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Acute migrainous vertigo: clinical and oculographic findings

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Summary

Migrainous vertigo (MV) is an increasingly recognized cause of episodic vertigo. However, the pathophysiology of MV is still a matter of speculation and it is not known to what extent the dysfunction is located in the central or peripheral vestibular system. The aim of this prospective study was to describe the clinical spectrum of acute MV and to clarify which structures of the vestibular system are involved. Testing of 20 patients with acute MV included neuro-otological examination, recording of spontaneous and positional nystagmus with 3D video-oculography, and audiometry. Pathological nystagmus was observed in 70% of patients during acute MV: six had isolated spontaneous nystagmus, five had isolated positional nystagmus and three had a combination of the two. Only a few patients showed additional ocular motor deficits. Imbalance was observed in all patients except one. Hearing was not affected in any patient during the attack. The findings during acute MV point to central–vestibular dysfunction in 10 patients (50%) and to peripheral vestibular dysfunction in three patients (15%). In the remaining seven patients (35%) the site of involvement could not be determined with certainty. MV should be considered in the differential diagnosis of vertigo with spontaneous and positional nystagmus and can present both as a central and a peripheral vestibular disorder.

Keywords: migraine; migrainous vertigo; nystagmus; vestibular; video-oculography

Abbreviations: IHS = International Headache Society; MV = migrainous vertigo; SPV = slow-phase velocity; VOG = video-oculography; VOR = vestibulo-ocular reflex

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Introduction

Over the last few decades, a syndrome that causally links vertigo to migraine has evolved from several case series (Slater, 1979; Moretti *et al*., 1980; Kayan and Hood, 1984; Cutrer and Baloh, 1992; Lempert *et al*., 1993; Bikhazi *et al*., 1997; Cass *et al*., 1997; Dieterich and Brandt, 1999; Neuhauser *et al*., 2001). The clinical association of migraine and vertigo has been supported by case-controlled studies showing that migraine is more common in patients presenting with dizziness than in age- and sex-matched controls (Neuhauser *et al*., 2001) and, inversely, that vertigo is more common in patients with migraine than in controls (Kuritzky *et al*., 1981; Kayan and Hood *et al*., 1984). In specialized dizziness clinics, migrainous vertigo (MV) accounts for at least 7% of diagnoses (Dieterich and Brandt, 1999; Neuhauser *et al*., 2001).

At present, the International Headache Society's (IHS) classification of headache disorders does not include a comprehensive category for MV (Headache Classification Subcommittee of the International Headache Society, 2004). MV may last anything from seconds to several days (Cutrer and Baloh, 1992; Neuhauser *et al*., 2001), and therefore often differs from a typical migraine aura which lasts between 5 and 60 min. The diagnostic criteria for basilar migraine are rarely fulfilled because this requires at least two aura symptoms from the posterior circulation territory (Cutrer and Baloh, 1982; Dieterich and Brandt, 1999). To resolve this situation,

our group has proposed diagnostic criteria for *definite* and *probable* MV which are based on a history of migrainous symptoms that are temporally related to recurrent vertigo (Neuhauser *et al*., 2001).

The pathophysiology of MV is still a matter of speculation; it is not even known whether the origin is in the central or peripheral vestibular system. In any paroxysmal disorder, the physical examination during the acute episode is indispensable for an understanding of the underlying pathophysiology. However, there are only a few case reports on clinical findings during an acute episode of MV (Moretti *et al*., 1980; Lempert *et al*., 1993; Dieterich and Brandt, 1999) and neurological and neuro-otological signs have never been assessed systematically in the symptomatic phase. The aim of this prospective study was to record and describe the spectrum of clinical findings during acute MV and to elucidate whether central or peripheral vestibular structures are involved.

Patients and methods

Criteria for migrainous vertigo

The diagnosis of definite MV was based on the following criteria (Neuhauser *et al*., 2001): (i) episodic vestibular symptoms of at least moderate severity (rotational vertigo, other illusionary self or object motion, positional vertigo, head motion intolerance); (ii) migraine according to the IHS criteria (Headache Classification Subcommittee of the International Headache Society, 2004); (iii) at least one of the following migrainous symptoms during at least two vertiginous attacks: migrainous headache, photophobia, phonophobia, visual or other auras; and (iv) other causes ruled out by appropriate investigations.

Note that the term 'head motion intolerance' used in this study indicates vestibular symptoms provoked by any movement of the head and is not to be confused with aggravation of headache by head movement, which is common with migraine.

The criteria for probable MV were (Neuhauser *et al*., 2001): (i) episodic vestibular symptoms of at least moderate severity; (ii) at least one of the following: migraine according to the criteria of the IHS; migrainous symptoms during vertigo; migraine-specific precipitants of vertigo, e.g. specific foods, sleep irregularities and hormonal changes; response to antimigraine drugs; and (iii) other causes ruled out by appropriate investigations.

Patients

Patients presenting to our dizziness clinic with MV usually lasting at least 2 h were asked to inform one of the authors (D. Z.) via mobile phone during an episode of vertigo. Patients were examined between August 1999 and January 2003 by D. Z. and a neuro-otologist (M. v. B., H. N. or T. L.) within 1 h after alert either at home or in our clinic. All patients were still symptomatic when we arrived for examination. One patient, in whom the diagnosis of MV had been made previously, was excluded from the study because she presented with a migraine attack and symptoms due to orthostatic dysregulation. Further patients were recruited from our emergency department. The study was approved by the local ethics committee. Informed consent was obtained from all participants prior to the measurements.

