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# Abduction paresis with rostral pontine and/or mesencephalic lesions: Pseudoabducens palsy and its relation to the so-called posterior internuclear ophthalmoplegia of Lutz

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## Abstract

**Background:** The existence of a prenuclear abduction paresis is still debated.

**Methods:** In a retrospective design, we identified 22 patients with isolated unilateral (n = 20) or bilateral (n = 2) abduction paresis and electrophysiologic abnormalities indicating rostral pontine and/or mesencephalic lesions. Another 11 patients had unilateral abduction paresis with additional ocular motor abnormalities indicating midbrain dysfunction. Eight of these 11 patients also had electrophysiological abnormalities supporting this location. Electrophysiological examinations in all patients included masseter and blink reflexes (MassR, BlinkR), brainstem auditory evoked potentials (BAEP), and direct current elctro-oculography (EOG).

**Results:** Unilateral MassR abnormalities in patients with unilateral abduction paresis were seen in 17 patients and were almost always (in 16 of 17 patients) on the side of the abduction paresis. Another 11 patients had bilateral MassR abnormalities. BlinkR was always normal. EOG disclosed slowed abduction saccades in the non-paretic eye in 6 patients and slowed saccades to the side opposite to the abduction paresis in another 5 patients. Re-examinations were done in 27 patients showing normalization or improvement of masseter reflex abnormalities in 18 of 20 patients and in all patients with EOG abnormalities. This was always associated with clinical improvement.

**Conclusions:** Electrophysiologically documented or clinically evident rostral pontine and/or mesencephalic lesions in our patients exclude an infranuclear intrapontine 6th nerve lesion and indicate the existence of an abduction paresis of prenuclear origin. An increased tone of the antagonistic medial rectus muscle during lateral gaze either by abnormal convergence or impaired medial rectus inhibition seems most likely.

## Background

In 1921, Anton Lutz postulated the existence of a prenuclear abduction paresis, the so-called "ophthalmoplegia internuclearis posterior" (posterior internuclear ophthalmoplegia, PINO) [1]. This concept, however, was based on an erroneous neuroanatomical concept: Lutz thought that the supranuclear fibers mediating horizontal gaze divide within the pons into a descending branch to lateral rectus motoneurons on one side and an ascending branch to medial rectus motoneurons on the other

side. The PINO was attributed to a lesion of the descending branch thought to be followed by a reduced or absent excitation of lateral rectus motoneurons. Although Lutz's basic neuroanatomical assumption was wrong, the existence of a PINO remained controversial, as a PINO was repeatedly discussed in patients, whose abduction paresis was thought to differ from a 6th nerve palsy. This included absence of strabismus and diplopia in the primary position [2–5], adduction nystagmus of the contralateral, i.e. non-paretic eye on lateral gaze [3,4,6], isolated impairment of abduction saccades, i.e. unrestricted abduction with following eye movements [7], preserved abduction sacccades with caloric testing, i.e. with vestibular (caloric) nystagmus [8,9], or preserved abduction with the vestibulo-ocular reflex [9]. There was little agreement on both, the location of the responsible lesion and the underlying mechanism. Some suggested impairment of the supranuclear pathways for lateral gaze running near the 3rd nerve nucleus [9]. Others postulated a decreased excitation of lateral rectus motoneurons due to a lesion of aberrant pyramidal tract fibers to the abducens nucleus [10], or an affection of the connection between the paramedian pontine reticular formation (PPRF) and the ipsilateral abducens nucleus [5,7]. An impaired inhibition of the antagonistic medial rectus muscle was discussed by Collard et al. [4] suggesting a medial longitudinal fasciculus (MLF) lesion contralateral to the paretic eye. Finally, some authors attributed such cases to a lesion of the intrapontine segment of the 6th nerve thereby rejecting a pre- or supranuclear origin of the abduction paresis [11–14].

We re-address this issue based on findings in 33 (including 8 previously reported [15] patients with unilateral or bilateral abduction paresis with electrophysiologically or clinically documented rostral pontine and/or mesencephalic lesions.

## Methods

We retrospectively identified 22 patients with isolated unilateral (n = 20) or bilateral (n = 2) abduction paresis, who also had electrophysiological abnormalities indicating rostral pontine and/or mesencephalic lesions. Another 11 patients with an unilateral abduction paresis as their main clinical symptom had additional clinical signs of midbrain dysfunction, which were supported by abnormal electrophysiological findings in 8 of them. None of the 33 patients had total abduction paresis. In most patients, abduction was limited to 20–30° from the midposition with saccadic and following eye movements. Electrophysiologic testing in all patients included masseter and blink reflexes (MassR, BlinkR), brainstem auditory evoked potentials (BAEP), and direct current electro-oculography (EOG) as described previously [15,16]. Criteria of MassR and BlinkR abnormalities were: (i) unilateral or bilateral delayed latency outside the age related mean + 2.5 standard deviations (SD), (ii) unilateral or bilateral loss (including partial MassR loss, i.e. loss of more than 4 responses out of 10 trials); (iii) right/left differences outside the age related mean + 2.5 SD; (iv) increase or shortening of the MassR latency at re-examination by 0.8 ms or more was interpreted in favor of deteriorating or improving acute lesions. [15,16]. Velocities of saccades outside the normal range were considered abnormal (normal ranges of our laboratory: 30°-abduction saccades: 320 to 640°/s; 30°-adduction saccades: 335 to 670°/s; interocular difference < 35°/s).

Magnetic resonance imaging (MRI) was done in 8 patients with 1.0 (Siemens Magnetom, Erlangen, Germany) or 1.5 Tesla (Philips S, Eindhoven, The Netherlands) superconducting systems before and after intravenous gadolinium. T1-weighted (repetition time: 500–750 ms, echo time: 20–50 ms) and T2-weighted (repetition time: 1800–2080 ms, echo time: 80–100 ms) images were obtained. Slice thickness was between 4 and 7 mm. CT was done in 19 patients with an EMI 1010 (London, United Kingdom) or Siemens Somatom ARP (Erlangen, Germany). Slice thickness was between 4 and 7 mm.

