Handbook of Clinical Neurology, Vol. 137 (3rd series)
Neuro-Otology
J.M. Furman and T. Lempert, Editors
http://dx.doi.org/10.1016/B978-0-444-63437-5.00022-4

Chapter 22

Vestibular migraine

M. VON BREVERN[1]* AND T. LEMPERT[2]

[1]*Department of Neurology, Park-Klinik Weissensee and Vestibular Research Group, Berlin, Germany*

[2]*Department of Neurology, Schlosspark-Klinik and Vestibular Research Group, Berlin, Germany*

Abstract

During the last decades a new vestibular syndrome has emerged that is now termed vestibular migraine (VM). The main body of evidence for VM is provided by epidemiologic data demonstrating a strong association between migraine and vestibular symptoms. Today, VM is recognized as one of the most common causes of episodic vertigo. The clinical presentation of VM is heterogeneous in terms of vestibular symptoms, duration of episodes, and association with migrainous accompaniments. Similar to migraine, there is no clinical or laboratory confirmation for VM and the diagnosis relies on the history and the exclusion of other disorders. Recently, diagnostic criteria for VM have been elaborated jointly by the International Headache Society and the Bárány Society. Clinical examination of patients with acute VM has clarified that the vast majority of patients with VM suffer from central vestibular dysfunction. Findings in the interval may yield mild signs of damage to both the central vestibular and ocular motor system and to the inner ear. These interictal clinical signs are not specific to VM but can be also observed in migraineurs without a history of vestibular symptoms. How migraine affects the vestibular system is still a matter of speculation. In the absence of high-quality therapeutic trials, treatment is targeted at the underlying migraine.

During the last three decades several new vestibular syndromes have emerged on the basis of clinical, epidemiologic, and pathophysiologic findings, such as vestibular migraine (VM), superior canal dehiscence syndrome, and vestibular paroxysmia. VM is by far the most common of these new disorders, gaining increasing recognition by clinicians and scientists. A PubMed search in 2015 yielded that 80% of papers on the association between migraine and vestibular symptoms have been published since the turn of the millennium.

Vertigo as a presentation of migraine was already recognized from the early days of neurology (Liveing, 1873; Escat, 1904; Boenheim, 1917), but systematic studies on the association between vertigo and migraine started only a hundred years later. Beginning with Slater's (1979) and Kayan and Hood's (1984) classic papers, the clinical features of VM have been well elucidated in several large case series (Cutrer and Baloh, 1992; Cass et al., 1997; Johnson, 1998; Dieterich and Brandt, 1999; Neuhauser et al., 2001; Reploeg and Goebel, 2002). To date, most dizziness clinic experts rank VM as one of the most common causes for episodic vertigo. Numerous synonyms have been used to designate vertigo caused by a migraine mechanism, including benign recurrent vertigo, migrainous vertigo, migraine-associated vertigo, migraine-associated dizziness, and migraine-related vestibulopathy. VM has been convincingly advocated as a term that stresses the particular vestibular manifestation of migraine and thus best avoids confounding with nonvestibular dizziness associated with migraine (Brandt and Strupp, 2006). Although there is still some debate on VM as an entity (Phillips et al., 2010; von Brevern et al., 2011), it is expected that the dissemination of recently developed diagnostic criteria for

*Correspondence to: Michael von Brevern, MD, Department of Neurology, Park-Klinik Weissensee and Vestibular Research Group Berlin, Schönstrasse 80, 13086 Berlin, Germany. Tel: +49-30-96283700, Fax: +49-30-96283705, E-mail: von.brevern@park-klinik.com

VM by the Bárány Society and the International Headache Society (Lempert et al., 2012) will enhance research and improve the quality of clinical care of patients with VM.

