

Adaptive Neural Mechanism for Listing's Law Revealed in Patients with Fourth Nerve Palsy

Agnes M. F. Wong,^{1,2} James A. Sharpe,^{1,2} and Douglas Tweed^{1,3}

PURPOSE. During fixation and saccades, human eye movements obey Listing's law, which specifies the eye's torsional angle as a function of its horizontal and vertical position. Torsion of the eye is in part controlled by the fourth nerve. This study investigates whether the brain adapts to defective torsional control after fourth nerve palsy.

METHODS. Thirteen patients with fourth nerve palsy (11 chronic, 2 acute), and 10 normal subjects were studied with scleral search coils. With the head immobile, subjects made saccades to a target that moved between straight ahead and eight eccentric positions. At each target position, fixation was maintained for 3 seconds before the next saccade. From the eye position data, we computed the plane of best fit, referred to as Listing's plane. Violations of Listing's law were quantified by computing the "thickness" of this plane, defined as the SD of the distances to the plane from the data points.

RESULTS. Both the paretic and nonparetic eyes in patients with chronic fourth nerve palsy obeyed Listing's law during fixation and saccades. However, Listing's planes in both eyes had abnormal orientations, being rotated temporally, meaning the eye excyclotorted during downgaze and incyclotorted during upgaze. In contrast, the paretic eye of patients with acute fourth nerve palsy violated Listing's law during saccades. During downward saccades, transient torsional deviations moved the paretic eye out of Listing's plane. Torsional drifts returned the paretic eye to Listing's plane during subsequent fixation.

CONCLUSIONS. During saccades, acute fourth nerve palsy violates Listing's law, whereas chronic palsy obeys it, indicating that neural adaptation can restore Listing's law by adjusting the innervations to the remaining extraocular muscles, even when one eye muscle remains paretic. The transient torsional deviations during downward saccades in acute palsy are attributed to pulse-step mismatch, as a result of lesions in the trochlear nerve that lead to an imbalance of phasic and tonic signals reaching the muscles. (*Invest Ophthalmol Vis Sci.* 2002;43:1796-1803)

During fixation, saccades, and smooth pursuit, the eye rotates freely in the horizontal and vertical dimensions, but torsion is constrained.¹⁻³ This restriction on ocular torsion is described by Donders' and Listing's laws.⁴ Donders' law

states that horizontal and vertical positions of the eye determine the torsional angle.^{2,4} Donders' law does not specify what torsional angle the eye assumes, but only that there is a unique torsional angle for each gaze direction. Listing's law is a special case of Donders' law and quantitatively specifies the torsional angle for each gaze direction. It states that, when the head is fixed, there is an eye position called the primary position and that the eye assumes only those orientations that can be reached from the primary position by a single rotation about an axis in a plane called Listing's plane.⁴ This plane, furthermore, is orthogonal to the gaze line when the eye is in primary position.

Listing's law is illustrated in Figure 1. The eye at the center is in the primary position, and the plane of the paper is Listing's plane. All the eye orientations drawn with solid lines are in accord with Listing's law, because they can be reached from the primary position by rotating around axes (straight black lines extending from the globes) in Listing's plane. But the position drawn with dashed lines in the illustration at top center violates Listing's law, because the rotation to that orientation from primary position has its axis (white line extending from the globe) tilted out of Listing's plane.

We have recently demonstrated that during fixation and saccades, eyes in patients with acute peripheral sixth nerve palsy violate Listing's law but obey Donders' law, whereas eyes in patients with chronic palsy obey both laws, indicating that the neural mechanism that enforces Listing's law is adaptive.⁵ In the current study, we investigated patients with unilateral fourth nerve palsy to determine whether Listing's law is obeyed in the acute and chronic state. We provide further evidence that the neural mechanism underlying Listing's law is adaptive, even when one eye muscle is abnormal.

METHODS

We recruited 13 patients with unilateral fourth nerve palsy from the Neuro-ophthalmology Unit at the University Health Network. 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, and any associated neurologic symptoms and signs were recorded. Patients with diplopia of less than 4 weeks' duration were classified as having acute palsy; all others were classified as having chronic palsy. Superior oblique palsy was diagnosed using the following clinical criteria⁶⁻⁸: deficient depression of the hypertropic eye in adduction, incomitant hypertropia that increased with adduction of the hypertropic eye and with head tilt toward the hypertropic eye, and presence of subjective excyclotorsion. Patients with a history of head tilt, diplopia, or strabismus dating to infancy or early childhood or prior surgery for strabismus were excluded from the study.

The magnitude of strabismus was measured objectively, with the prism-and-cover test, and subjectively, with the Maddox rod-and-prism test. The range of ductions was estimated independently by one of two examiners (AMFW, JAS), 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.

