Vertical Misalignment in Unilateral Sixth Nerve Palsy

Agnes M. F. Wong, MD, PhD,[1,2] Douglas Tweed, MD, PhD,[1,3] James A. Sharpe, MD[1,2]

Objective: To detect and determine the magnitude of vertical deviation in patients with unilateral sixth nerve palsy.

Design: Prospective consecutive comparative case series.

Participants: Twenty patients with unilateral peripheral sixth nerve palsy, 7 patients with central palsy caused by brainstem lesions, and 10 normal subjects.

Methods: Subjects were tested by the prism and cover test, Maddox rod and prism test, and magnetic search coil recordings in nine diagnostic eye positions. They were also tested during static lateral head tilt by the prism and cover, and Maddox rod and prism tests.

Main Outcome Measures: The magnitudes of horizontal and vertical deviations.

Results: All patients had an abduction deficit and incomitant esodeviation that increased in the field of action of the paretic muscle, indicating sixth nerve palsy. Mean vertical deviations, for all positions of gaze in peripheral palsy were 0.3 $\pm$ 0.8 prism diopters (PD) by prism and cover test, 1.3 $\pm$ 1.6 PD by Maddox rod and prism test, and 2.0 $\pm$ 1.4 PD by coil recordings. Mean vertical deviations in normal subjects were 0.0 $\pm$ 0.0 PD by prism and cover test, 1.0 $\pm$ 0.9 PD by Maddox rod and prism test, and 1.9 $\pm$ 2.1 PD by coil recordings. Therefore, peripheral palsy did not cause abnormal vertical deviation. In central palsy, for all positions together mean vertical deviations were 0.9 $\pm$ 1.3 PD by prism and cover test, 1.4 $\pm$ 1.6 PD by Maddox rod and prism test, and 2.5 $\pm$ 1.6 PD by coil recordings; they were not different from normal values. During static head roll, patients with peripheral palsy had a right hyperdeviation on right head tilt and a left hyperdeviation on left head tilt, regardless of the side of the palsy. In contrast, in central palsy, head tilt caused vertical strabismus that remained on the same side on head tilt to either side.

Conclusions: Small vertical deviations in sixth nerve palsy are consistent with normal hyperphorias that become manifest in the presence of esotropia. In peripheral sixth nerve palsy, static head roll to either side induces hyperdeviation in the eye on the side of the head tilt. Hyperdeviation of the same eye induced by head tilt to either direction implicates a brainstem lesion as the cause of paretic abduction. Quantitative study of sixth nerve palsy demonstrates that if a vertical deviation falls within the normal range of hyperphoria, multiple cranial nerve palsy or skew deviation may not be responsible. Conversely, vertical deviation $>$ 5 PD indicates skew deviation or peripheral nerve palsy in addition to abduction palsy. *Ophthalmology 2002;109:1315–1325 © 2002 by the American Academy of Ophthalmology.*

Sixth nerve palsy is the most common ocular motor nerve palsy. It is characterized by incomitant esotropia with or without a visible limitation of abduction. When a vertical strabismus accompanies defective abduction, multiple cranial nerve palsy or skew deviation from a brainstem lesion should be considered in the differential diagnosis.

Although the abducens nerve and lateral rectus muscle function to abduct the eye, effects of palsy suggest that they play a role in the vertical alignment of the eyes.[1–3] Evidence for this has been sparse, based on subjective testing, and not quantified. Our preliminary clinical observations suggested that patients with isolated sixth nerve palsy could have a small vertical strabismus, the magnitude of which changed with lateral head tilt. Roll of the head about its nasooccipital axis activates the torsional vestibulo-ocular reflex, causing the eyes to rotate around their visual axes. The torsional vestibulo-ocular reflex has a dynamic counterroll component[4–7] during head roll and a static counterroll component after the head comes to rest in a position of lateral tilt.[8] By use of objective and subjective techniques and magnetic search coil oculography, we investigated patients with unilateral sixth nerve palsy from a peripheral cause to determine the vertical alignment of their eyes and their responses

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[1] Division of Neurology, the University of Toronto, and University Health Network–Toronto Western Hospital, Toronto, Ontario, Canada.

[2] Department of Ophthalmology, the University of Toronto, and University Health Network–Toronto Western Hospital, Toronto, Ontario, Canada.

[3] Department of Physiology, the University of Toronto, and University Health Network–Toronto Western Hospital, Toronto, Ontario, Canada.

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Reprint requests to James A. Sharpe, MD, Division of Neurology, University Health Network–Toronto Western Hospital, WW5-440, 399 Bathurst Street, Toronto, Ontario, Canada M5T 2S8.

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to static change in head roll. They were compared with normal subjects and patients with central sixth nerve palsy caused by brainstem lesions.

Material and Methods

Twenty-seven consecutive patients with unilateral sixth nerve palsy were recruited from the Neuro-ophthalmology Unit at the University Health Network, Toronto, Ontario, Canada. A complete history was taken, and detailed ophthalmic and neurologic examinations were performed. The age of onset, the presence or absence of risk factors for ischemia (diabetes mellitus and hypertension), duration of diplopia, range of duction, horizontal and vertical deviations (see Orthoptic Assessment), and associated neurologic symptoms and signs were recorded. When indicated, appropriate tests were performed to rule out myasthenia gravis, thyroid ophthalmopathy, other orbital diseases, or intracranial lesions. Informed consent was obtained from each subject.

Orthoptic Assessment

The range of ductions was examined, and the degree of abduction defect was graded according to the estimated percentage of the normal abduction in the fellow eye. Vertical ductions were also recorded.

The amounts of horizontal and vertical deviation were measured in nine diagnostic positions. This was achieved by turning the patient's head in the appropriate direction to put the eyes into the desired positions.[9] The nine diagnostic positions were (1) the straight-ahead position; (2) four secondary positions, i.e., 10° to the right and left (by turning the face to the left and right), and 10° up and down (by depressing and elevating the chin); and (3) four tertiary positions, i.e., 10° up and right, up and left, down and right, and down and left (by a combination of face turn and chin depression/elevation).[9] The amounts of vertical deviation were also measured by tilting the patient's head 30° toward each shoulder. Both primary deviation (nonparetic eye fixating) and secondary deviation (paretic eye fixating) were measured.