EPIDEMIOLOGY

The scientific basis for our current understanding of VM is provided mainly by epidemiologic studies. However, the interrelations between vertigo and migraine are complex. First, both migraine and vertigo are common complaints in the general population and may coexist in a patient just by coincidence. Second, some vertigo syndromes have been shown to be epidemiologically associated with migraine. According to our current understanding, these disorders are linked to, but not caused by, migraine. They include Menière's disease, benign paroxysmal positional vertigo (BPPV), motion sickness, rare cerebellar disorders, and several psychiatric syndromes that may manifest with vertigo and dizziness (Lempert and Neuhauser, 2009). Finally, there is VM that is conceptualized as migraine manifesting predominantly with episodic vertigo.

Epidemiologic association of migraine and vertigo

As both vertigo and migraine rank among the most common complaints in medicine, it is crucial to ask for the evidence supporting a specific link between vestibular symptoms and migraine beyond a chance concurrence. In several studies, the prevalence of migraine in unselected dizziness clinic patients has been found to be higher than expected (Aragones et al., 1993; Savundra et al., 1997). Furthermore, all case-control studies published to date indicate a more than chance association of migraine with vertigo. The prevalence of migraine was 1.6 times higher in 200 dizziness clinic patients than in 200 age- and sex-matched controls (Neuhauser et al., 2001). Conversely, in migraineurs, the prevalence of vertigo is higher as compared to nonmigraineurs. In a seminal study by Kayan and Hood (1984), 27% of unselected migraine patients reported vertigo, compared with 8% of patients with tension-type headache. Similarly, several other case-control studies found an increased prevalence of vertigo and dizziness in migraineurs (Kuritzky et al., 1981; Vukovic et al., 2007; Akdal et al., 2013).

Even more striking is the preponderance of migraine in patients with recurrent spontaneous vertigo, not fulfilling diagnostic criteria for Menière's disease. Cha et al. (2009) found that 87% of 208 patients with "benign recurrent vertigo" met the criteria for migraine and that 70% of these fulfilled diagnostic criteria for VM. In 72 patients with recurrent vertigo of unknown cause, the prevalence of migraine was six times higher as compared to an age- and sex-matched control group (61% vs. 10%) (Lee et al., 2002). Likewise, in patients with recurrent vertigo of unknown cause, Rassekh and Harker (1992) found a prevalence of migraine of 81% as compared to 22% in patients with Menière's disease.

The intersection of vertigo and migraine has also been examined on the population level. Assuming a lifetime prevalence of migraine of 14% (Jensen and Stovner, 2008) and a lifetime prevalence of vertigo of 7.4% (Neuhauser et al., 2005), a chance coincidence of 1% can be calculated. Notably, a large epidemiologic study of the general population found that three times more adults have a history of both vertigo and migraine than would be expected by chance alone (Neuhauser et al., 2006).

Epidemiology of vestibular migraine

In specialized dizziness clinics, VM is the most common cause of spontaneous recurrent vertigo, accounting for about 10% of diagnoses (Brandt, 1999; Neuhauser et al., 2001; van Omberg et al., 2015). VM is still widely underdiagnosed, as shown by a study from a dizziness clinic in Switzerland, where VM accounted for 20.2% of the diagnoses in young patients, but was suspected by the referring doctors in only 1.8% (Geser and Straumann, 2012). In a large two-stage population-based study with screening interviews followed by expert telephone interviews, the lifetime prevalence of VM in the general population has been estimated at 0.98% (Neuhauser et al., 2006). In a community-based sample of middle-aged women in Taiwan, VM was identified in 5% of the whole group and in 30% of those with migraine (Hsu et al., 2011).

VM may occur at any age (Cutrer and Baloh, 1992; Cass et al., 1997), although rarely after the sixth decade of life (Dieterich and Brandt, 1999). In most patients, migraine begins earlier in life than VM (Dieterich and Brandt, 1999; Neuhauser et al., 2001). Similar to migraine, VM has a female preponderance, with a female-to-male ratio between 1.5 and 4.5 to 1 (Dieterich and Brandt, 1999; Neuhauser et al., 2006). Familial occurrence has been reported in some patients, indicating an autosomal-dominant pattern of inheritance with decreased penetrance in men (Oh et al., 2001). Some migraineurs have been free from migraine attacks for years when VM first manifests itself (Dieterich and Brandt, 1999). Often, migraine headaches are replaced by vertigo attacks in women around menopause (Park and Viirre, 2010).

