

Adaptations and Deficits in the Vestibulo-Ocular Reflex After Third Nerve Palsy

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Objective: To analyze the vestibulo-ocular reflex (VOR) in patients with unilateral peripheral third nerve palsy.

Participants and Methods: Ten patients and 15 healthy subjects were studied using magnetic search coils. Subjects made sinusoidal $\pm 10^\circ$ head-on-body rotations in yaw, pitch, and roll in darkness and during monocular viewing in light.

Results: Horizontal VOR and visually enhanced VOR (VVOR) gains of the paretic eye were decreased during both abduction and adduction. Vertical VOR and VVOR gains of the paretic eye were decreased during both elevation and depression. Dynamic and static torsional VOR and VVOR gains of the paretic eye were reduced during both excyclotorsion and incyclotorsion. Horizontal, vertical, and torsional VOR and VVOR gains were normal in the nonparetic eye.

Conclusions: Adducting VOR gains were reduced as anticipated from medial rectus palsy. Abducting gains were also reduced; the reduction is attributed to an adaptive decrease in innervation to the lateral rectus to achieve symmetry of the horizontal VOR in the paretic eye. Torsional VOR gains were reduced during excyclotorsion from palsy of the inferior oblique muscle. Gains were also reduced during incyclotorsion, which can be explained by an adaptive decrease in innervation to the superior oblique to restore symmetry of the torsional VOR in the paretic eye.

Clinical Relevance: Monocular adaptation in the VOR of the paretic eye reduces asymmetrical movement of retinal images during head motion, prevents nystagmus, and reduces retinal image disparity.

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THE EFFECTS of third nerve palsy on the vestibulo-ocular reflex (VOR) have not been systematically investigated. Clinical testing of ocular motor nerve palsies emphasizes examination of static deviations of the eyes. The VOR stabilizes retinal images by generating compensatory smooth eye movements that are nearly equal in amplitude and opposite in direction to head rotations. Adaptive changes in the VOR occur in response to visual stimuli.¹⁻⁵ When healthy subjects wear reversing prisms for several days, VOR gains are substantially reduced.³ After 3 to 4 weeks of vision reversal, the phase of the VOR actually reverses; head rotations cause eye rotations in the *same* direction, so that retinal images are once again stabilized.³ Disconjugate VOR adaptation has been elicited in response to different prisms in each eye⁶ and experimental weakening of the horizontal rectus muscles of one eye in monkeys.^{7,8} Adaptive changes in the VOR might also im-

prove defective visual stabilization of images caused by third nerve palsy.

In this study, we investigated patients with unilateral third nerve palsy to examine their VORs and their adaptations, if any, in 3 dimensions. The third (oculomotor) nerve innervates 4 extraocular muscles: the medial rectus, superior rectus, inferior rectus, and inferior oblique. Because the primary action of the medial rectus is adduction, we hypothesized that weakness of the medial rectus in third nerve palsy would cause a reduction in VOR gains during adduction. We also anticipated a decrease in vertical VOR gains during both elevation and depression in third nerve palsy, as these are the primary actions of the superior and inferior rectus muscles.⁹ Similarly, because the primary action of the inferior oblique is excyclotorsion,⁹ we also predicted a decrease in VOR gains during excyclotorsion in third nerve palsy. We identified changes in the VOR that signify monocular adaptation by the vestibulo-ocular system.

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PARTICIPANTS AND METHODS

CLINICAL ASSESSMENT AND IMAGING STUDIES

We recruited 10 patients with unilateral peripheral third nerve palsy from the Neuro-ophthalmology Unit at the University Health Network, Toronto, Ontario. A complete history was taken, and detailed ophthalmic and neurologic examinations were performed, recording the duration and age at onset of diplopia, the presence or absence of risk factors for ischemia (diabetes mellitus and hypertension), and associated neurologic symptoms and signs. The magnitude of strabismus was measured objectively using the prism and cover test and subjectively using the Maddox rod and prism test. The range of ductions was estimated independently by 2 examiners (A.W. and J.A.S.), and the degree of duction defect was graded according to the estimated percentage of the normal duction in the fellow eye. When indicated, appropriate tests were performed to rule out myasthenia gravis, thyroid ophthalmopathy, other orbital diseases, or intracranial lesions. Informed consent was obtained for all subjects.

In this investigation, magnetic resonance (MR) or computed tomographic (CT) imaging was performed on all patients, although imaging is not our standard practice for all such patients. We obtained CT images of the head with contrast in all patients with ischemic risk factors and for patients older than 50 years. Those with abnormal findings on CT scans were further investigated with MR imaging. Serial axial and sagittal T1-weighted and T2-weighted MR images with gadolinium enhancement were obtained (slice thickness, 5 mm) for all patients younger than 50 years. In addition, MR imaging was performed on all patients with pupillary involvement; if the MR image was normal, cerebral angiography was performed.

