
Internuclear ophthalmoplegia: recovery and plasticity

M. J. Doslak, L. B. Kline, L. F. Dell'Osso, and R. B. Daroff

We studied reflexional eye movements of a patient during the gradual resolution of an internuclear ophthalmoplegia (secondary to head trauma) in an attempt to determine the relative contributions of both medial longitudinal fasciculus (MLF) recovery and secondary central plastic changes. Adduction-reflexional eye movements in the affected eye consisted of an initial fast (saccadic) portion followed by a slow drift toward the new intended eye position. The fast and slow components of the movements reflected, respectively, the pulse and step increases in neural innervation. Shortly after the traumatic insult, the affected eye exhibited low adduction gain (pulse gain 0.34; step gain 0.37) and slow saccades with peak velocities of 55% and durations of 278%, normalized for achieved, rather than intended, amplitudes. Several months later the pulse and step gains, peak velocities, and durations of the saccades improved to 0.81, 0.92, 87%, and 146%, respectively. The increased gains and faster velocity were accomplished by increases in the firing frequency of the pulse and step, reflecting recovery of MLF axons, rather than saccadic system plasticity, which would have resulted in increased duration of the saccadic pulse.

Key words: internuclear ophthalmoplegia, ophthalmoplegia, eye movements, plasticity, recovery

Internuclear ophthalmoplegia (INO) designates impairment of versional (saccadic, pursuit, and vestibulo-ocular) adduction secondary to a lesion in the ipsilateral medial longitudinal fasciculus (MLF) between the sixth and third cranial nerve nuclei.¹ Convergence is usually intact, and the opposite, abducting eye demonstrates horizontal nystagmus. Strictly speaking, INO should refer to cases

in which there is absolute inability to cross the midline in a versional adduction, and the term internuclear ophthalmoparesis should describe those cases where adduction past the midline occurs but is impaired. The impairment, ranging from mild to marked, consists of decreased velocity and usually amplitude limitation. An acute INO from almost any cause (brainstem neoplasm being the usual exception) often improves with time, sometimes completely. The characteristics of such improvement have never been documented by sequential quantitative eye movement recording, so that it is uncertain as to whether the improvement represents enhanced MLF axonal conduction (recovery) or plastic alterations within central nervous system firing patterns in response to the MLF lesion (plasticity). Such a distinc-

From the Ocular Motor Neurophysiology Laboratory, Miami Veterans Administration Medical Center, and the Departments of Ophthalmology and Neurology, University of Miami School of Medicine, Miami, Fla. Supported in part by U.S. Public Health Service grant IT 32EY-07021-04.

Submitted for publication Oct. 9, 1979.

Reprint requests: L. F. Dell'Osso, Ph.D., Neurology Service (127A), V. A. Medical Center, Cleveland, Ohio 44106.

tion could be made with quantitative oculography, and we attempted this during the recovery of an INO following head trauma.

Case report

A 13-year-old boy struck the right side of his head on the trunk of a tree while swinging on a rope. He was unconscious for approximately 15 sec and, upon recovery, complained of dizziness and horizontal diplopia. When examined 1 hr after the accident, he was alert, oriented, and cooperative. Neurological examination revealed no abnormalities except for extraocular movements. His eyes were straight in primary position. Gaze to the right and downward appeared full, conjugate, and without nystagmus. There was a small-amplitude upward-beating nystagmus on sustained up-gaze. On leftward gaze, there was absolute inability to adduct the right eye beyond the midline to all versional stimuli. The left eye fully abducted but had sustained left-beating nystagmus. Both eyes converged normally. The clinical impression was a right INO.

Skull x-rays and computerized tomography scan were normal. The patient was hospitalized for 5 days of observation. He was then re-examined as an outpatient 12 days after the accident, when the first eye movement recording was performed.

