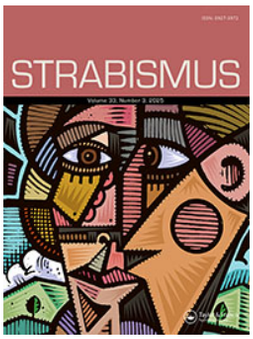

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Comparison of subjective cyclovertical deviation and objective ocular torsion in sagging eye syndrome and superior oblique palsy

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ABSTRACT

Purpose: To compare the differentiating clinical features of subjective cyclovertical deviation and objective ocular torsion in elderly patients with cyclovertical sagging eye syndrome (CSES) versus superior oblique palsy (SOP). *Study design*: Prospectivestudy. *Methods*: Patients with CSES ($n = 22$) and unilateral SOP ($n = 20$) aged ≥50 years were included. Subjective cyclovertical deviation was measured in the primary, secondary, and third-gaze positions using a synoptophore. The disc-fovea angle (DFA), which evaluates objective ocular torsion, was measured using fundus photographs. *Results*: The subjective vertical deviation of the primary position was 1.3° (median) in the CSES group and 4.3° in the SOP group ($p < .001$). Vertical deviation was larger in the SOP than CSES group in all gaze positions ($p < .05$). The subjective cyclodeviation of the primary gaze was −6.0° (-: excyclo) in the CSES and SOP groups($p = .48$). Cyclodeviation was larger in the SOP group in downgaze positions ($p < .05$). The mean DFAs were −11.5° in CSES group and −11.8° in SOP group for the hypertrophic eye ($p = .85$), and −12.2° in CSES group and −16.3° in SOP group for the hypotropic eye ($p < .01$). The ratio of patients with a larger DFA in the hypertropic than hypotropic eye was 9/22 (41.0%) in the CSES group and 4/20 (20%) in the SOP group. *Conclusions*: SOP has a larger hypertropia than SES. Excyclotorsion does not help distinguish in primary position but if it is somewhat larger in downgaze more likely SOP. DFA showed no obvious clinical differences; it is difficult to distinguish the two diseases from DFA.

KEYWORDS

Cyclovertical strabismus; disc-fovea angle; ocular torsion; sagging eye syndrome; superior oblique palsy

Introduction

Epidemiological studies of strabismus in the elderly show that sagging eye syndrome (SES) and superior oblique (SO) palsy (SOP) account for the highest percentage of cases.[1,2] Both these conditions have different mechanisms, with SES due to structural abnormalities, and SOP due to neuropathic etiology. SES is caused by the age-related degeneration or disappearance of orbital connective tissue, comprising collagen, elastin, and smooth muscle.[3–5] Accordingly, SES shows elongation, rupture, or disappearance of the orbital connective tissue and pulley and downward deviation of the lateral rectus (LR) muscle on magnetic resonance imaging (MRI).[4,6] SES can manifest as cyclovertical SES (CSES) [4], which accounts for 65% of SES cases,[2] or age-related distance esotropia (ARDE). Conversely, SOP is caused by muscle atrophy, deficiency or palsy of the SO muscle, which is innervated by the trochlear nerve. SOP is a disturbance of the SO's function, mainly infraduction and intorsion, resulting in vertical and extorsional strabismus.

CSES and SOP are both characterized by cyclovertical strabismus; it is therefore sometimes difficult to distinguish CSES from SOP in patients with late-onset strabismus. In a previous report[7] that compared the characteristics of SES and SOP, the Parks three-step test was positive in patients with CSES, and the clinical findings were confounded with unilateral SOP. Additionally, the accuracy of disease differentiation in machine learning is imperfect.[7]

The treatments for CSES and SOP may clinically overlap, primarily with the goal of eliminating diplopia. However, if diplopia due to acute neurological lesions occurs, further investigations and

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treatment are required. Therefore, there is potential for subjective and objective evaluations other than an MRI to be useful as a diagnostic aid. Particularly, there are no reports comparing cyclodeviation. We compared subjective cyclovertical deviations in different gaze positions and objective ocular torsion between elderly patients with CSES and SOP diagnosed from clinical findings.