Diagnosis of brainstem infarction was based on (a) sudden onset, (b) presence of at least one relevant risk factor for the development of cerebrovascular diseases (diabetes, hypertension, previous strokes or transient ischemic attacks, atrial fibrillation, heavy smoking, hypercholesterolemia, signs of general arteriosclerosis), and (c) subsequent improvement or recovery. Multiple sclerosis was diagnosed according to the criteria given by Poser et al. [17] and Paty et al. [18].

## Results

Brainstem ischemia was diagnosed in 24 and multiple sclerosis in 4 patients. One patient had an undiagnosed inflammatory disease. In the remaining 4 patients the etiology remained undetermined.

Abnormal electrophysiologic findings are given in detail in table 1. Seventeen patients with unilateral abduction paresis, which was the only clinical signs in 12 and associated with additional clinical signs of midbrain dysfunction in 5, had unilateral MassR abnormalities. These abnormalities were ipislateral in 16 and contralateral in one patient. One of these patients (#9) also had a delayed BAEP wave V ipsilateral to the abduction paresis and the MassR abnormality. Another 11 patients with unilateral abduction paresis, which was the only clinical signs in 8 and associated with additional clinical signs of midbrain dysfunction in 3, had bilateral MassR abnormalities, which were more pronounced on the side of the abduction paresis in 3 and without a relevant side difference in

**Table 1: Abnormal electrophysiological and/or clinical findings**

| No. | Age *(years)* | Sex | Etiology | Clinical findings | Electrophysiological findings | | |
|---|---|---|---|---|---|---|---|
| 1 | 75 | female | ischemia | abduction paresis **right** eye | MassR | **right** | **loss ⇒ 8.3 ms** |
| | | | | | | left | 8.0 ms ⇒ 7.9 ms |
| | | | | | EOG | slowed abduction saccades left eye[N] | |
| 2 | 76 | female | ischemia | abduction paresis **right** eye | MassR | **right** | **9.2 ms ⇒ 8.8 ms** |
| | | | | | | left | 8.5 ms ⇒ 8.7 ms |
| 3 | 51 | Male | undetermined | abduction paresis **right** eye | MassR | **right** | **9.1 ms** ⇒ 8.4 ms |
| | | | | | | left | 7.9 ms ⇒ 8.0 ms |
| 4 | 58 | female | ischemia | abduction paresis **right** eye | MassR | **right** | **8.9 ms ⇒ 8.0 ms** |
| | | | | | | left | 8.2 ms ⇒ 7.9 ms |
| | | | | | EOG | Slowed abduction saccades left eye[N] | |
| 5 | 33 | female | Multiple sclerosis | abduction paresis **left** eye | MassR | right | 6.6 ms ⇒ 7.1 ms |
| | | | | | | **left** | **7.4 ms ⇒ 7.9 ms** |
| | | | | | EOG | Slowed abduction saccades right eye[N] | |
| 6 | 74 | Male | ischemia | abuction paresis **right** eye | MassR | **right** | **7.3 ms**⇒ 7.2 ms |
| | | | | | | left | 6.6 ms ⇒ 7.2 ms |
| 7 | 68 | male | ischemia | abduction paresis **right** eye | MassR | **right** | **9.8 ms** |
| | | | | | | left | 9.1 ms |
| 8 | 78 | female | ischemia | abduction paresis **right** eye | MassR | **right** | **9.6 ms** |
| | | | | | | left | 8.9 ms |
| | | | | | EOG | slowed saccades to the **left** [N] | |
| 9 | 51 | male | ischemia | abduction paresis **left** eye | MassR | right | 7.4 ms |
| | | | | | | **left** | **9.0 ms** |
| | | | | | BAEP | right | 5.8 ms ⇒ 5.9 ms |
| | | | | | | **left** | **6.1 ms** ⇒ 5.9 ms |
| | | | | | EOG | Slowed abduction saccades right eye[N] | |
| 10 | 77 | male | ischemia | abduction paresis **right** eye | MassR | **right** | **8.6 ms** |
| | | | | | | left | 8.0 ms |
| 11 | 67 | male | ischemia | abduction paresis **right** eye | MassR | **right** | **8.0 ms** |
| | | | | | | left | 7.3 ms |
| 12 | 39 | female | inflammation | abduction paresis **left** eye | MassR | **right** | **6.9 ms** |
| | | | | | | left | 6.1 ms |
| | | | | | EOG | Slowed abduction saccades right eye[N] | |
| 13 | 74 | female | ischemia | abduction paresis **right** eye | MassR | **right** | **loss ⇒ loss** |
| | | | | | | **left** | **loss** ⇒ 7.3 ms |
| 14 | 34 | female | Multiple sclerosis | abduction paresis **right** eye | MassR | **right** | **9.4 ms** |
| | | | | | | **left** | **8.5 ms** |
| | | | | | EOG | Slowed saccades to the left[N] | |
| 15 | 26 | male | Multiple sclerosis | abduction paresis **right** eye | MassR | **right** | **8.8>4 ms** |
| | | | | | | **left** | **9.0 ms** |
| | | | | | EOG | Slowed saccades to the **left** [N] | |
| 16 | 68 | female | ischemia | abduction paresis **left** eye | MassR | **right** | **9.4 ms** ⇒ 8.0 ms |
| | | | | | | **left** | **9.2 ms** ⇒ 8.0 ms |
| 17 | 73 | male | ischemia | abduction paresis **right** eye | MassR | **right** | **9,3 ms** ⇒ 8.5 ms |
| | | | | | | **left** | **9.6 ms** ⇒ 8.5 ms |
| | | | | | EOG | Slowed abduction saccades left eye[N] | |
| 18 | 68 | female | ischemia | abduction paresis **left** eye | MassR | **right** | **9.4 ms** ⇒ 8.0 ms |
| | | | | | | **left** | **9.2 ms** ⇒ 8.0 ms |
| 19 | 73 | male | ischemia | abduction paresis **right** eye | MassR | **right** | **9,3 ms** ⇒ 8.5 ms |
| | | | | | | **left** | **9.6 ms** ⇒ 8.5 ms |
| 20 | 70 | male | ischemia | abduction paresis **right** eye | MassR | **right** | **9.1>4 ms** |
| | | | | | | **left** | **8.9>4 ms** |
| | | | | | EOG | Slowed saccades to the **left** [N] | |
| 21 | 65 | male | ischemia | abduction paresis **left > right** eye | MassR | **right** | **loss** ⇒ 8.3 ms |
| | | | | | | left | 8.6 ms ⇒ 8.6 ms |
| 22 | 55 | male | undetermined | abduction paresis **right > left** eye | MassR | **right** | **11.8 ms ⇒ 10.3 ms** |
| | | | | | | left | 9.4 ms ⇒ 9.0 ms |
| 23 | 48 | male | ischemia | abduction paresis ***plus*** | MassR | right | 7.9 ms ⇒ 8.1 ms |

