# Internuclear ophthalmoplegia: MR-anatomic correlation.

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# Internuclear Ophthalmoplegia:
## MR-Anatomic Correlation

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**Internuclear ophthalmoplegia is a gaze disorder characterized by impaired adduction on the side of a lesion involving the medial longitudinal fasciculus with dissociated nystagmus of the abducting eye. Eleven patients with internuclear ophthalmoplegia (nine with clinical multiple sclerosis, two with clinical infarction) underwent MR imaging with spin-echo techniques on a 1.5-T system. Nine patients also had CT. MR showed focal or nodular areas of high signal intensity on T2-weighted images in the region of the medial longitudinal fasciculus in 10 of 11 patients. In one of four patients with internuclear ophthalmoplegia who had MR after intravenous gadolinium-DTPA, an enhancing ring lesion was seen in the region of the medial longitudinal fasciculus on short TR/TE images, indicating active blood-brain-barrier disruption, which correlated with this patient's recent-onset internuclear ophthalmoplegia. CT failed to show the lesions in all nine patients examined. This report demonstrates the superiority of MR in evaluating gaze disorders attributable to brainstem dysfunction, such as internuclear ophthalmoplegia, and correlates MR findings with the relevant neuroanatomy of the medial longitudinal fasciculus.**

Internuclear ophthalmoplegia (INO) is a disorder of eye movement, classically characterized by impaired adduction on the side of a lesion involving the medial longitudinal fasciculus (MLF) with dissociated nystagmus of the abducting eye (Fig. 1) [1, 2]. In young patients, this syndrome is most commonly caused by multiple sclerosis (MS) [1, 3–6]; in fact, INO is the most common oculomotor manifestation of MS [3]. The same eye-movement disorder in an older age group is usually attributed to cerebrovascular disease. MR is a highly sensitive imaging technique for detecting MS plaques [7–10], and it has become the technique of choice for evaluating suspected brainstem disease [11–13]. MR is thus ideally suited to evaluate gaze disorders, such as INO [14, 15]. This report describes the MR findings in 11 patients with INO and correlates these findings with the relevant neuroanatomy of the MLF.

### Subjects and Methods

Eleven patients (eight women, three men; ages 18–80 years) with INO were evaluated with MR. Nine of the 11 were also evaluated with CT, which was performed on a high-resolution scanner (GE 9800) using 5-mm contiguous axial sections through the brainstem in all cases. Two patients had noncontrast CT only. Seven patients had high-iodine CT with intravenous infusion of 88.1 g/l. MR was performed with spin-echo techniques on a GE 1.5-T Signa scanner. Spin-echo images were obtained by using repetition time (TR) = 600 msec with echo time (TE) = 20–25 msec (short TR/TE), and TR = 2000–2500 msec with TE = 20–80 msec (short–long TE). Four patients had MR performed both before and after intravenous gadolinium (Gd)-DTPA (0.1 mmol/kg). MR images were obtained in axial, coronal, and sagittal planes.

Four of 11 patients had a clinical diagnosis of "definite MS" on the basis of the presence of clinical signs and symptoms localized to at least two anatomic regions of the CNS and a

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course of relapses and remissions separated by at least 1 month [16]. Five other patients had a clinical diagnosis of "probable MS" [16]. Two patients were diagnosed as having had infarctions. Of the nine patients with definite or probable clinical MS, six had bilateral INO and three had unilateral INO. The two patients with infarctions both had unilateral INO.

## Results

CT did not detect brainstem abnormalities in the region of the MLF in any of the nine patients so examined. By MR, however, the brainstem was seen as abnormal in 10 of 11 patients. In these cases, long TR images showed focal or nodular regions of high signal intensity in the area of the MLF (Figs. 2–5). In all 11 cases, short TR/TE images without Gd-DTPA failed to show the lesion. In one of four patients who had post-Gd-DTPA MR, an enhancing ring lesion was shown on post-Gd-DTPA short TR/TE images at the pontomesencephalic junction posteriorly (Fig. 6). In one patient with clinically diagnosed infarction, no lesion was detected on MR.