EYE MOVEMENT RECORDINGS

Experimental Protocol

With one eye occluded, subjects viewed a red laser spot 0.25° in diameter that was rear-projected on a uniformly gray vertical flat screen 1 m from the nasion. Subjects made active sinusoidal $\pm 10^\circ$ head-on-body rotations in yaw to elicit the horizontal VOR and in pitch to elicit the vertical VOR at approximately 0.5 and 2 Hz. Torsional VOR was elicited by head rotation in roll at approximately 0.5, 1, and 2 Hz. Head movements were paced by a periodic tone. The examiner placed his or her hands on each parietal area of the subject's skull to maintain the desired amplitude and frequency of head movements. The procedure was performed in light with one eye viewing to elicit the visually enhanced VOR (VVOR) then repeated with the other eye fixating and the fellow eye occluded. The VOR was then recorded in complete darkness while subjects were instructed to fixate on an imaginary earth-fixed target.

To measure the static torsional VOR, subjects fixated on the center target with one eye occluded as we measured their ocular responses to static head rolls of about 30° toward each shoulder, as measured with search coils. The procedure was then repeated with the other eye

fixating and the fellow eye occluded and also in total darkness.

Recordings of Eye Movement and Calibration

The positions of each eye were simultaneously measured by a 3-dimensional magnetic search coil technique, using an 183-cm (6-ft) diameter coil field arranged in a cube (CNC Engineering, Seattle, Wash). In each eye, the subject wore a dual-lead scleral coil annulus designed to detect horizontal, vertical, and torsional gaze positions (Skalar Medical, Delft, the Netherlands). Head position was recorded by another coil taped to the subject's forehead. Each subject's head was centered in the field coils. Horizontal, vertical, and torsional movements were calibrated by attaching the scleral coil to a rotating protractor before each experiment. After scleral coils were inserted in the subject's eyes, horizontal and vertical eye movements were calibrated with saccades from the straight-ahead reference position to steps of a laser target. Consistency of calibrated positions before and after coils were inserted provided evidence that the gimbal calibrations were valid. Because torsional eye position depended on the same magnetic field as vertical eye position, the accuracy of vertical calibration before and after coil insertion provided further evidence that the torsional calibration was also accurate. Phase detectors employing amplitude modulation as described by Robinson¹⁰ provided signals of torsional gaze position within the linear range. Torsional precision was about $\pm 0.2^\circ$. There was minimal cross-talk; large horizontal and vertical movements produced deflections in the torsional channel of less than 4% of the amplitude of the horizontal and vertical movement. Any coil slippage was assessed by requiring subjects to repeatedly refixate at the straight-ahead reference position after each eye movement. Consistency of calibrated torsional coil signals 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 data were also displayed in real time by a rectilinear thermal array recorder (Model TA 2000; Gould Electronics Inc, Eastlake, Ohio).

Data Analyses

Eye position was derived by subtracting head position from gaze position signals. Fast phases of vestibular nystagmus were identified by a computer program using velocity and acceleration criteria.¹¹ Results of fast-phase identification were edited on a video monitor, allowing the operator to verify cursor placement for fast-phase removal. Eye positions between 80 milliseconds before and after the identified fast phases were removed, and the gaps were replaced with quadratic fits. The average slopes were used to calculate the contribution of the ongoing slow phase during the fast phase. The offset due to the fast phase was then removed, and the ongoing slow phase was interpolated to yield a cumulative trace of eye position.

Using position data, each cycle of rotation was identified by marking adjacent peaks with the opposite direction, and the frequency was computed. Using a least-square sinusoidal fit,¹² eye and head positions were fitted with one

Continued on next page

cycle, and the phase and amplitude were computed. The ratio of the amplitude of the eye and the amplitude of the head was the gain, and the difference between the phase of the eye and the phase of the head was the phase shift.

To calculate the gain in each direction, eye and head position data from each half cycle were used and reflected to form a full cycle. Each cycle was then fitted using a least-square sinusoidal fit,¹² and the gain was computed for each direction. In addition, we plotted head velocity against eye velocity and performed a linear regression for each direction. The slopes of the fitted lines were the gains, and the results were comparable to those computed by the least-square sinusoidal fit technique (**Figure 1**).

Subjects wore spectacles, if habitually worn, during VOR testing. To account for the prismatic effect or rotational magnification induced by spectacle adaptation,^{5,13} horizontal and vertical VOR gains were adjusted by using the formula: $M_{pred} = 40 / (40 - D)$, where D is the lens power in diopters and M_{pred} is the predicted magnification.^{5,13} For example, a patient with hyperopia who habitually wears +10 D spherical lenses has an M_{pred} of $40 / (40 - 10)$ or 1.3. This means that while wearing +10 D, a VOR gain of 1.3, instead of 1.0, is required to prevent the visual scene from moving on the retina during head rotations.

For the measurement of static torsional VOR, head and gaze position signals were sampled for 6 seconds in each of 20 positions of 30° lateral tilt. The position of the eye in the head was derived from the difference between head and gaze position signals. Head and eye positions were computed off-line over each 6-second period after the eye had come to a torsional resting position (defined as having angular velocity less than 1° per second). Responses containing blinks or rapid drifts were not analyzed. Change of torsional eye position was plotted as a function of static change of head position after roll, and a linear regression was performed. Static torsional VOR gain, defined as the change in torsional eye position divided by the change in head position in static roll, was calculated from the slope of the regression line.