To standardize the amount of head turn and gaze positions, patients wore a cervical range of motion instrument (Performance Attainment Associates, Roseville, MN), which measures the amount of cervical rotation (face turn), extension and flexion (chin elevation and depression), and lateral flexion (head tilts) in degrees.[10,11] The cervical range of motion instrument consists of inclinometers that are attached to a frame similar to that for glasses: one in the sagittal plane for chin up and down position, a second in the frontal plane for head tilt, and a third in the horizontal plane for face turn.[10,11] Two of these inclinometers have gravity-dependent needles (in the sagittal and frontal planes). The other has a magnetic needle (in the horizontal plane) directed to a trunk-fixed magnet placed in midline of the upper chest and back.[10–12] The cervical range of motion instrument has high reliability and validity, with intratester and intertester correlation coefficients > 0.80 and high correlation with radiographic measurement of cervical spine movement.[10–12]

The amounts of horizontal and vertical deviation were measured both objectively using the prism and cover test (prism-cover test), and subjectively using the Maddox rod and prism test (Maddox test). For the prism-cover test, which measured the magnitude of tropia (i.e., manifest deviation),[9] patients fixated at a 20/30 Snellen symbol at a distance of 6 m. A cover was placed in front of one eye while patients fixated with the other eye. Prisms of increasing power were used not only until refixation movement had stopped but also until a reversal of the direction of movement was noted.[9] The increase in prism strength was tailored to each patient and was not performed in uniform steps. The highest prism strength used immediately before the reversal of refixation movement was recorded.

The Maddox test measured the magnitude of phoria (i.e., latent deviation).[9] For horizontal deviation, a red Maddox rod was placed over the right eye with the small glass rods oriented horizontally while patients fixated a small white light at a distance of 6 m. Prisms of increasing strength were used until the red streak was reported to go through the white light. Vertical deviation was measured with the small glass rods oriented vertically. Ten normal subjects served as controls.

Eye Positions and Alignment from Eye Movement Recordings

Visual Stimuli and Experimental Protocol. In addition to using clinical techniques, we also measured eye deviations in nine diagnostic positions with magnetic search coils while patients fixated a red laser spot 0.25° in diameter, rear-projected onto a vertical flat screen 1 m away from the nasion. The laser was programmed to appear in nine different target positions, arranged in a 3×3 square. The middle row of this array was at eye level and the other two 10° above and below. In each row, the center target lay in the patient's midsagittal plane and the other two 10° right and left of it.

With one eye covered, patients were instructed to follow the laser spot as it stepped among positions. At each position the laser halted for 3 seconds. In the horizontal target sequence, the laser started in the center, then stepped to the 10° right position, then back to center, then 10° left, cycling through this pattern 20 times for each eye. The vertical sequence was the same but with the laser stepping center—up—center—down; the two diagonal sequences stepped along oblique lines between opposite corners of the target array. Recordings were then made with the other eye fixating and the fellow eye occluded.

Recordings of Eye Movement and Calibration. The position of each eye was simultaneously measured in the nine diagnostic positions by a three-dimensional magnetic search coil technique, using a 6-foot (183 cm) diameter coil field arranged in a cube (CNC Engineering, Seattle, WA). Eye positions were not measured during static lateral head tilt with magnetic search coils. Phase detectors that use amplitude modulation as described by Robinson[13] provided signals of torsional gaze position within the linear range. In each eye, the patient wore a dual-lead scleral coil annulus designed to detect horizontal, vertical, and torsional gaze positions (Skalar Instrumentation, Delft, The Netherlands). Head position was detected by another coil taped to the patient's forehead. The patient's head was immobilized and centered in the field coils. Horizontal and vertical eye movements were calibrated with saccades to steps of the laser target. Head and torsional eye movements were calibrated by attaching the scleral coil to a rotating protractor. Torsional precision was approximately $\pm$ 0.2°. There was minimal crosstalk; large horizontal and vertical movements produced deflections in the torsional channel of $< 4\%$ of the amplitude of the horizontal and vertical movement. Any coil slippage was assessed by monitoring offsets in torsional eye position signal during testing. Consistency of calibrated positions after each eye movement provided evidence that the coil did not slip on the eye. Eye position data were filtered with a bandwidth of 0 to 90 Hz and digitized at 200 Hz. They were recorded on disc for off-line analysis. Analog recordings were also displayed in real time by a thermal array recorder (Model TA 2000, Gould Inc., Cleveland, OH).

Data Analyses. Eye position and angular velocity were computed from coil signals.[14,15] Eye positions were expressed by use of Helmholtz angles in degrees.[16] To exclude saccades, we ana-

Table 1. Characteristics of Patients with Sixth Nerve Palsy Caused by a Presumed Peripheral Lesion

Patient	Age/ Gender	Side of Lesion	Duration (Months)	Abduction Deficit (% Normal)	Imaging	Comments
1 (TM)	50/F	Right	66	30	Normal MRI	Idiopathic
2 (TH)	77/M	Right	30	60	Normal MRI	Idiopathic
3 (PL)	21/M	Right	2 wks	0	Normal MRI	Improved after 4 months
4 (JM)	46/M	Right	2 wks	0	Normal MRI	Resolved after 3 months
5 (NR)	75/F	Right	4	90	Normal MRI	Idiopathic
6 (RL)	77/F	Right	10	95	Normal MRI	Idiopathic
7 (EF)	52/M	Right	3 wks	95	Normal MRI	Idiopathic
8 (AM)	75/F	Right	2	70	Normal CT	Resolved after 6 months (HTN)
9 (GD)	64/M	Right	15	90	Normal CT	Claustrophobia
10 (KE)	75/F	Right	2	10	Normal CT	Resolved after 4 months (HTN, DM)
11 (THA)	57/M	Right	2	90	Normal CT	Resolved after 4 months (HTN, DM)
12 (SC)	66/M	Right	3 wks	80	Normal CT	Resolved after 4 months (DM)
13 (DW)	65/M	Left	96	70	Normal MRI	Idiopathic
14 (GC)	57/M	Left	34	90	Normal MRI	Idiopathic
15 (VI)	65/F	Left	36	50	Normal MRI	Idiopathic
16 (SCH)	50/F	Left	24	80	Normal MRI	Idiopathic
17 (JM2)	46/M	Left	3 wks	80	Normal MRI	Resolved after 6 months (HTN)
18 (IW)	75/F	Left	12	90	Normal MRI	Idiopathic
19 (EM)	64/M	Left	3 wks	80	Normal CT	Resolved after 5 months (HTN)
20 (LC)	54/F	Left	60	80	Normal MRI	Idiopathic

CT = computed tomography; DM = diabetes mellitus; F = female; HTN = hypertension; M = male; MRI = magnetic resonance imaging.

lyzed only data in which both eyes were turning at less than 10°/second. For each subject we computed a set of best-fit functions, expressing each eye's torsion as a function of its horizontal and vertical angles and expressing the horizontal and vertical angles of the nonviewing eye as a function of the horizontal and vertical angles of the viewing eye. Using these fitted functions, we then computed the typical torsions of both eyes and the typical horizontal and vertical positions of the nonviewing eye when the viewing eye fixated the nine targets in our array. To quantify ocular alignment in these nine positions, we calculated the difference (right minus left) between the two eyes' horizontal, vertical, and torsional angles. Exodeviation, right hyperdeviation, and excyclotorsion (of the nonviewing eye) were positive; esodeviation, left hyperdeviation, and incyclotorsion (of the nonviewing eye) were negative. The horizontal, vertical, and torsional deviations between the two eyes were then converted from degrees to prism diopters using the formula:

$$\Delta = 100 \tan \theta$$

where Δ is angle in prism diopters, and θ is angle in degrees.[17]

This relationship between the angle in prism diopters and angle in degrees is nonlinear. However, it approximates linearity for deviations up to 30°.[17] In this study, only 1 of 27 patients had horizontal deviations of more than 20°. No patients had vertical deviations of more than 4°. Relative to the precision of clinical measurement, the relation between prism diopters and degrees is linear within this range.