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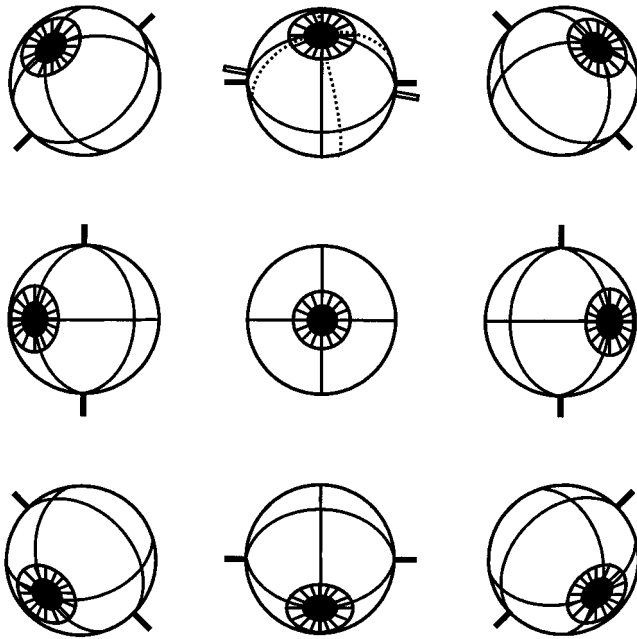


FIGURE 1. The nine orientations drawn in *solid lines* are in accordance with Listing's law, because they are attainable by rotating from the primary position (center) around axes lying in Listing's plane (the plane of the paper). The position drawn in *dashed lines at top center* does not fit Listing's law, because the rotation to this position from the primary position occurs around an axis that is tilted out of primary position.

In this investigation, magnetic resonance (MR) or computed tomographic (CT) imaging were performed in all patients, although imaging is not our standard practice for all such patients. CT images of the head with contrast were obtained in all patients with ischemic risk factors and in patients more than 50 years of age. Those with abnormal CT images underwent further investigation, with MR imaging. Serial axial and sagittal T_1 - and T_2 -weighted MR images with gadolinium enhancement were obtained (slice thickness, 5 mm) in all patients less than 50 years of age.

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

Eye Movement Recordings

Visual Stimuli and Experimental Protocol. Eye position was measured with search coils while subjects fixated a red laser spot of 0.25° 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, with the other two 10° above and below. In each row, the center target lay in the subject's midsagittal plane, the other two 10° to the right and left of it.

With the head immobilized and with one eye covered, subjects 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 to the 10° left position—cycling through this pattern 20 times in 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 were not made during binocular viewing. To avoid fatigue, breaks were provided approximately every 2 minutes for 1 to 3 minutes.

Recordings of Eye Movement and Calibration. Eye positions were measured by a three-dimensional (3-D) magnetic search coil technique, using a 6-ft (183-cm) diameter coil field arranged in a

cube (CNC Engineering, Seattle, WA). In each eye, the subject wore a dual-lead scleral coil annulus (Skalar Instrumentation, Delft, The Netherlands). Horizontal, vertical, and torsional movements were calibrated by attaching the scleral coil to a rotating protractor before each experiment. The coil was first calibrated for $\pm 30^\circ$ torsionally in the straight-ahead position. The protractor was then rotated 30° to the right, and the signal was measured again as the mounted coil was rotated $\pm 30^\circ$ torsionally. The same procedure was performed with the protractor rotated 30° up. Phase detectors using amplitude modulation as described by Robinson⁹ provided signals of torsional gaze position within the linear range. There was minimal crosstalk. Horizontal and vertical movements produced deflections in the torsional channel of less than 4% of the amplitude of the horizontal and vertical movements. The difference in torsional deflections between the straight-ahead and 30° right (or up) positions was less than 4%. Torsional precision was approximately $\pm 0.2^\circ$.

To measure the offset of coil signal, during the gimbal calibration, the coil was rotated through 360° to measure its maximum and minimum readings. If there was no offset, these two readings would be equal and opposite. If they were not, the mean of the two readings was the offset, which was then subtracted from all coil recordings.

After the scleral coils were inserted onto 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 (see later description of reference position and Listing's primary position). Consistency of calibrated positions before and after insertion of the coils 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 insertion of the coils provided further evidence that the torsional calibration was also accurate.

The reference position, relative to which all eye positions were expressed, was defined by measuring the coil readings while the subject fixated a target straight ahead. To assess torsional coil slippage, throughout the experiment, the subject was required to fixate the same straight-ahead target repeatedly. Any discrepancy in voltage readings associated with reference position was corrected for by resetting the torsional position to the setting measured at the beginning of a trial during each straight-ahead fixation.

Eye position data were filtered with a bandwidth of 0 to 90 Hz and digitized at 200 Hz. They were recorded on disk for off-line analysis. Analog data were also displayed in real time by a rectilinear thermal array recorder (model TA 2000; Gould Inc., Cleveland, OH).