Methods

Horizontal eye movements from both eyes were recorded with infrared oculography. The full-system bandwidth was DC to 100 Hz. Eye velocity was determined by electronically differentiating the eye position signal. The patient was seated at the center of a 1.14 m radius arc in a modified dental chair with chin rest and head brace. He refixated between red light-emitting diodes located on the arc. The refixations were from center to right (15°, 20°, or 25°), to left (15°, 20°, or 25°), and back to center.

This examination was performed initially 12 days after the accident and again 5 weeks and 18 weeks after the event. Saccadic peak velocities and durations were measured and related to both total saccadic amplitudes and amplitudes of the pulse portion of the saccade. Initially, the saccadic pulse durations and pulse amplitudes were determined from the tracings of the adduction saccades. However, since the adduction movement results from a pulse-step of innervation distorted by the MLF lesion, a better method of estimating true brainstem pulse duration and, from that, pulse ampli-

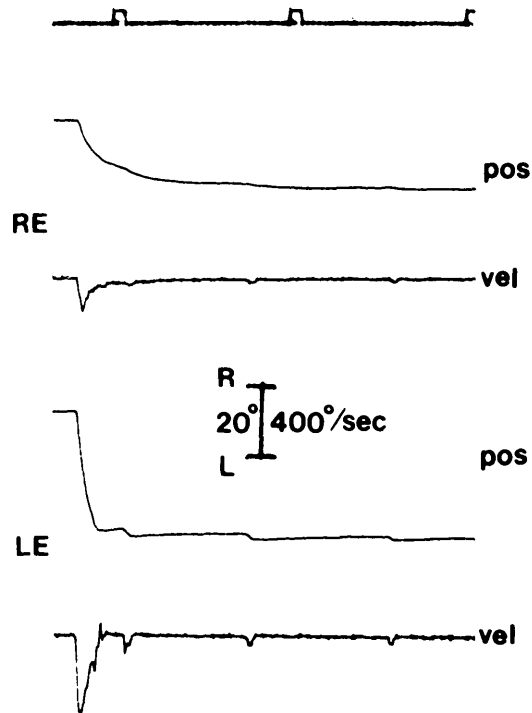


Fig. 1. Refixational movements 12 days after the accident (adducting eye viewing). The position traces started at 15° to the right. Timing marks were at 1 sec intervals. RE, right eye; LE, left eye; pos, eye position; vel, eye velocity.

tude was devised from the pulse duration of the yoked abducting eye, determined from its velocity trace. The motion of the abducting eye reflects the duration of the innervating pulse, regardless of the accuracy of the saccade.

Results

Ocular motility recordings indicated that the velocity of the left eye in adduction was slightly slowed compared to the yoked right eye in abduction, indicating a subtle left INO that was not clinically detected. We have restricted our data analysis and discussion to contralateral movements of the more dramatic right INO; the recovery pattern was analogous in the less evident left INO.

Between the immediate postaccident period and the initial oculographic examination, the right INO had improved somewhat. Although adduction past the midline was impossible 1 hr after trauma, the patient was