Oculography was performed at one point in each patient's course (**Table 1**). Thus, deviations from normal results, rather than serial intrasubject changes, were analyzed. Statistical analyses of horizontal, vertical, and torsional VOR and VVOR gains and phases were performed using *t* tests with 2-tailed, unequal variance. Values were defined as significant when $P < .05$.

RESULTS

GENERAL CHARACTERISTICS OF PATIENTS

The mean ± SD age was 54 ± 13 years (median age, 54 years; age range, 38-70 years). There were 8 women. The duration of symptoms ranged from one week to 50 months, with a mean duration of 18 months. Mean follow-up duration was 38 months (range, 11-72 months). In all patients, the third nerve palsy affected both the superior and inferior divisions, with or without pupillary involvement. No patients had any clinical signs of misdirection

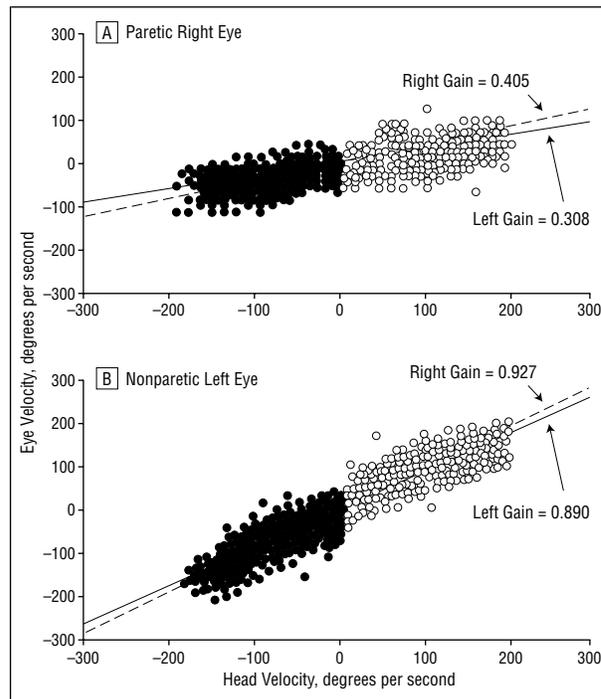


Figure 1. Plots of head velocity vs eye velocity of the paretic right eye (A) and the nonparetic left eye (B) of Patient 1 with severe right third nerve palsy during horizontal head rotation about an earth-vertical axis at 2 Hz in darkness. Gains in the vestibulo-ocular reflex, defined as the slopes of the lines of best fit, were reduced in the paretic right eye in both directions (A), whereas gains were normal in the nonparetic left eye in both directions (B). Open circles indicate data during rightward movements; dashed line, line of best fit for data during rightward movements; filled circles, data during leftward movements; and solid line, line of best fit for data during leftward movements.

involving the eyelid or pupil. Six patients had idiopathic, presumed ischemic, peripheral lesions. Four had normal MR images, and 2 had normal CT scans. Four of these 6 patients had ischemic factors, namely hypertension or diabetes, and had a complete resolution of their palsy within 4 to 6 months. Four other patients had intracranial lesions: head injury (n=1), neurosarcoidosis with enhanced meninges at the cavernous sinus (n=1), posterior communicating artery aneurysm (n=1), and pituitary tumor extending into the cavernous sinus (n=1). All 4 patients with intracranial lesions had neurologic symptoms and signs in addition to diplopia. None of them had signs or MR evidence of involvement of the third nerve nucleus or fascicle. Fifteen healthy subjects served as controls (mean ± SD age, 52 ± 15 years; median age, 58 years; age range, 19-69 years; 8 women).

GAIN AND PHASE IN THE VOR

In darkness (**Figure 2A**), horizontal VOR gains of the paretic eye were reduced symmetrically ($P < .05$) during both abduction and adduction, whereas those of the nonparetic eye remained normal in both directions (**Table 2**). During viewing with either eye in light (**Figure 2B and C**), horizontal VVOR gains of the paretic eye were low in both directions ($P < .05$), whereas VVOR gains of the nonparetic eye were normal (**Table 2**). In light and darkness, the mean phase differences between the eye and