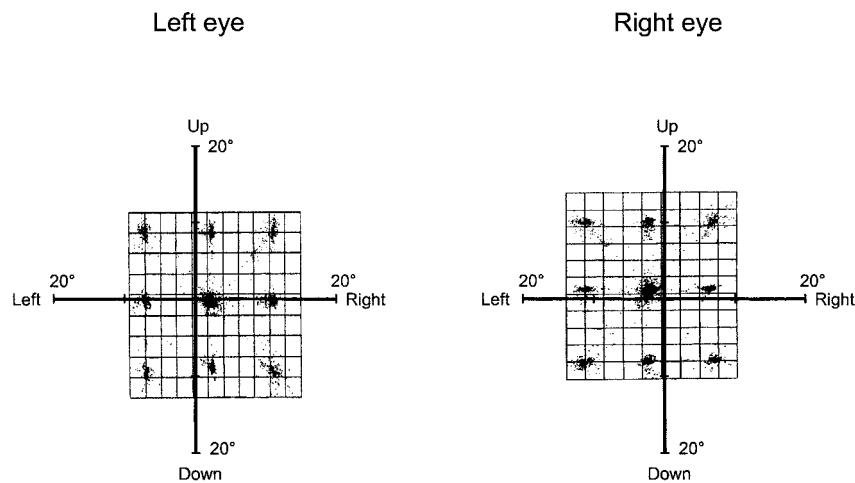
Data Analyses and Statistical Methods

Eye position and angular velocity were computed from coil signals.^{10,11} For analysis, fixations were defined as periods when eye velocity was less than 20 deg/sec, and saccades when eye velocity exceeded 50 deg/sec. Coil signals were converted into eye-position quaternions, by a method described previously.¹¹ Quaternions represent each eye position as a fixed-axis rotation from a reference position. This reference position was recorded when subjects looked straight ahead at the center target. Listing's law predicts that during fixation and saccades, the quaternion vectors of eye positions lie in a plane. This plane is not necessarily Listing's plane, unless the reference position happens to be the primary position, but by computing the orientation of the plane with respect to the gaze direction at reference position, one can determine the primary position and the orientation of Listing's plane.¹¹ Listing's primary position is not the primary position commonly used clinically, which refers to the straight-ahead gaze position and roughly corresponds to the center of the oculomotor range. In this study, all plots of eye position were set up so that the origin of the coordinate system (the zero position) was the straight-ahead reference position.

Figure 2 shows the 3-D eye position data from a normal subject fixating nine target positions. Listing's plane is the best-fit plane through the data cloud of eye positions. To assess the scatter in the data, we measured the distance of each eye position from the plane of best fit. The SD of these distances we called the "thickness" of the plane. The less the thickness, the better the data fit Listing's law.

Normal subject (KQ)

(A) Behind View



(B) Top View

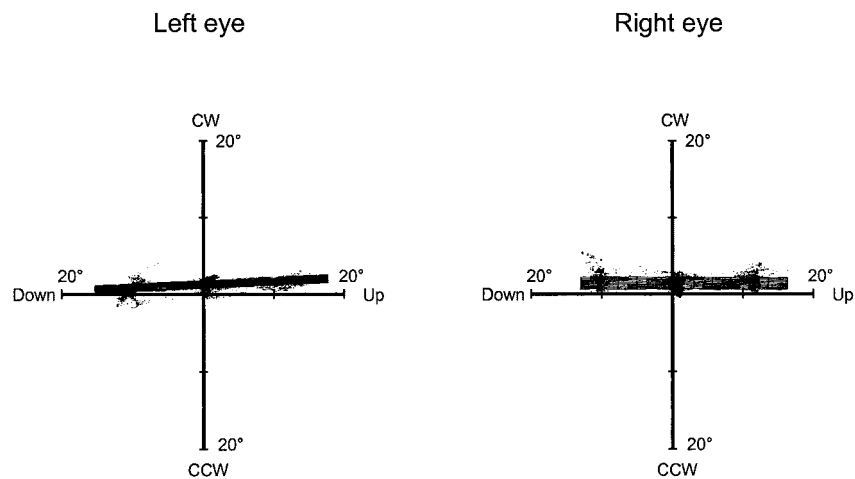


FIGURE 2. Plots of eye positions relative to primary position of a normal subject KQ, during fixation at nine target positions, 1 m away from the nasion. **(A) Behind view:** Listing's plane is the best-fit plane through the data cloud of eye positions. The central cloud among the nine small clouds of eye positions represents Listing's primary position and is shifted away from the zero position of the coordinate system (intersection of left-right and up-down axes), which is the straight-ahead gaze position. Note that Listing's primary position and straight-ahead gaze position are different. **(B) Top view:** A small temporal rotation of Listing's plane is demonstrated in both eyes. CW-CCW axis denotes rotation about the line of sight, clockwise (CW) or counterclockwise (CCW) from subject's point of view. The up-down axis denotes rotation around the interaural axis.

For a distant target, Listing's plane is approximately parallel to the frontal plane of the head. During near viewing, however, the Listing's planes of the two eyes rotate temporally in normal subjects.¹²⁻¹⁴ This is also illustrated in Figure 2, when a normal subject viewed a target 1 m away from the nasion. This temporal rotation of Listing's plane means that both eyes undergo excyclotorsion during downgaze and incyclotorsion during upgaze. Thus, during vergence in normal subjects, eye positions remain restricted to a plane, and therefore obey Listing's law, although the planes are turned.

We defined the direction of torsion from the subject's point of view. Rotation of the upper pole of the iris toward the subject's right shoulder was designated clockwise (CW), whereas rotation of the upper pole of the iris toward the subject's left shoulder was designated counterclockwise (CCW).

Oculography was performed at one point in each patient's course (Table 1). Thus, changes from normal, rather than serial intrasubject changes, were available for analyses. The eye that patients habitually used for fixation was not controlled. We compared the thickness of Listing's plane between patients and normal subjects. In the Results section, we report only the thickness of Listing's plane during parietic eye viewing. The results during nonparietic eye viewing were similar.