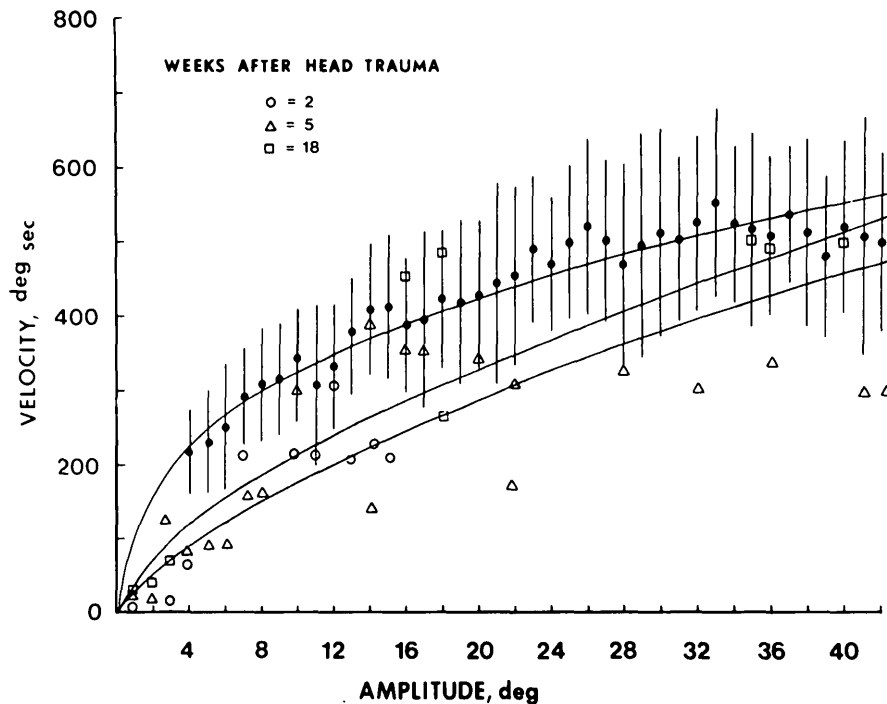


Fig. 2. Peak velocity vs. total saccadic amplitude of eye movements, illustrating normal values and patient data from the three recording sessions conducted over a period of approximately 4 months. The normal values are indicated by filled circles and their regression curve; the error bars are standard deviations. The lowest and the center solid curves are linear regressions utilizing power function relationships of the patient data at 5 and 18 weeks, respectively, after the accident.

able to adduct the right eye to 10° past the midline 12 days later. The velocity of the adducting right eye was slow, and the left eye had abduction nystagmus (Fig. 1). The saccadic adduction in the right eye consisted of an initial fast (pulse) portion followed by a slow drift toward the intended eye position (Fig. 1). The velocity-amplitude relationship determined by plotting peak velocities of the saccades against total amplitudes of the eye movements was lower than normal (Fig. 2).

Five weeks after the accident, the patient was able to adduct the right eye to 20° past the midline (Fig. 3). The velocity of adduction in the right eye had increased since the previous recording but was still abnormally slow (Fig. 2).

Eighteen weeks after the accident, the patient was able to adduct the right eye fully, and there was no nystagmus of the abducting

eye (Fig. 4). Adduction velocity was nearly normal (Fig. 2).

The waveform of the abnormal versional adduction consisted of an initial saccade followed by a slower (glissadic) portion.² In Fig. 2, we plotted the peak velocity of the saccade against the total amplitude of the movement which included both the fast and slow portions. After separating the segments of the eye movement (Fig. 5), we then plotted the peak velocity of the initial pulse segment (S'_p) against amplitude for the three testing sessions (Fig. 6, dashed lines). The velocities were subnormal on the first test (12 days) as expected but appeared "supranormal" near the end of the recovery period (18 weeks). This perplexing finding prompted us to redefine saccadic parameters based upon analysis of the saccades of the yoked normal eye from which we derived true pulse duration

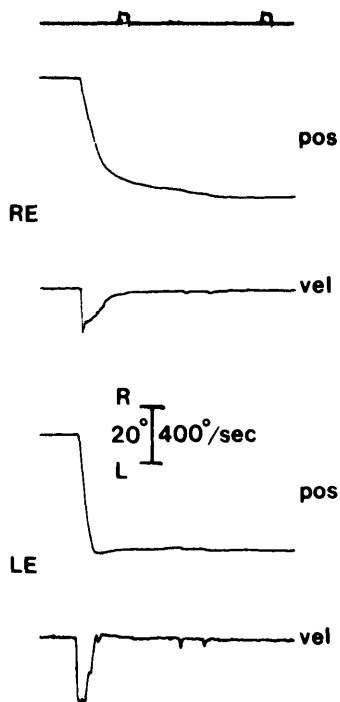


Fig. 3. Eye movements 5 weeks after the accident (adducting eye viewing). The position traces start at 20° to the right. For abbreviations see legend to Fig. 1.