In total, 20 patients participated in the study, 13 from the dizziness clinic and seven from the emergency department. Thirteen patients were female (65%) and seven male (35%). Their ages ranged from 18 to 77 years with an average of 49.4 ± 15.0 years (Table 1). Thirteen patients reported migraine without aura, six patients had migraine with aura and one patient had a probable migraine according to the criteria of the IHS (Headache Classification Subcommittee of the International Headache Society, 2004). Seventeen patients were

Table 1 *Clinical characteristics of 20 patients with migrainous vertigo by history*

Patient	Sex	Age (years)	Age at onset (years)	Vestibular complaint	Migraine symptoms	Migrainous symptoms during MV	MV
1	F	44	34	**PV**, HMI	MO	Phono	Definite
2	F	41	37	CV	MO	–	Probable
3	M	25	24	**PV**, CV	MO	Photo	Definite
4	M	77	56	**PV**, CV	MA	Photo, phono	Definite
5	F	63	63	**HMI**, CV, PV	MO	H, photo	Probable
6	F	60	59	**PV**, CV	MA	H, photo, phono	Definite
7	M	59	54	PV	MO	H	Definite
8	F	47	27	**PV**, HMI	MA	H, photo, phono	Definite
9	F	61	36	**CV**, HMI	MA	H, photo, phono	Definite
10	F	45	36	**CV**, HMI	MA	Photo, aura	Definite
11	M	49	39	**CV**, PV, HMI	MO	H, photo, phono	Definite
12	F	18	17	CV	MO	Photo	Definite
13	F	54	54	CV	PM	Photo	Probable
14	M	40	30	**HMI**, CV	MO	H, photo, phono	Definite
15	F	24	22	**PV**, CV	MO	H, photo	Definite
16	F	56	44	**HMI**, CV	MA	H, photo	Definite
17	F	70	66	**PV**, CV, HMI	MO	H, photo	Definite
18	M	56	53	**HMI**, CV	MO	H	Definite
19	F	48	47	**HMI**, CV	MO	H	Definite
20	M	51	49	**HMI**, CV, PV	MO	H, photo	Definite

Vestibular complaints in bold type indicate predominant symptoms. CV = constant vertigo; PV = positional vertigo; HMI = head motion intolerance (vertigo, dizziness or imbalance which is provoked by head motion); MO = migraine without aura; MA = migraine with aura; PM = probable migraine; H = headache; photo = photophobia; phono = phonophobia.

diagnosed as definite MV and three patients as probable MV. Recurrent temporal association of vestibular and migrainous symptoms were reported by 18 patients, 12 of whom had also experienced isolated episodes of vertigo. The mean age of manifestation of migraine was 22.3 years (range 10–53 years). The mean age of onset of vertigo was 42.5 years with a range from 18 to 63 years. The onset of migraine preceded the manifestation of vestibular symptoms in all but one patient. Patients with any additional vestibular or neurological disorder were excluded from the study. The consumption of sedating drugs or alcohol within 24 h and of tobacco within 6 h before examination was an exclusion criterion; however, this criterion proved unnecessary in the patients examined. Prophylactic medication had been taken in some cases: β-blockers in three and betahistine in two patients. In the case of the examined attack, one patient had taken naratriptan and another aspirin. Testing was repeated in 18 patients during the symptom-free interval, and two patients did not return for follow-up.

The median latency between onset of MV and examination was 14.5 h (range 3–72 h, data not normally distributed). Ten patients were examined during maximum intensity and eight patients during high intensity of symptoms. Two patients stated that their vertigo had significantly improved (but not disappeared) at the time of examination. Several patients reported that they had felt too unwell for an examination earlier during the attack.

History and clinical testing during acute MV

Patients were asked about onset, type and severity of vestibular and migrainous symptoms as well as autonomic and auditory accompaniments by means of a structured interview. The neurological examination included observation of spontaneous and positional nystagmus in the upright, supine and right and left lateral positions with and without Frenzel's glasses, a cover test for ocular palsies and bedside testing of horizontal and vertical smooth pursuit and saccades. Gaze-evoked nystagmus was tested in eccentric positions in light in the horizontal (30–35°) and vertical (25–30°) plane, and was considered positive when present for more than 10 s. For testing of the horizontal vestibulo-ocular reflex (VOR), the examiner performed head impulses in the horizontal plane, while the patient was instructed to fixate the nose of the examiner (head thrust test) (Halmagyi and Curthoys, 1988). Coordination was examined with the Romberg test, the tandem Romberg test with both feet in line, walking and tandem walking with eyes open, diadochokinesis, and the finger–nose and heel–chin tests. Full neurological examination was not included in order to limit the duration of testing to a tolerable length in these acutely ill patients. However, all patients received a full neurological examination at some point. For the same reason, the Dix–Hallpike test was not performed.