Imaging Studies and Follow-up

Serial axial and sagittal T1- and T2-weighted magnetic resonance (MR) images with gadolinium enhancement were obtained (slice thickness = 5 mm) for all patients younger than 50 years of age and those with other neurologic signs. In this investigation, computed tomography (CT) images of the head with contrast were obtained in all patients with ischemic risk factors and for patients older than 50 years of age, although CT imaging is not our standard practice for such patients. If CT imaging was normal, patients were followed at approximately 3 months. Those without improvement at 3 months and those with an abnormal CT scan were further investigated with MR imaging.

Data Analyses and Statistical Methods

In all 27 patients and by all three measuring techniques—prism-cover test, Maddox test, coils recordings—the secondary deviations (with the paretic eye fixating) were always greater than the primary deviations (with the nonparetic eye fixating). In what follows, we report only the primary deviations; the results for secondary deviations were similar. Analyses of variance (ANOVA) were used to compare mean deviations between patients with peripheral palsy and normal controls, as well as between central palsy and normal controls. Correlations between the degree of abduction defect and the magnitude of hyperdeviation were assessed using linear regressions. Fisher exact tests were used to examine the relationship between the side of palsy and the side of hyperdeviation. To assess whether the vertical deviations were comitant, the mean differences of vertical deviations between upgaze and downgaze were calculated and compared using ANOVA. The difference in vertical deviations on right and left head tilt between patients and normal subjects was assessed using ANOVA. Torsional alignment is the subject of a separate report.[18]

Results

General Characteristics of Patients

Twenty patients had peripheral palsy caused by an idiopathic, presumed ischemic, peripheral lesion (Table 1). The mean age was 61 ± 14 years (age range, 21–77 years; median age, 64 years); 11 of them were men. The duration of symptoms ranged from 2 weeks to 96 months, with a mean duration of 20 ± 17 months. Mean follow-up duration was 10 months (range, 8–22 months). Fourteen

Table 2. Characteristics of Patients with Sixth Nerve Palsy Caused by a Central Lesion in the Brainstem

Patient	Age/Gender	Side of Lesion	Duration (months)	Abduction Deficit (% Normal)	Imaging	Presenting Symptoms
21 (CS)	79/F	Right	19	0	MRI: Right pontine meningioma	Diplopia, right facial paresthesia
22 (AK)	75/M	Right	1 wk	70	MRI: Right pontine demyelinating lesion	Diplopia, ataxia (MS for 27 yrs)
23 (MD)	75/M	Left	240	40	MRI: Left caudal pontine infarct	Dysarthria, tinnitus, limb weakness
24 (WS)	59/M	Left	52	90	MRI: Left pontomedullary cavernoma and hematoma	Headache, right paresthesia, ataxia
25 (RC)	56/F	Left	132	70	MRI: Left pontomedullary cavernoma and hematoma	Left facial palsy and paresthesia
26 (JP)	36/F	Left	3	80	MRI: Left pontomedullary and middle cerebellar peduncle demyelinating lesions	Diplopia, right leg paresthesia, ataxia
27 (WR)	30/F	Left	2 wks	70	MRI: Left pontomedullary demyelinating lesion	Diplopia, ataxia

F = female; M = male; MRI = magnetic resonance imaging; MS = multiple sclerosis.

had normal MR imaging and six had normal CT scanning of the brain. Five of the six patients with normal CT scan had ischemic risk factors, such as hypertension or diabetes, and had a complete resolution of their palsy within 4 to 6 months.

Seven patients had sixth nerve palsy caused by central brainstem lesion, as shown by MR imaging (Table 2). The mean age was 59 ± 20 years (age range, 30–79 years; median age, 59 years); three of them were men. The duration of symptoms ranged from 1 week to 240 months, with a mean duration of 64 ± 91 months. Mean follow-up duration was 16 months (range, 10–24 months). Lesions included demyelination (three patients), pontomedullary cavernous hemangioma (two patients), meningioma compressing the pons (one patient), and infarct (one patient). All seven patients had neurologic symptoms and signs in addition to abduction paresis but no other ocular motor signs.

Ten normal subjects served as controls (five men; mean age 49 ± 12 years; median age 55 years; age range, 19–69 years).

Horizontal Deviations in the Nine Diagnostic Positions

The mean horizontal deviations in all 27 patients in the nine diagnostic positions are shown in Figure 1. Consistent with a paralytic strabismus, all patients had an incomitant esodeviation, which increased in the field of action of the paretic muscle. In general, the magnitudes of esodeviation measured by the prism-cover test were slightly smaller than those measured by the Maddox test or coil recordings; however, these differences were not statistically significant (NS) (ANOVA).

Vertical Deviations in Nine Diagnostic Positions

The prism-cover test showed hyperdeviation in at least one eye position in four (20%) patients with peripheral palsy and two (29%) patients with central palsy. The Maddox test revealed hyperdeviation in 15 (75%) patients with peripheral and 5 (71%) patients with central palsy. Coil recordings identified hyperdeviation in all 27 (100%) patients. No vertical duction deficits were found in any patient.

Peripheral Palsy. Mean vertical deviations in nine diagnostic positions are shown in Figure 2. Mean vertical deviations, averaged across the 20 patients and nine eye positions, were 0.3 ± 0.8 prism diopters (PD) by prism-cover test, 1.3 ± 1.6 PD by Maddox test, and 2.0 ± 1.4 PD by coil recordings (Fig 3A). Mean vertical deviations in normal subjects were 0.0 ± 0.0 PD by prism-cover test, 1.0 ± 0.9 PD by Maddox test, and 1.9 ± 2.1 PD by coil recordings (Fig 3A). Thus, peripheral palsy did not cause abnormal vertical deviation (ANOVA, NS). There was no correlation between the degree of abduction defect and the magnitude of hyperdeviation in any diagnostic position (linear regression, NS). No correlation was found between the side of palsy and the side of hyperdeviation (Fisher's exact test, NS). No patients exhibited any pattern of vertical deviation consistent with an associated vertical rectus or oblique muscle paresis. The vertical deviations were comitant in individual patients and in normal subjects, as were the group means (Fig 2) (ANOVA, NS). The maximum difference between hyperdeviation on upgaze and downgaze in any individual patients was 3 PD.