Diagnostic criteria for vestibular migraine

During the last three decades the International Classification of Headache Disorders (ICHD) has been developed by the International Headache Society as a widely used framework to define operational diagnostic criteria for

Table 22.1

Diagnostic criteria for migraine without aura

A. At least five attacks fulfilling criteria B–D
B. Headache attacks lasting 4–72 hours
C. Headache has at least two of the following characteristics:
   1. Unilateral localization
   2. Pulsating quality
   3. Moderate or severe pain intensity
   4. Aggravation by or causing avoidance of routine physical activity
D. During headache at least one of the following:
   1. Nausea and/or vomiting
   2. Photophobia and phonophobia
E. Not attributable to another disorder

Reproduced from Headache Classification Subcommittee of the International Headache Society (2013).

headache disorders such as migraine (Table 22.1). In the previous ICHD (ICHD-2), vertigo was not included as a migraine symptom in adults, except for basilar-type migraine (now termed migraine with brainstem aura), which presents with vertigo in more than 60% of patients (Sturzenegger and Meienberg, 1985; Kirchmann et al., 2006). As a symptom of migraine with brainstem aura, vertigo should last between 5 and 60 minutes and should be accompanied or followed by migraine headache. In addition, at least one more aura symptom originating from the brainstem is required. Fewer than 10% of patients with VM fulfilled the criteria for basilar-type migraine/migraine with brainstem aura (Cass et al., 1997; Johnson, 1998; Dieterich and Brandt, 1999), which makes this diagnosis an inappropriate category for most of these patients.

Neuhauser and coworkers (2001) proposed diagnostic criteria for VM that have been widely used for clinical and research purposes. These criteria have a high positive predictive value. A re-evaluation of 75 patients 105 ± 16 months after the initial diagnosis of VM confirmed this diagnosis in 84%, whereas a competing diagnosis was considered in 16% (Radtke et al., 2011).

Recently, the Bárány Society, which represents the international community of basic scientists, otolaryngologists, and neurologists committed to vestibular research, and the International Headache Society have jointly refined these diagnostic criteria, defining VM and probable VM (Lempert et al., 2012). These criteria have been included in the third edition of the ICHD (ICHD-3), published in 2013. VM appears in the appendix of the ICHD-3 for new disorders that need further research for validation. In addition, the classification of VM is part of the evolving International Classification of Vestibular Disorders (ICVD) of the Bárány Society. The new ICHD-3 includes only VM, while the ICVD also contains probable VM (Table 22.2). The recent classification of VM is a major step forward and should allow for broader acceptance of the disorder and more accurate recognition.

SYMPTOMS

Types of vertigo

Patients with VM typically report episodic spontaneous or positional vertigo. Some experience a sequence of spontaneous vertigo transforming into positional vertigo after several hours or days. Altogether, 40–70% of patients experience positional vertigo in the course of the disease, but not necessarily with every attack. This positional vertigo is distinct from BPPV with regard to duration of individual attacks (often as long as the head position is maintained in VM versus only seconds in BPPV), duration of symptomatic episodes (minutes to days in VM versus weeks in BPPV), and nystagmus findings (von Brevern et al., 2004). A frequent additional symptom is head motion-induced dizziness, i.e., imbalance, illusory motion, and nausea aggravated or provoked by head movements (Kuritzky et al., 1981; Cass et al., 1997). Visually induced vertigo, i.e., vertigo provoked by moving visual scenes such as traffic or movies, can be another prominent feature of VM (Cass et al., 1997; Waterston, 2004; Radtke et al., 2012). The combination of different types of vertigo distinguishes VM from other neurotologic disorders such as BPPV or Menière's disease, which typically present with monosymptomatic vertigo. The duration of symptomatic episodes ranges from minutes to hours and several days, sometimes even in the same patient (Kayan and Hood, 1984; Cutrer and Baloh, 1992; Dieterich and Brandt, 1999; Neuhauser et al., 2001). Although the core attack with objective clinical signs rarely exceeds 72 hours, for some patients it may take considerably longer to fully recover from an episode.