Eye movement recording

Horizontal, vertical and torsional eye movements were recorded monocularly with a custom made portable video-oculography system (VOG; A. Clarke, Berlin, Germany). Eye movements were recorded around primary gaze in darkness (after instructing the patients to look straight ahead) in four head positions: upright, supine, and lying with the left and right ear down. In addition, spontaneous eye movements were recorded in light with the non-recorded eye fixating. Each position was maintained for at least 60 s. Off-line VOG processing yielded horizontal and vertical eye positions at a sample rate of 50 Hz and torsional eye position at a sample rate of 25 Hz. Nystagmus slow-phase velocity (SPV) was quantified as the mean of 10 representative slow phases, measured by hand from the eye position trace. In two patients, VOG recording could not be performed due to technical problems; however, eye movements were clinically examined and documented.

Definition of pathological nystagmus

Nystagmus in darkness with an SPV below 3°/s was considered insignificant and was not further analysed. Spontaneous or positional nystagmus was rated pathological when it was absent in the symptom-free interval or when the SPV of nystagmus during the acute episode of migrainous vertigo exceeded the SPV of the interval by >50%. The term 'spontaneous nystagmus' refers to nystagmus that was observed in the primary position of gaze with the patient upright. Positional nystagmus refers to nystagmus that was exclusively present after positioning, that changed direction after the patient had been brought from upright to a lying position or that showed a change of SPV of >100% between upright and supine positions.

Definition of vestibular syndromes

A diagnosis of peripheral vestibular dysfunction was made when all of the following criteria were met: (i) direction-fixed, predominantly horizontal spontaneous nystagmus; (ii) >50% decrease of SPV of spontaneous nystagmus with fixation; (iii) semicircular canal paresis contralateral to the direction of nystagmus on head impulsive testing (Halmagyi and Curthoys, 1988); and (iv) absence of signs of CNS involvement

A diagnosis of central vestibular dysfunction was made when at least one of the following criteria was fulfilled: (i) purely vertical or torsional spontaneous nystagmus; (ii) <50% decrease of SPV of spontaneous nystagmus with fixation; (iii) positional nystagmus not fulfilling criteria for canalolithiasis and cupulolithiasis (Brandt and Steddin, 1993; Baloh *et al*., 1993, 1995); and (iv) gaze-evoked nystagmus, saccadic pursuit or other ocular motor abnormality present during the acute episode, but with normal findings in the interval.

Other testing procedures

Pure-tone audiometry with air conduction measurements was performed with a mobile audiometer (Grason-Stadler) at 0.5, 1 and 2 kHz. To test for orthostatic dizziness, which may accompany migraine attacks, blood pressure was measured in the supine position and immediately after standing up repeatedly for 2 min. A decrease in systolic blood pressure during orthostasis of at least 20 mm Hg was considered pathological.

Results

Symptoms during the recorded attack

In six patients (30%) the leading vestibular symptom was constant vertigo during the recorded attack. Seven patients (35%) reported positional vertigo in addition to constant vertigo of lesser intensity and one further patient had isolated positional vertigo. Six patients (30%) reported head motion intolerance (dizziness, vertigo or imbalance provoked by head

Table 2 *Symptoms in 20 patients during acute migrainous vertigo*

Symptom	*n*	%
Vestibular		
Constant vertigo	6	30
Positional vertigo	8	60
Head motion intolerance	6	30
Cochlear		
Aural pressure	4	20
Hearing loss	0	0
Tinnitus	0	0
Autonomic		
Nausea	19	95
Vomiting	10	50
Diarrhoea	2	10
Polyuria	1	5
Visual		
Oscillopsia	10	50
Migrainous		
Photophobia	14	70
Headache	13	65
Osmophobia	3	15
Phonophobia	2	10
Aura	2	10

movements) as the main vestibular symptom (Table 2). The entire duration of the acute episode ranged from 7 h to 4 weeks. The duration of the documented episode was less than 24 h in six patients, 24 h to 1 week in eight patients and more than 1 week in four patients. Vertigo subsided in all patients after less than 1 week; vestibular head motion intolerance often prevailed for a longer period. For two patients there was no information available on the resolution of the attack because they did not return for follow-up.

During the examined attack, migrainous symptoms were present in 19 of the 20 patients, 12 of whom reported multiple migrainous symptoms. The most common migrainous symptoms were photophobia and headache (Table 2). One patient had a visual aura with a fortification spectrum during the vertigo and a second reported a somatosensory aura with slowly progressing facial paraesthesias, which she had often experienced with her headaches. The initial symptom was vestibular in 10 patients. Vestibular and migrainous symptoms started coincidentally in four patients. Five patients reported headache as the first symptom. One patient with probable MV had no migrainous symptom during the recorded vertiginous episode but reported a constant temporal relationship between her menstrual cycle and either vertigo or migraine.

None of our patients noticed hearing loss during the vertigo. Four patients reported bilateral aural pressure for seconds to minutes at the beginning of the episode. Two patients had chronic tinnitus that did not change during the attack. Almost all patients had autonomic symptoms during migrainous vertigo (Table 2). Visual complaints included apparent motion of the visual surround (oscillopsia), which was horizontal in eight patients and vertical in two patients.

Nystagmus

Pathological spontaneous or positional nystagmus was present in 14 patients (70%) when examined during the acute episode (Table 3). One further patient showed transient torsional nystagmus (SPV 8°/s) after shaking the head in the horizontal plane, which was only performed in this patient after testing for spontaneous and positional nystagmus was normal (patient 18).