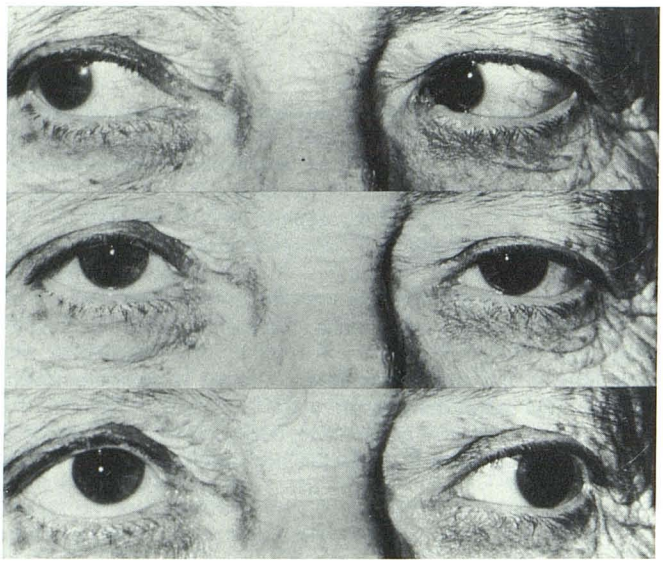

**Fig. 1.—Eye movements in unilateral (right) internuclear ophthalmoplegia. Note inability of right eye to fully adduct on leftward gaze (*bottom*).**

## Discussion

The MLF is a dorsally situated bundle of fibers arising from brainstem vestibular nuclei that ascends on either side of midline to project primarily on nuclei controlling the extraocular muscles (Figs. 7, 8). The MLF also carries various descending tracts, mainly arising from the pontine reticular formation, the medial vestibular nucleus, the interstitial nucleus of Cajal (an accessory oculomotor nucleus), and the superior colliculus. Fibers descend as far as the thoracic cord [17]. The nucleus of the sixth cranial nerve, in the inferior aspect of the dorsal pons, sends axonal connections across the midline that ascend via the MLF to synapse on third-nerve nucleus motorneurons in the midbrain, at the level of the superior colliculi (Fig. 9) [17, 18]. Lesions in the MLF in this region, between the abducens and contralateral oculomotor nuclei, result in INO.

Clinical deficits caused by MLF lesions depend upon the precise anatomic site of the lesion. Generally, rostral lesions that involve the oculomotor nucleus may result in impaired convergence, whereas more caudally located lesions do not [19]. Bilateral MLF involvement has traditionally been highly suggestive of MS, whereas unilateral MLF lesions are often vascular in origin [1, 3, 4, 20]. However, unilateral INO is

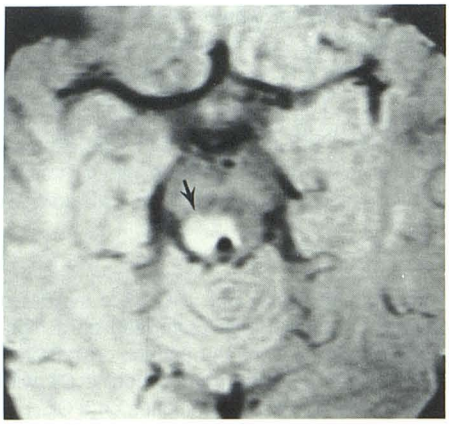

**Fig. 2.—Axial MR scan (TR = 2500, TE = 30 msec) in patient with multiple sclerosis and bilateral internuclear ophthalmoplegia. Note large focus of high signal intensity in posterior midbrain (*arrow*) that encircles periaqueductal region and extends from region of right medial longitudinal fasciculus (MLF) to also involve left MLF.**