Often patients with VM report episodic vestibular symptoms as well as persistent dizziness and imbalance (Neff et al., 2012). In many patients this latter symptom can be attributed to secondary psychiatric morbidity (Furman et al., 2005a; Eckhardt-Henn et al., 2008; Boldingh et al., 2011; Neff et al., 2012). About 50% of patients with VM have a psychiatric comorbidity, most commonly anxiety, phobic and somatoform disorders (Lahmann et al., 2015). In addition, patients with VM are often affected by motion sensitivity even between attacks (Jeong et al., 2010), which may also lead to a chronic type of dizziness. These two components of interictal dizziness, psychogenic dizziness, and motion sensitivity, may not be easily discriminated in individual patients (Furman et al., 2005a).

Table 22.2

Diagnostic criteria for vestibular migraine

1. Vestibular migraine
   A. At least five episodes with vestibular symptoms[1] of moderate or severe intensity,[2] lasting 5 minutes to 72 hours[3]
   B. Current or previous history of migraine with or without aura according to the *International Classification of Headache Disorders* (ICHD)[4]
   C. One or more migraine features with at least 50% of the vestibular episodes[5]:
      - Headache with at least two of the following characteristics: one-sided location, pulsating quality, moderate or severe pain intensity, aggravation by routine physical activity
      - Photophobia and phonophobia[6]
      - Visual aura[7]
   D. Not better accounted for by another vestibular or ICHD diagnosis[8]
2. Probable vestibular migraine
   A. At least five episodes with vestibular symptoms[1] of moderate or severe intensity,[2] lasting 5 minutes to 72 hours[3]
   B. Only one of the criteria B and C for vestibular migraine is fulfilled (migraine history or migraine features during the episode)
   C. Not better accounted for by another vestibular or ICHD diagnosis[8]

Reprinted from Lempert T, Olesen J, Furman J, et al. (2012). Vestibular migraine: Diagnostic criteria. Consensus document of the Bárány Society and the International Headache Society. J Vest Res 22:167-172 with permission from IOS Press. Available at IOS Press through http://dx.doi.org/10.1007/s00115-013-3768-x.

[1]Vestibular symptoms, as defined by the Bárány Society's Classification of Vestibular Symptoms and qualifying for a diagnosis of vestibular migraine, include:

- Spontaneous vertigo including:
  - Internal vertigo, a false sensation of self-motion, and
  - External vertigo, a false sensation that the visual surround is spinning or flowing
- Positional vertigo, occurring after a change of head position
- Visually induced vertigo, triggered by a complex or large moving visual stimulus
- Head motion-induced vertigo, occurring during head motion
- Head motion-induced dizziness with nausea. Dizziness is characterized by a sensation of disturbed spatial orientation. Other forms of dizziness are currently not included in the classification of vestibular migraine.

[2]Vestibular symptoms are rated "moderate" when they interfere with, but do not prohibit, daily activities and "severe" if daily activities cannot be continued.

[3]Duration of episodes is highly variable: about 30% of patients have episodes lasting minutes, 30% have attacks for hours, and another 30% have attacks over several days. The remaining 10% have attacks lasting seconds only, which tend to occur repeatedly during head motion, visual stimulation, or after changes of head position. In these patients, episode duration is defined as the total period during which short attacks recur. At the other end of the spectrum, there are patients who may take 4 weeks to fully recover from an episode. However, the core episode rarely exceeds 72 hours.

[4]Migraine categories 1.1 and 1.2 of the ICDH-2.