Nine patients (45%) presented with pathological spontaneous nystagmus (Fig. 1). The SPV of spontaneous nystagmus without fixation ranged between 3.0°/s and 33.3°/s (Table 3). The predominant direction of spontaneous nystagmus was horizontal in five patients, vertical in two and torsional in two. In four patients, spontaneous nystagmus was only apparent with Frenzel's goggles. In three patients with horizontal spontaneous nystagmus the head-thrust test revealed a deficit of the vestibulo-ocular reflex contralateral to the direction of nystagmus.

Pathological positional nystagmus was present in eight patients (40%) and persisted as long as the precipitating head position was maintained in all of them. In five patients nystagmus was only present after positioning, while three patients with spontaneous nystagmus showed a change of nystagmus direction with positional testing (Table 3). In three patients positional nystagmus changed direction with different supine positions (Fig. 2).

In all patients, nystagmus had disappeared on follow-up. The only exception was one patient with spontaneous (torsional) and positional nystagmus (downbeating in the supine and left lateral positions) during the attack, who presented on follow-up without spontaneous nystagmus and a different positional nystagmus (torsional in right lateral position) (patient 5). One further patient had identical nystagmus during the attack and on follow-up which was apogeotropic horizontal in the left lateral position (4°/s) and upbeat in the supine position (5°/s) in the dark (patient 19). She was therefore not included in the group of patients with attack-specific findings. One patient with spontaneous horizontal nystagmus and contralateral VOR deficit (and normal hearing) had a persistent unilateral loss of vestibular function on follow-up. The course of the disease resembled vestibular neuritis but we decided to include this patient because he had experienced several similar attacks of shorter duration previously, which were all accompanied by migrainous symptoms, as was his recorded attack.

Other ocular motor findings

Five patients had mild to moderate saccadic pursuit eye movements in the acute episode. This finding persisted in three patients in the interval. Saccades were fast and accurate in all patients. Two patients showed unilateral horizontal gaze-evoked nystagmus that was also present in the interval.

Cerebellar signs, stance and gait

The finger–nose test, heel–shin test and diadochokinesis were normal in all patients. In contrast, 19 patients (95%) showed

Table 3 *Ocular-motor and vestibulospinal findings during acute MV*

Patient	Nystagmus					VOR deficit	GEN	Saccadic pursuit	Gait ataxia	Romberg test	Findings in the interval
	Upright with fixation	Upright without fixation	Supine	Right ear down	Left ear down						
Central vestibular syndrome											
1	U 4°/s;	U 3°/s	U (A)	–	–	–	–	+ L	+	+	–
2	–	TL 3°/s	TL 3°/s	TL (A)	TL (A)	–	–	–	+	+	–
3	–	R 5°/s	R 25°/s	TR 16°/s	TL 8°/s	–	–	–	–	–	n.a.
4	D 9°/s;	D 5°/s	–	R 5°/s	–	–	–	+ R/L	n.f.	n.f.	Hypoacusis
5	–	TL 6°/s	D 6°/s	–	D 3°/s	–	–	–	+	+	Positional nystagmus, hypoacusis
6	–	–	U 16°/s	TR 14°/s	TL 19°/s	–	–	–	+	+	Hypoacusis
7	–	–	R 7°/s	R 8°/s	L 8°/s	–	–	–	–	–	–
8	–	–	–	–	TL 10°/s	–	–	–	+	+	–
9	–	–	–	–	TL 6°/s	–	–	+ R	+	+	Saccadic pursuit, hypoacusis
10	–	–	–	L (A)	–	–	–	–	–	–	–
Peripheral vestibular syndrome											
11	R 4°/s;	R 15°/s	R 14°/s	R 15°/s	R 15°/s	+ L	–	–	+	+	VOR deficit left
12	R 4°/s;	R 33°/s	R 31°/s	R 33°/s	R 31°/s	+ L	–	–	+	+	n.a.
13	R	R	R	R	R	+ L	–	–	+	+	–
Vestibular syndrome of uncertain origin											
14	–	–	–	–	–	–	–	–	–	–	–
15	–	–	–	–	–	–	–	–	+	+	–
16	–	–	–	–	–	–	–	–	–	+	Romberg +
17	–	–	–	–	–	–	+ L	+ L	+	+	GEN; saccadic pursuit, Romberg +
18	–	–	–	–	–	–	–	–	+	+	–
19	–	–	U 5°/s	–	R 4°/s	–	–	–	–	+	Positional nystagmus as in attack
20	–	R	R	R	R	–	+ L	+ R/L	–	–	GEN; saccadic pursuit

GEN = gaze-evoked nystagmus; U = upward; D = downward; R = rightward; L = leftward; TR = torsional to the patient's right side; TL = torsional to the patient's left side; A = quantification not possible due to artefacts; n.a. = not available; n.f. = not feasible. Note that only main directions of nystagmus are presented.

disturbed stance and gait. Thirteen patients (65%) had difficulty walking with eyes open; one of them was unable to stand and walk (Table 3). Tandem walking with eyes open was abnormal in 16 patients, three of them veered to one side and five were unable to perform the test. Fourteen patients (70%) showed a positive Romberg test (i.e. increased body sway after eye closure), eight of whom had a directed lateral sway and one showed a tendency to fall backwards. The tandem Romberg test was pathological in 18 patients.