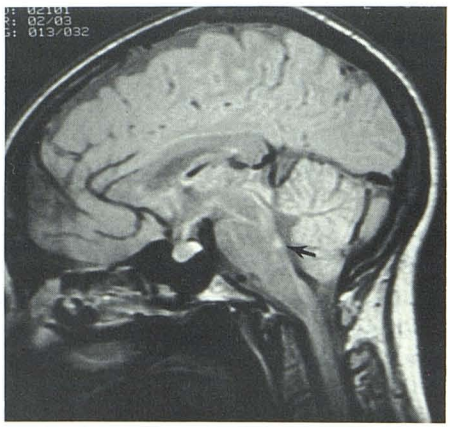

**Fig. 3.—Sagittal MR scan (TR = 2500, TE = 30 msec) in patient with multiple sclerosis and internuclear ophthalmoplegia. High-signal-intensity lesion (*arrow*) in medial longitudinal fasciculus at level of mid-pons.**

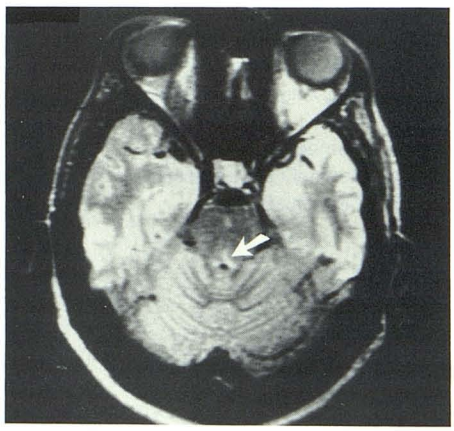

**Fig. 4.—Axial MR scan (TR = 2500, TE = 20 msec) in patient with infarction and left internuclear ophthalmoplegia. Nodular region of high signal intensity just left of midline involves left medial longitudinal fasciculus (*arrow*).**

Fig. 5.—Sagittal MR scan (TR = 2500, TE = 80 msec) in patient with infarction and internuclear ophthalmoplegia. Lesion (*arrow*) in midbrain at level of medial longitudinal fasciculus entering area of third nerve nucleus.

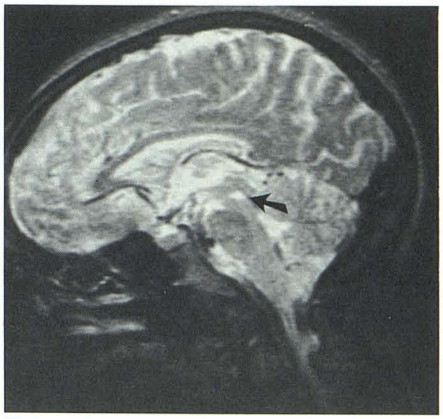

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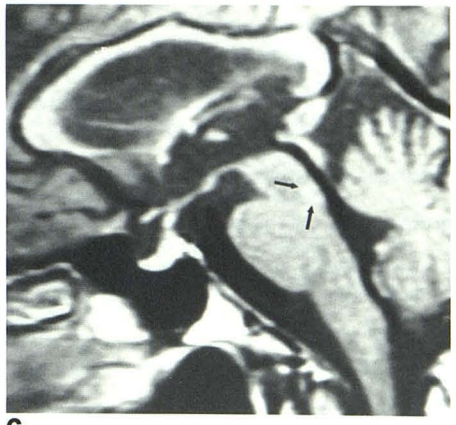
Fig. 6.—Sagittal MR scan (TR = 600, TE = 25 msec), after Gd-DTPA, in patient with recent-onset internuclear ophthalmoplegia and multiple sclerosis. Ring area of enhancement (*arrow*) involving medial longitudinal fasciculus at pontomesencephalic junction representing area of active blood-brain-barrier disruption.



