Reflex vertical gaze and the medial longitudinal fasciculus

L. R. Jenkyn, G. Margolis, and A. G. Reeves

From the David Prosser Neurology Research Laboratory, Division of Neurology, Department of Medicine, Dartmouth-Hitchcock Medical Center, and the Department of Pathology, Dartmouth Medical School, Hanover, New Hampshire, USA

Summary. Extraocular movements were investigated in a patient with bilateral vascular lesions of the medial longitudinal fasciculus. The patient showed voluntary and reflex horizontal gaze consistent with his lesion, but had absent reflex vertical gaze. Voluntary vertical gaze was present. Necropsy was performed, and the findings suggest that the medial longitudinal fasciculi in the pons convey impulses for reflex vertical gaze, but are not required for voluntary vertical gaze.

Lesions of the medial longitudinal fasciculus (MLF) produce characteristic neuro-ophthalmological findings. Bilateral lesions are most common in demyelinating processes but are also observed with occlusive vascular disease and neoplasm (Smith and Cogan, 1959; Christoff et al., 1960; Cogan, 1970; Gonyea, 1974). With complete bilateral involvement, there is paralysis of adduction of both eyes with nystagmus in the abducting eye. Vertical nystagmus is usually present on upgaze, and convergence may or may not be preserved. Skew deviation is rarely observed (Smith and Cogan, 1959). In less complete lesions, there may be only paresis of adduction with nystagmus of both eyes in the direction of gaze (Christoff et al., 1960). Unilateral lesions are caused more commonly by occlusive vascular disease than by demyelinating processes (Cogan et al., 1950; Fine and MacGlashan, 1956; Harrington et al., 1966; Kupfer and Cogan, 1966; Ross and DeMyer, 1966). The paresis or paralysis of adduction is seen ipsilateral to the side of the lesion. Abduction nystagmus is usually present contralateral to the and vertical nystagmus occurs frequently. Convergence is preserved. Skew deviation is common with the elevated eye usually on the side of the lesion (Smith and Cogan, 1959; Cogan, 1970; side of the lesion. Vertical gaze is usually intact, Keane, 1975). A mechanism for the eye movements seen in internuclear ophthalmoplegia has been postulated by Pola and Robinson (1976), and recently confirmed by electro-oculographic analysis of 25 patients (Kirkham and Katsarkas, 1977). Unilateral hot or cold caloric stimulation of the semicircular canals results in reflex conjugate horizontal gaze (Bender, 1959; Shanzer and Bender, 1959). The reflex response, also known as the slow component of nystagmus, is thought to originate in the hair cells of the horizontal semicircular canals and to follow a path to the contralateral paramedian pontine reticular formation via the vestibular nuclei of the side stimulated. This area of the reticular formation is thought to be the source of integration of both voluntary and reflex conjugate horizontal eye movements (Bender and Shanzer, 1964; Cohen, 1971; Sharpe et al., 1974). With the subject in the supine position, unilateral cold stimulation results in reflex gaze toward the side irrigated, while warm stimulation directs gaze to the opposite side. The cerebral hemispheres are thought to generate a checking or fast component in the direction opposite to the slow component that determines the direction of the specified nystagmus—that is, nystagmus to the left means fast component to the left (Bender, 1955; Pasik et al., 1960). While some authors cite the usefulness of double simultaneous caloric irrigation in eliciting reflex vertical gaze, we have found few reports investigating the neural connections of this mechanism in man (Bender, 1959, 1960; Shanzer and Bender, 1959; Shanzer, 1964; Shanzer et al., 1964).
In primates, including man, voluntary vertical gaze is thought to be mediated in the pretectal region of the midbrain (Bender and Shanzer, 1960; Christoff et al., 1962; Shanzer et al., 1964). Voluntary upgaze is thought to require an intact pretectum and posterior commissure (Bender, 1959; Christoff et al., 1962; Pasik et al., 1969a, b), while intact structures dorsomedial to the red nuclei are considered necessary for voluntary downgaze (Bender, 1959; Christoff et al., 1962; Jacobs et al., 1973; Cogan, 1974; Halmagyi et al., 1978). Recent studies in monkeys have confirmed that bilateral lesions of the MLF eliminate reflex vertical eye movements and impair fixation in extremes of vertical gaze while not affecting voluntary vertical saccades (King et al., 1976; Evinger et al., 1977). We report a case of bilateral MLF involvement and impaired reflex vertical gaze with preserved voluntary vertical gaze which suggest that the pathway mediating reflex vertical gaze in man includes the medial longitudinal fasciculi.