**Table 1: Abnormal electrophysiological and/or clinical findings *(Continued)***

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | superior oblique palsy **left eye** | | **left** | **9.3 ms** ⇒ 8.5 m |
| 24 | 69 | male | ischemia | abduction paresis ***plus*** superior oblique **left eye** | MassR | **right**<br>**left** | **12.4>4 ms** ⇒ 9.4 ms<br>**10.2 ms** ⇒ 9.2 ms |
| 25 | 79 | male | ischemia | aduction paresis ***plus*** elevation paresis **left eye** | MassR | right<br>**left** | 8.6 ms ⇒ 8.9 ms<br>**9.2 ms** ⇒ **9.5 ms** |
| 26 | 71 | female | ischemia | abduction paresis ***plus*** elevation paresis **right eye** | MassR | **right**<br>**left** | **8.2 ms** ⇒ 7.4 ms<br>**10.0 ms** ⇒ **8.4 ms** |
| 27 | 68 | male | ischemia | abduction paresis ***plus*** elevation paresis **right eye** | | | |
| 28 | 63 | female | multiple sclerosis | abduction paresis **right eye *plus*** upgaze palsy | EOG | slowed saccades to the **left** [N] | |
| 29 | 63 | female | ischemia | abduction paresis **right eye *plus*** up- and downgaze palsy | MassR | **right**<br>left | **8.9 ms** ⇒ 8.0 ms<br>8.2 ms ⇒ 8.2 ms |
| 30 | 40 | male | undetermined | abduction paresis **right eye *plus*** up- and downgaze palsy & gaze paresis to the **left** | MassR | **right**<br>left | **8.2>4 ms**<br>8.0 ms |
| 31 | 21 | male | undetermined | abduction paresis **right eye *plus*** up- and downgaze palsy & convergence-retraction nystagmus | | | |
| 32 | 75 | female | ischemia | Abduction paresis **right eye *plus*** unsteady tandem walking with falling to the **right** | MassR | **right**<br>left | **loss** ⇒ 8.1 ms<br>8.0 ms ⇒ 7.9 ms |
| 33 | 73 | male | ischemia | abduction paresis **right eye *plus*** unsteady tandem walking with falling to the **right** | MassR | **right**<br>**left** | **9.3 ms** ⇒ 8.5 ms<br>**9.6 ms** ⇒ 8.5 ms |

the remaining patients. Both patients with bilateral abduction paresis (#21 and #22) had unilateral MassR abnormalities. BlinkR was normal in all patients.

EOG disclosed slowed abduction saccades in the opposite eye in 6 patients with velocities ranging between 379 and 523°/s, which was by 123 to 199°/s slower than adduction saccades in the non-paretic eye. Another 5 patients had slowed saccades to the side opposite to the abduction paresis with velocities for 30°-saccades ranging between 323 and 478°/s, which was by 109 to 228°/s slower than adduction saccades in the non-paretic eye.

Re-examinations were done in 27 patients documenting normalized or improved MassR abnormalities in 18 and unchanged abnormal MassR findings in 2 patients. The delayed BAEP wave V latency (patient #9) was normal at re-examination. EOG documented saccadic slowing had improved or normalized in all patients.

MRI (8 patients) and CT (19 patients) revealed no brainstem lesions except MRI documented bilateral symmetrical pontine hyperintensities without signs of acute infarctions in one patient with vertebrobasilar ischemia. (MRI disclosed multiple periventricular hyperintense lesions in two patients with multiple sclerosis and multiple

supratentorial white matter lesions in 6 patients with risk factors for cerevbrovascular disease.

## Discussion

Thirty of our patients had electrophysiologically documented rostral pontine and/or mesencephalic lesions. Unilateral MassR abnormalities were almost always on the side of the abduction paresis, which argues against a random association. Pre-existing electrophysiological abnormalities were unlikely, as almost all (19 of 21) re-examined patients showed improvement or normalization of abnormal MassR and BAEP findings, which strongly suggests acute lesions. This was always associated with improvement of the abduction paresis, which strongly indicates that both, clinical and electrophysiological abnormalities, were caused by the same actual lesion. Abnormal MassR findings in patients with normal trigeminal nerve sensory and motor function indicate lesions involving the ipsilateral trigeminal mesencephalic tract and nucleus [see for review [19,20]]. This corresponds to the rostral pons and mesencephalon between the level of the 5th nerve entry zone and the 3rd nerve nucleus level. An abnormal R1-component of the BlinkR (Blink-R1) with normal R2 components and normal trigeminal and facial nerve functions indicates an ipsilateral pontine lesion between the trigeminal nerve entry zone and the facial nucleus [see for review [19,20]]. Abnormal MassR findings with normal BlinkR-R1 as seen in 30 of our patients indicate rostral pontine and/or mesencphalic lesions [19,20]. Midbrain dysfunction was also evident from vertical gaze palsies and convergence nystagmus [21], which were seen in 4 of our patients. Such lesion location is clearly rostral to the intrapontine segment of the 6th nerve excluding an infranuclear intrapontine 6th nerve lesion in our patients.