Methods

This prospective, cross-sectional observational study was approved by the Kitasato University Ethics Committee (B19–124) and complied with the principles of the Helsinki Convention. Patients were provided with the opportunity to refuse research consent through an opt-out method. This study included 22 and 20 patients with CSES and unilateral SOP, respectively, aged ≥50 years who visited the Kitasato University Hospital between September 2019 and March 2023. The diagnostic criteria for CSES[4,5] were as follows: 1) acquired binocular diplopia; 2) cyclovertical strabismus at a distance (5 m) or near (1/3 m) (+3.00 D addition) manifested with the alternate prism cover test; 3) no underaction and overaction such as SOP, confirmed with the Hess screen test;[2] 4) normal range of ocular ductions, except for supraduction limitation (saccade was normal);[8] 5) Bielschowsky head tilt test (BHTT) difference < 5 prism diopter (PD, Δ); 6) sunken upper eyelid in facial appearance;[9,10] 7) elongation, rupture, or disappearance of the LR-superior rectus (SR) band 3–6 mm anterior to the optic nerve attachment and downward deviation of the LR muscle on MRI; and 8) neurogenic, neuromuscular junction, and myogenic causes excluded through laboratory and imaging scans.

The diagnostic criteria for SOP were as follows: 1) congenital or acquired cyclovertical strabismus; 2) underaction of the affected eye in the inferonasal gaze and overaction in the superonasal gaze position, confirmed with the Hess screen test; 3) abnormal head position with a tilt toward the fellow side; and 4) BHTT difference ≥ 6 Δ.

Patients who were diagnosed by two physicians and fulfilled all the above criteria were included in this study. Patients with suspected superotemporally displaced globes on orbital MR images were not included, and those with myopia >-6.00 D or an axial length of ≥27.00 mm on the IOL master (Carl Zeiss Meditec, Jena, Germany) were excluded, as high myopia may cause displacement of the extraocular muscles.[11]

Subjective cyclovertical deviation was measured using a synoptophore (Haag-Streit UK Ltd., Harlow, UK). The slides used for the measurements were A17 and A18 of a heterogeneous, cross-shaped figure with a 20-mm diameter (visual angle: 7°; Figure 1).

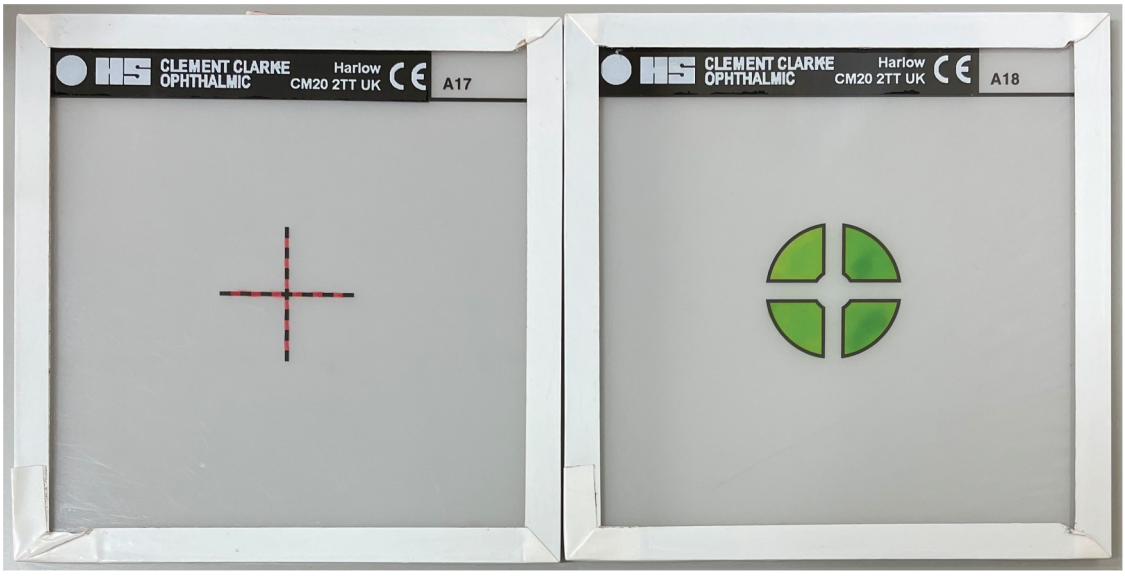

Figure 1. Slides for measuring subjective cyclovertical deviation.

Patients wore glasses or contact lenses with complete correction and looked into the synoptophore tube. The synoptophore started with horizontal, vertical, and torsion scales set at 0°, with slide A17 set in the hypertropic eye and slide A18 in the hypotropic eye. Patients manipulated the horizontal arm of the A17 slide, and the examiner turned the vertical and torsion knobs to rotate the A17 slide and confirm that simultaneous perception was achieved. This measurement was performed in nine directions: primary, secondary, and tertiary gazes at 15°. A certified orthoptist conducted all tests (MK).