Donders' law implies that the eye position data lie in some two-dimensional surface, which is not necessarily a plane. To assess whether Donders' law was obeyed when Listing's law was violated, we also computed the second-order and third-order surfaces of best fit, by a method described previously (see Appendix).² The thickness (one SD) of the fitted curved surface was then compared in patients and normal subjects. Statistical analyses were performed using analysis of variance. Results were defined as significant when $P < 0.05$.

The research protocol was approved by the University Health Network Ethics Committee and adhered to the tenets of the Declaration of Helsinki. Informed consent was obtained from all subjects.

RESULTS

General Characteristics of Patients

The characteristics of the 13 patients with fourth nerve palsy are shown in Table 1. The mean age was 54 ± 16 years (median, 55; range, 23-81). There were eight women. The duration of symptoms ranged from 1 week to 132 months, with a mean duration of 35 months. Mean follow-up duration

TABLE 1. Characteristics of Patients with Fourth Nerve Palsy

Patient	Age	Sex	Side of Palsy	Duration (mo)	Hypertropia in primary position (PD)	Imaging	Comments
KG	23	M	R	48	4 RHT	Normal MRI & MRA	—
MA	75	F	R	60	12 RHT	Normal MRI	—
ER	49	F	R	42	3 RHT	Normal MRI	—
KS	39	F	R	1 week	3 RHT	Normal MRI	Hypertension
SD	66	M	R	3 weeks	2 RHT	Normal CT	Hypertension
GW	67	M	L	39	7 LHT	Normal CT	Trauma
SF	59	M	L	24	12 LHT	Normal MRI	Trauma
JG	53	F	L	24	10 LHT	Normal CT	—
CG	59	M	L	9	2 LHT	Normal MRI	—
HL	41	F	L	19	3 LHT	Normal MRI	—
LA	55	F	L	12	6 LHT	Normal CT	—
EB	81	F	L	132	8 LHT	Normal MRI	—
SW	37	F	L	40	4 LHT	Normal MRI & MRA	—

PD, prism diopter; R, right; L, left; RHT, right hypertropia; LHT, left hypertropia; MRA, MR angiogram.

was 49 months (range, 13–165). No patients had any associated neurologic symptoms or signs. Eleven patients had chronic palsy, whereas two had acute palsy. All patients had normal findings on neuroimaging: nine had normal findings on MR imaging and four had normal findings on CT imaging of the head.

Chronic Fourth Nerve Palsy

Figure 3 shows the 3-D eye position data and the fitted Listing's plane of a patient (SF) with chronic left fourth nerve palsy, during fixation with the paretic left eye. The thickness of Listing's plane was 1.0° in the right and left eyes. Listing's planes rotated temporally 15.4° in the right eye and 9.1° in the left eye. In this patient, Listing's law was obeyed, with temporal rotation of Listing's planes in both eyes.

The same was observed in each of 11 patients with chronic fourth nerve palsy, regardless of the severity of the palsy. The thickness of Listing's plane, averaged across all patients, was $0.7 \pm 0.3^\circ$ in the paretic eye and $0.6 \pm 0.4^\circ$ in the nonparetic eye, compared with $0.8 \pm 0.3^\circ$ in control subjects during both fixation and saccades. During fixation, rotation of Listing's plane, averaged across the 11 patients, was $21.0 \pm 2.3^\circ$ temporally in the paretic eye and $12.8 \pm 3.1^\circ$ temporally in the nonparetic eye, compared with $0.8 \pm 0.4^\circ$ temporally in the control subjects ($P < 0.001$). During saccades, rotation of Listing's plane was $20.4 \pm 1.9^\circ$ temporally in the paretic eye and $13.7 \pm 2.0^\circ$ temporally in the nonparetic eye, compared with $0.8 \pm 0.3^\circ$ temporally in control subjects ($P < 0.001$). Listing's law held in chronic fourth nerve palsy, but with abnormally rotated planes.

Acute Fourth Nerve Palsy

During saccades, the thickness of Listing's plane of the paretic eye, averaged across the two patients with acute palsy, was $8.3 \pm 0.4^\circ$ ($P < 0.001$), which was 10 times the thickness in normal control subjects. The plane of the nonparetic eye was of normal thickness. When we fit the data from the paretic eye with curved surfaces rather than planes, the thickness scarcely diminished. It averaged $8.0 \pm 1.2^\circ$ when the surface was second order and $7.7 \pm 1.2^\circ$ when it was third order, compared with $0.7 \pm 0.3^\circ$ and $0.6 \pm 0.3^\circ$, respectively, in normal control subjects ($P < 0.001$). Thus, during saccades in acute fourth nerve palsy, not only was Listing's law violated but also Donders' law—that is, the paretic eye did not show one consistent angle of torsion in any given gaze direction, but rather an abnormally wide range of torsional angles.

Figure 4A shows the eye movements made by patient KS while the paretic right eye viewed a target that stepped from center to 10° up, to center, to 10° down. When the target

stepped downward (that is, from 10° up to center and from center to 10° down), the paretic right eye made hypermetric downward and leftward saccades. Overshoot saccades were each followed immediately without interval by corrective upward and rightward movements (Fig. 4A, top panel, vertical and horizontal traces). At the same time, it made rapid clockwise movements, defined as rotations of the upper pole of the iris toward the subject's right shoulder, which were each followed by slow counterclockwise drifts (Fig. 4A, top panel, torsional trace). In the nonparetic left eye, vertical saccades were of normal amplitude, and were not associated with overshoot saccades or transient torsion (Fig. 4A, bottom panel). The same pattern was also observed in the other patient with acute right fourth nerve palsy.