Our patients correspond to a number of previously reported patients, most of them with pathologically or radiologically proven midbrain or meso-diencephalic lesions, showing an abduction paresis with additional clinical signs of midbrain dysfunction like upgaze palsy, convergence paresis, or convergence nystagmus [3,7,9,22–29]. Such location was also obvious in another 2 patients with transient abduction paresis after ipsilateral mesencephalotomy [30]. These observations and our data leave no doubt on the existence of an abduction paresis with ipsilateral rostral pontine and/or mesencephalic lesions, even though we were unable to demonstrate CT or MRI documented brainstem lesions. Small brainstem lesions definitely escape observation by CT and "routine" MRI (=T1- and T2-weighted imaging with thick (4–7 mm) slices) as shown with pathologically documented brain stem infarctions [31,32], internuclear ophthalmoplegia [33–35], monocular elevation paresis [36], isolated 3rd, 4th, 6th, 7th, and 8th nerves palsies in multiple sclerosis [37–41], and electrophysiologically documented brainstem lesions [15,36,39,42–49]. Thinner slicing and other recent techniques (e.g. diffusion weighted imaging, perfusion imaging, fluid attenuated inversion recovery) have increased MRI sensitivity [50–54]. Such techniques, however, were not applied to our patients. Moreover, lesions impairing the function of certain brainstem structures not necessarily impair the structural integrity and therefore may escape detection by MRI even with thinner slicing and diffusion weighted imaging [54,55]. Functional abnormalities, both clinical and electrophysiological, can be estimated equal reliable in indicating the location of a brainstem lesion if they have been correlated with imaging or pathologically documented lesion locations, which has been worked out for brainstem reflexes and clinical signs [see for review [19–21].

Supranuclear excitatory connections mediating horizontal gaze simultaneously activate lateral rectus motoneurons and, via abducens nucleus internuclear neurons, medial rectus motoneurons [56,57]. Lesions of these fibres within the midbrain are followed by horizontal gaze disorders simultaneously affecting abduction in one and adduction in the other eye [56,57]. Abduction paresis in one without impaired adduction in the other eye as in our patients can not be attributed to a lesion of descending excitatory fibres mediating horizontal gaze, which excludes supranuclear impairment of lateral rectus activation as the working mechanism in our patients. Abduction paresis in our patients were most likely caused by abnormal convergence or impaired medial rectus inhibition during lateral gaze. Both conditions create an increased tone of the antagonistic medial rectus muscle causing abduction paresis despite normal lateral rectus activation.

Abduction paresis with organic and non-organic convergence spasm documents the functional significance of an abnormal convergence during lateral gaze [58–61]. Abduction paresis may also occur (not infrequently in association with convergence or convergence-retraction nystagmus as in patient #31) as one sign of the dorsal midbrain syndrome and is generally attributed to an abnormal convergence tone during lateral gaze [62,63]. Such mechainsm was discussed as the most likely cause in patients with unilateral or bilateral abduction paresis with or without esotropia of the affected eye occurring with meso-diencephalic infarctions [24,26–29] and called "pseudo-sixth" [24] or "pseudoabducens palsy" [29]. Convergence neurons are located within the mesencephalic reticular formation. Their discharge is time-coupled to convergence eye movements and encodes their velocity [see for review [64]]. The supranuclear control of these neurons is not fully understood, but may

involve several connections. In primates, there is evidence for an excitatory projection from area 19 and 22 to the midbrain. Stimulation in these areas was followed by ipsilateral or ipsilaterally pronounced convergence movements with or without miosis depending on the intensity and exact location of the stimulation [65,66]. Another bilateral, mainly ipsilateral, projection from the frontal lobe to the midbrain was also shown in primates [67,68] and considered to exert direct inhibition of a subgroup of rectus medialis motorneurons (27), the group C of Büttner-Ennever und Akert, which is thought to be primarily involved in convergence eye movements [69]. A lesion of this connection within the midbrain would be followed by a disinhibition of convergence neurons creating an increased convergence tone during lateral gaze because of the preponderance of the excitatory projection from area 19 and 22 [27]. More recently, Pullicino et al. [29] provided convincing evidence, that the region of the interstitial nucleus of Cajal, which has a close proximity to convergence neurons in the monkey [70], may be critical for the occurrence of a "pseudoabducens palsy" due to a lesion of a descending pathway just before it reaches the convergence neurons.

Lesions involving rostral parts of the central MassR arc may extend beyond this level reaching the meso-diencephalic junction thereby involving the region of the interstitial nucleus of Cajal. Such localized lesions were likely in a number of our patients because of additional clinical signs such as vertical gaze palsies (patients #29–31), monocular elevation paresis (patients #25–27), and convergence retraction nystagmus (patient #31), which was associated with ipsilateral MassR abnormalities in 4 of them. All previously described patients with an abduction paresis due to upper brainstem infarcts had additional clinical signs of rostral midbrain dysfunction (e.g. vertical gaze palsies, convergence retraction nystagmus) [24,26–29]. Such signs, however, were not seen in most of our patients indicating either more restricted rostral midbrain lesions involving descending fibres to convergence neurons with sparing of adjacent structures, or more caudally located, rostral pontine and/or pontomesencephalic lesions. Such lesion location is caudal to the level of the convergence neurons, which excludes damage of descending fibres involved in the control of convergence thereby also excluding abnormal convergence as the underlying mechanism of the abduction paresis in these patients.

Inhibition of antagonistic eye muscles may cause paresis of vertical and horizontal eye movements despite normal excitation of agonistic eye muscles [23,71–73]. Impaired medial rectus inhibition may occur with midbrain lesions as documented in a patient with an unilateral convergence paresis as a clinical sign of an ipsilateral midbrain dysfunction, who also had an ipsilateral abduction paresis with grossly impaired medial rectus inhibition and normal lateral rectus excitation [23]. Medial rectus inhibition was attributed to several different mechanisms. Pola and Robinson [74] proposed the existence of inhibitory fibres ascending within the medial longitudinal fasciculus (MLF). As MLF fibre activity is always associated with contraversive eye movements, i.e. ipsilateral to the adducting eye [74,75], inhibitory MLF fibers would have to cross at the 3rd nerve nucleus level to reach the medial rectus motoneurons on the side of the abducting eye [74]. Such crossing of MLF fibres, however, has not been demonstrated so far [76,77].

Pierrot-Deseilligny [78] discussed an inhibition of excitatory abducens nucleus internuclear neurons ("disfacilitation") as the working mechanism of medial rectus inhibition. This inhibition was attributed to the activity of inhibitory burst neurons located within the dorsomedial pontine reticular formation, which receive afferents from the ipsilateral PPRF and project to contralateral abducens nucleus neurons [79,80]. Bilateral interruption of this connection and of both MLF, however, was followed by bilateral INO and bilateral loss of lateral rectus inhibition but only mild impairment of medial rectus inhibition [71]. Moreover, loss of excitatory MLF fibre activity is not associated with a reduced tonic resting activity of the medial rectus muscle [81–83]. These findings do not support the concept that inhibition of excitatory abducens nucleus internuclear neurons is important for medial rectus inhibition.