Case report

A 63 year old white man was transferred on 30 October 1974 to the White River Junction Veterans Administration Hospital with the chief complaint of increasing lethargy and confusion over four days. He had a longstanding history of diabetes mellitus and severe peripheral vascular disease. Abnormal general findings included a soft mid-systolic murmur and a fourth heart sound. The left leg had no pulses, and the right leg had been amputated above the knee for occlusive vascular disease. On neurological examination the patient was arousable and oriented. He had a Cheyne-Stokes pattern of respiration while sleeping. He had no visual field defect, equal pupils with normal direct and consensual light reflexes bilaterally, normal direct and consensual corneal reflexes bilaterally, decreased gag reflexes bilaterally, and dysarthria with slight deviation of the tongue to the left. Eye movement abnormalities are described below. He was able to move all extremities to command. Paratonia (resistance to movements in all directions) was present diffusely, and there was a slight drift with pronation of his right upper extremity. Biceps and triceps reflexes were normal bilaterally. Knee and ankle jerks were absent in the left leg, and the left plantar response was flexor. Sucking, forced biting, and rooting reflexes were present. Abnormal laboratory values were blood glucose of 19.4 mmol/l and blood urea nitrogen of 10 mmol/l. An old septal myocardial infarct was detected on electrocardiography. Skull radiography showed calcification in the carotid arteries. Cerebrospinal fluid study revealed protein of 1.12 g/l and glucose of 8.2 mmol/l with all other parameters within normal limits. EEG and brain scan were normal.

NEURO-OPHTHALMOLOGICAL FINDINGS (Fig. 1)

At rest a skew deviation was present with the left eye 3 mm above the right. Attempts to converge after instruction without fixating on a visual target yielded no eye movements. With tracking of a visual target, 2 mm of adduction of the right eye and 1 mm of adduction of the left eye were seen.

An incomplete bilateral MLF syndrome was present. On voluntary gaze to the right, the right eye abducted 7 mm with nystagmus to the right, while the left eye came to the midline without nystagmus. On left lateral gaze, the left eye abducted 7 mm with nystagmus to the left, while the right eye adducted 2 mm past the midline.
without nystagmus. Vertical tracking of an object resulted in 2 mm upgaze bilaterally with conjugate nystagmus upwards, and in 7 mm downgaze in the right eye and 5 mm downgaze in the left eye without nystagmus.

Optokinetic responses were elicited by use of an optokinetic drum while the patient was alert. Optokinetic nystagmus was seen in the right eye, greater on movement of the stimulus from left to right than on right to left. In the left eye, there was full abduction with the stimulus moving to the patient's left and absent adduction with it moving to the right and no nystagmus in either direction. Vertical presentation of the optokinetic stimulus produced no change in the eyes from midposition.

Horizontal oculocephalic reflex evaluation showed only abduction without nystagmus bilaterally.

Vertical oculocephalic testing revealed a 2 mm deviation of the eyes upward when the chin was flexed toward the chest. Frenzel glasses were not used, and visual fixation was not controlled with this manoeuvre. With brisk extension of the head the eyes remained in midposition.

With the head raised 30 degrees above the horizontal, caloric irrigation was performed with 60 ml of ice water both unilaterally and bilaterally and hot tap water bilaterally, with five minutes between irrigations. Cold stimulation on the right elicited 7 mm abduction of the right eye without nystagmus and no adduction or nystagmus of the left eye. Cold stimulation on the left elicited 7 mm abduction of the left eye with depressed, intermittent checking and 2 mm adduction of the right eye with active checking. Double simultaneous ice water stimulation resulted in a 4 mm depression of the right eye with a variable nystagmus sometimes to the right and sometimes vertically, and no depression or nystagmus of the left eye. Double simultaneous hot stimulation resulted in no response from the midposition in either eye. Upward and outward deviation of both eyes on forced closure of the lids (Bell's phenomenon) was observed.

COURSE
The patient developed gangrene of the left lower extremity, and died two months later with no change in his neurological status.

PATHOLOGY
Gross findings included a recent focal infarct of the myocardial septum and an old extensive antero- and postero-septal infarct. The heart was enlarged with left ventricular hypertrophy and dilatation. There was pulmonary congestion and oedema. Atherosclerosis was severe in the aorta and moderate in the coronary arteries. The cerebral circulation exhibited mild atherosclerosis without significant narrowing.

