SHORT REPORT

Torsional deviations with voluntary saccades caused by a unilateral midbrain lesion

Olympia Kremmyda, Jean A Büttner-Ennever, Ulrich Büttner, Stefan Glasauer

Three dimensional eye rotations were measured using the magnetic search coil technique in a patient with a lesion of the right rostral interstitial nucleus of the medial longitudinal fasciculus (RIMLF) and in four control subjects. Up to 10° contralesional torsional deviations with each voluntary saccade were revealed, which also could be seen during bedside examination. There was no spontaneous nystagmus. Based on MRI criteria, the lesion involved the RIMLF but spared the interstitial nucleus of Cajal. To date, this deficit has not been described in patients. Our results support the hypothesis that the vertical–torsional saccade generator in humans is organised similarly as in monkeys: each RIMLF encodes torsional saccades in one direction, while both participate in vertical saccades.

Two major premotor structures in the mesencephalon are related to the generation of saccadic eye movements: the rostral interstitial nucleus of the medial longitudinal fasciculus (RIMLF) for the generation of torsional–vertical saccades and, adjacent to it, the interstitial nucleus of Cajal (INC), the vertical–torsional integrator, which is responsible for holding the eyes steady in eccentric gaze following saccades.[1] On the basis of lesion studies in the monkey, it has been proposed that the saccade burst generator in the RIMLF is organised symmetrically to the midline similar to the coordinate systems of the extraocular muscles or the vestibular semicircular canals.[2] Accordingly, bilateral activation of the RIMLF would generate purely vertical saccades, whereas appropriate unilateral activation would lead to torsional saccades, if expressed in the intrinsic coordinate system of the saccade generator.[3]

Because of the proximity of the RIMLF and INC, lesions in patients usually affect both regions, causing a mixture of signs such as tonic torsional deviation, torsional nystagmus, slowing of vertical saccades and a vertical gaze holding deficit.[1] For this reason, it has not been possible to clearly demonstrate that the properties of the human vertical–torsional saccade generator in the RIMLF are consistent with the scheme derived in the monkey.

Here we report for the first time visually guided saccades in a clinical case, in which only the RIMLF, without the INC, was involved. Spontaneous nystagmus was not observed. Instead, three dimensional eye movement recordings revealed that with each saccade the eye rotated counter clockwise by up to 10°. Our results support the assumption that the human RIMLF on each side encodes signals for both upward and downward, but only for ipsitorsional, saccades.[2 4 5]

PATIENT AND METHODS
Case report
A 59-year-old woman woke up with the right side of her mouth drooping, a falling tendency to the left, clumsiness of the right hand and dysarthric speech.

Neurological examination on the same day showed a head tilt to the left with a slight skew deviation (the right higher than the left eye). Vertical saccades were slow and deviated from pure vertical in a counter clockwise direction (direction always refers to the patient's point of view)—that is, the upper pole of the eye deviated to the left. There were no spontaneous or gaze evoked nystagmus, no ptosis, no complaint of double vision and no strabismus. Pupil reactions and convergence were intact. Smooth pursuit was slightly saccadic. Fundoscopy showed 2° (right) and 9.5° (left) excyclotorsion, which falls within the normal range of ocular torsion.[6] MRI revealed a recent right antero-paramedian thalamus infarct that affected the mecencephalon up to the RIMLF, but spared the INC (fig 1B), using the same criteria of identification as previously described.[7]

METHODS
Eye movement recordings were performed 5 days after the infarction with the patient's informed, written consent, according to the Declaration of Helsinki. Head tilt was no longer present (it disappeared 2 days after the infarct). A dual search coil (Skalar, Breda, the Netherlands; Remmel Labs, Ashland, Massachusetts, USA) was used to record three-dimensional eye movements monocularly (left eye) at 1 kHz. The local ethics committee of the Medical Faculty of the University of Munich approved the recordings.

