR, both of which favor incyclotorsion of the paretic eye or contralateral excyclotorsion via Hering's law of reciprocal changes. These should be confirmed by forced duction test results of the SO and SR; however, the majority of study patients could not perform the test as they did not undergo operation, and further investigations should verify this assumption.

Some limitations of this study need to be considered. First, this study was based on objective torsion measured on fundus photographs; therefore fusion was artificially disrupted by the occlusion of one eye during photographic examination. There was a possibility of an instant shift in excyclotorsion caused by improper fixation. Moreover, incidental artifacts such as an imbalance due to facial asymmetry may have occurred. Thus, we tried to minimize these errors by introducing the net torsional angle between eyes, which would compensate for inborn variations or incidental artifacts. Second, the time of diagnosis after symptom onset was largely heterogeneous in our study, which may affect ocular motility and torsion.

In conclusion, absence of the trochlear nerve and smaller size of the paretic SO may account for net excyclotorsion in the paretic eye of unilateral SOP. Conversely, a normal trochlear nerve, larger paretic SO size, and greater hypertropia during ipsilateral gaze are associated with net incyclotorsion of the paretic eye in unilateral SOP.

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