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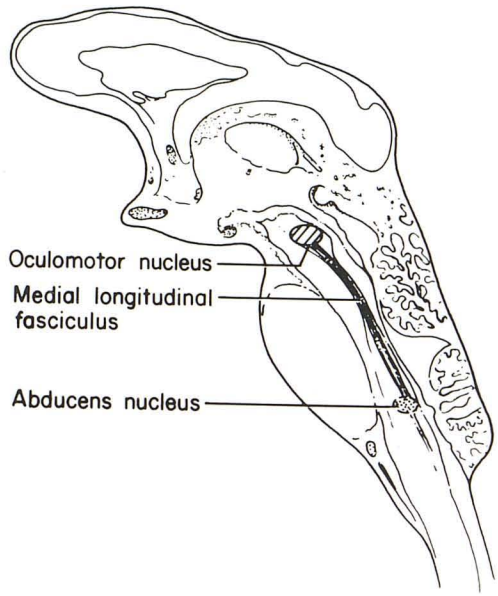


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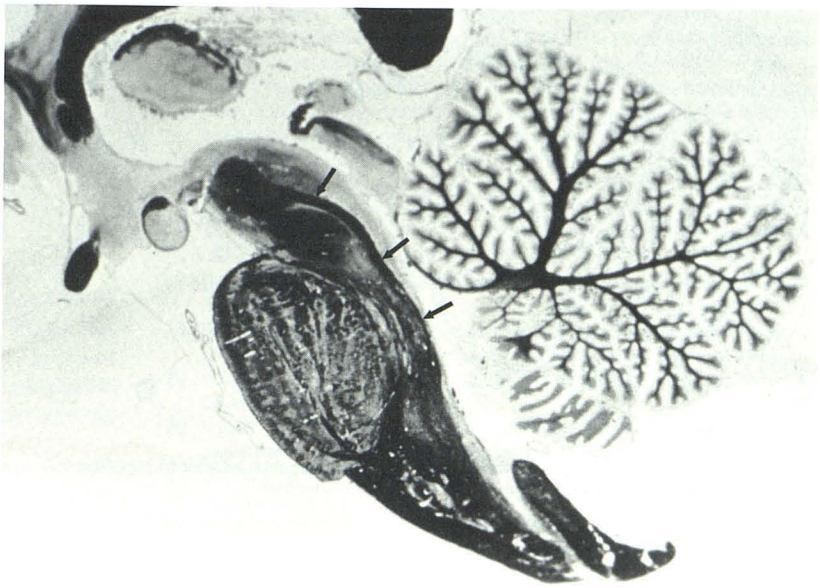

B

Fig. 7.—Sagittal anatomy of medial longitudinal fasciculus.
*A*, Artist's conception.
*B*, Necropsy specimen, myelin stain. The medial longitudinal fasciculus (*arrows*) ascends from abducens nucleus to oculomotor nucleus in dorsal aspect of brainstem.

common in MS and was present in three of nine MS patients in our series, corroborating other authors' experience in larger series [6]. A list of causes of INO is presented in Table 1 [19]. Most INOs improve spontaneously, but some patients with advanced MS are left with permanent neurologic deficit [21].

In our series, MR was highly sensitive (10 of 11 cases) in detecting clinically suspected lesions in the region of the MLF. Long TR spin-echo pulse sequences were superior for showing these lesions, which appeared as focal or nodular areas of high signal intensity. These focal abnormalities must be distinguished from the frequently present "pseudo-MLF hyperintensity"—a thin, strictly midline, linear area of hyperintensity just anterior to the aqueduct and fourth ventricle in normal patients (Fig. 10). The origin of this potentially confusing region of hyperintensity remains uncertain, although it may be normal signal from the gray-matter nuclei of the median raphe. In contradistinction, true MLF lesions are nodular, more prominent, and slightly off the midline, corresponding to the paramedian anatomic site of the MLF. CT was of no value in detecting these lesions.

In one of four patients with INO who had Gd-DTPA MR, an enhancing lesion in the MLF was shown on short TR/TE images indicating active blood-brain-barrier disruption [22–24]. This corresponded to the fact that this patient had recent-onset INO. The three other patients whose scans did not