Table 1. Characteristics of Patients With Third Nerve Palsy*

Patient No.	Age, y/Sex/ Duration of Third Nerve Palsy	Side of Lesion	Normal Adduction, %†	Normal Elevation, %†	Normal Depression, %†	Deviations in Primary Position, PD	Ptosis	Pupils	Misdirection	Imaging	Comments
1	48/F/16 mo	R	80	0	20	14 XT, 6 LHT	Y	Affected	N	MRI results, angiogram: PCA aneurysm	Surgical clipping
2	39/F/2 wk	R	10	90	10	10 XT, 8 LHT	Y	Spared	N	MRI results: enhanced meninges	Neurosarcoidosis
3	44/F/23 mo	R	60	70	90	14 XT, 2 LHT	Y	Spared	N	Normal MRI results	...
4	69/F/14 mo	R	90	50	80	16 XT, 6 LHT	Y	Spared	N	Normal CT scan	Diabetes mellitus
5	70/F/2 wk	R	0	0	0	40 XT, 16 LHT	Y	Spared	N	Normal CT scan	Diabetes mellitus, hypertension
6	59/M/24 mo	R	90	20	0	30 XT, 16 LHT	Y	Affected	N	Normal MRI results, angiogram	...
7	66/F/1 wk	R	0	0	0	16 XT, 6 LHT	Y	Affected	N	Normal MRI results, angiogram	Diabetes mellitus, hypertension
8	67/M/38 mo	L	90	80	80	4 XT, 4 RHT	Y	Spared	N	Normal MRI results	Diabetes mellitus, hypertension
9	42/F/15 mo	L	80	0	10	6 XT, 8 RHT	Y	Affected	N	MRI results: subarachnoid hemorrhage	Head trauma
10	38/F/50 mo	L	80	80	70	6 XT, 4 RHT	Y	Affected	N	MRI results: pituitary tumor extending to cavernous sinus	Surgical debulking

*PD indicates prism diopters; F, female; M, male; R, right, L, left; XT, exotropia; LHT, left hypertropia; RHT, right hypertropia; MRI, magnetic resonance imaging; PCA, posterior communicating artery; CT, computed tomographic; and ellipses, not applicable.
†Percentage of normal duction.

head positions approximated 180°, designated as zero phase shift.

In darkness (**Figure 3A**), vertical VOR gains of the paretic eye were reduced ($P < .01$) during both elevation and depression, whereas gains of the nonparetic eye were normal (Table 2); upward and downward gains did not differ. In light, during paretic or nonparetic eye viewing (Figure 3B and C), vertical VVOR gains of the paretic eye remained reduced ($P < .05$), whereas gains in the nonparetic eye were normal (Table 2). Neither eye showed any significant phase shift from zero in light or darkness.

In darkness (**Figure 4A**), torsional VOR gains of the paretic eye were reduced during both incyclotorsion and excyclotorsion ($P < .01$), whereas gains of the nonparetic eye were normal (Table 2). In light, and during viewing with either eye (Figure 4B and C), torsional VVOR gains of the paretic eye remained reduced ($P < .01$), whereas gains in the nonparetic eye were normal (Table 2). Neither eye showed any significant phase shift from zero in light or darkness.

Static torsional VOR gains did not differ between viewing with the paretic or nonparetic eye. Therefore, they are reported as the pooled mean for each eye with either eye fixating, in light and darkness (**Table 3**). Static torsional VOR and VVOR gains of the paretic eye were

reduced during incyclotorsion and excyclotorsion ($P < .05$); they were normal in the nonparetic eye.

COMMENT

In subjects with third nerve palsy, horizontal VOR and VVOR gains of the paretic eye were decreased during both abduction and adduction, whereas gains in the nonparetic eye were normal. Vertical VOR and VVOR gains of the paretic eye were decreased during both elevation and depression, consistent with palsy of the superior and inferior rectus muscles in third nerve palsy. In the nonparetic eye, vertical gains were normal. Dynamic and static torsional VOR and VVOR gains of the paretic eye were reduced during incyclotorsion and excyclotorsion. Torsional gains were normal in the nonparetic eye. In light, horizontal, vertical, and torsional VVOR gains in the paretic eye remained reduced, indicating that visual input does not enhance VVOR to normal in third nerve palsy.

Changes in the VOR in our patients, who were tested at one point in the course of their palsies, are expressed as changes from normal, rather than serial intrasubject changes. Any recovery toward normal values was not assessed. Abnormalities are interpreted as deficits or adaptations to those deficits.