There is some experimental data supporting the concept of an inhibitory projection to medial rectus motoneurons: Fibre degeneration studies in rabbits [84] and primates [85] and autoradiographic studies in cats [86] and primates [76,87] demonstrated an uncrossed connection between the pontine reticular formation and the 3rd nerve nucleus. This projection originates from neurons in the pontine reticular formation between the level of the 4th and 6th cranial nerve nuclei [88] ascending adjacent but separate from the MLF [76,85], and approaching medial rectus motoneurons [87]. Stimulation of these neurons in animals with bilaterally destructed MLFs was followed by monosynaptic inhibitory potentials in ipsilateral 3rd nerve nucleus neurons and ipsilateral medial rectus motoneurons [88–90]. If this connection mediates medial rectus inhibition, its lesion would be followed by an abduction paresis with normal lateral rectus activation but impaired medial rectus inhibition.

The locations of the responsible lesions thought to be followed by an impaired medial rectus inhibition or abnormal convergence during lateral gaze are in accordance to

both, abnormal electrophysiological and clinical findings, and to an ischemic origin of the lesions as diagnosed in most of our patients. The regions in question, i.e. the midbrain area containing convergence neurons, the region of the uncrossed inhibitory connection, and the trigeminal mesencephalic tract and nucleus forms a watershed zone. It is supplied by long penetrating branches of the basilar artery with additional contributions from paramedian, lateral, and dorsolateral branches of the posterior cerebral artery and the superior cerebellar artery [91,92]. Occlusion of a long penetrating artery may cause unilateral or bilateral lesions, as these arteries often show an asymmetric termination [91,92], which explains bilateral MassR abnormalities in our patients. EOG documented slowed abduction saccades on non-paretic may also be attributed to asymmetric bilateral lesions. The close relation of the mesencephalic tract and nucleus of the trigeminal nerve to both, mesencephalic convergence neurons and the probably inhibitory connection between the pontine reticular formation and the medial rectus subnucleus, explains abnormal MassR findings in our patients. Slowed contraversive saccades (in 5 of our patients) may also occur with lesions near the 3rd nerve nucleus, if such lesions involve the descending excitatory fibres to the paramedian pontine reticular formation before its crossing at the 3rd/4th nerve nucleus level. A combined abduction and superior oblique palsy in the same eye and an ipsilateral MassR abnormality, which is caused by a single responsible lesions, can only be attributed to a midbrain lesion involving the intra-axial segment of the crossed 4th nerve, which runs closely related to the probably inhibitory connection and the trigeminal mesencephalic tract and nucleus. Monocular elevation paresis and abduction paresis in the same eye may also be caused by a single ipsilateral midbrain lesion involving the probably inhibitory connection and the intramesencephalic 3rd nerve, as monocular elevation paresis may also be caused by intraaxial 3rd nerve lesions [93].

## Conclusions

Our data add further evidence on the existence of an abduction paresis with rostral pontine or mesencephalic lesions. With such locations, the most likely explanation is an increased tone of the antagonistic medial rectus muscle during lateral gaze, which may be due to abnormal convergence or impaired medial rectus inhibition. Both mechanisms are followed by "a failure of ocular abduction which is not due to dysfunction of the sixth nerve" [24]. Such ocular motor disorder resembles the ominous and unsettled "posterior internuclear ophthalmoplegia" of Lutz only with respect to its prenuclear origin, but not its mechanism. An impaired excitation of the lateral rectus muscle in one eye without impaired excitation of the medial rectus muscle in the other eye, as proposed by Anton Lutz, is not compatible with the proven prenuclear organisation of horizontal eye movements. All kinds of horizontal eye movements (saccades, pursuit, vestibulo-ocular-reflex) are generated by an excitation of both, abducens nucleus motoneurons and internuclear neurons [see for review [57]]. This is followed by the simultaneous activation of the lateral rectus muscle in one eye (via projections of lateral rectus motoneurons) and the medial rectus muscle in the other eye (via the projections of abducens nucleus internuclear neurons, which cross at the abducens nucleus level and ascend in the medial longitudinal fasciculus to medial rectus motoneurons). Impaired excitation of the lateral rectus muscle without excitation of the medial rectus muscle in the opposite eye can not occur with lesions of prenuclear excitatory connections mediating horizontal gaze. This is only seen with infranuclear lesions of the 6th nerve. An increased tone of the antagonistic medial rectus muscle during lateral gaze is the only possible mechanism of an abduction paresis, which is not caused by a sixth nerve lesion. Such an ocular motor disorder should be called "pseudoabducens palsy" [29] or "pseudo-sixth" [24], because the term "posterior INO" was introduced on the basis of an erroneous neuroanatomical concept. Moreover, Cogan [94] had his own anterior and posterior types of internuclear ophthalmoplegia (INO) using the term "posterior INO" for the well known INO (= adduction paresis on lateral gaze and preserved adduction during convergence), and the term "anterior INO" for an INO with convergence paresis, which further confuses terminology [95].

Diagnosis of a pseudoabducens palsy should only be considered in patients with clinical, electrophysiological, or morphological evidence of an ipsilateral rostral pontine or mesencephalic lesion. In our experience, such an eye movement disorder is very rare with an incidence of less than one tenth as compared to the incidence of the well known internuclear ophthalmoplegia with adduction paresis on lateral gaze but usually preserved adduction during convergence.