Objective ocular torsion was assessed using fundus photography.[12] Fundus photographs were captured in a semi-dark room using a VX-20α camera (Kowa Company, Nagoya, Japan). Images were acquired under mydriatic or nonmydriatic conditions while gazing at the internal fixation light in the primary mode. This procedure allowed simultaneous macula and optic nerve head imaging at a 45° viewing angle. Fundus photographs were obtained with the patient's chin resting on the chin rest, forehead resting against the forehead band, and head fixed in the primary position with a headband. Fundus photographs were converted to JPEG and analyzed using ImageJ software (National Institutes of Health, Bethesda, MD, USA) to measure the fundus torsion angle. For analysis, the center of the optic nerve head was determined by tracing the limbus of the optic nerve head with the free hand. The disc-fovea angle (DFA) was defined as the angle formed by two lines: one line passing through the center of the optic nerve head and fovea, and a horizontal line passing through the center of the optic nerve head (Figure 2).[13]

Data were shown as the mean and standard deviation for normally distributed variables, and as the median and interquartile range values p.25 (first quartile), p.75 (third quartile) for non-normally distributed variables. Statistical analyses were performed using the R software (version 4.2.3; The R Foundation for Statistical Computing, Vienna, Austria). The CSES and SOP groups were compared using the *t* test or Mann – Whitney U test. Statistical significance was set at *P*-values <.05.

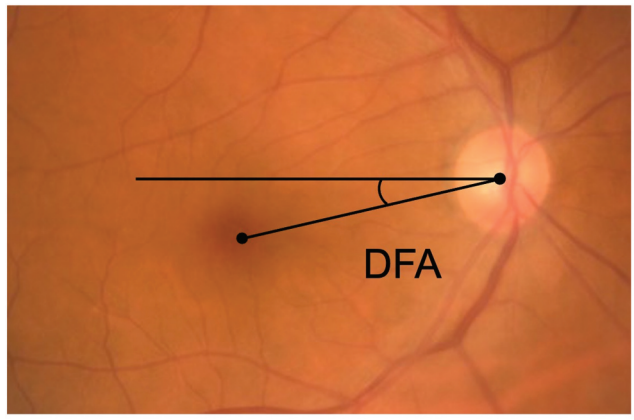

Figure 2. The disc-fovea angle (DFA) was defined as the angle formed by two lines: One line passing through the center of the optic nerve head and fovea, and a horizontal line passing through the center of the optic nerve.

Results

The ages of the patients were 75.0 ± 7.9 (mean ± standard deviation) years in the CSES group (n = 22) and 66.1 ± 10.2 years in the SOP group (n = 20) (p < .01). The ratio of hypertropic eyes in the CSES group was right:left = 13:9, and the ratio of paretic eyes in the SOP group was right:left = 9:11. The etiology of SOP was congenital, vascular, brain disease (including microinfarction), trauma, and unknown in six, five, four, one, and four patients, respectively.

Subjective vertical deviation of the Primary position was 1.3° [1.0°, 2.5°] (median [first quartile, third quartile]) in the CSES group and 4.3° [2.3°, 8.0°] in the SOP group (p < .001). Figure 3a shows the subjective vertical deviation values for the CSES and SOP groups in various gaze positions, as well as a comparison between groups. The data are reflected as necessary to appear as left hypertropic eye. The vertical deviation was larger in the SOP than CSES group for gaze positions (Up, Temporal: p < .05, Nasal up, Temporal down: p < .01, Primary, Nasal, Down, Nasal down: p < .001).

Subjective cyclodeviation of the Primary position was −6.0° [−7.0°, −4.3°] (-: excyclo) in the CSES group and −6.0° [−7.3°, −5.0°] in the SOP group for hypertropic eyes (p = .48). Figure 3b

a Subjective vertical deviation

Temporal up CSES: 2.0 [1.0, 2.0] SOP: 2.8 [1.4, 5.0]	**Up** CSES: 2.0 [0.5, 2.9] SOP: 2.8 [1.4, 5.3] *	**Nasal up** CSES: 2.0 [0.6, 2.9] SOP: 3.5 [2.0, 7.3] **
Temporal CSES: 1.0 [0.6, 3.0] SOP: 4.0 [1.8, 7.3] *	**Primary** CSES: 1.3 [1.0, 2.5] SOP: 4.3 [2.3, 8.0] ***	**Nasal** CSES: 2.3 [1.0, 4.0] SOP: 5.0 [3.0, 8.0] ***
Temporal down CSES: 1.0 [0, 2.8] SOP: 2.8 [1.5, 7.3] **	**Down** CSES: 1.5 [1.0, 3.4] SOP: 4.0 [3.0, 7.5] ***	**Nasal down** CSES: 2.0 [2.0, 4.0] SOP: 6.0 [4.0, 10.0] ***