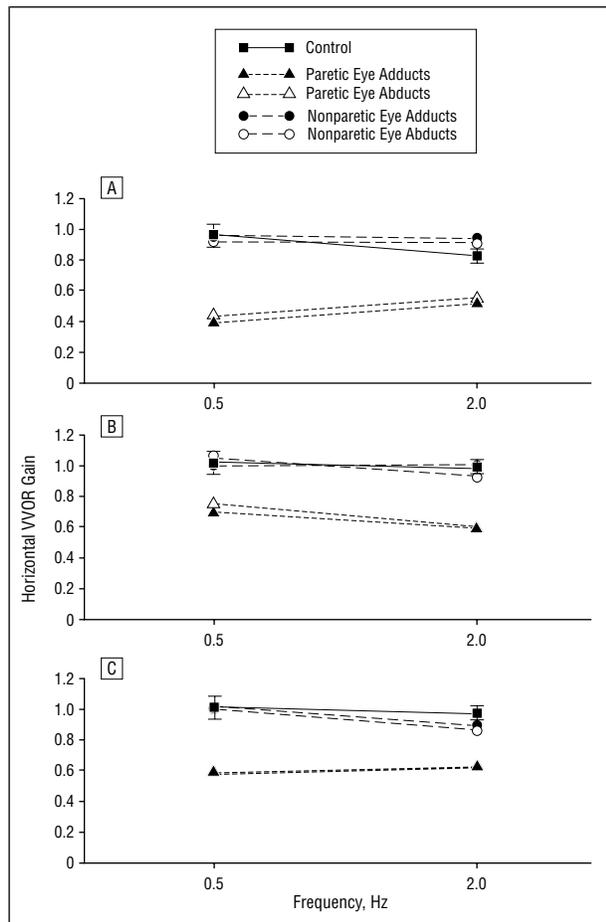


Figure 2. Mean horizontal vestibulo-ocular reflex (VOR) gains in controls (n=15) and patients with peripheral third nerve palsy (n=10) in darkness (A); and mean horizontal visually enhanced VOR (VVOR) gains in light during paretic (B) and nonparetic (C) eye viewing. Adducting and abducting VOR and VVOR gains are reduced symmetrically in the paretic eye, so their VVOR plots overlap (B and C). Error bars indicate one SD.

HORIZONTAL VOR IN UNILATERAL THIRD NERVE PALSY

During rotation in darkness, horizontal VOR gains were reduced during adduction of the paretic eye in all patients, as anticipated in palsy of the medial rectus muscle from third nerve palsy. VOR gains during abduction of the paretic eye were also reduced. In contrast, in the nonparetic eye, VOR gains were normal during both abduction and adduction (Figure 2). Apparently, the innervation to the lateral rectus of the paretic eye is reduced, along with the reduced innervation to the medial rectus resulting from the palsy, without changes in the innervation to the horizontal rectus muscles of the nonparetic eye.

A functional adaptation to unilateral third nerve palsy can explain this adjustment in abducting VOR gain. Without it, the VOR would be asymmetrical in the paretic eye, being reduced in adduction but normal in abduction. The asymmetry would drive the paretic eye farther into abduction with each cycle of head rotation, soon “pinning” it at its temporal limits and aggravating the patient’s diplopia. There are several strategies that might seem to rectify this problem. The brain might increase its innervation to the paretic medial rectus to increase

VOR gain during adduction, but this strategy is limited by the palsy itself. Or, the brain might generate adducting saccades in the paretic eye to correct for low VOR gains during adduction. However, adduction paresis would limit the saccades. Moreover, if common premotor signals are sent to both the abducens motoneurons and internuclear neurons in the abducens nucleus, the result might be unwanted abducting saccades in the nonparetic eye, taking it off its target. A better option would be to reduce the innervation just to the lateral rectus of the paretic eye, decreasing its abduction gain to make the VOR symmetrical in that eye, while leaving the VOR in the nonparetic eye intact. Apparently, the brain adopts this adaptive strategy when challenged by retinal image disparity caused by paresis of the medial rectus muscle.

TORSIONAL VOR IN UNILATERAL THIRD NERVE PALSY

In third nerve palsy that affects both the superior and inferior divisions, 3 of 4 cyclovertical extraocular muscles are involved, namely, the superior rectus, inferior rectus, and inferior oblique muscles. The cyclotorsional actions of the superior rectus and the inferior rectus are opposed; the superior rectus incyclotorts, and the inferior rectus excyclotorts.⁹ If both vertical rectus muscles were equally palsied, the net effects of third nerve palsy on torsional VOR would be determined by weakness of the inferior oblique, whose primary action is excyclotorsion. As anticipated, dynamic and static torsional VOR gains are reduced during excyclotorsion. However, we found that torsional VOR gains are also reduced during incyclotorsion. Unequal involvement of the superior and inferior rectus muscles, with the superior rectus being more severely affected than the inferior rectus, might make some contributions to reduction of incyclotorting gains. However, symmetry of upward and downward gains indicate that differential paresis of the vertical rectus muscles was not a factor.

The reduced VOR gains during incyclotorsion in the paretic eye, without any change in gains in the nonparetic eye, can be attributed to a functional adaptation in unilateral third nerve palsy. Without it, the VOR would be asymmetrical in the paretic eye: weak in excyclotorsion but normal in incyclotorsion. The asymmetry would drive the paretic eye farther into incyclotorsion with each cycle of head rotation, resulting in increased torsional disparity between the 2 eyes and diplopia. Using similar rationale discussed for the horizontal VOR, this adaptation in the paretic eye could be achieved by decreasing the innervation to the ipsilateral superior oblique (but not to the yolked contralateral inferior rectus) of the paretic eye.

PROPRIOCEPTION AND VOR ADAPTATION

A decrease in proprioceptive signals from extraocular muscles of the paretic eye might have also contributed to the VOR changes in our patients. Extraocular muscle afferents leave the ocular motor nerves near the apex of the orbit or in the region of the cavernous sinus and travel via the ophthalmic branch of the trigeminal nerve and

Table 2. Horizontal, Vertical, and Torsional VOR and VVOR Gains in Patients With Third Nerve Palsy*