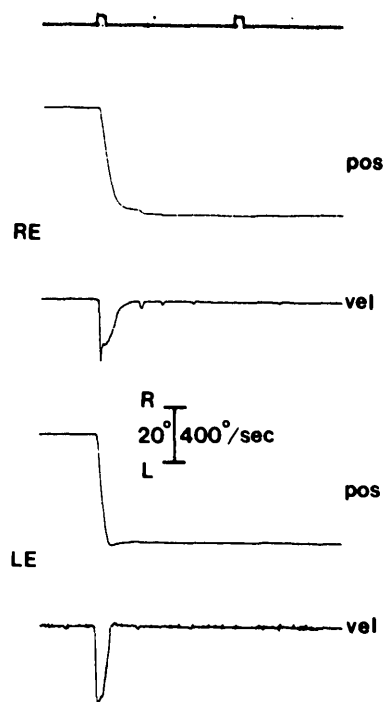


Fig. 4. Eye movements 18 weeks after the accident (adducting eye viewing). The position traces start at 20° to the right. For abbreviations see legend to Fig. 1.

(Fig. 7). In addition to providing true pulse duration, the velocity trace of the abducting eye showed evidence that it, too, was affected by the INO; it was bimodal. These new peak velocities related to the true saccadic pulse amplitudes (S_p) shown in solid lines in Fig. 6 were initially slow (55%)³ and gradually improved to approximately 87% of normal near the end of the recovery period. The normalized pulse duration (PD) decreased from 278% to 140% and 146% of normal value⁴ (Fig. 8). The pulse gain (the fraction of the intended eye displacement achieved by the pulse increase of neural innervation) and step gain (the fraction achieved by the pulse and the step) improved from 0.34 and 0.37 to 0.81 and 0.92, respectively, in conjunction with the peak velocity improvements.

Discussion

Central nervous system adaptation to a peripheral paresis is accomplished by pro-

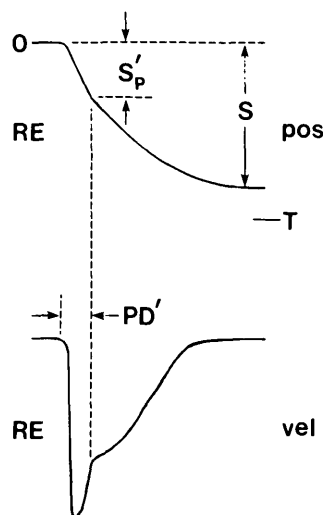


Fig. 5. Illustration of key parameters used in the initial analysis of the paretic eye data. S'_p , saccadic pulse amplitude; S , total saccadic amplitude; PD' , apparent neural pulse duration obtained from the velocity recording of the affected eye; T , target position. For other abbreviations see legend to Fig. 1.