Central Palsy. Mean vertical deviations in the nine diagnostic positions are shown in Figure 4. Mean vertical deviations, averaged across the seven patients and nine eye positions, were 0.9 ± 1.3 PD by prism-cover test, 1.4 ± 1.6 PD by Maddox test, and 2.5 ± 1.6 PD by coil recordings (Fig 3A). They were not statistically different than normal values (ANOVA). No patient had features of an associated vertical rectus or oblique muscle paresis. Two patients with a right rostral pontomesencephalic lesion had a right (ipsilateral) hyperdeviation (when tested with coil recordings), whereas five patients with a left caudal pontomedullary lesion had a right (contralateral) hyperdeviation. The vertical deviations were comitant in individual patients, as were the group means (Fig 4) (ANOVA, NS). The maximum difference between hyperdeviation on upgaze and downgaze in any individual patient was 2 PD.

Vertical Deviations During Static Head Roll

Peripheral Palsy. During static lateral head roll, 18 of the 20 patients with *peripheral palsy* exhibited a right hyperdeviation on lateral head tilt to the right shoulder (right head tilt) and a left hyperdeviation on lateral tilt toward the left shoulder (left head tilt) on testing with the Maddox test, regardless of the side of palsy (Fig 2). Two other patients had hyperdeviation on head roll to one side only. The Maddox test detected a mean of 4.3 ± 4.0 PD right hyperdeviation (range, 1–14 PD) on *right* head tilt and 2.9 ± 2.1 PD left hyperdeviation (range, 0–8 PD) on *left* head tilt. The difference in vertical deviations between right and left static head roll was statistically significant (ANOVA, $P < 0.001$). Among 10 normal subjects, 5 had a small hyperphoria (maximum, 1 PD) on lateral head tilt. The side of hyperphoria did not correlate with the side of head tilt (Fisher's exact test, NS). The mean vertical deviations in normal subjects were 0.3 ± 0.5 right hyperphoria (range, 0–1 PD) on both *right* and *left* head tilt using the Maddox test. The difference in vertical deviations on head tilt between patients with peripheral palsy and normal subjects was statistically significant (ANOVA, $P < 0.001$).

Central Palsy. In contrast to patients with peripheral palsy, four of the seven patients with *central* palsy had hyperdeviation

Prism cover test			Maddox rod and prism test			Coil recordings		
Right 6th nerve palsy (n = 14)								
16.93*	6.57*	2.43*	18.50*	7.14*	3.29	17.96*	8.17*	4.72
(± 13.38)	(± 9.22)	(± 4.24)	(± 13.70)	(± 9.88)	(± 4.34)	(± 12.68)	(± 8.44)	(± 4.07)
16.93*	6.71*	3.14*	18.36*	7.86*	3.57	18.56*	8.46*	4.94*
(± 13.38)	(± 9.36)	(± 4.42)	(± 13.81)	(± 9.87)	(± 4.52)	(± 12.63)	(± 8.71)	(± 4.62)
17.14*	6.21*	2.57*	18.36*	6.71	3.79	18.00*	8.98*	5.37*
(± 13.27)	(± 8.52)	(± 4.33)	(± 13.81)	(± 9.13)	(± 4.93)	(± 12.29)	(± 8.88)	(± 4.23)
Left 6th nerve palsy (n = 13)								
7.54*	10.46*	19.38*	8.77*	12.31*	20.00*	10.19*	11.97*	19.50*
(± 10.65)	(± 11.67)	(± 12.99)	(± 10.35)	(± 10.42)	(± 12.80)	(± 11.57)	(± 10.01)	(± 13.42)
8.00*	12.31*	19.85*	8.62*	13.31*	20.38*	9.24*	12.48*	20.27*
(± 10.39)	(± 10.89)	(± 13.29)	(± 10.31)	(± 10.87)	(± 13.19)	(± 11.02)	(± 10.93)	(± 13.25)
8.54*	10.92*	18.85*	8.62*	12.38*	20.38*	9.73*	12.82*	20.06*
(± 10.35)	(± 11.71)	(± 14.36)	(± 10.31)	(± 10.84)	(± 13.19)	(± 10.71)	(± 11.53)	(± 13.30)
Normal subjects (n = 10)								
0.00	0.00	0.00	1.50	1.70	2.00	1.41	1.80	2.14
(± 0.00)	(± 0.00)	(± 0.00)	(± 1.35)	(± 1.42)	(± 1.94)	(± 1.31)	(± 1.42)	(± 2.12)
0.00	0.00	0.00	1.40	1.70	1.70	1.44	1.85	1.79
(± 0.00)	(± 0.00)	(± 0.00)	(± 1.35)	(± 1.64)	(± 2.11)	(± 1.41)	(± 1.65)	(± 2.26)
0.00	0.00	0.00	1.60	1.80	1.80	1.55	1.89	1.92
(± 0.00)	(± 0.00)	(± 0.00)	(± 1.43)	(± 1.81)	(± 2.10)	(± 1.47)	(± 1.91)	(± 2.23)

Figure 1. Mean horizontal esodeviations ± 1 standard deviation (in prism diopters), measured by prism and cover test, Maddox rod and prism test, and magnetic search coil recordings, in nine diagnostic positions of 27 patients with sixth nerve palsy, as viewed by the examiner. (* indicates $P < 0.05$)

that remained on the same side during static lateral head tilt to either side on testing with the Maddox test (Fig 4). Two other patients had hyperdeviation on head tilt to one side only. One patient had no vertical deviation during head tilt. The Maddox test detected a mean of 2.1 ± 1.7 PD right hyperdeviation (range, 0–4 PD) on *right* head tilt and 1.3 ± 1.5 PD right hyperdeviation (range, 0–4 PD) on *left* head tilt. The difference in vertical deviations between right and left head tilt was not statistically significant (ANOVA). However, the difference in vertical deviations during head tilt between patients with central palsy and normal subjects was significant (ANOVA, $P < 0.01$).

Discussion

Information about vertical strabismus in sixth nerve palsy is sparse. Kestenbaum[1] stated that "in abducens paresis a vertical component is sometimes found," and this slight vertical component can be up to 3 diopters before one can conclude that a vertical muscle is involved pathologically.[1] Smith[2] cited Dr. F. Walsh, stating that "one could accept up to 2 to 3 prism diopters of vertical deviation with a VI nerve palsy alone, but any amount more than that was significant."[2] They[1,2] did not present data or clinical documentation.

Slavin et al[19] examined 61 normal subjects subjectively with the Maddox test and found that up to 77% showed a vertical misalignment of 2 to 10 PD in any field of gaze. In another study, Slavin[3] examined 16 patients with isolated unilateral sixth nerve palsy using the same method. He[3] concluded, in contrast to Kestenbaum and Walsh,[1,2] that a large amount of hyperdeviation, up to 16 PD, could be detected in these patients in different gazes, as well as during head tilt.