	VOR Gain								
	Darkness (VOR)			Paretic Eye Viewing (VVOR)			Nonparetic Eye Viewing (VVOR)		
	0.5 Hz	1 Hz	2 Hz	0.5 Hz	1 Hz	2 Hz	0.5 Hz	1 Hz	2 Hz
Horizontal VOR									
Controls (n = 15)	0.96 (0.07)	...	0.92 (0.04)	1.01 (0.07)	...	0.97 (0.05)
Paretic eye adducts	0.39 (0.21)†	...	0.51 (0.26)‡	0.69 (0.33)§	...	0.59 (0.24)‡	0.58 (0.31)‡	...	0.62 (0.28)‡
Paretic eye abducts	0.45 (0.19)†	...	0.55 (0.26)‡	0.74 (0.31)§	...	0.59 (0.27)‡	0.59 (0.30)‡	...	0.62 (0.29)‡
Nonparetic eye abducts	0.96 (0.20)	...	0.94 (0.17)	0.99 (0.32)	...	0.98 (0.17)	1.00 (0.04)	...	0.87 (0.14)
Nonparetic eye adducts	0.93 (0.31)	...	0.90 (0.21)	1.05 (0.38)	...	0.91 (0.15)	1.02 (0.07)	...	0.90 (0.10)
Vertical VOR									
Controls (n = 15)	0.90 (0.13)	...	0.91 (0.10)	1.07 (0.10)	...	0.99 (0.13)
Paretic eye elevates	0.37 (0.26)†	...	0.48 (0.27)‡	0.67 (0.36)§	...	0.57 (0.35)‡	0.52 (0.30)†	...	0.58 (0.30)‡
Paretic eye depresses	0.45 (0.39)†	...	0.52 (0.31)‡	0.67 (0.37)§	...	0.56 (0.35)‡	0.51 (0.29)†	...	0.58 (0.29)‡
Nonparetic eye elevates	0.73 (0.23)	...	1.02 (0.35)	1.07 (0.33)	...	1.06 (0.26)	1.10 (0.09)	...	1.05 (0.18)
Nonparetic eye depresses	0.75 (0.25)	...	1.02 (0.27)	1.08 (0.30)	...	1.07 (0.26)	1.09 (0.12)	...	1.05 (0.14)
Torsional VOR									
Controls (n = 15)	0.49 (0.09)	0.51 (0.10)	0.56 (0.08)	0.56 (0.10)	0.56 (0.08)	0.63 (0.08)
Paretic eye excyclotorts	0.18 (0.11)†	0.24 (0.12)†	0.33 (0.16)‡	0.28 (0.10)†	0.26 (0.13)†	0.36 (0.20)‡	0.23 (0.10)†	0.27 (0.11)†	0.33 (0.15)†
Paretic eye incyclotorts	0.18 (0.12)†	0.22 (0.12)†	0.32 (0.15)‡	0.23 (0.16)†	0.24 (0.14)†	0.33 (0.22)‡	0.24 (0.09)†	0.25 (0.14)†	0.34 (0.16)†
Nonparetic eye incyclotorts	0.42 (0.16)	0.40 (0.14)	0.50 (0.13)	0.45 (0.20)	0.45 (0.15)	0.57 (0.14)	0.54 (0.12)	0.51 (0.11)	0.61 (0.10)
Nonparetic eye excyclotorts	0.46 (0.13)	0.41 (0.14)	0.51 (0.15)	0.46 (0.16)	0.46 (0.15)	0.59 (0.15)	0.55 (0.08)	0.51 (0.09)	0.60 (0.09)

*Data given as mean (SD). VOR indicates vestibulo-ocular reflex; VVOR, visually enhanced VOR; and ellipses, not applicable.

†P<.001.

‡P<.01.

§P<.05.

the gasserian ganglion to reach the spinal trigeminal nucleus.¹⁴⁻¹⁹ There is disagreement as to whether some afferents also project centrally via the ocular motor nerves.¹⁹⁻²⁴ Sectioning of the trigeminal nerve reduced horizontal VOR gains in rabbits²⁵⁻²⁷ and pigeons.²⁸ Immediately after unilateral sectioning of the trigeminal nerve in pigeons, horizontal VOR gains of the deafferented eye were dramatically reduced, whereas gains in the contralateral eye were little affected.²⁸ In our patients, horizontal VOR gains of the paretic eye were reduced in both directions, whereas gains of the nonparetic eye remained normal. Our results might be explained by defective transmission of afferent signals from the paretic eye to the brainstem because of a lesion in the oculomotor nerve, which normally carries proprioceptive signals from extraocular muscles to the ophthalmic branch of the trigeminal nerve and the spinal trigeminal nucleus.

ORBITAL MECHANICS AND VOR ADAPTATION

Changes in normal orbital plant mechanics might contribute to the decreased VOR gains of the paretic eye in third nerve palsy. The relative contribution of agonist contraction and antagonist relaxation varies with orbital position,²⁹ and it may be altered when one muscle

of an agonist-antagonist pair is palsied. In paralytic strabismus, "contracture" (shortening and increased stiffness) occurs in the nonparetic antagonist muscle,³⁰⁻³³ whereas the paretic muscle lengthens in response to a change in orbital position of the globe. Anatomical and histological study³⁴ showed that shortening or contracture of the nonparetic antagonist is associated with a decrease in the number of sarcomeres, whereas lengthening of the paretic muscle is accompanied by an increase in its number of sarcomeres.³⁴ In addition, denervation atrophy in the paretic muscle and changes in orbital tissues have been documented in paralytic strabismus.^{35,36} These changes may alter VOR gains in both directions of the 3 axes of rotation.