## Competing interests

None declared

## References

1. Lutz A: **Über die Bahnen der Blickwendung und deren Dissoziierung. (Nebst eines Falles von Ophthalmoplegia internuclearis anterior in verbindung mit Dissoziierung der Bogengänge).** *Klin Monatsbl Augenheilkd* 1923, **70**:213-235
2. Larmande A-M: **La paralysie supranucléaire du VI.(dite ophthalmoplégie internucléaire postérieure).** *Arch d' Ophtalmol (Paris)* 1969, **29**:521-530
3. Schiffter R: **Die internukleären Ophthalmoplegien. Klinische Analyse von 25 Kranheitsfällen.** *Nervenarzt* 1975, **46**:116-127
4. Collard M, Eber AM, Streicher D, Rohmer F: **L'ophthalmoplégie internucléaire postérieure-existe-t-elle? A propos de onze observations avec oculographie.** *Rev Neurol* 1979, **135**:293-312

5. Topilow HW: **Posterior internuclear ophthalmoplegia of Lutz.** *Ann Ophthalmol* 1981, **13**:221-226
6. Bogousslavsky J, Regli F, Ostinelli B, Rabinowicz T: **Paresis of lateral gaze alternating with so-called posterior internuclear ophthalmoplegia. A partial pontine reticular formation-abducens nucleus syndrome.** *J Neurol* 1985, **232**:38-42
7. Kommerell G: **Internuclear ophthalmoplegia of abduction. Isolated impairment of phasic ocular motor activity in supranuclear lesions.** *Arch Ophthalmol* 1975, **93**:531-534
8. Walsh FB, Hoyt WF: **Clinical Neuro-Ophthalmology,** *Baltimore, Williams & Wilkins* 1969, **Vol. 1**:239-243
9. Yokota JI, Imai H, Mizuno Y, Hishii M, Ito M: **Unilateral supranuclear abducens palsy in a pineal tumor.** *No-To-Shinkei* 1994, **46**:291-295
10. Rothstein TL, Alvord EC: **Posterior internuclear ophthalmoplegia. A clinicopathological study.** *Arch Neurol* 1971, **24**:191-202
11. Fine M, Mac Glashan CB: **Unilateral internuclear ophthalmoplegia of vascular origin.** *Arch Ophthalmol* 1956, **56**:327-337
12. Henn V, Büttner U, Büttner-Ennever JA: **Supranukleäre Organisation der Okulomotorik-physiologische und anatomische Grundlagen.** *In: Augenbewegungsstörungen. Neurophysiologie und Klinik (Edited by Kommerell G) München, Bergmann* 197829-141
13. Oliveri RL, Bono F, Quattrone A: **Pontine lesion of the abducens fasciculus producing so-called posterior internuclear ophthalmoplegia.** *Eur Neurol* 1997, **37**:67-69
14. Wiest G, Wanschitz J, Baumgärtner C, Trattnig S, Deecke L, Mueller C: **So-called posterior internuclear ophthalmoplegia due to a pontine glioma: a clinicopathological study.** *J Neurol* 1999, **246**:412-415
15. Thömke F, Hopf HC, Krämer G: **Internuclear opththalmoplegia of abduction. Clinical and electrophysiological data on the existence of an abduction paresis of prenuclear origin.** *J Neurol Neurosurg Psychiatry* 1992, **55**:105-111
16. Thömke F, Hopf HC: **Pontine lesions mimicking acute peripheral vestibulopathy.** *J Neurol Neurosurg Psychiatry* 1999, **66**:340-349
17. Poser CM, Paty DW, Scheinberg L, McDonald WI, Davis FA, Ebers GC, Johnson KP, Sibley WA, Silberberg DH, Tourtelotte WW: **New diagnostic criteria for multiple sclerosis: Guidelines for research protocols.** *Ann Neurol* 1983, **13**:227-231
18. Paty DW, Asbury AK, Herndon RM, McFarland HF, McDonald WI, McIlroy WJ, Prineas JW, Scheinberg LC, Wolinsky JS: **Use of magnetic resonance imaging in the diagnosis of multiple sclerosis: Policy statement.** *Neurolgy* 1986, **36**:1575
19. Hopf HC: **Topodiagnostic value of brain stem reflexes.** *Muscle Nerve* 1994, **17**:475-484
20. Thömke F: **Isolated cranial nerve palsies due to brainstem lesions.** *Muscle Nerve* 1999, **22**:1168-1176
21. Leigh RJ, Zee DS: **Ocular motor syndromes caused by lesions of the mesencephalon.** *In: The Neurology of Eye Movements (by Leigh RJ, Zee DS) New York, Oxford University Press* 1999511-526
22. Körney S: **Blickstörungen bei vasculären Herden des mesodiencephalen Übergangsgebietes.** *Arch Psychiat Z ges Neurol* 1959, **198**:535-543
23. Orlowski WJ, Slomski P, Wojtowicz S: **Bielschowsky-Lutz-Cogan syndrome.** *Am J Ophthalmol* 1965, **59**:416-430
24. Caplan LR: **"Top of the basilar" syndrome.** *Neurology* 1980, **30**:72-79
25. Weisberg LA: **Mesencephalic hemorrhages: clinical and computed tomographic correlations.** *Neurology* 1986, **36**:713-716
26. Rousseaux M, Petit H, Hache JC, Devos P, Dubois F, Warot P: **La motricite oculaire et cephalique dans les infarctus de la region thalamique.** *Rev Neurol* 1985, **141**:391-403
27. Gomez CR, Gomez SM, Selhorst JB: **Acute thalamic esotropia.** *Neurology* 1988, **38**:1759-1762
28. Namer IJ, Öztekin MF, Kansu T, Zilli T: **Pseudo-sixth nerve palsy with thalamo-mesencephalic junction lesion. Report of two cases.** *Neuro-ophthalmology* 1990, **10**:69-72