The Maddox test usually reduces fusional vergence by creating dissimilar images between the eyes and reveals the magnitude of heterophoria (i.e., latent deviation) or heterotropia. In this investigation, we also used the prism-cover test that measures the magnitude of heterotropia (i.e., manifest deviation). However, when a horizontal heterotropia exists (as in our patients with sixth nerve palsy), any vertical heterophoria becomes manifest and is measured as if it were a heterotropia. Because approximately 80% of our normal subjects have a vertical heterophoria, any vertical heterotropia, as measured by the prism-cover test, in patients with sixth nerve palsy cannot be considered a genuine vertical heterotropia, unless it exceeds the magnitude of the range of vertical heterophoria in normal subjects.

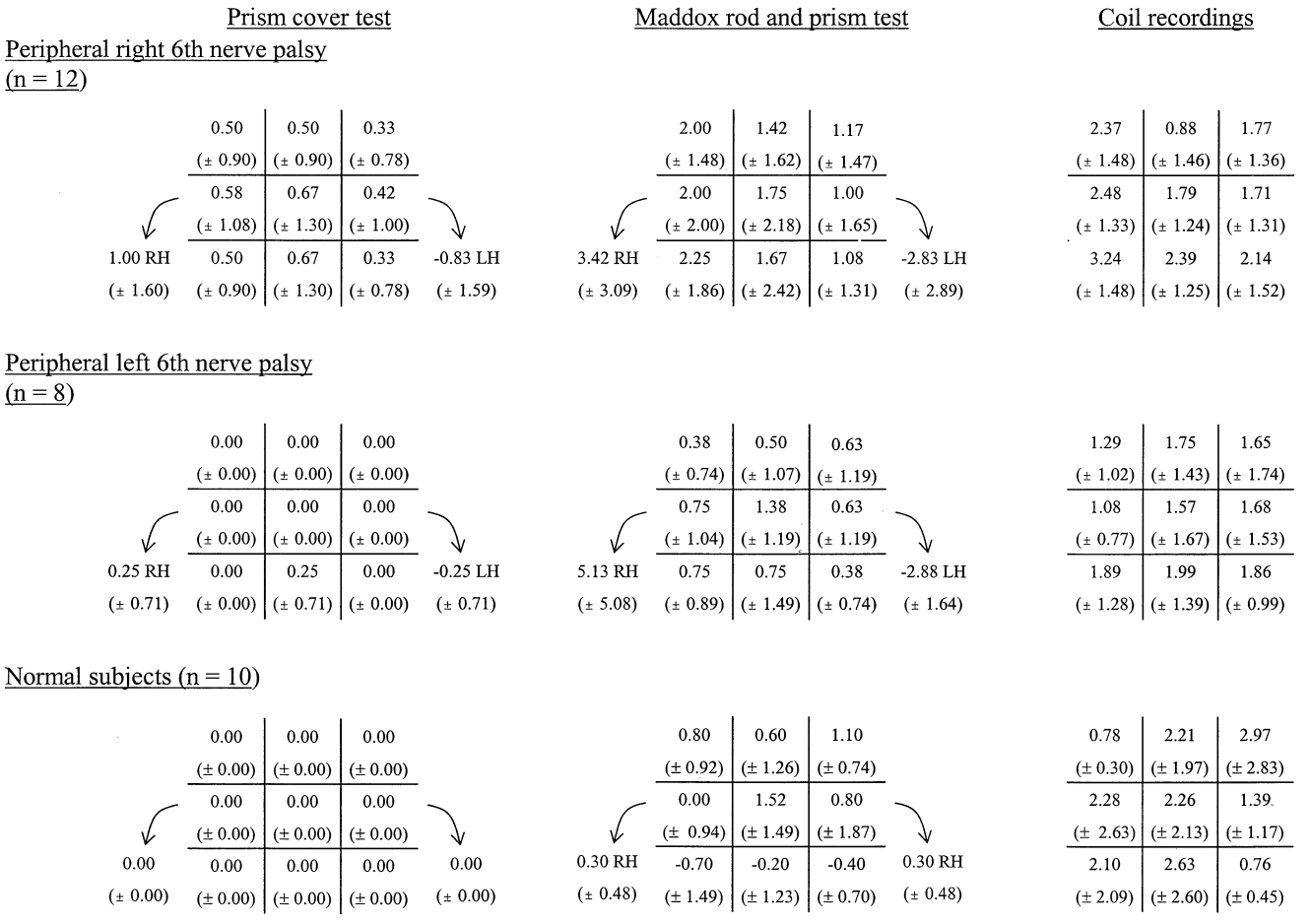

Figure 2. Mean vertical deviations ± 1 standard deviation (in prism diopters) in nine diagnostic positions and during static lateral head tilt in 20 patients with peripheral sixth nerve palsy, as viewed by the examiner. Negative values indicate left hyperdeviation; unsigned values indicate right hyperdeviation. LH = left hyperdeviation; RH = right hyperdeviation. Arrows on left (counterclockwise arrows) denote deviation during right head tilt, arrows on right (clockwise arrows) denote deviation during left head tilt. The mean deviation of a right hypertropia in both right and left sixth nerve palsy is simply a group result, whereas individual patients had either right or left hyperdeviation with either right or left sixth nerve palsy.

Vertical Misalignment in Peripheral Sixth Nerve Palsy

In our study, most normal subjects (80%) were found to have a vertical heterophoria in at least one of the nine diagnostic positions. Three of them had a vertical deviation in the straight-ahead position. The vertical phoria ranged from 0 to 5 PD, as measured by the Maddox test. Our findings were comparable with those from a previous study,[19] although we found a smaller maximum deviation (5 PD vs. 10 PD[19]).

In isolated peripheral sixth nerve palsy, the Maddox test showed that 75% of our 20 patients had a vertical deviation in at least one eye position. This is in contrast to a prior study,[3] which found that all 16 patients had a vertical deviation. In addition, we found that the maximum magnitude of hyperdeviation was smaller (6 PD vs. 16 PD[3]). These discrepancies may be due to methodologic differences[3]: fixation target distance was 14 inches; only 5 of 16 patients had CT scan or MR imaging to exclude brainstem involvement of vertically acting muscles; and the duration of follow-up was not specified.[3]

With the prism-cover test, the maximum hypertropia measured in any of our patients with peripheral sixth nerve palsy was 4 PD (Fig 3B). The estimates by Kestenbaum and Walsh[1,2] of the magnitude of vertical strabismus associated with sixth nerve palsy are consistent with the results of our quantitative investigation. Hypertropia in our patients varied idiosyncratically with gaze direction and always fell within the range of hyperphoria seen in our normal subjects (maximum, 5 PD) (Fig 3B). Normal hyperphoria that becomes manifest in paralytic strabismus explains these findings.

Comparison of the Prism-Cover Test, Maddox Test, and Magnetic Search Coil Methods

Deviations estimated by the prism-cover test were usually slightly smaller than those estimated by the Maddox test and by coil recordings. This discrepancy can be explained by several factors. As mentioned, whereas the prism-cover test measured the amount of heterotropia, the Maddox test and coil recordings measured heterophoria plus heterotropia, if present.