MONOCULAR ADAPTATION IN UNILATERAL THIRD NERVE PALSY

Hering³⁷ suggested that the brain circuitry controlling gaze consists of 2 systems: one for conjugate movements, the other for vergence. Conjugate control operates in the vestibulo-ocular, saccade, smooth pursuit, and optokinetic systems. Premotor neurons encode common signals to both abducens motoneurons and internuclear neurons in the abducens nucleus.³⁸⁻⁴⁰ The abducens motoneurons innervate the ipsilateral lateral rectus, whereas the

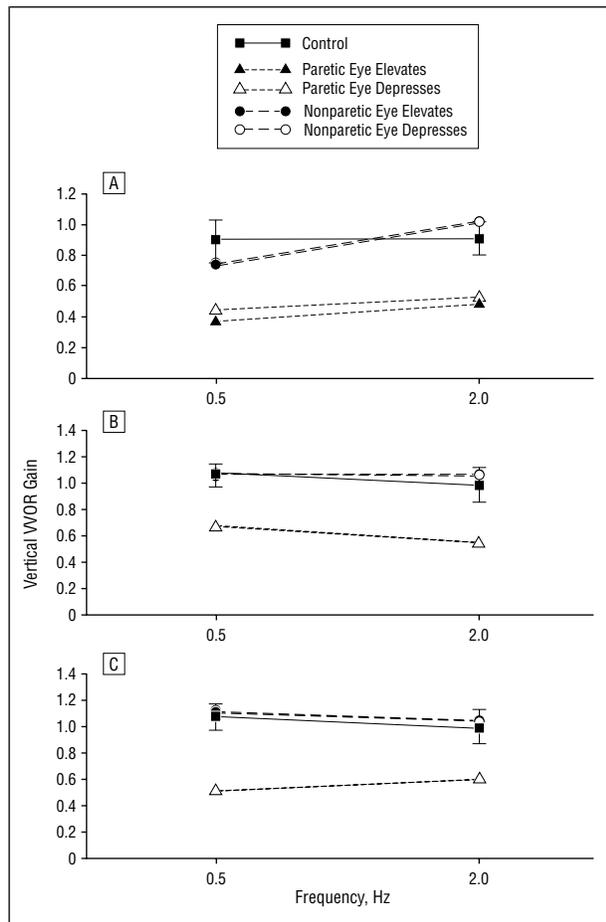


Figure 3. Mean vertical vestibulo-ocular reflex (VOR) gains in controls (n=15) and patients with peripheral third nerve palsy (n=10) in darkness (A); and mean vertical visually enhanced VOR (VVOR) gains in light during paretic (B) and nonparetic (C) eye viewing. Upward and downward VOR and VVOR gains are reduced symmetrically in the paretic eye, so their VVOR plots overlap (B and C). Error bars indicate one SD.

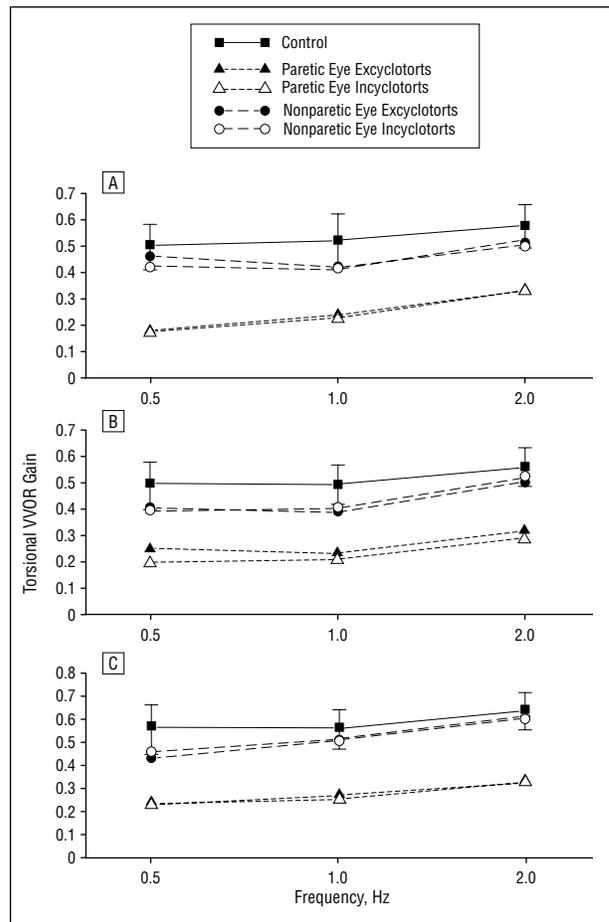


Figure 4. Mean dynamic torsional vestibulo-ocular reflex (VOR) gains in controls (n=15) and patients with peripheral third nerve palsy (n=10) in darkness (A); and mean torsional visually enhanced VOR (VVOR) gains in light during paretic (B) and nonparetic (C) eye viewing. Excyclotorting and incyclotorting VOR and VVOR gains are reduced symmetrically in the paretic eye. Error bars indicate one SD.