The brain showed a 2 mm cystic infarct in the right cerebral peduncle at the junction of the medial and lateral portions. The peduncle medial to this zone was palpably softened. In the rostral pons, a vertically oriented zone of softening involved the tegmentum on the left side from the ventricular surface to the pars basalis. At this point, it forked into a Y that extended diagonally across into the pars basalis of the contralateral side (Fig. 2). The lesion extended caudally 5 mm from the uninvolved left fourth nucleus. The remainder of the brainstem was normal. There was also a 30 mm infarct of the left frontal operculum. There was no involvement of the midbrain tectum, tegmentum, or periaqueductal region. The mamillary bodies appeared normal, and there was no atrophy of the substantia nigra. The cerebral cortex showed mild generalised atrophy, with moderate dilatation of the ventricular system.

Microscopic analysis of the lesion in the midpons showed a malacic zone in the left tegmentum involving the anatomical regions formerly occupied by the medial longitudinal fasciculus, and the dorsal, ventral, and superior segmental nuclei (Fig. 3, top). The lesion extended to the pars basalis of the pons where it crossed the midline. The cystic area was partially occupied by

Fig. 2 Transverse gross section through rostral pons showing destruction of left medial longitudinal fasciculus and underlying tegmentum, now evident as a sharply defined cystic zone. No gross alterations of the right medial longitudinal fasciculus are recognisable.
Reflex vertical gaze and the medial longitudinal fasciculus

foamy macrophages and remnants of blood vessels. There was a diffuse astroglial reaction in the surrounding tissues. Throughout the right medial longitudinal fasciculus there was a scattered loss of myelinated fibres producing a moth-eaten appearance (Fig. 3, bottom). There were also scattered, swollen, degenerating axons spread throughout the fasciculus. In the surrounding tissues, there was an astroglial reaction involving the dorsal and superior tegmental nuclei. The remainder of the brainstem, including the pretectum, was normal.

Discussion

The patient showed signs of diffuse bilateral cerebral dysfunction and bilateral involvement of the MLF. There was no reflex upgaze in either eye and minimal reflex downgaze on the side of the incompletely involved MLF during double simultaneous caloric stimulation. The presence of upgaze on oculocephalic testing suggests either that the patient was fixating visually during the head flexion manoeuvre (which obscured the reflex component), or that the bilateral hot caloric stimulation was not sufficient to elicit the response. It must be considered that the pathway for reflex upgaze may differ from that of reflex downgaze. The post-mortem findings, and the presence of a bilateral MLF syndrome response on caloric stimulation of each side, imply that the vestibular connections to the paramedian pontine reticular formation were intact bilaterally. There was complete destruction of the paramedian pontine reticular formation.

Fig. 3 Top: transverse microscopic section through rostral pons. The absence of parenchyma on the left demarcates the cystic lesion which has effaced the left medial longitudinal fasciculus. At this low magnification, the right medial longitudinal fasciculus appears approximately normal, except for a few vacuolar zones (Luxol fast blue—haematoxylin eosin, original magnification $\times 45$). Bottom: detail of enclosed area from top of figure showing subtle structural lesions which are compatible with functional defects in right medial longitudinal fasciculus. These consist of proliferation of astrocytes ($A$), vacuoles indicating loss of individual myelinated fibres ($B$), and swollen degenerating axons ($C$) (original magnification $\times 250$).
only in the rostral pons on the left as well as of the left MLF, while the right paramedian pontine reticular formation was not involved at all, and the right MLF only partially so. This suggests that the absence of reflex vertical gaze in the left eye may have been caused by reticular formation involvement as well as MLF destruction, while impaired but detectable reflex downgaze of the right eye was a function of the intact reticular formation on the right or only partial involvement of the right MLF. Despite these hypothetical objections, it seems that bilateral lesions in the MLF were the major factor contributing to impairment of reflex vertical eye movements in this patient.

A recent report of seven cases of the "locked-in" syndrome described one patient with bilateral reflex downgaze on double simultaneous ice water caloric stimulation. Postmortem findings showed bilaterally intact medial longitudinal fasciculi, while the basis pontis and both paramedian reticular formations were destroyed. The author does not comment on the basis for the preserved reflex response (Hawkes, 1974). On double simultaneous caloric stimulation, the observed vertical conjugate deviation of the eyes results from thermally-induced currents in the endolymph of either the unopposed anterior (resulting in reflex upgaze) or posterior (resulting in reflex downgaze) semicircular canals after antagonistic reflex gaze signals from the horizontal semicircular canals neutralise each other (Szentagothai, 1950; McMasters et al., 1966; Pasik et al., 1969a). It has been shown experimentally in monkeys that ascending fibres from the vestibular nuclei project to the extraocular motor nuclei primarily via the medial longitudinal fasciculi, and that most axons in the MLF rostral to the abducens nuclei arise from both vestibular nuclear complexes (Carpenter et al., 1963; Carpenter and McMasters, 1963; Carpenter and Strominger, 1965; McMasters et al., 1966). Vertical vestibulo-ocular responses have been abolished by sectioning the MLF in primates (Evinger et al., 1977). Thus the clinical and experimental evidence support the concept that the medial longitudinal fasciculi carry the innervation for reflex vertical gaze from the vestibular nuclei to the oculomotor and trochlear nuclei.