Performance on gait and balance testing had normalized in almost all patients on follow-up. Three patients had improved considerably but still showed some unsteadiness on tandem Romberg testing.

Audiometry

Pure-tone audiometry was normal in 16 patients. Four patients had abnormal audiograms, which were unchanged when measured again in the asymptomatic interval. In three patients there was a longstanding history of non-fluctuating hearing loss, whereas in one patient (mild) audiographic abnormalities were an incidental finding. Two patients (aged 60 and 63 years) had mild bilateral high-frequency hearing loss, compatible with presbyacusis. One patient (61 years) showed moderate bilateral high-frequency hearing loss, in whom presbyacusis likewise appeared to be the most likely diagnosis. The fourth patient (77 years) had moderate to severe bilateral hearing loss (from 35 dB at low frequencies to 80–90 dB at high frequencies) of unknown aetiology. None of the patients with hearing loss presented with a peripheral type of nystagmus during the attack.

Blood pressure

In the supine position, systolic blood pressure ranged between 100 and 160 mm Hg (127.5 ± 19.0) and diastolic pressure between 60 and 110 mm Hg (79.1 ± 12.5). Systolic blood pressure decreased by 20 mm Hg in two patients without evoking orthostatic symptoms.

Vestibular syndromes

According to the criteria described above, findings in ten patients (50%) were classified as a central vestibular syndrome, in three patients (15%) as a peripheral vestibular syndrome, whereas in seven patients (35%) the site of dysfunction could not be determined with certainty (Table 3). Five patients with

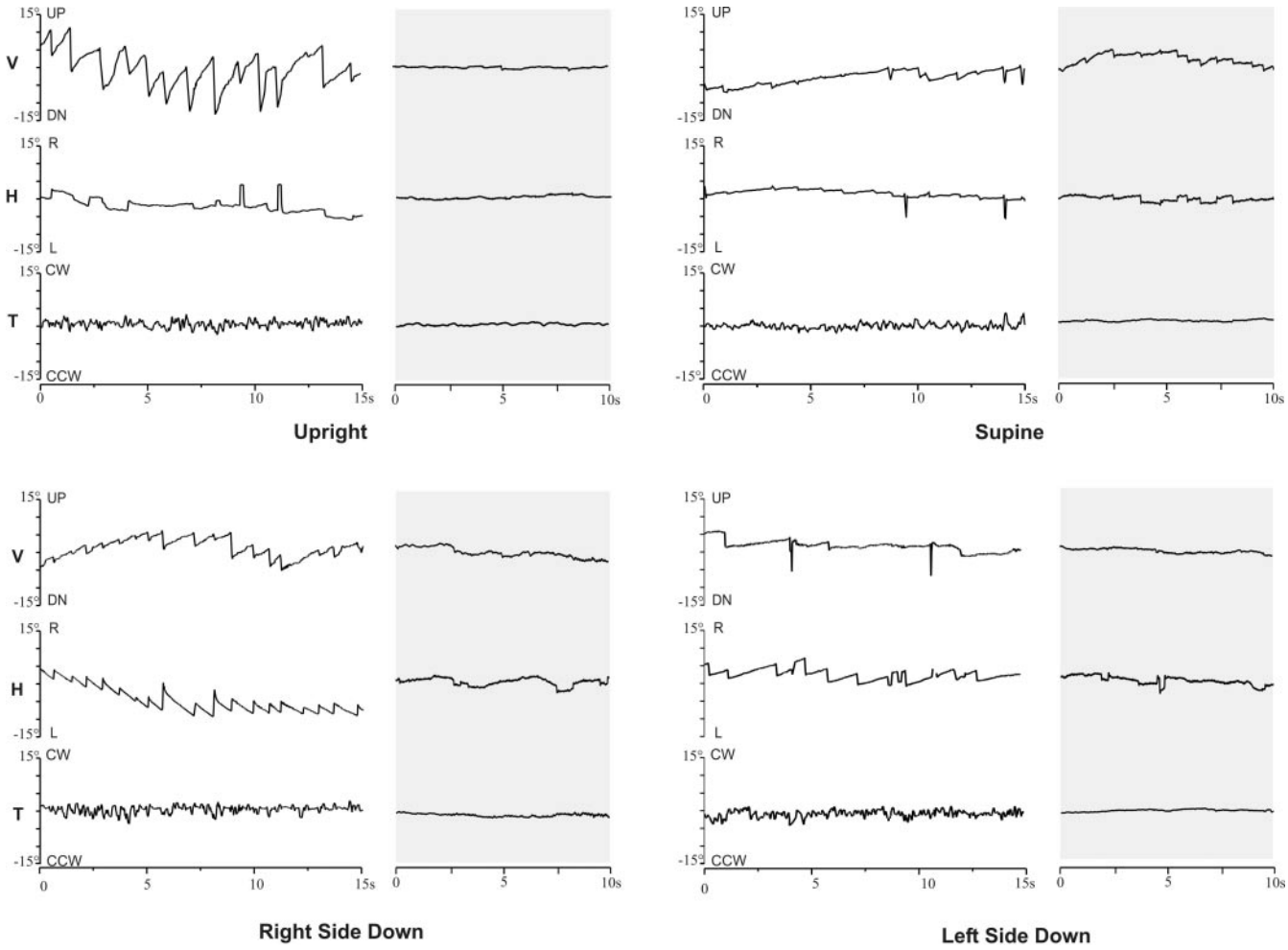

Fig. 1 VOG recording of spontaneous and persistent positional nystagmus in a patient (patient 4) with acute MV and during the symptom-free interval (grey shading). Vertical (V), horizontal (H) and torsional (T) eye movement components are shown. Note the downbeating nystagmus in the upright position, which ceases in the supine position. In the lateral positions a predominantly horizontal, geotropic nystagmus appears which reaches more than 3°/s SPV only on the right side. Note that in all figures torsional eye movements are defined as clockwise (CW) or counterclockwise (CCW) from the patient's point of view. Video examples of eye movements can be seen on www.medizin.fu-berlin.de/hno/vestibularlab/videos.html.