In addition, a small deviation may not be detected by the prism-cover test. The smallest refixation movement detect-

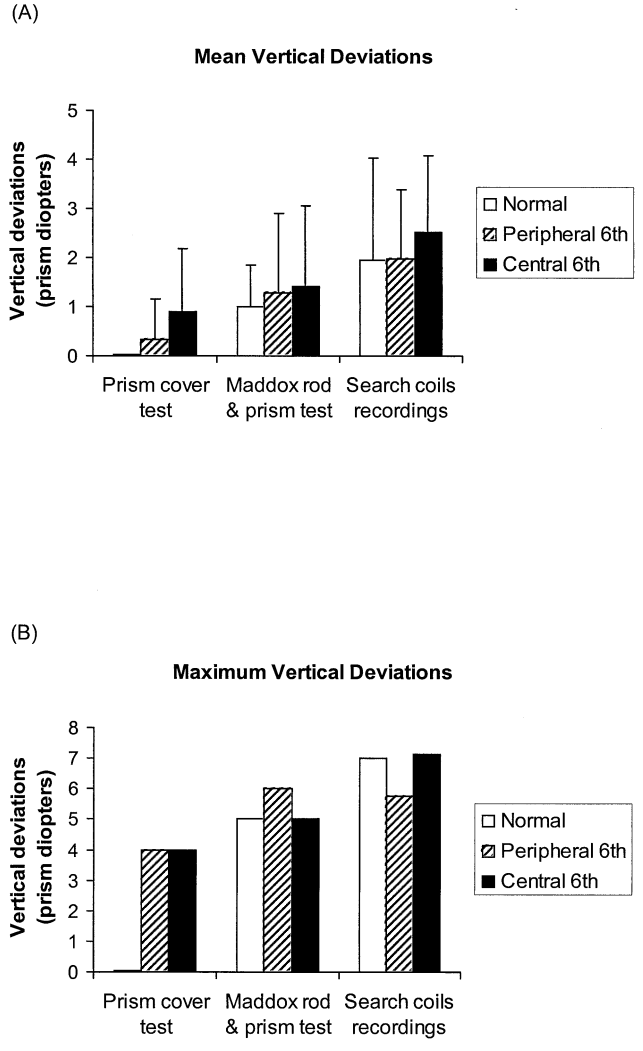

Figure 3. A, Mean vertical deviations (in prism diopters) of all nine diagnostic positions in normal subjects and patients with peripheral and central sixth nerve palsy. Error bars indicate 1 standard deviation. **B,** Maximum vertical deviations (in prism diopters) measured in any diagnostic position in a normal subject and in any single patient with peripheral or central sixth nerve palsy.

able with the prism-cover test has been estimated to be from 1 to 4 PD.[20–22] Ludvigh[21] and Romano and von Noorden[22] reported that 2 PD (about 1.1°) should be considered the smallest deviation detectable by the prism-cover test with the unaided eye. The absence of detectable refixation movement means that a deviation, if present, is probably < 2 PD but does not exclude strabismus.[22] In agreement with early studies,[21,22] we found that the prism-cover test detected vertical deviation in fewer normal subjects than the other two techniques, and measurements obtained by the prism-cover test were 1 to 2 PD lower.

Furthermore, the testing conditions and the underlying physiologic basis for the three techniques are different. In the prism-cover test, the refixation movement is a visually guided saccade that occurs in both eyes when one eye refixates, bringing the image of the target to the fovea. Prisms of increasing power in front of the eye bring the image of the target closer and closer to the fovea, decreasing the refixation movement and allowing for *objective* measurement of the angle of deviation.[9] In the Maddox test, the measurement is based on the diplopia principle. One determines the subjective localization of a single object point imaged on the fovea of the fixating eye and an extrafoveal retinal area in the other eye. The distance of the double images is then a *subjective* measure of the deviation that can be quantified by using prisms until a single image is seen.[9]

Although the prism-cover and the Maddox tests are commonly used clinically, the scleral search coil technique is available in few laboratories. Dual search coils allow one to measure simultaneously the three-dimensional positions of both eyes; from these data the three-dimensional misalignment of the two eyes can be computed. The coil method allows measurements with high temporal and spatial resolution,[23] detecting eye movements as small as 30 seconds of arc.[24] This study, to our knowledge, is the first to systematically compare two standard clinical methods of measuring ocular deviation with the scleral search coil technique. Although deviations measured by the prism-cover test tend to be smaller than those measured by the Maddox test and by coil recordings, the differences were not statistically significant, indicating that all three methods were concordant in clinical usefulness. The search coil technique provides objective, high-resolution determination of changes in eye position.

The difference in viewing distance between the three techniques might contribute to the discrepancy of measured deviations. The fixation distance was 6 m for the prism-cover and the Maddox tests compared with 1 m for the search coils technique. Differences in horizontal eye positions could affect the amounts of vertical deviation. However, in normal subjects, vertical misalignment of the eyes is small and varies idiosyncratically with viewing distance.[25] In addition, both the prism-cover and the Maddox tests were performed using a fixation target at 6 m, the discrepancy of measured vertical deviations between these two techniques cannot be explained by fixation distance.

Vertical Misalignment in Central Sixth Nerve Palsy

Brainstem or acute peripheral vestibular lesions that disrupt the otolith-ocular pathway cause large amounts of vertical (skew) deviation and ocular torsion. Brandt and Dieterich[26] reported a mean skew deviation of 4° (ranging from 1° to 20°) in 56 patients with unilateral brainstem infarction. Rostral pontomesencephalic lesions were associated with ipsilesional hypertropia and caudal pontomedullary lesions with contralesional hypertropia.[26] Abnormal ocular torsion was also present. The mean ocular torsion was 8° (ranging from 2° to 28°), with the hypertropic eye incyclotorted and the hypotropic eye excyclotorted.[26]

We investigated seven patients with central sixth nerve palsy caused by brainstem lesions. All patients had associated neurologic symptoms and signs in addition to abduction paresis but no other ocular motor signs. MR imaging showed unilateral lesions in the brainstem tegmentum. Caudal pontomedullary lesions were associated with contralat-