The patient was seated with her head on a chin rest in complete darkness and was instructed to follow a laser dot (size 0.1°) on a projection screen (distance 145 cm). The dot, which jumped every 3.5 s between a central and eight eccentric positions ($\pm 18°$ from the centre on the horizontal and vertical meridians and $\pm 25.46°$ on the two oblique meridians), was only visible for 500 ms around the jump. Eye positions were expressed as rotation vectors. Saccades were detected automatically and could be corrected in interactive software. Three dimensional eye velocity was calculated from eye position. To determine the time constants of the slow drift, the dependence of three dimensional slow phase velocity on three dimensional eye position was computed using MatLab (The Mathworks). Further details on the mathematical analysis and the calibration procedure are described elsewhere.[8]

Control subjects
Four healthy, age matched control subjects (three females and one male, aged 54–62 years) without a known history of ocular motor disorders were tested using the protocol described above.

RESULTS
Vertical gaze displacements larger than 15° consisted of a series of smaller saccades up to 10° (fig A, animation of the data; fig A can be viewed on the *J Neurol Neurosurg Psychiatry* website at

Abbreviations: INC, interstitial nucleus of Cajal; RIMLF, right rostral interstitial nucleus of the medial longitudinal fasciculus
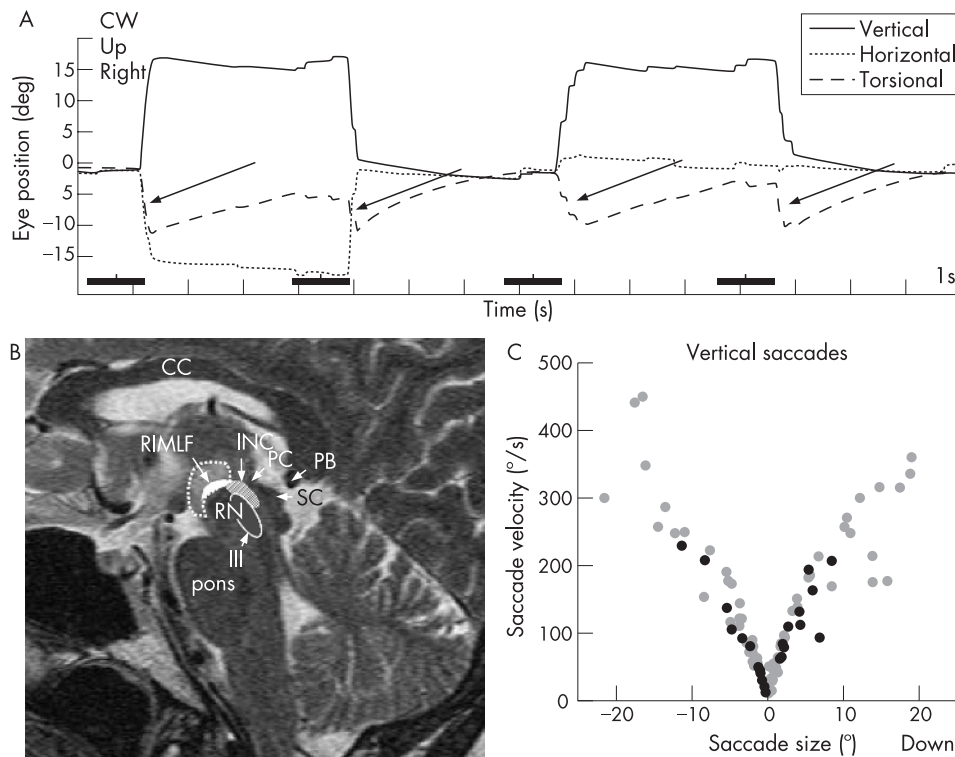
Figure 1 (A) Eye positions (vertical, horizontal, torsional) during saccades to a visual target, which jumped every 3.5 s and was visible for ±500 ms (black bars) around the target jump. During each saccade, the eye rotated counter clockwise up to 10° (arrows, contralesional torsional deviation) followed by a slow compensatory drift (average time constant 3.8 s) towards a torsional null position. CW, clockwise. (B) T2 weighted sagittal image of brain MRI. Broken line indicates the lesioned area which includes the right rostral interstitial nucleus of medial longitudinal fasciculus (RIMLF) but not the interstitial nucleus of Cajal (INC). CC, corpus callosum; III, oculomotor nucleus; PB, pineal body; PC, posterior commissure; RN, red nucleus; SC, superior colliculus. (C) Angular eye velocity plotted over saccade size for all vertical saccades of the patient (black) and four age matched control subjects (gray). The patient's vertical saccades were smaller (up to 10°) but clearly not slower than comparable control saccades.