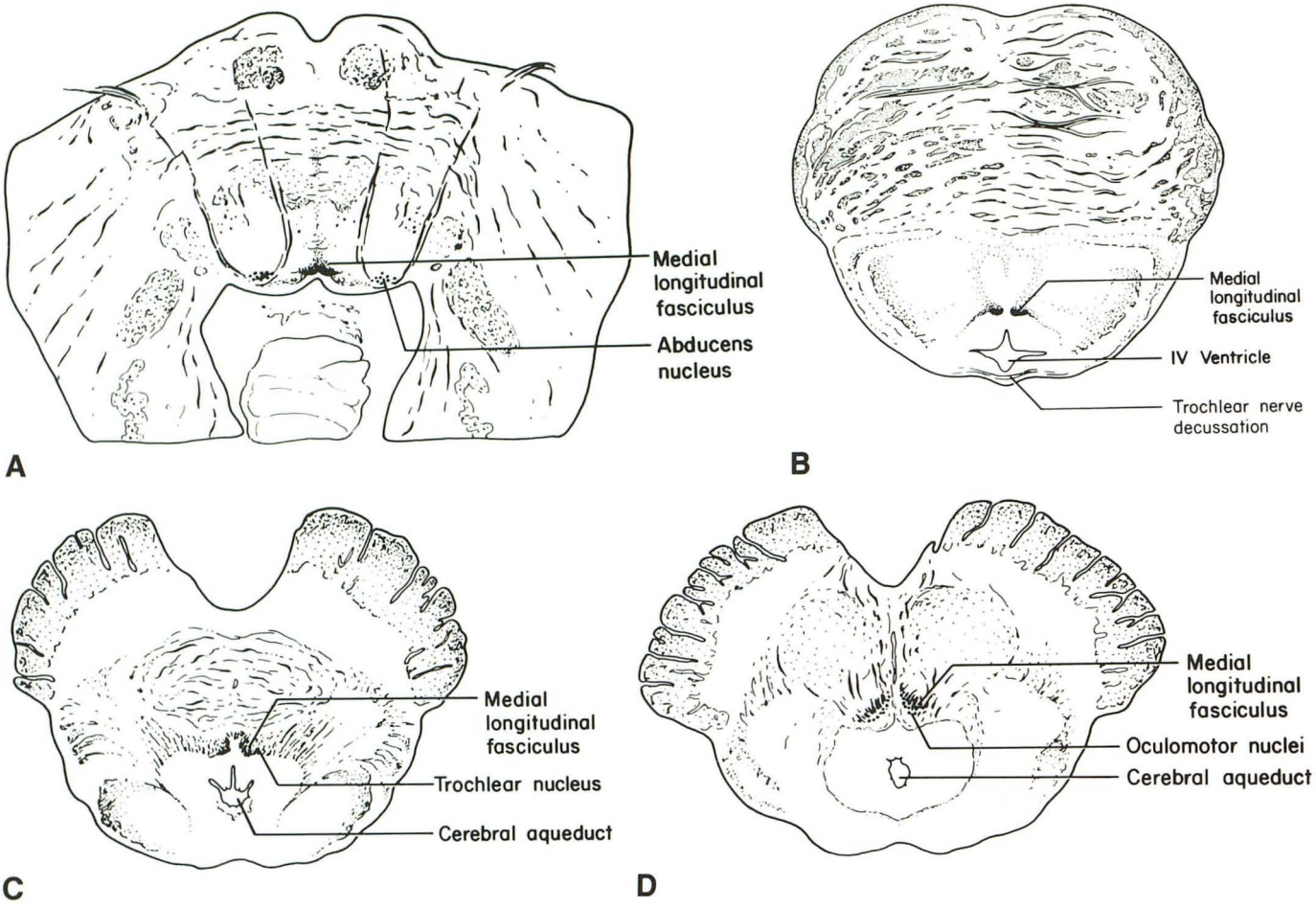


Fig. 8.—*A–D*, Axial anatomy of medial longitudinal fasciculus, inferior to superior, lower pons to midbrain (modified from [17]). Note paramedian location of medial longitudinal fasciculus in dorsal aspect of brainstem.