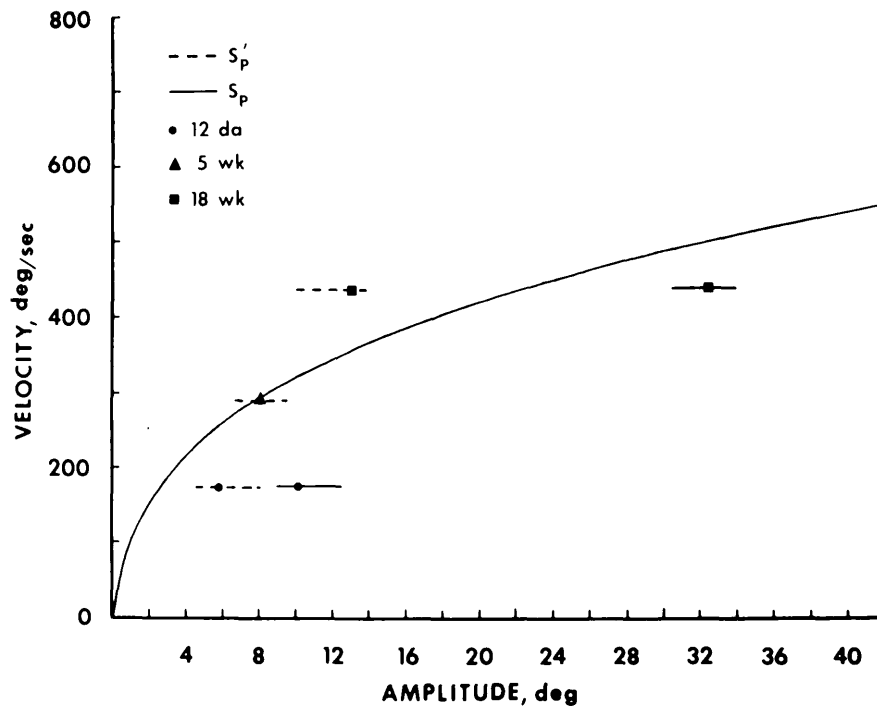


Fig. 6. Averages of peak velocity vs. saccadic pulse amplitude (S'_p and S_p) from the three patient tests compared to normal (solid curve). Amplitude means (symbols) and ranges (line segments) are indicated. The sample sizes and standard errors for the 12 day, 5 week, and 18 week data are (6, 6.6), (11, 7.6), and (9, 4.7), respectively.

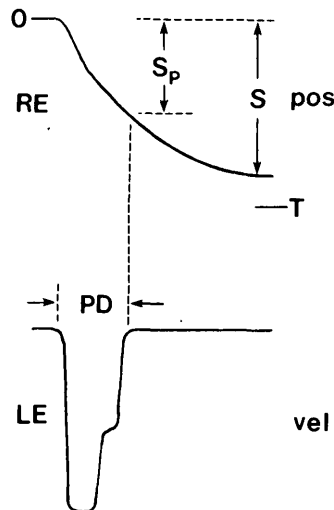


Fig. 7. Illustration of key parameters used in the revised analysis of the paretic eye data. The top trace is the paretic eye position; the bottom trace is the normal eye velocity. S_p , saccadic pulse amplitude; S , total saccadic amplitude; PD , actual neural pulse duration obtained from the velocity recording of the normal eye; T , target position. For other abbreviations see legend to Fig. 1.

longed duration of the brainstem pulse of increased firing frequency that triggers a saccadic eye movement rather than an actual increase in the frequency of spikes.⁵ We studied refixational eye movements over a period of several months during the gradual resolution of a unilateral INO in an attempt to determine the relative contributions of both central plastic changes secondary to the injury and MLF recovery. Adduction-refixational eye movements in the affected eye consisted of an initial fast (pulse) portion followed by a slow drift toward the new intended eye position. The two components of the movements reflected, respectively, the pulse and step increases in neural innervation. In the early stage of the study (i.e., 12 days after trauma), the affected eye exhibited low adduction gain (pulse gain 0.34; step gain 0.37) and slow saccades with normalized peak velocities of 55% and durations of 278% (normalized for achieved rather than intended saccadic amplitudes). The long pulse durations probably reflected central nervous