29. Pullicino P, Lincoff N, Truax BT: **Abnormal vergence with upper brainstem infarcts. Pseudoabducens palsy.** *Neurology* 2000, **55**:352-358
30. Nashold BS, Gills JP: **Ocular signs from brain stimulation and lesions.** *Arch Opthalmol* 1967, **77**:609-618
31. Alberts MJ, Faulstich ME, Gray L: **Stroke with negative brain magnetic resonance imaging.** *Stroke* 1992, **23**:663-667
32. Besson G, Hommel M, Clavier I, Perret J: **Failure of magnetic resonance imaging in the detection of pontine lacune.** *Stroke* 1992, **23**:1535-1536
33. Rumbach L, Eber AM, Dietemann JL, Bataillard M, Tranchant C, Warter JM, Collard M: **Apport de l'I.R.M. au diagnostic topographique des troubles oculomoteurs dans la sclérose en plaques.** *Rev Neurol* 1990, **146**:30-35
34. Bronstein AM, Rudge P, Gresty MA, du Boulay G, Morris J: **Abnormalities of horizontal gaze. Clinical, oculographic and magnetic resonance imaging findings. II. Gaze palsy and internuclear ophthalmoplegia.** *J Neurol Neurosurg Psychiatry* 1990, **53**:200-207
35. Mutschler V, Eber AM, Rumbach L, Dietemann JL, Bataillard M, Collard M: **Internuclear ophthalmoplegia in 14 patients. Clinical and topographic correlation using magnetic resonance imaging.** *Neuro-ophthalmology* 1990, **10**:319-235
36. Thömke F, Hopf HC: **Aquired monocular elevation paresis – An asymmetric upgaze palsy.** *Brain* 1992, **115**:1901-1910
37. Newmann NJ, Lessell S: **Isolated pupil-sparing third-nerve palsy as the presenting sign of multiple sclerosis.** *Arch Neurol* 1990, **47**:817-818
38. Rose JW, Digre KB, Lynch SG, Harnsberger RH: **Acute VIth cranial nerve dysfunction in multiple sclerosis.** *J Clin Neuro-ophthalmol* 1993, **12**:17-20
39. Thömke F, Lensch E, Ringel K, Hopf HC: **Isolated cranial nerve palsies in multiple sclerosis.** *J Neurol Neurosurg Psychiatry* 1997, **63**:682-685
40. Jacobson DM, Moster ML, Eggenberger ER, Galetta SL, Liu GT: **Isolated trochlear nerve palsy in patients with multiple sclerosis.** *Neurology* 1999, **53**:877-879
41. Fukazawa T, Moriwaka F, Hamada T, Tashiro K: **Facial palsy in multiple sclerosis.** *J Neurol* 1997, **244**:631-633
42. Comi G, Martinelli V, Medaglini S, Locatelli T, Filippi M, Canal N, Triulzi F, DelMaschio A: **Correlation between multimodal evoked potentials and magnetic resonance imaging in multiple sclerosis.** *J Neurol* 1989, **236**:4-8
43. Hopf HC, Gutmann L: **Diabetic 3rd nerve palsy: evidence for a mesencephalic lesion.** *Neurology* 1990, **40**:1041-1045
44. Uncini A, Faricelli A, Assetta M, Serio A, Tartaro A, Gambi D: **Electrophysiological and magnetic resonance imaging correlates of brainstem demyelinating lesions.** *Electromyogr clin Neurophysiol* 1990, **30**:233-238
45. Tettenborn B: **Multifocal ischemic brain-stem lesions.** *In: Brainstem localization and function (Edited by Caplan LR, Hopf HC) Berlin Springer* 199323-31
46. Thömke F, Tettenborn B, Hopf HC: **Third nerve palsy as the sole manifestation of midbrain ischemia.** *Neuro-ophthalmology* 1995, **15**:327-335
47. Thömke F: **Isolated abducens palsies due to pontine lesions.** *Neuro-ophthalmology* 1998, **20**:91-100
48. Thömke F, Hopf HC: **Pontine lesions mimicking acute peripheral vestibulopathy.** *J Neurol Neurosurg Psychiatry* 1998, **66**:340-349
49. Thömke F, Hopf HC: **Isolated superior oblique palsies with electrophysiologically documented brainstem lesions.** *Muscle Nerve* 2000, **23**:267-270
50. Hanstock CC, Faden AI, Bendall MR, Vink R: **Diffusion-weighted imaging differentiates ischemic tissue from traumatized tissue.** *Stroke* 1994, **25**:843-848
51. Fisher M, Prichard JW, Warach S: **New magnetic resonance technique for acute ischemic stroke** *JAMA* 1995, **274**:908-911
52. Rydberg JN, Riederer SJ, Rydberg CH, Jack CR: **Contrast optimization of fluid-attenuated inversion recovery (FLAIR) imaging.** *Magn Reson Med* 1995, **34**:868-877
53. Ashikaga R, Araki Y, Ishida O: **MRI of head injury using FLAIR.** *Neuroradiology* 1997, **39**:239-242
54. Mika-Grüttner A, Thömke F, Marx JJ, Urban PP, Ringel K, Hopf HC: **MRI versus electrophysiologic testing in internuclear ophthalmoplegia.** *2nd European Meeting on Brainstem Reflexes, Functions and Related Movement Disorders. Amsterdam. Movement Disorders [Abstract],* 2001
55. Marx JJ, Thömke F, Fitzek S, Vucurevic G, Fitzek C, Mika-Grüttner A, Urban PP, Stoeter P, Hopf HC: **Topodiagnostic value of blink reflex R1 changes – A digital postprocessing MRI correlation study.** *Muscle & Nerve,*
56. Bender MB, Shanzer S: **Oculomotor pathways definded by electrical stimulation and lesions in the brainstem of monkey.** *In:*