internuclear neurons innervate the medial rectus motoneurons in the contralateral oculomotor nucleus.⁴¹⁻⁴³

Because the neuronal connectivity is suitable for conjugate motion, it might be presumed that only conjugate plasticity is possible. However, experiments on primates have shown that ocular motor systems are capable of selective, monocular adaptation.^{7,8,44} In monkeys, surgical weakening of the horizontal rectus muscles of one eye elicits an adaptation that selectively increases saccadic and VOR gains in the affected eye, whereas those of the unaffected eye remained normal.^{7,8} Disconjugate ocular motor adaptation has also been demonstrated in normal humans^{45,46} and monkeys⁶ in response to image disparity induced by anisometric spectacles⁴⁵ or prisms.⁶ Disconjugate saccades and pursuit are generated to compensate for the disparate retinal errors produced by the optical displacement of images.^{45,46}

This investigation is the first, to our knowledge, to demonstrate monocular adaptive change in the VOR in humans with third nerve palsy. We found that VOR gains are selectively decreased during abduction and incyclotorsion of the paretic eye, without a conjugate decrease in gains of the nonparetic eye. These results exemplify monocular adaptation in humans with peripheral neu-

Table 3. Static Torsional VOR Gain (Ocular Counterroll) in Controls and Patients With Third Nerve Palsy*

	Light		Darkness	
	Paretic Eye	Nonparetic Eye	Paretic Eye	Nonparetic Eye
Controls (n = 10)				
Incyclotort	...	0.21 (0.11)	...	0.20 (0.13)
Excyclotort	...	0.22 (0.09)	...	0.21 (0.13)
Patients (n = 10)				
Incyclotort	0.11 (0.06)†	0.23 (0.10)	0.08 (0.06)†	0.23 (0.07)
Excyclotort	0.11 (0.09)‡	0.23 (0.14)	0.09 (0.10)‡	0.22 (0.15)

*Data given as mean (SD). VOR indicates vestibulo-ocular reflex; ellipses, not applicable.

† $P < .01$.

‡ $P < .05$.

romuscular deficits. Differences in slippage of retinal images between the 2 eyes is a stimulus that can drive the monocular adaptation we have recorded.

Changes in neural drive to each eye might occur independently at the level of motoneurons. Selective adaptation might be achieved by changing the sensitivity

of each motoneuron pool to innervation from premotor neurons. The cerebellum, which mediates ocular motor adaptation, may have direct projections to ocular motoneurons.⁴⁷ Using the Nauta method for tracing wallerian degeneration, Carpenter and Strominger⁴⁷ suggested that cerebello-oculomotor fibers from all parts of the dentate nucleus project to the inferior rectus subdivision of the contralateral oculomotor nucleus, whereas fibers from ventral portions of the dentate nucleus project to the superior rectus subdivision of the contralateral oculomotor nucleus. However, a more modern retrograde tracer technique identified no afferents from the dentate nucleus to the oculomotor nucleus.^{48,49}

Supranuclear neural circuitry is not exclusively conjugate. For example, for saccades, different populations of burst neurons mediate a pulse of innervation to each eye. In monkeys, 79% of premotor excitatory burst neurons in the caudal pontine paramedian reticular formation that were thought to encode conjugate velocity commands for saccades³⁸⁻⁴⁰ actually encode monocular commands for either the ipsilateral or contralateral eye.⁵⁰ Similarly, different populations of vestibular neurons provide innervation to the horizontal muscles of each eye. In addition to a major excitatory horizontal VOR pathway that mediates conjugate eye movements via motoneurons and internuclear neurons in the abducens nucleus, a second direct excitatory horizontal VOR pathway exists. This second pathway originates from the ventral lateral vestibular nucleus and ascends through the ascending tract of Deiters to the ipsilateral medial rectus subdivision of the oculomotor nucleus.^{51,52} Furthermore, neurons in the feline medial vestibular nucleus are activated antidromically only by local stimulation of the contralateral abducens nucleus,⁵³ whereas another group of medial vestibular nucleus neurons are activated only by stimulation of the ipsilateral medial rectus motoneurons pool, but not by stimulation of the contralateral abducens nucleus.⁵³

The cerebellum plays important roles in adaptive control of saccades⁵⁴⁻⁵⁷ and the VOR, including disconjugate control.^{55,58-61} Experimental inactivation of the deep cerebellar nuclei (including the fastigial nucleus) causes disconjugate saccadic dysmetria, so that both saccade magnitude and peak velocity differ in the 2 eyes.⁶² Patients with cerebellar degeneration or dysgenesis also show disconjugate dysmetria during and immediately after horizontal or vertical saccades,⁶³ although brainstem circuits are typically not spared in spinocerebellar degenerations or malformations. The flocculus modulates VOR responses, and unilateral lesions of the rabbit flocculus cause different VOR gain changes in the 2 eyes.⁶⁴ Thus, the cerebellum exerts selective, dysconjugate control and may participate in the monocular adaptation of the horizontal and torsional VOR that we have identified after third nerve palsy.

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