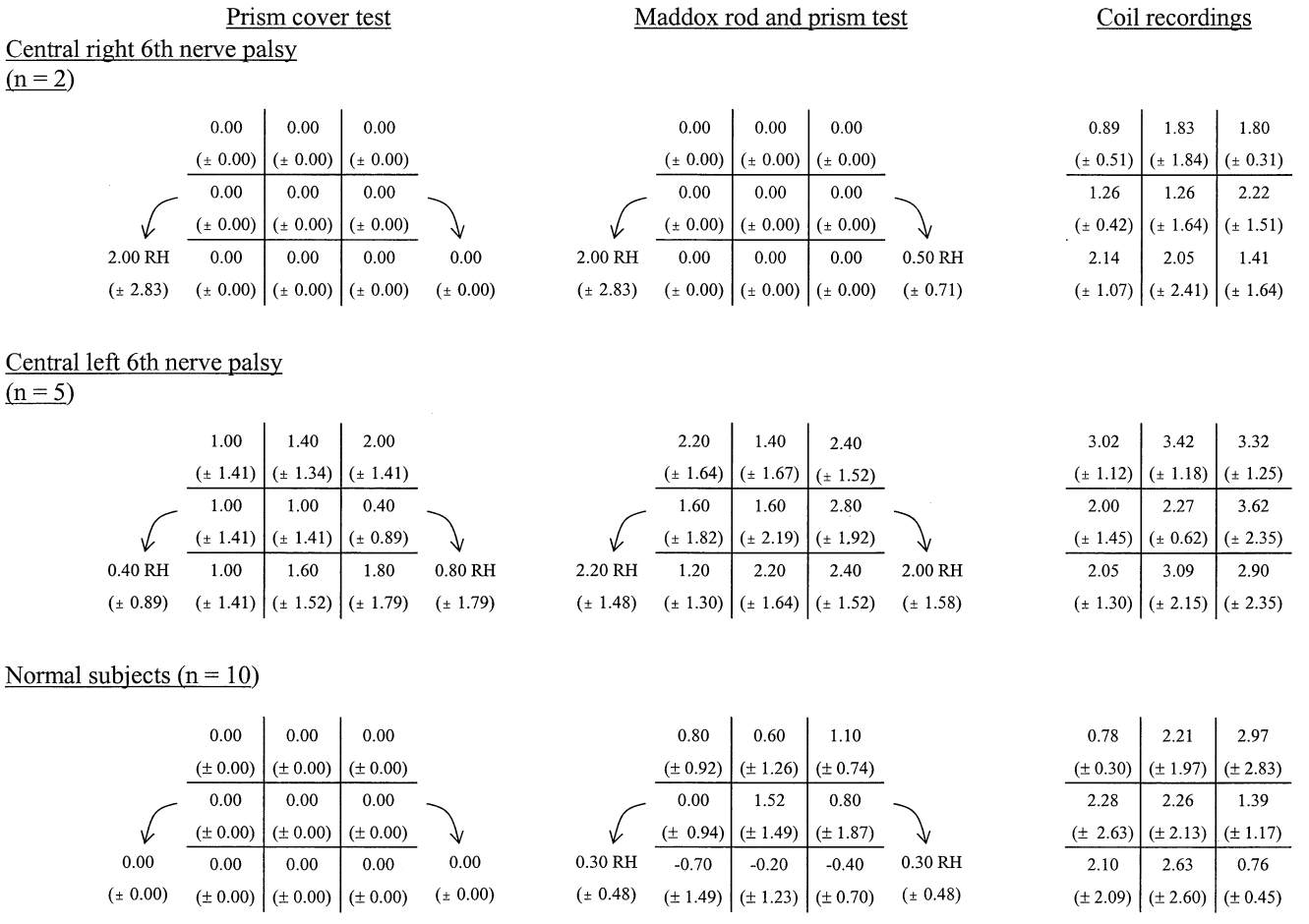

Figure 4. Mean vertical deviations ± 1 standard deviation (in prism diopters) in nine diagnostic positions and during static lateral head tilt in seven patients with central sixth nerve palsy, as viewed by the examiner. LH = left hyperdeviation; RH = right hyperdeviation. Arrows on left (counterclockwise arrows) denote deviation during right head tilt, arrows on right (clockwise arrows) denote deviation during left head tilt.

eral hyperdeviation, whereas rostral pontomesencephalic lesions were associated with ipsilateral hyperdeviation. The hyperdeviation did not exhibit any pattern that could localize a palsy to one of the vertical rectus or oblique muscles, using the three-step test.[27] In addition, the hyperdeviation was comitant, with the maximum difference between upgaze and downgaze never exceeding 2 PD in any of our patients. Their vertical strabismus might represent a small skew deviation caused by disruption of the otolith-ocular pathway. However, because the magnitude of hyperdeviation in individual patients (maximum, 4 PD) did not differ from normal subjects (maximum, 5 PD) (Fig 3B), their vertical strabismus was consistent with normal vertical heterophoria that became manifest in the presence of esotropia.

Vertical Misalignment during Static Ocular Counterroll in Peripheral and Central Sixth Nerve Palsy

Sustained head roll evokes compensatory changes in torsional eye position, called "static ocular counterroll," that are mediated mainly by the otolith-ocular reflex from inputs of the utricles.[8] In humans, static head tilt causes sustained conjugate counterroll of the eyes and a small vertical misalignment,[25] with static counterroll gain (eye torsion/head tilt) ranging from 0.10 to 0.24, depending on target distance.[25,28,29]

One study[25] quantified the change in vertical alignment of the eyes during static head roll while subjects fixated binocularly. In normal subjects, the hypertropia was small (up to 3.6° for a 20° head roll) and varied idiosyncratically with viewing distance.[25] In general, during viewing of a distant target (7.2 m), a right head tilt was associated with a left hyperdeviation, and a left head tilt was associated with a right hyperdeviation. The reverse was observed during viewing of a near target (20 cm): a right head tilt was associated with a right hyperdeviation, and a left head tilt was associated with a left hyperdeviation.[25] This vertical misalignment was not accompanied by subjective diplopia in normal subjects.[25] In the same study, four patients with skew deviation were investigated, and their vertical deviation did not change with head tilt.[25]

In our normal subjects, prism-cover testing did not identify a vertical hypertropia in static head roll, with a detection threshold of approximately 2 PD (about 1.1°). Maddox rod testing detected a vertical heterophoria in five normal subjects during static head roll, with a detection threshold of