[5]One symptom is sufficient during a single episode. Different symptoms may occur during different episodes. Associated symptoms may occur before, during, or after the vestibular symptoms.

[6]Phonophobia is defined as sound-induced discomfort. It is a transient and bilateral phenomenon that must be differentiated from recruitment, which is often unilateral and persistent. Recruitment leads to an enhanced perception and often distortion of loud sounds in an ear with decreased hearing.

[7]Visual auras are characterized by bright scintillating lights or zigzag lines, often with a scotoma that interferes with reading. Visual auras typically expand over 5–20 minutes and last for less than 60 minutes. They are often, but not always, restricted to one hemifield. Other types of migraine aura, e.g., somatosensory or dysphasic aura, are not included as diagnostic criteria because their phenomenology is less specific and most patients also have visual auras.

[8]History and physical examinations do not suggest another vestibular disorder or such a disorder is considered but ruled out by appropriate investigations or such disorder is present as a comorbid or independent condition, but episodes can be clearly differentiated. Migraine attacks may be induced by vestibular stimulation. Therefore, the differential diagnosis should include other vestibular disorders complicated by superimposed migraine attacks.

Relation to headaches

VM often misses not only the duration criterion for a migraine aura as defined by the ICHD, but also the temporal relationship to migraine headaches: vertigo can precede headache as would be typical for an aura, may begin with headache, or may appear late in the headache phase. Most patients experience attacks both with and without headache (Cutrer and Baloh, 1992; Johnson, 1998; Dieterich and Brandt, 1999). Quite frequently, patients have an attenuated headache with their vertigo as compared to their usual migraine (Behan and Carlin, 1982; Johnson, 1998). Often patients develop VM after the intensity of their migraine headaches has

Table 22.3

Diagnostic criteria for benign paroxysmal vertigo of childhood

A.	At least five attacks fulfilling criterion B
B.	Multiple episodes of severe vertigo, occurring without warning and resolving spontaneously after minutes to hours
C.	Normal neurologic examination, audiometric and vestibular functions between attacks
D.	Normal electroencephalogram

Reproduced from Headache Classification Subcommittee of the International Headache Society (2013).

declined during their lifetime. Thus, the dominant clinical feature of VM is usually vertigo, not headache. In some patients, vertigo and headache never arise together (Cutrer and Baloh, 1992; Johnson, 1998; Neuhauser et al., 2001). Misdiagnosis of VM as "cervical vertigo" may occur when accompanying pain is mainly localized in the neck, which is quite common in patients with migraine (Yacovino and Hain, 2013).

Other symptoms

Autonomic symptoms with nausea and vomiting are frequent but nonspecific accompaniments of acute VM (von Brevern et al., 2005; Polensek and Tusa, 2010). Along with the vertigo, patients may experience photophobia, phonophobia, osmophobia, and visual or other auras. These phenomena are of diagnostic importance, since they may represent the only clinical connection of vertigo and migraine. Patients need to be asked specifically about these migraine symptoms since they often do not volunteer them. A dizziness diary can be useful for prospective recording of associated features.

Auditory symptoms, including hearing loss, tinnitus, and aural pressure, have been reported in up to 38% patients with VM (Kayan and Hood, 1984; Parker, 1991; Cass et al., 1997; Johnson, 1998; Neff et al., 2012). Hearing loss is usually mild and transient, without or with only minor progression in the course of the disease (Johnson, 1998). About 20% develop mild bilateral downsloping hearing loss over the years (Radtke et al., 2012). In contrast, unilateral moderate to severe hearing loss starting in the low-frequency range would rather favor a diagnosis of Menière's disease.