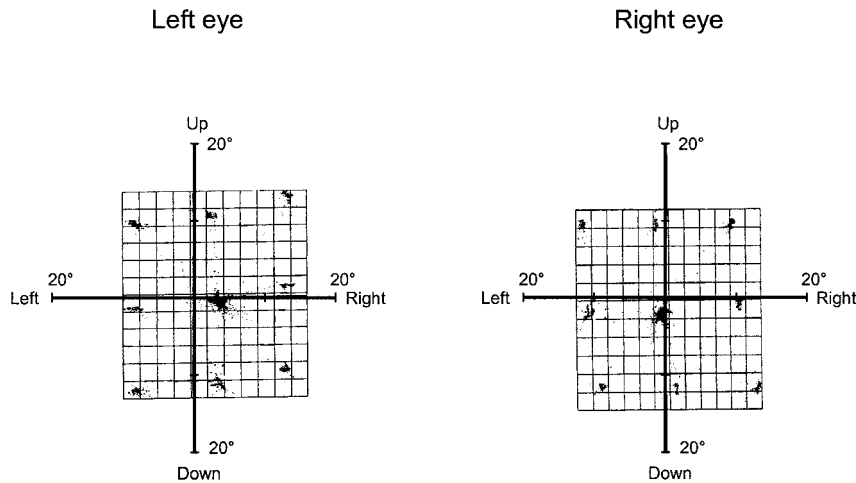
Figure 5 shows the 3-D eye position data and the fitted Listing's plane of the patient (KS) shown in Figure 4A (acute right fourth nerve palsy), during viewing with the paretic right eye. Because we defined fixation as periods when eye velocity was less than 20 deg/sec , when we fit Listing's plane including the corrective movements that followed the overshoot saccades, the thickness of Listing's plane was abnormal in the paretic right eye, with a mean of $10.0 \pm 1.1^\circ$, but normal in the nonparetic left eye (Figs. 5A, 5B). However, when we fit a Listing's plane excluding the corrective movements—that is, by fitting positions of the paretic eye that were more than 1.5 seconds after the saccade offset—the thickness returned to normal, with a mean of $1.1 \pm 0.9^\circ$ (Figs. 5C, 5D). The orientation of this Listing's plane, measured after the corrective movements were excluded, was also normal, with a mean temporal rotation of $1.2 \pm 0.9^\circ$. Thus, in patients with acute fourth nerve palsy, the paretic eye made abnormal torsional excursions during and immediately after saccades, and then it drifted back to Listing's plane during steady fixation.

DISCUSSION

The diagnosis of fourth nerve palsy is generally made on the basis of incomitant hypertropia, which increases with adduction of the hypertropic eye and during lateral head tilt toward the hypertropic eye (positive Bielschowsky head-tilt test). Because the primary action of the superior oblique is incyclotorsion, abnormal excyclotorsion is also associated with fourth nerve palsy, as demonstrated by double Maddox rods and fundus photography.¹⁵ One would predict that in fourth nerve palsy, the paretic eye might adopt abnormal eye positions and violate Listing's law. This was the case in acute fourth nerve palsy during saccades, but in chronic fourth nerve palsy, although Listing's plane is rotated temporally, meaning that the eye undergoes excyclotorsion during downgaze and incy-

Chronic left fourth nerve palsy (SF)

(A) Behind View



(B) Top View

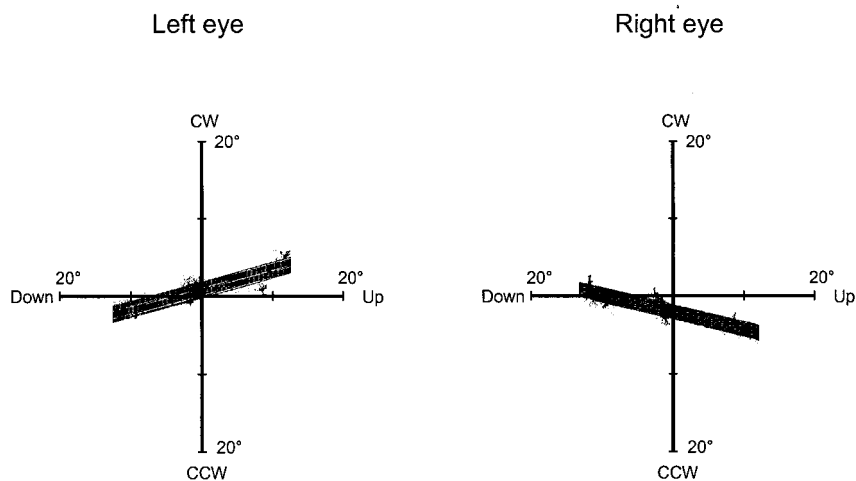


FIGURE 3. Plots of eye positions relative to primary position of patient SF, with chronic left fourth nerve palsy, during fixation of nine target positions with the paretic left eye. (A) Behind view and (B) top view. Note that Listing's planes were of normal thickness, but were rotated temporally in each eye. Axes are described in Figure 2.

clotorsion during upgaze, the eye positions remained restricted to planes and therefore obeyed Listing's law. Thus, in chronic fourth nerve palsy, the abnormality is not that Listing's law fails but that Listing's plane has an abnormal orientation.