http://www.jnnp.com/supplemental). Overall, the maximal vertical velocity was restricted to 200°/s, which was about half the maximal vertical velocity of the age matched control subjects (fig 1C), but for saccades of comparable size the vertical angular eye velocity did not differ from that of the control subjects. For oblique saccades larger than 15°, the vertical component of eye velocity was slower than in controls; it was saturated between 180 and 250°/s in the patient. During the intermittent dark periods, the horizontal and vertical gaze holding function was normal with time constants larger than 50 s.[1] The most prominent feature was a large counter clockwise torsional eye rotation (up to 10°, maximum velocity 115°/s) with each voluntary saccade (fig 1A), followed by a drift back to the torsional null position (time constant 3.8 s). Additional results are provided in the supplementary material (the supplementary material can be viewed on the *J Neurol Neurosurg Psychiatry* website at http://www.jnnp.com/supplemental)

DISCUSSION

To our knowledge, this is the first clinical case in which a patient presented with a unilateral midbrain lesion and a pronounced torsional deviation (up to 10°) during each voluntary saccade, which could be observed clinically in vertical saccades. The following slow drift back to the torsional null position became particularly obvious, when the eye was held in an eccentric position without visual feedback. Clinically, a counter clockwise deviation of the upper pole of the eye during vertical saccades was noted. These ocular motor findings agree well with loss of the torsional–vertical saccade generator, as previously described in monkeys.[2][4] Single cell recordings in the monkey show that each RIMLF contains neurons that fire both for upward and downward directions, but only for the ipsilateral torsional direction. For vertical saccades, both RIMLF are active, so that the overall saccadic torsion remains zero. With a unilateral lesion, the remaining functional RIMLF determines the torsion, causing the torsional deviations

observed in our patient (see also supplementary material; the supplementary material can be viewed on the *J Neurol Neurosurg Psychiatry* website at http://www.jnnp.com/supplemental). RIMLF lesions caused a contralateral tonic torsional offset, torsional deviations with each saccade, but no lasting head tilt, as seen with larger lesions.[9] The small torsional nystagmus previously described in monkey experiments[4] might actually reflect torsional deviations, which are difficult to distinguish in untrained monkeys performing many saccades.

The loss of ipsilateral quick phases of torsional nystagmus previously described in patients with RIMLF lesions[10] corresponds to our finding that the eye never returned towards Listing's plane with a torsional quick phase, as found in healthy subjects.[11] Rather, following the torsional deviation, the eye slowly drifted back to the torsional null position with a time constant of 3.8 s. As the torsional time constant is 2 s in healthy subjects,[12] our data do not indicate a gaze holding deficit, as one would expect in an INC lesion. The sparing of the INC might also be the reason why our patient did not show any spontaneous nystagmus.

In patients, it has been suggested that ipsilesional torsional nystagmus indicates an INC and contralesional nystagmus and RIMLF involvement.[7] Most of the latter patients also had additional INC lesions, in contrast with the present case where the lesion was rather more rostral. Thus it remains to be determined why additional INC involvement leads to contralesional nystagmus.

Pathological torsional deviations (''blips'') have been seen after a lower brainstem lesion, have a short time constant (250–300 ms) and probably reflect some torsional dysmetria.[13] Torsional pulsion (torsional deviations during voluntary horizontal or vertical saccades) has also been seen with lateral medullary syndrome.[14] These patients however had saccadic dysmetria, which is typical of Wallenberg's syndrome.

Surprisingly, the velocity of purely vertical saccades in our patient was not slower than comparable saccades of the control subjects. Analysis of quick phases of optokinetic nystagmus in

patients with slower vertical saccades caused by progressive supranuclear palsy[15] showed that only larger saccades had reduced velocities compared with controls. Our patient's maximal vertical saccade size was restricted to about 10° (fig 1C).[4] This suggests that the local feedback loop controlling burst generation successfully increased burst size as long as possible (ie, up to around 200°/s) so that the patient had to make up to four smaller saccades to reach an 18° vertical target (fig 1A). Clinically, this was seen as slower saccades.

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Fig A, animation of the data and supplementary material can be viewed on the *J Neurol Neurosurg Psychiatry* website at http://www.jnnp.com/supplemental

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