a central vestibular syndrome had spontaneous nystagmus (patients 1–5) and eight had positional nystagmus (patients 3–10).

Discussion

Migrainous vertigo: a vestibular syndrome

In this prospective study we found pathological spontaneous and positional nystagmus in 70% of patients during acute MV. Accordingly, most of our patients experienced vestibular symptoms such as vertigo, oscillopsia and imbalance. The findings confirm the vestibular origin of the syndrome.

We found the neuro-otological manifestations of acute MV to be heterogeneous. Five patients showed spontaneous nystagmus indicative of central vestibular dysfunction. In cases with predominantly torsional spontaneous nystagmus, a dysfunction of the vestibular nuclei at the pontomedullary junction (Lopez *et al*., 1992) or midbrain (Helmchen *et al*., 2002) is most likely, while downbeating nystagmus indicates dysfunction of the vestibulocerebellum or underlying medulla and upbeating nystagmus is commonly reported with midline medullary lesions (Leigh and Zee, 1999). Eight patients demonstrated positional nystagmus not compatible with any variant of benign paroxysmal positional vertigo (Baloh *et al*., 1993, 1995; Brandt and Steddin, 1993). Positional nystagmus of a central type has been reported in posterior fossa lesions adjacent to the fourth ventricle (Brandt, 1990), presumably involving an inhibitory loop between midline archicerebellar structures and the vestibular nuclei. One further patient showed perverted head-shaking nystagmus as a probable sign of central vestibular dysfunction (Leigh and Zee, 1999). In contrast, findings in three patients with predominantly horizontal spontaneous nystagmus and contralateral semicircular canal paresis pointed to acute peripheral vestibular dysfunction.