Neural Implementation of Listing's law

Listing's law holds during fixation, saccades, and smooth pursuit, but fails during sleep^{16,17} and during vestibulo-ocular reflex (VOR).¹⁸ Its failure shows that the eye muscles are capable of violating Listing's law, and it is therefore not the muscles but the neural commands driving fixation, saccades, and pursuit that constrain the eye to obey the law.^{2,19} The muscles may, however, be arranged in a way that simplifies the brain's work in implementing Listing's law,²⁰⁻²⁶ as in the "active-pulley hypothesis,"²⁵ which says that contraction of the global layer of the extraocular muscles rotates the globe, whereas contraction of the orbital layer displaces the connective tissue sleeves, or pulleys, that direct the paths of the muscles.

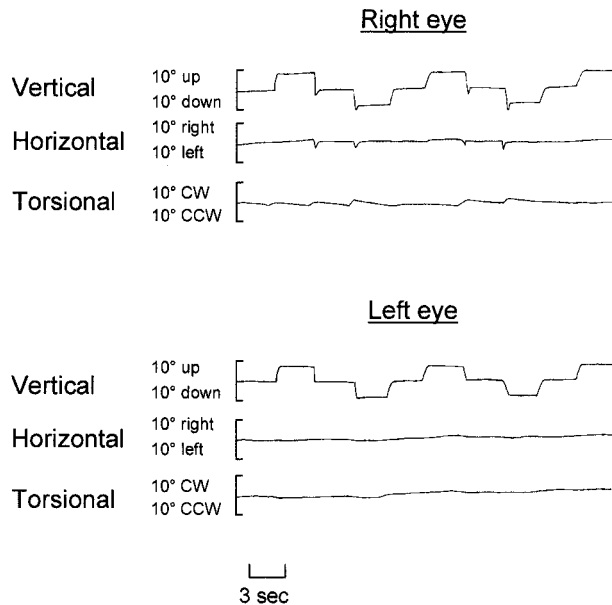
In our patients with acute fourth nerve palsy, Listing's law was violated in the paretic eye during saccades. In patients

with chronic fourth nerve palsy, both eyes obeyed Listing's law, even though the superior oblique in the paretic eye was still markedly weak, as indicated by restricted duction and incomitant hypertropia. This recovery shows that the neural circuitry underlying Listing's law is adaptive, restoring the law despite a palsied muscle. Neural adaptation must work by readjusting the innervations to the remaining extraocular muscles. It may also adjust the pulleys of the horizontal and vertical rectus muscles²⁷ (but not the trochlear pulley, because it is fixed), although, theoretically, Listing's law could be restored with or without a new pattern of pulley placement and motion.

Functional Significance of Listing's law

Chronic fourth nerve palsy has abnormal torsion, as indicated in the temporal shift of Listing's plane, but nonetheless obeys Listing's law. That Listing's law was reestablished in these patients without restoration of normal torsion suggests that there is some advantage to Listing's law that goes beyond any specific set of torsional angles. That is, there is some advantage to keeping the axes of eye rotations in a plane, and the orientation of the plane may not matter so much.

(A) Patient KS - Right acute fourth nerve palsy



(B) Patient SF - Left chronic fourth nerve palsy

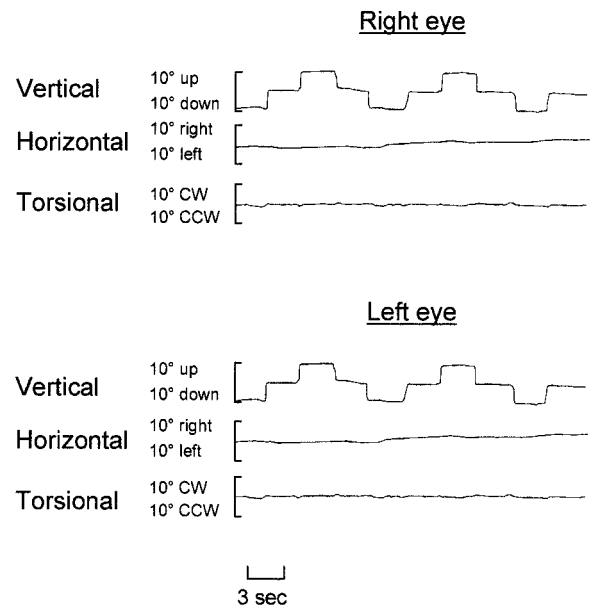


FIGURE 4. (A) Eye positions plotted against time in patient KS with acute right fourth nerve palsy, while the paretic right eye viewed a target that stepped from center to 10° up to center to 10° down. When the target stepped downward, the paretic right eye made hypermetric downward and leftward saccades. Overshoot saccades were each followed by corrective upward and rightward movements. Fast CW eye rotation movements occurred in the paretic right eye, which were each followed by slow, CCW drifts back to initial torsional eye positions. In the nonparetic left eye, vertical saccades were normal in amplitude and direction. (B) Similar tracings for patient SF, who had chronic left fourth nerve palsy, during viewing with the paretic left eye. No overshoot saccades were observed. Rotation of the upper pole of the iris toward the subject's right shoulder was designated CW, whereas rotation of the upper pole of the iris toward the subject's left shoulder was designated CCW.