*The Oculomotor System (Edited by Bender MB) New York, Harper and Row* 196481-140
57. Leigh RJ, Zee DS: **Brain stem connections for horizontal conjugate movements.** *In: The Neurology of Eye Movements (by Leigh RJ, Zee DS) New York, Oxford University Press* 1999215-221
58. Griffin JF, Wray SH, Anderson DP: **Misdiagnosis of spasm of the near reflex.** *Neurology* 1976, **26**:1018-1020
59. Guiloff RJ, Whiteley A, Kelley RE: **Organic convergence spasm.** *Acta neurol scand* 1980, **61**:252-259
60. Dagi LR, Chrousos GA, Cogn DC: **Spasm of the near reflex associated with organic disease.** *Am J Ophthalmol* 1987, **103**:582-585
61. Moster ML, Hoenig EM: **Spasm of the near reflex associated with metabolic encephalopathy.** *Neurology* 1989, **38**:150
62. Ochs AL, Stark L, Hoyt WF, D'Amico D: **Opposed adducting saccades in convergence-retraction nystagmus. A patient with sylvian aqueduct syndrome.** *Brain* 1979, **102**:497-508
63. Keane JR: **The pretectal syndrome. 206 patients.** *Neurology* 1990, **40**:684-690
64. Leigh RJ, Zee DS: **Vergence eye movements.** *In: The Neurology of Eye Movements (by Leigh RJ, Zee DS) New York, Oxford University Press* 1999286-318
65. Jampel RS: **Representation of the near response on the cerebral cortex of the macaque.** *Am J Ophthalmol* 1959, **48**:573-582
66. Jampel RS: **Convergence, divergence, pupillary reactions and accomodation of the eyes from faradic stimulation of the macaque brain.** *J Comp Neurol* 1960, **115**:371-397
67. Leichnetz GR: **The prefrontal cortico-oculomotor trajectories in the monkey. A possible explanation for the effects of stimulation/lesion experiments on eye movements.** *J Neurol Sc* 1981, **49**:387-396
68. Leichnetz GR, Spencer RF, Hardy SGP, Astruc J: **The prefrontal corticotectal projection in the monkey. An anterograde and retrograde horseradish peroxidase study.** *Neuroscience* 1981, **6**:1023-1041
69. Büttner-Ennever JA, Akert K: **Medial rectus subgroups of the oculomotor nucleus and their abducens nucleus internuclear input.** *J. Comp Neurol* 1981, **197**:17-27
70. Mays LE: **Neural control of vergence eye movements: convergence and divergence neurons in midbrain.** *J Neurophysiol* 1984, **51**:1091-1108
71. Burde RM, Lehman RAW, Roper-Hall G, Brooks J, Keltner JL: **Experimental internuclear ophthalmoplegia.** *Brit. J. Ophthalmol* 1977, **61**:233-239
72. Pinhas I, Pinhas A, Goldhammer V, Braham J: **Progressive supranuclear palsy: Electromyographic examinations of eye muscles.** *Acta neurol scandinav* 1978, **58**:304-308
73. Agnetti V, Traccis S, Depperu PV, Azzera GB: **Internuclear ophthalmoplegia of abduction: Ocular EMG patterns.** *In: Neurogenetics and Neuro-ophthalmology (Edited by Huber A, Klein D) Amsterdam, Elsevier* 1981263-266
74. Pola J, Robinson DA: **An explanation of eye movements seen in internuclear ophthalmoplegia.** *Arch Neurol* 1976, **33**:447-452
75. King WM, Lisberger SG, Fuchs AF: **Responses of fibers in the medial longitudinal fasciculus (MLF) of alert monkeys during horizontal and vertical conjugate eye movements evoked by vestibular or visual stimuli.** *J Neurophysiol* 1976, **39**:1135-1149
76. Büttner-Ennever JA, Henn V: **An autoradiographic study of the pathways from the pontine reticular formation involved in horizontal eye movements.** *Brain Res* 1976, **108**:155-164
77. Steiger HJ, Büttner-Ennever JA: **Oculomotor nucleus afferents in the monkey demonstrated with horseradish peroxidase.** *Brain Res* 1979, **160**:1-15
78. Pierrot-Deseiligny C: **Circuits oculomoteurs centraux.** *Rev Neurol* 1985, **141**:349-370
79. Highstein SM, Maekawa K, Steinacker A, Cohen B: **Synaptic input from the pontine reticular nuclei to abducens motoneurons and internuclear neurons in the cat.** *Brain Res* 1976, **112**:162-167
80. Scudder CA, Fuchs AF, Langer TP: **Characteristics and functional identification of saccadic inhibitory burst neurons in the alert monkey.** *J Neurophysiol* 1988, **59**:1430-1454
81. Loeffler JD, Hoyt WF, Slatt B: **Motor excitation and inhibition in internuclear palsy.** *Arch Neurol* 1966, **15**:664-671
82. Gonzalez C, Reuben RN: **Ocular electromyography in the syndrome of the median longitudinal fasciculus. Patterns of inhibition and excitation.** *Am J Ophthalmol* 1967, **64**:916-926
83. Pierrot-Deseilligny C, Rigolet MH, Chain F: **Etude électromyographique de deux cas d'ophtalmoplégie internucléaire: Déductions physiopathologiques.** *Rev Neurol* 1979, **135**:143-152
84. Matano S: **Experimental Studies on the medial longitudinal fasciculus in the rabbit. V. Ascending fibers from the reticular formation and the oculomotor system.** *J Hirnforsch* 1970, **12**:241-253
85. Goebel HH, Komatsuzaki A, Bender MB, Cohen B: **Lesions of the pontine tegmentum and conjugate gaze paralysis.** *Arch Neurol* 1971, **24**:431-440
86. Graybiel AM: **Direct and indirect preoculomotor pathways of the brainstem: An autoradiographic study of the pontine reticular formation in the cat.** *J Comp Neurol* 1977, **175**:37-78
87. Büttner-Ennever JA, Miles TA, Henn V: **The role of the pontine reticular formation in oculomotor function.** *Exp Brain Res* 1975, **23(Suppl)**:31
88. Remmel RS, Skinner RD, Pola J: **Cat pontomedullary reticular neurons projecting to the regions of the ascending MLF and the vestibular nuclei.** *Control of gaze by brain stem neurons (Edited by Baker A, Berthoz A) Amsterdam, Elsevier* 1977163-166
89. Highstein SM, Cohen B, Matsunami K: **Monosynaptic projections from the pontine reticular formation to the IIIrd nucleus in the cat.** *Brain Res* 1975, **75**:340-344
90. Grantyn A, Grantyn R, Gaunitz U, Robin KP: **Sources of direct excitatory and inhibitory inputs from the medial rhombencephalic tegmentum to lateral and medial rectus motoneurons in the cat.** *Exp Brain Res* 1980, **39**:49-61
91. Hassler O: **Arterial pattern of human brainstem. Normal appearance and deformation in expanding supratentorial conditions.** *Neurology* 1967, **17**:368-375
92. Duvernoy AM: **Human brainstem vessels.** *Berlin, Springer* 1978
93. Gauntt CD, Kashii S, Nagata I: **Monocular elevation paresis caused by an oculomotor fascicular impairment.** *J Clin Neuro-Ophthalmol* 1995, **15**:11-14
94. Cogan DG: **Neurology of the ocular muscles.** *Springfield, Charles C. Thomas* 1956
95. Zee DS: **Supranuclear and internuclear ocular motor disorders.** *In: Walsh & Hoyt's Clinical Neuro-Ophthalmology, Vol. I (Edited Miller NR, Newman NJ). Baltimore; Williams & Wilkins* 19981283-1349