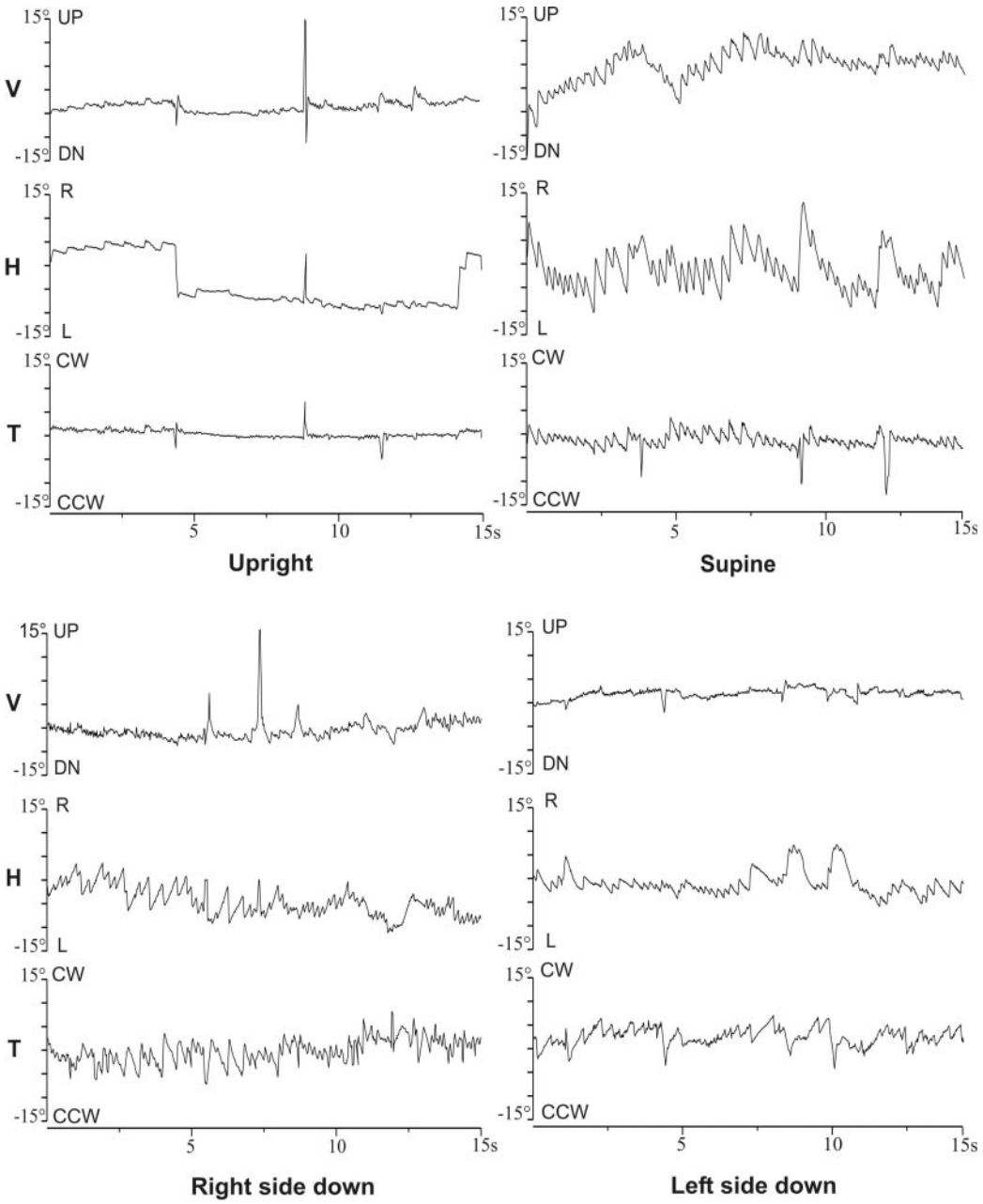

Fig. 2 VOG recording of persistent positional nystagmus in one patient (patient 3) with acute MV. A complex positional nystagmus with vertical, horizontal and torsional components manifests in the supine position. In the left and right lateral supine positions there is a direction-changing horizontal torsional nystagmus, providing strong evidence of a central vestibular origin.

Reports on clinical findings in patients with MV during the acute episode are scarce. Most reported patients had ocular motor signs indicating central or peripheral vestibular dysfunction. Transient spontaneous nystagmus has been described in eight patients with MV examined in the attack, three of whom also had severe vertical positional nystagmus (Dieterich and Brandt, 1999). Another case series found nystagmus in seven patients examined during the vertiginous episode, six due to central and one due to peripheral vestibular dysfunction. Follow-up examination was normal in all patients (Lempert *et al*., 1993). In another report, two out of three patients with vertigo related to migraine showed only mild gaze-evoked nystagmus during the acute episode (Moretti *et al*., 1980).

In summary, the available evidence indicates that MV affects the vestibular system mainly at the brainstem and cerebellar levels and less commonly in the periphery.

Definition of pathological nystagmus

Nystagmus intensity, as measured by its SPV, ranged between 3.0 and 33.3°/s, and was thus comparable with caloric irrigation or with other acute vestibular disorders. In normal subjects, some degree of spontaneous and positional nystagmus is

rather common in darkness (McAuley *et al*., 1996; Bisdorff *et al*., 2000). The American Academy of Neurology (1996) proposed an SPV of 6°/s as the upper limit for positional nystagmus in normal subjects. In this study, analysis of eye movements both during the acute episode and in the asymptomatic interval allowed a more specific approach to the identification of pathological nystagmus by comparison of the two stages. Eye drift ranging below 3°/s was considered insignificant and was not analysed further. Only one patient showed nystagmus with an SPV of >3°/s during acute MV that was also present at follow-up. In all other patients nystagmus was absent or grossly reduced in the interval. Thus, all nystagmus above 3°/s observed during the acute stage alone was most likely related to MV.

Vestibular symptoms

The spectrum of vestibular symptoms in our group of patients with MV includes spontaneous vertigo, positional vertigo and vestibular head motion intolerance in any combination. A transition from spontaneous to positional vertigo and finally to head motion intolerance was often reported. This heterogeneity of symptoms in MV is reflected in several case series that have reported the occurrence of spontaneous vertigo in 21–83% of patients (Cutrer and Baloh, 1992; Bikhazi *et al*., 1997; Cass *et al*., 1997, Johnson, 1998; Dieterich and Brandt, 1999), positional vertigo and dizziness in 17–65% (Kayan and Hood, 1984; Johnson, 1998; Dieterich and Brandt, 1999) and head motion intolerance in 31 and 77% (Cutrer and Baloh, 1992; Cass *et al*., 1997). In our study, eight patients reported positional vertigo as their leading symptom. MV is a neglected differential diagnosis of episodic positional vertigo and can even mimic benign paroxysmal positional vertigo. The observation of positional nystagmus during the acute stage will lead to the correct diagnosis (von Brevern *et al*., 2004).

The duration of vestibular symptoms in our group ranged from several hours to weeks, thus differing from a migraine aura. Notably, it has been reported that 10–30% of patients have vertigo with the typical duration of a migraine aura, i.e. 5–60 min (Dieterich and Brandt, 1999; Neuhauser *et al*., 2001) and 20–30% of patients have even shorter attacks (Cutrer and Baloh, 1992; Dieterich and Brandt, 1999, Neuhauser *et al*., 2001). A limitation of our study is that the median latency between onset of MV and examination was 14.5 h, so that only patients with long-lasting MV were examined. In contrast, patients with a duration of vertigo corresponding to a migraine aura could not be investigated. Therefore, it is possible that patients with short attacks of MV present with clinical findings that differ from the spectrum of our series.

Migrainous symptoms

The recurrent simultaneous occurrence of migrainous and vestibular symptoms can confirm the diagnosis of MV. In this study, symptoms were recorded during the acute attack, whereas previous case series were based on patients' recall. All patients except one reported migrainous complaints during the observed episode, photophobia and headache being most frequent. However, these migrainous symptoms should be specifically inquired about, as patients often do not volunteer them. Furthermore, many patients experience attacks of vertigo both with and without accompanying migrainous symptoms (Cutrer and Baloh, 1992; Johnson, 1998; Neuhauser *et al*., 2001).