The functional significance of Listing's law is uncertain. Hering²⁸ and Helmholtz⁴ proposed that it optimizes certain aspects of image flow across the retina, thereby simplifying the neural processing of visual information. Because optical flow depends on the eye's motion relative to space, both theories tacitly assume that the eyes rotates relative to space in the way dictated by Listing's law. But, in fact, it is eye rotation relative to the head that follows Listing's law, whereas, owing to head movement, eye rotation relative to space does not.²⁹⁻³¹ Thus, theories based on optical flow probably do not explain Listing's law.

Fick and Wundt proposed that Listing's law enhances motor efficiency by minimizing eccentricity during motion of the eye.⁴ Minimizing eccentricity during movement may reduce the elastic recoiling force acting on the eye and therefore reduce the work load on the eye muscles, or it may bring the eye the same advantage that staying near the center court brings a squash player, namely swift and flexible responses to incoming stimuli. By ensuring that all gaze shifts toward and away from primary position are made along the shortest path, Listing's law permits quick responses to unpredictable targets that may appear from any direction.

These motor advantages may be regained when Listing's law is reestablished in patients with chronic fourth nerve palsy. After adaptation, the only difference from normal individuals is that primary position, and therefore Listing's plane, is farther temporal. Each of our 11 patients with chronic palsy showed temporal rotation of Listing's plane in both eyes, in contrast to 1 reported patient with nasal rotation in the nonparetic eye.³² This temporal rotation may serve some functional purpose, or it may be an unavoidable consequence of the palsy. The inferior rectus attempts to compensate for the deficits of the palsied superior oblique, causing abnormal excyclotorsion on downgaze, and so rotating Listing's plane in the paretic eye.

The temporal rotation of Listing's plane of the nonparetic eye can be explained by a conjugate increase in activity of the inferior rectus of the nonparetic eye.

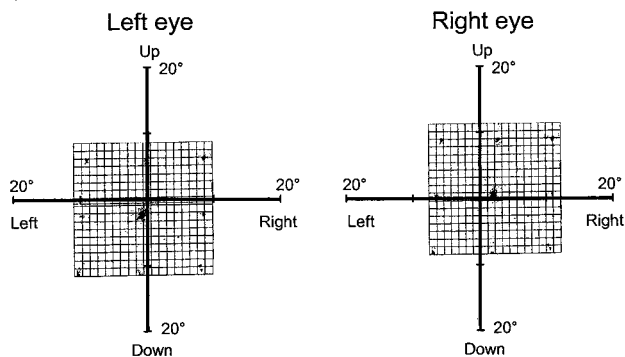
Transient Torsional Deviations in Acute Fourth Nerve Palsy

Abnormal torsional deviations have been reported in patients with medullary and cerebellar lesions. Torsional pulsion of saccades (torsionpulsion), consisting of torsional fast eye movements away from the side of lesion (from examiner's viewpoint), induced during saccades downward or away from the side of lesion, has been recorded in patients with lateral medullary infarction.³³ Torsional blips, consisting of torsional fast eye movements followed by slow exponential drifts in the opposite direction during horizontal and vertical saccades, were observed in a patient with infarction of the dorsolateral medulla and cerebellum.³⁴ Damage to the medulla and the cerebellum may disturb the neural commands that normally prevent or correct torsional deviations during saccades.

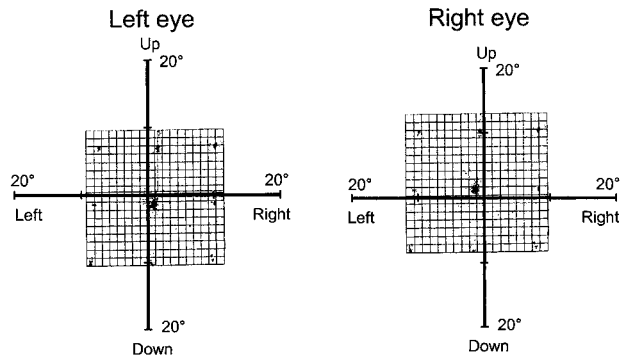
We found that in acute fourth nerve palsy, both Listing's and Donders' laws failed during saccades, but the eye then drifted back into Listing's plane during steady fixation. This behavior indicates a pulse-step mismatch. In normal saccades, a pulse of innervation, consisting of a high-frequency burst of phasic activity in the agonist motoneurons drives the eye rapidly to its target.^{35,36} Once the eye has reached its target, agonist motoneurons assume a new, higher-than-resting level of tonic innervation, constituting saccadic step of innervation, which holds the eye in its new position.^{35,36} If the pulse drives the eye to some position that does not correspond to the step command, a pulse-step mismatch occurs, so that the eye drifts, after every saccade, to a position dictated by the step command.