b Subjective cyclodeviation

Temporal up CSES: -6.0 [-7.0, -4.0] SOP: -6.0 [-8.0, -4.8]	**Up** CSES: -5.0 [-7.0, -3.0] SOP: -6.5 [-9.3, -3.0]	**Nasal up** CSES: -5.5 [-8.0, -4.0] SOP: -7.0 [-9.3, -4.8]
Temporal CSES: -6.0 [-8.0, -5.0] SOP: -7.0 [-9.3, -6.0]	**Primary** CSES: -6.0 [-7.0, -4.3] SOP: -6.0 [-7.3, -5.0]	**Nasal** CSES: -6.0 [-8.0, -5.0] SOP: -7.0 [-9.0, -5.0]
Temporal down CSES: -7.0 [-8.0, -5.3] SOP: -9.0 [-11.0, -7.8] *	**Down** CSES: -7.0 [-8.0, -5.0] SOP: -8.5 [-10.3, -7.5] **	**Nasal down** CSES: -7.0 [-7.8, -5.3] SOP: -7.5 [-10.3, -6.0]

Figure 3. Comparison of the subjective cyclovertical deviation values between cyclovertical sagging eye syndrome (CSES), superior oblique palsy (SOP) in various gaze positions. The data are reflected as necessary to appear as left hypertropic eye. (a) indicates vertical deviation; (b) indicates cyclodeviation. Median [first quartile, third quartile], Unit: degree, -: excyclo *$p < .05$, **$p < .01$, ***$p < .001$

shows the subjective cyclodeviation values for the CSES and SOP groups in various gaze positions, as well as a comparison between groups. The SOP group had larger excyclotorsion at the Temporal down ($p < .05$) and Down ($p < .01$) positions compared with the CSES group.

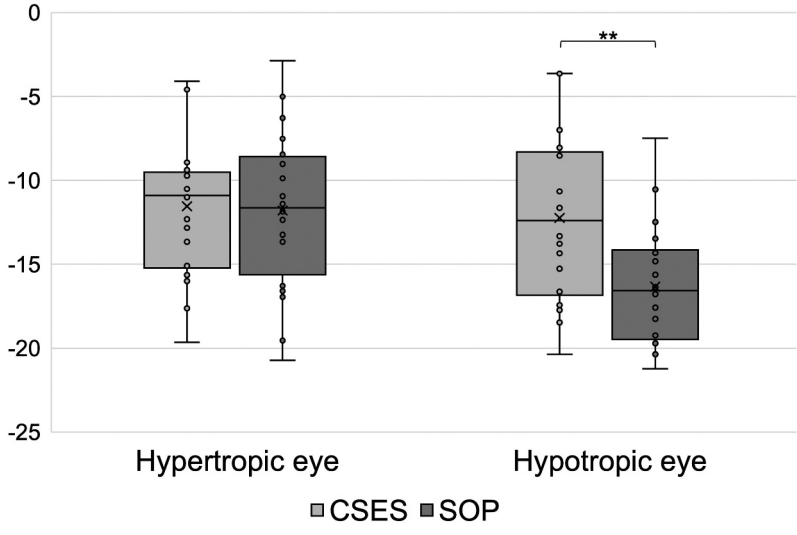

Figure 4. Comparison of the disc-fovea angle (DFA) between cyclovertical sagging eye syndrome (CSES), superior oblique palsy (SOP). Unit: degree, -: excyclo, **$p < .01$

Figure 4 shows the objective ocular torsion for the CSES and SOP groups. The respective DFAs were −11.5 ± 4.1° in CSES group and −11.8 ± 4.7° in SOP group for the hypertropic eye (p=.85), and −12.2 ± 4.8° in CSES group and −16.3 ± 3.6° in SOP group for the hypotropic eye ($p < .01$). The ratio of patients with a larger DFA in the hypertropic than hypotropic eye was 9/22 (41.0%) in the CSES group and 4/20 (20%) in the SOP group.