Cochlear symptoms

Hearing loss did not occur in our patients during acute MV. However, four patients reported short-lasting aural pressure during the episode. There is clinical evidence that migraine can damage the inner ear, leading to permanent hearing loss (Lipkin *et al*., 1987; Olsson, 1991). Cochlear symptoms such as hearing loss, tinnitus and sensations of aural fullness, sometimes mimicking Menière's disease, have been reported in MV (Kayan and Hood, 1984; Olsson, 1991). A possible link between migraine and Menière's disease was originally suggested by Prosper Menière (Menière, 1861) himself and has been reported by other authors (Atkinson, 1962; Kayan and Hood, 1984). A recent study demonstrates that the lifetime prevalence of migraine is significantly higher in patients with Menière's disease compared with a control group. In addition, 45% of patients with Menière's disease always experienced migrainous symptoms during vertigo attacks (Radtke *et al*., 2002). It has been speculated that these findings may be due to a common pathophysiological mechanism or diagnostic overlap between MV and Menière's disease (Atkinson 1962; Radtke *et al*., 2002). However, the absence of cochlear symptoms makes an alternative diagnosis of Menière's disease highly unlikely in our patients.

Postural symptoms

Almost all patients had unsteadiness of stance and gait in the symptomatic period; most of them had lateral or backward pulsion, which can occur with peripheral and central vestibular, lateral medullary, thalamic and cerebellar dysfunction. Typically, body sway was abnormal with eyes open and further increased with eye closure, indicating vestibulospinal dysfunction. In contrast, testing of neocerebellar function proved normal and ocular motor signs, such as saccadic pursuit and gaze-evoked nystagmus, were present only in a few patients, indicating that the vestibulo-cerebellum is not the predominant site of involvement in MV.

Orthostatic hypotension

Orthostatic hypotension is a common complaint in migraine (Raskin and Knittle, 1976) and can lead to dizziness and dysequilibrium, which may be confounded with MV. Only

two of our patients had borderline positive results in orthostatic testing without concurrent symptoms. Consequently, dizziness and imbalance in MV cannot be attributed to global cerebral hypoperfusion resulting from orthostatic hypotension.

Persistent vestibular abnormalities in patients with MV

In the asymptomatic interval, we found mostly minor vestibular findings in several patients, including one with persistent unilateral loss of vestibular function. Persistent vestibular abnormalities have been documented before in patients with MV during the symptom-free interval, including semicircular canal paresis, central vestibular findings (Kayan and Hood, 1984; Cutrer and Baloh, 1992; Cass *et al*., 1997) as well as mild ocular motor abnormalities (Dieterich and Brandt, 1999). However, most of these studies are flawed by the lack of controls and explicit diagnostic criteria for migraine and migrainous vertigo. Furthermore, a similar incidence of (mostly minor) abnormal vestibular test results and ocular motor abnormalities has been reported in migraine patients unselected for vestibular symptoms (Toglia *et al*., 1981; Harno *et al*., 2003). Therefore, further well-designed studies are needed to assess permanent vestibular dysfunction in patients with MV.

Pathophysiology of MV

How is vestibular dysfunction related to migraine? Various hypotheses have been proposed for MV, all of which are derived from the presumed pathophysiology of migraine. The migraine aura is likely to be the clinical equivalent of a spreading depression and vertigo is the most common manifestation of an aura in basilar artery migraine (Sturzenegger, 1985). Hence, a spreading depression affecting brainstem structures has been proposed to account for short-lasting episodes of MV (Dieterich and Brandt, 1999). Secondly, vasospasm of the internal auditory artery could explain peripheral vestibular and auditory symptoms in migraine (Baloh, 1997), similar to retinal vasospasm observed in retinal migraine (Killer *et al*., 2003). Thirdly, functional imaging studies using PET during acute migraine attacks have identified activation of brainstem regions in projection to the locus coeruleus and the dorsal raphe nucleus, suggesting that these neural structures are involved in the initiation of migraine attacks (Weiller *et al*., 1995). As the vestibular nuclei receive noradrenergic projections from the locus coeruleus (Schuerger and Balaban, 1999) and serotonergic input from the dorsal raphe nucleus (Halberstadt and Balaban, 2003), it is conceivable that activation of these structures in migraine also affects central vestibular processing (Furman *et al*., 2003). Similarly, calcitonin gene-related peptide and other neuropeptides that are released during migraine attacks have a neuromodulatory role in the peripheral and central vestibular system (Cutrer and Baloh, 1992). Fourthly, it has been proposed that defects of ion channels are involved in migraine. A channelopathy could account for central and peripheral vestibular dysfunction and appears to be the most promising hypothesis for migrainous vertigo, since other paroxysmal disorders that often present with both migraine and vertigo have been found to result from mutations in the calcium channel gene CACNA1A, namely familial hemiplegic migraine and episodic ataxia type 2 (Ophoff *et al*., 1996). Searching for mutations in the CACN1A1 gene was negative in several patients with familial migraine with vertigo (Kim *et al*., 1998), but further candidate gene loci have still to be tested. Our study suggests that MV is a heterogeneous vestibular disorder and it is plausible to assume that various pathomechanisms may be involved.

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