Acute right fourth nerve palsy (KS)

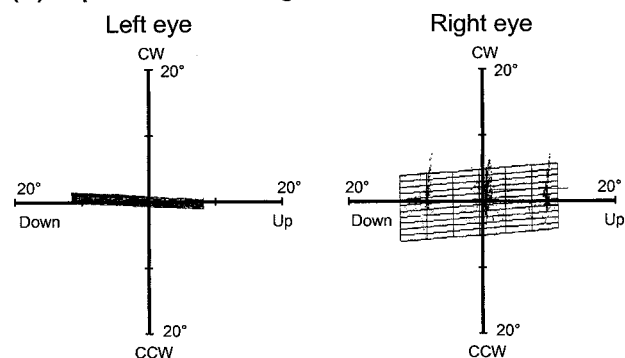
(A) Behind View – including corrective movements



(C) Behind View – excluding corrective movements



(B) Top View – including corrective movements



(D) Top View – excluding corrective movements

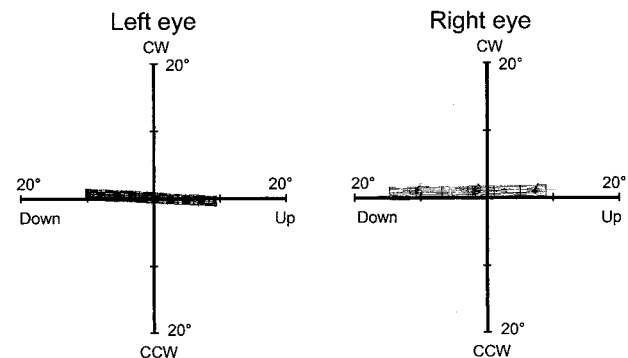


FIGURE 5. Plots of eye positions relative to primary position of a patient (KS) with acute right fourth nerve palsy, during viewing with the paretic right eye. When we fit a Listing's plane that *included* the corrective movements that followed each overshoot saccade, the thickness of Listing's plane was abnormal in the paretic right eye, but normal in the nonparetic left eye. (A) Behind view. (B) Top view. When we fit a Listing's plane *excluding* the corrective movements—that is, by fitting positions of the paretic eye that occurred more than 1.5 seconds after the saccade offset—the thickness of Listing's plane in the paretic right eye returned to normal. (C) Behind view. (D) Top view. Note that the orientation of this Listing's plane, measured after the corrective movements were excluded, was also normal. Axes are described in Figure 2.

In peripheral nerve palsy, both the burst neurons and the neural integrator are presumed to be normal, generating the correct pulse and step commands, which are sent to the peripheral nerve. We postulate that peripheral nerve damage affects the normal transmission of these commands to motoneurons, resulting in a pulse-step mismatch. There are several ways a nerve lesion might cause pulse-step mismatch: (1) The damaged nerve might be unable to transmit the high firing rates seen during the pulse; (2) it may be unable to respond to the rapid changes in firing rate at the start and the end of the pulse (that is, acting as a low-pass filter), distorting its temporal shape; or (3) it may alter the balance of forces among the muscles, perhaps repositioning the muscle pulleys. Whatever the mechanism, our findings show that in patients with acute fourth nerve palsy, phasic neural activity drove the eye into abnormal torsional angles, but the sustained step command specified a torsional position in Listing's plane. During saccades, both Listing's and Donders' laws failed, but afterward, during fixation, both laws were restored as the eye drifted back into Listing's plane.

On the basis of this finding, we can predict similar deficits in other eye movements in acute fourth nerve palsy. During saccades between tertiary positions, we would expect larger violations of Listing's and Donders' laws than we found in the largely radial movements, to and from the center, in the current study, because nonradial movements involve more torsional velocity, and therefore provide more opportunity for torsional pulse-step mismatch. We would also expect violations of both laws during pursuit, especially in tertiary posi-

tions, but these violations should be slight, because pursuit is slower than saccades, and the velocity commands that drive the eye out of Listing's plane are therefore smaller, and eye motion is dominated by the position commands. Similarly, we would expect the VOR to rotate the eyes about axes that tilt in an abnormal way as a function of eye position, with larger effects at higher speed of rotation.^{18,37}

APPENDIX

We used the angular position vector \mathbf{q} and the angular velocity vector $\boldsymbol{\omega}$ for describing eye position and velocity. Details of these representations and the algorithms for computing them from search coil signals are described previously.¹¹

The angular position vector \mathbf{q} (actually the vector part of the quaternion for that position) expresses the 3-D orientation of the eye in terms of its rotational displacement from some reference position—usually the primary position. The vector lies along the axis of the rotation according to the right-hand rule; its length is $\sin(a/2)$, where a is the amplitude of the rotation. The component q_T indicates the amount of rotation away from reference position in the clockwise direction (i.e., around a forward-pointing axis); q_V is the downward component and q_H is the leftward component.

To quantify adherence to Listing's law, we fitted \mathbf{q} to a plane by approximating the torsional component of \mathbf{q} , q_T , with an affine, or first-order polynomial, function of the vertical and horizontal components, q_V and q_H

$$q_T = f + f_V q_V + f_H q_H \quad (1)$$

To quantify adherence to Donders' law, we fitted \mathbf{q} to a quadratic surface instead of a plane, by approximating q_T with the second-order function

$$q_T = f + f_V q_V + f_H q_H + f_{VV} q_V^2 + f_{VH} q_V q_H + f_{HH} q_H^2 \quad (2)$$

and the third-order function

$$q_T = f + f_V q_V + f_H q_H + f_{VV} q_V^2 + f_{VH} q_V q_H + f_{HH} q_H^2 + f_{VVV} q_V^3 + f_{VVH} q_V^2 q_H + f_{VHH} q_V q_H^2 + f_{HHH} q_H^3 \quad (3)$$

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