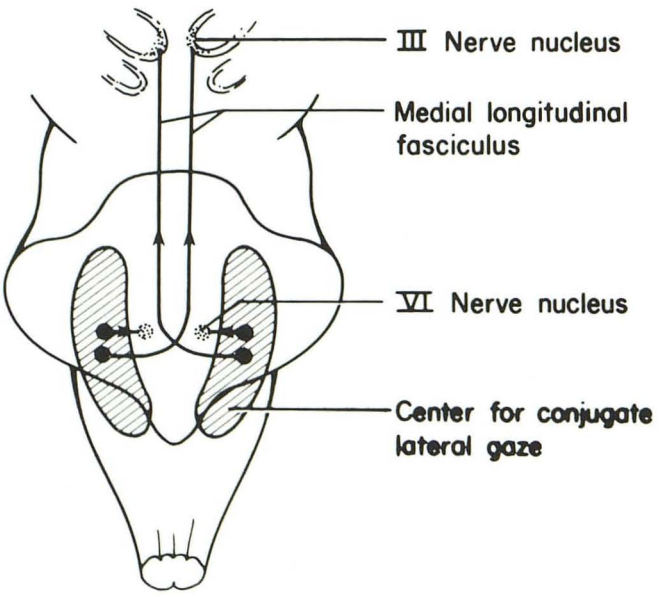


Fig. 9.—Coronal schematic view of medial longitudinal fasciculus pathways (modified from [3]). Decussation of medial longitudinal fasciculus is depicted in relation to sixth and third nerve nuclei.

**TABLE 1: Origins of Internuclear Ophthalmoplegia**

| |
|---|
| Demyelinating disease (MS) |
| Infarction |
| Hematoma |
| Mass effect |
| Trauma |
| Infection (i.e., encephalomyelitis) |
| Neoplasm |
| Radiation |
| Drugs (phenothiazines, tricyclic antidepressants) |
| Chiari malformation with syringobulbia |
| Wernicke's encephalopathy |
| Metabolic disorders (hepatic encephalopathy) |
| Degenerative disorders (progressive supranuclear palsy) |
| Syphilis |

show Gd-DTPA enhancement of their MLF lesion were clinically stable and had unchanged INO for months. In our experience, Gd-DTPA has been useful in detecting clinically active lesions (i.e., correlating to symptoms or signs of recent onset) on MR in patients with MS [22].

In conclusion, we suggest that MR is the technique of choice for evaluating gaze disorders attributable to brainstem

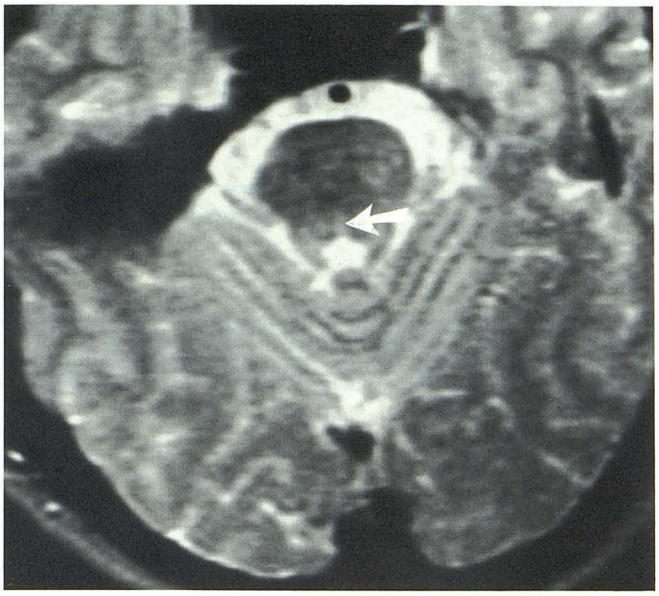

**Fig. 10.—Axial MR scan (TR = 2500, TE = 80 msec), "pseudomedial longitudinal fasciculus hyperintensity" in normal volunteer. Thin, strictly midline linear area of high signal intensity (*arrow*) should not be confused with lesion in medial longitudinal fasciculus.**

dysfunction, such as INO. The presence of additional lesions (i.e., multiple high-signal-intensity periventricular white-matter lesions), in combination with clinical information, may suggest the origin of such gaze disorders. Specific neuroanatomic sites of abnormality predicted by clinical evaluation can be documented and correlated to MR.

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