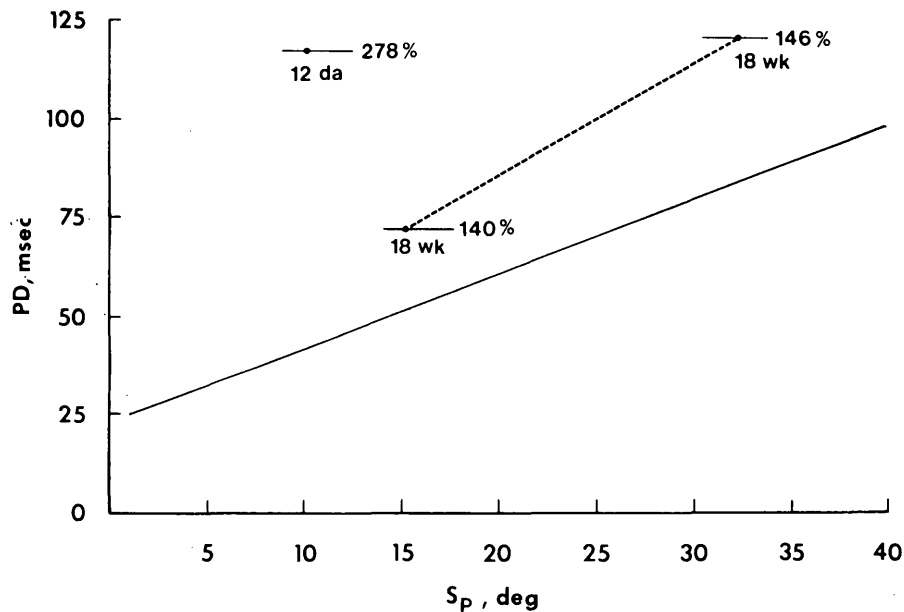


Fig. 8. Averages of pulse durations (PD) vs. saccadic pulse amplitude (S_p) from the first and last patient recording compared to normal (solid line). Amplitude means (filled circles) and ranges (line segments) are indicated. The sample sizes and standard errors for the 12 day and 18 week (low and high amplitude) data are (6, 3.7), (8, 2.5) and (9, 3.2), respectively.

system adaptation⁵; the bimodal nature of the pulse, inferred from the velocity traces of the abducting eye (Fig. 7), was also presumed to represent neural plasticity. The bimodal velocity pulse apparently results from two closely spaced pulses of firing frequency. In the abducting eye the first drives the eye through most of its excursion, and the second completes the movement. Thus the innervation of the "normal" left eye has been affected by the right MLF impairment⁶ and the resultant plastic changes. Equal-duration innervating pulses are reduced and distorted by the MLF lesion on their way to the yoked adducting eye, causing a much reduced movement which is completed by a glissade. Several months later the pulse and step gains, normalized peak velocities, and normalized durations of the saccades improved to 0.81, 0.92, 87%, and 140% to 146%, respectively.

We conclude that the increased gains, associated with faster velocities, were accomplished by recovery of MLF axons reflected in their enhanced ability to conduct higher-frequency activity. There was, indeed, initial

plastic adaptation (evidenced by the 278% normalized pulse duration) and readaptation (evidenced by its return nearer to normal (140% to 146%) as the INO recovered). The shorter time constant of plastic changes (approximately 1 day)⁵ allowed return of saccadic gain toward normal as the recovery took place at a much slower rate (18 weeks):

REFERENCES

1. Cogan DG: Internuclear ophthalmoplegia, typical and atypical. *Arch Ophthalmol* 84:583, 1970.
2. Dell'Osso LF, Robinson DA, and Daroff RB: Optokinetic asymmetry in internuclear ophthalmoplegia. *Arch Neurol* 31:138, 1974.
3. Schmidt D, Abel LA, Dell'Osso LF, and Daroff RB: Saccadic velocity characteristics: intrinsic variability and fatigue. *Aviat Space Environ Med* 50:393, 1979.
4. Troost BT and Daroff RB: The ocular motor defects in progressive supranuclear palsy. *Ann Neurol* 2:397, 1977.
5. Abel LA, Schmidt D, Dell'Osso LF, and Daroff RB: Saccadic system plasticity in humans. *Ann Neurol* 4:313, 1978.
6. Pola J and Robinson DA: An explanation of eye movements seen in internuclear ophthalmoplegia. *Arch Neurol* 33:447, 1976.