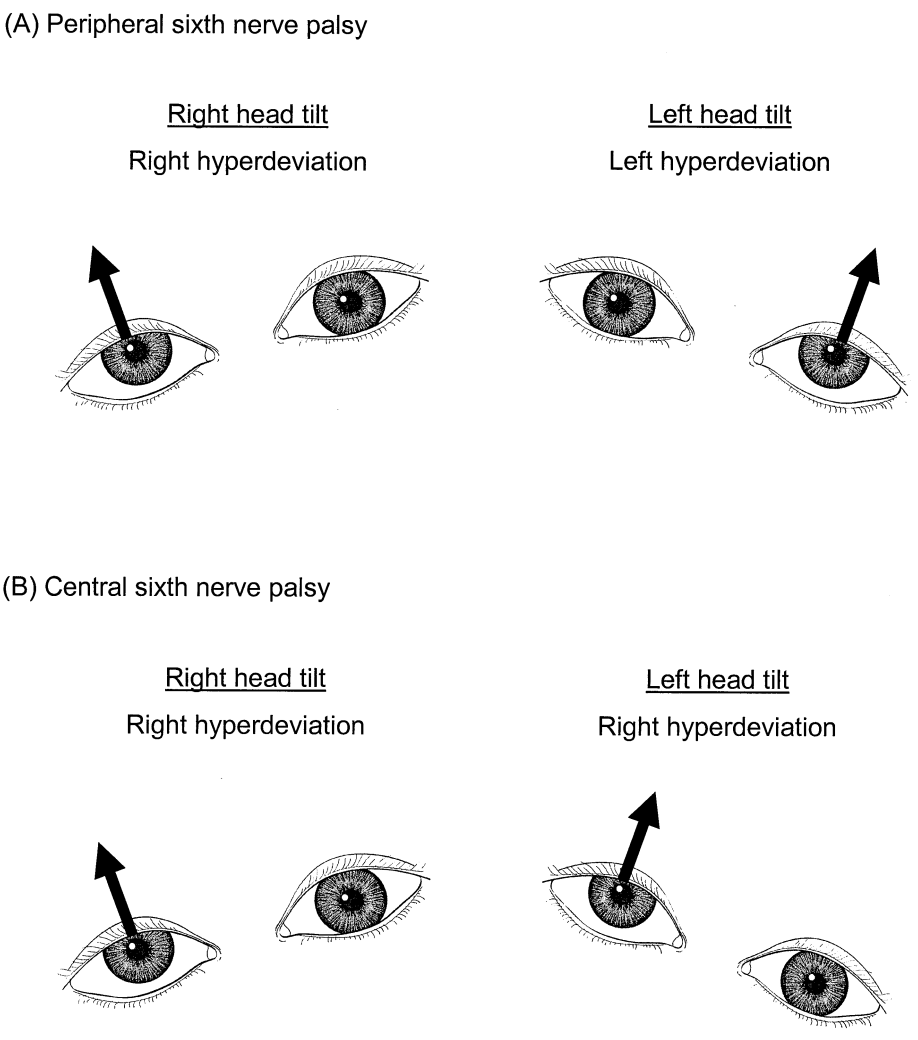

Figure 5. Diagrammatic summary of changes in vertical deviation during lateral head roll. **A,** In peripheral sixth nerve palsy, right head tilt is associated with right hyperdeviation and left head tilt with left hyperdeviation. **B,** In central palsy, the side of hyperdeviation does not change on head tilt to either side.

approximately 1 PD (about 0.6°). However, the magnitude was small (maximum, 1 PD), and no specific pattern was detected. In contrast to a prior study,[25] we did not record vertical strabismus after static head roll with coil recordings.

In sixth nerve palsy, we observed a distinct pattern of vertical misalignment using the Maddox test (Fig 5). In peripheral palsy, right head tilt was associated with right hyperdeviation, and left head tilt was associated with left hyperdeviation. In contrast, in central palsy, the side of hyperdeviation did not change on head tilt to either side. This pattern of hyperdeviation during static head tilt in peripheral palsy cannot be attributed to a concurrent bilateral fourth nerve palsy; in fourth nerve palsy, the hypertropia typically increases during adduction and depression, but this was not the case in our patients.

Using magnetic search coils, Averbuch-Heller et al[25] reported that during near viewing, normal subjects exhibited a small right hyperdeviation on right head tilt and a small left hyperdeviation on left head tilt. We did not detect any pattern of vertical misalignment during head tilt in our normal subjects using the Maddox test, which is less sensitive than coil recordings. However, in our patients with peripheral palsy, we detected a pattern of right hyperdeviation on right head tilt and left hyperdeviation on left head tilt similar to that reported in their normal subjects in a previous study.[25] This pattern of vertical misalignment in peripheral palsy may represent an exaggerated response to static head roll.

Static head tilt stimulates receptors in the macula of the utricle, leading to ocular counterroll and a small change in vertical alignment in normal subjects.[25,29] However, when the otolith-ocular reflex pathway is disrupted, ocular torsion and skew deviation are observed.[26] This indicates that under normal circumstances, the otolith-ocular reflex is symmetrical and balanced; it is also suppressed during static head roll. This suppression is probably mediated, in part, by visual mechanisms. Disruption of binocular vision may remove the suppression on the otolith-ocular reflex and lead to the pattern of right hyperdeviation on right head tilt and left hyperdeviation on left head tilt observed in patients with peripheral palsy. In contrast, in patients with central sixth nerve palsy, unilateral lesions that disrupt the balance of the otolith-ocular reflex may lead to the pattern of vertical

deviation that we recorded, with hyperdeviation remaining on the same side regardless of the direction of head roll.

Clinical Implications

Sixth nerve palsy in patients older than 50 years of age is usually presumed to be caused by ischemia, occurring with greater frequency in patients with diabetes mellitus or hypertension.[30] Because most patients recover within 3 months,[31] they require little investigation at the time of initial presentation if they have no other neurologic symptoms or signs. However, if vertical misalignment is found in a patient with an abduction defect, the physician should consider involvement of vertically acting muscles or additional cranial nerves or skew deviation indicating brainstem dysfunction. In this situation, imaging studies, and possibly cerebral angiography and lumbar puncture, are indicated.

Our results indicate that a small hypertropia can be detected in patients with peripheral and central sixth nerve palsy. This hypertropia falls within the normal range of hyperphoria seen in healthy subjects, indicating that it is a normal hyperphoria that becomes manifest in the presence of esotropia. In normal subjects, the mean vertical deviation in the straight-ahead position is 1.5 ± 1.5 PD. Thus, in patients with sixth nerve palsy, if a hypertropia is detected in the straight-ahead position, which is ≤ 5 PD (normal mean + 2 standard deviations), multiple cranial nerve palsy or skew deviation should not be considered responsible. Conversely, vertical deviations > 5 PD suggest skew deviation or peripheral nerve or muscle damage in addition to abduction palsy. In addition, a distinct pattern of hyperdeviation is observed in more than 90% of patients during static head roll. In peripheral palsy, right head tilt is associated with a right hyperdeviation, and left head tilt is associated with a left hyperdeviation. This contrasts with central palsy, in which the same eye hyperdeviates during head tilt to either side. This second pattern of hyperdeviation induced by lateral head tilt may warrant investigation for a brainstem lesion as the cause of paretic abduction.

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Historical Image

Lachrymatory, c. 2000 ybp. Tear vases were used in the Mediterranean area to catch and hold tears of bereaved friends of the dead. In some cases, mourners' tears were melded with a balm as an offering to the gods or to a loved one.

"Dr. Ennio Benedetti, an Alcon Research Institute awardee, presented this lachrymatory to Scientific Advisory Chairman Dr. Steven Podos in 1991. Dr. Benedetti observed that sometimes, perhaps when a jilted lover sought revenge, poison was put in containers such as this. A tan coloring is an indication that a bottle once held poison."

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