Discussion

In this study, the subjective vertical deviation was larger for SOP than CSES, particularly in the Primary, Nasal, Down and Nasal down positions. Subjective cyclodeviation did not differ between CSES and SOP in the Primary position, while SOP was larger in the Down and Temporal down positions. Wei et al.[7] compared the horizontal and vertical deviation characteristics of SES and unilateral SOP based on the Hess screen test. The study reported that the horizontal deviation was not significantly different, whereas the vertical deviation was significantly difference. Our study also found that the vertical deviation was more significantly downward, and the results were generally similar to those of the previous study. The differences in subjective vertical deviations of gaze position in this study depended on the respective disease mechanism. SES causes displacement of the LR and tends to cause hypotropia of the more affected eye, but may result normal saccadic movements;[8] thus, SES is unlikely to be of neuropathic etiology. SO has a stronger action in the downgaze, and SOP causes defects in the action of the SO in its specific field of action.[14] Regarding atrophic SOP, muscle volume increases in the ipsilateral inferior rectus (IR), LR, and contralateral SR muscles,[15] and contractions in the ipsilateral IR[16] and contralateral SR[17] muscles are enhanced. Therefore, SOP may also reflect slight hypertrophy and increased contractility of other extraocular muscles due to the prolonged SO muscle weakness.

The result of cyclodeviation comparing CSES and SOP was revealed for the first time in this study. SOP had a larger excyclotorsion at the Temporal down and Down positions. This is because the intorsional action of paralyzed SO does not work. Meanwhile,16.6% of patients with SOP had ipsilateral SR contracture,[18] which may decrease excyclotorsion at downgaze. It should be noted that elderly patients with congenital SOP leads sometimes to fibrosis of the SR due to long-term contracture.

In this study, the objective ocular torsion of both CSES and SOP exceeded 10°. The reported DFA in normal individuals aged >60 years is −6.57 ± 3.48°;[19] therefore, the DFA was larger in both the CSES and SOP groups than in normal individuals. Age-related nonparalytic hypertropia involving SES was reported as −11.0 ± 4.8° in the right eye and −11.6 ± 3.9° in the left,[20] which was also the case for CSES in this study.

In 41% of patients with CSES in this study, the DFA was not larger in the hypotropic eye than in the hypertropic eye. Even in the previous report,[20] the hypotropic eye was not the eye with a larger DFA in 39% of the cohort. Orbital MRI in CSES is characterized by downward deviation and tilt of the LR muscle, a finding that is significantly more common in hypotropic than hypertropic eyes.[4,6] Therefore, the downward deviation of the LR muscle is one of the features in hypotropic eyes. However, as the DFA tends to show a larger angle of ocular torsion in the left than right eye (even in normal individuals,[21] and due to the influence of the dominant eye,[22] it was considered that the objective ocular torsion does not completely match structural abnormalities in CSES. In SOP, ocular torsion occurs in either eye in 61.1% of congenital unilateral SOP cases and 46.5% of acquired unilateral SOP cases. Particularly, congenital unilateral SOP is characterized by ocular torsion in the fellow eye or both eyes.[23] Therefore, the relationship between the hypertropic and hypotropic eyes in objective ocular torsion in SOP may be considered to vary between individuals depending on the pathology. Based on the results of DFA, it is difficult to distinguish between CSES and SOP.

This study has a limitation; first, the diagnosis was made by clinical findings in elderly patients, and the position of the extraocular muscles was not quantified by MRI. Recent cases with clinical findings of SOP have been reported due to masquerading SOP[24] and displacement of the rectus muscle pulley,[25,26] and those who only exhibited the eye movements and clinical patterns of patients with

SOP may have been included in this study. Therefore, additional studies based on detailed MRI features are needed in the future. Second, congenital and acquired SOP are not homogeneous by definition and affect not only the affected eye but also the fellow eye. Because of the differences in their characteristics, future comparisons of the two are necessary.

In conclusion, this study was conducted to compare the characteristics of subjective cyclovertical deviation and objective ocular torsion in elderly patients with CSES and SOP. The subjective vertical deviation was larger in patients with SOP than CSES, and the excyclotorsion was larger in patients with SOP in the downgaze. The findings of this subjective cyclovertical deviation can help differentiate CSES from SOP in the elderly and may contribute to the understanding of the pathogenesis of both diseases. Objective ocular torsion showed excyclotorsion > 10° in both CSES and SOP. It was suggested that the balance between the hypertropic and hypotropic eyes was significantly influenced by other factors. Future studies should attempt to validate the findings presented here to determine how accurately the torsion criteria can predict the diagnosis and figures.

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Disclosure statement

No potential conflict of interest was reported by the author(s).

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Data availability statement

The data supporting the findings of this study are available from the corresponding author, TG, upon reasonable request.

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