Our patient demonstrated voluntary vertical gaze, although the range of movement of upgaze was limited. This observation has been made in other patients with diffuse cortical dysfunction (Critchley, 1956; Hurwitz, 1968; Adams and Hurwitz, 1974; Jenkyn et al., 1977). Additionally, it has been suggested that the neuronal pathways for vertical gaze are not direct, but proceed from the pretectum to the rostral paramedian pontine reticular formation before turning cephalad to enter the oculomotor and trochlear nuclei (Christoff, 1974). This conclusion was based on the absence of vertical gaze observed in three patients with infiltrating gliomas of the pons which did not extend into the midbrain, and four patients with focal infarctions of the pontine tegmentum which extended across the midline. The patholog y reported in the "locked-in" syndrome demonstrates preserved voluntary vertical gaze in cases with bilateral destruction of the caudal paramedian pontine reticular formation (Halsey et al., 1967; Kemper and Romanul, 1967; Chase et al., 1968; Nordgren et al., 1971; Hawkes, 1974). No reports could be found describing vertical eye movements in patients with bilateral destruction of the rostral paramedian pontine reticular formation. The above observations suggest that cortical innervation of vertical eye movements in man is mediated by structures caudal to the midbrain in the rostral pons, and this is supported by the experimental evidence in monkeys (Bender and Shanzer, 1964).

Skew deviation was observed in our patient. The hypertropic eye was ipsilateral to the completely destroyed MLF. A review of the subject documents the observation that the elevated eye is ipsilateral to the lesion in unilateral internuclear ophthalmoplegia (Keane, 1975). It is possible that hypertropia on the side of the lesion results from loss of a tonic downward component originating in the vestibular nuclei and carried by a disrupted MLF. The release of a tonic upward component, possibly of vestibular origin and conveyed by the contralateral MLF, may also explain the origin of the upward deviation of the eye in unilateral or incomplete bilateral MLF syndromes. It would follow that the relatively infrequent occurrence of skew deviation with complete bilateral MLF lesions results from a balanced loss of upward and downward tonic influences.

Other lesions abolishing reflex vertical gaze would include labyrinthine, eighth nerve, and vestibular nuclear involvement bilaterally. Recent reports suggest that pretectal lesions may also impair reflex vertical gaze in the absence of complete third and fourth nerve nuclear destruction (Halmagyi et al., 1978; Reagan and Trautmann, 1978). In these syndromes, however, voluntary vertical gaze is also significantly impaired.

We have reported a case of bilateral MLF involvement and impaired reflex vertical gaze with preserved voluntary vertical gaze. In addition, we have noted a case in the literature of intact reflex downgaze with the medial longitudinal fasciculi as the only preserved ascending extraocular motor pathways. We conclude that the major pathways
Reflex vertical gaze and the medial longitudinal fasciculus

for reflex vertical gaze in man are the medial longitudinal fasciculi. These observations do not imply a centre for reflex vertical gaze. Rather, they stress the importance of separate pathways (Fig. 4) for voluntary and reflex vertical conjugate eye movements and the probable role played by the medial longitudinal fasciculi in mediating reflex vertical gaze.

We wish to thank Judy Murphy for her efforts in preparation of the manuscript, and Val Page for the medical illustrations.
L. R. Jenkyn, G. Margolis, and A. G. Reeves


McMasters, R. E., Weiss, A. H., and Carpenter, M. B. (1966). Vestibular projections to the nuclei of the...


Reflex vertical gaze and the medial longitudinal fasciculus

L. R. Jenkyn, G. Margolis and A. G. Reeves

*J Neurol Neurosurg Psychiatry* 1978 41: 1084-1091
doi: 10.1136/jnnp.41.12.1084

Updated information and services can be found at:
http://jnnp.bmj.com/content/41/12/1084

These include:

**Email alerting service**

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/