Precipitating factors

Asking for migraine-specific precipitants of vertigo attacks may provide valuable diagnostic information, e.g., provocation by deficient sleep, excessive stress, skipped meals, lack of fluid and exposure to sensory stimuli, such as bright or scintillating lights, intense smells or noise. In women, VM can be precipitated by hormonal changes, appearing just before menses, similar to migraine headaches. The influence of specific foods and weather conditions is probably overestimated. Sometimes, migraine accompaniments and typical precipitants may be missing, but VM is still considered the most likely diagnosis after other potential causes have been investigated and appear unlikely. In this case a favorable response to antimigraine drugs may support the suspicion of an underlying migraine mechanism. However, apparent efficacy of a drug should not be regarded as a definite confirmation of the diagnosis, since spontaneous improvement, placebo response, and additional drug effects (e.g., anxiolytic or antidepressant) have to be taken into account.

VESTIBULAR MIGRAINE IN CHILDHOOD

Migraine-related vestibular syndromes are the most common cause of episodic vertigo in children. About 30–50% of children and adolescents with vestibular symptoms report headache associated with their vertigo and a migraine mechanism has been suspected in about a third of children suffering from dizziness and vertigo (Riina et al., 2005; Szirmai, 2010; Jahn et al., 2011; Langhagen et al., 2015). The clinical presentation of VM is similar in children and adults, although difficulties describing their symptoms and a shorter medical history may hamper establishing the diagnosis (Langhagen et al., 2015). Motion sickness and a family history of migraine have been reported in about 50% of affected children (Jahn et al., 2011).

Benign paroxysmal vertigo of childhood is a migraine-related vestibular syndrome manifesting before puberty that is recognized by the International Headache Society as a precursor of migraine (Table 22.3). It has been estimated that 2.6% of children between the ages of 6 and 12 years are affected by benign paroxysmal vertigo of childhood (Abu-Arafeh and Russell, 1995), although this diagnosis seems to be less common in children than VM (Langhagen et al., 2015). Benign paroxysmal vertigo of childhood is characterized by sudden brief attacks of vertigo with imbalance, occurring without warning and lasting minutes, rarely hours, in otherwise healthy children (Basser, 1964). The attacks may be accompanied by nausea, vomiting, pallor, sweating, and nystagmus, but headache and other migrainous symptoms are lacking. Thus, the diagnosis is less specific than VM and rests mainly on the exclusion of other disorders. The ictal ocular motor findings of benign paroxysmal vertigo of childhood have not been well documented. The interictal clinical examination is typically normal (Langhagen et al., 2015). Usually the condition ceases spontaneously after a few years. Many of

these children have a family history of migraine and later develop migraine headache, often years after vertigo attacks have ceased (Krams et al., 2011).

CLINICAL AND LABORATORY TESTING

There is no specific testing abnormality in VM, either in the acute episode or in the interictal interval. However, laboratory testing can be useful to exclude other diseases and to reassure the patient. It is important to bear in mind that minor signs of peripheral and central vestibular dysfunction are not uncommon in patients with VM in the symptom-free interval. Many older studies on laboratory findings in patients with VM are limited by the fact that they lack specific diagnostic criteria for VM, control groups, and normative data, but studies overcoming these limitations have been published recently. In the following, findings during the acute episode and in the symptom-free interval are summarized.

Findings during the episode

Examination during an episode of VM usually yields pathologic nystagmus, indicating central vestibular dysfunction in most patients. A prospective study of 20 patients during the acute phase of VM recorded pathologic nystagmus in 70% of patients by means of three-dimensional video-oculography (von Brevern et al., 2005). A peripheral type of spontaneous nystagmus with a unilateral deficit of the horizontal vestibulo-ocular reflex (VOR) was observed in 3 patients, a central type of spontaneous nystagmus in 3, a central positional nystagmus in 5, and a combined central spontaneous and positional nystagmus in 4 patients during the acute episode of VM (Fig. 22.1). Hearing was not affected in any patient during the episode. Saccadic pursuit was noted in 5 patients during the attack and in 3 of them also in the interval. Overall, findings pointed to central vestibular dysfunction in 10 patients (50%), to peripheral vestibular dysfunction in 3 patients (15%), and were

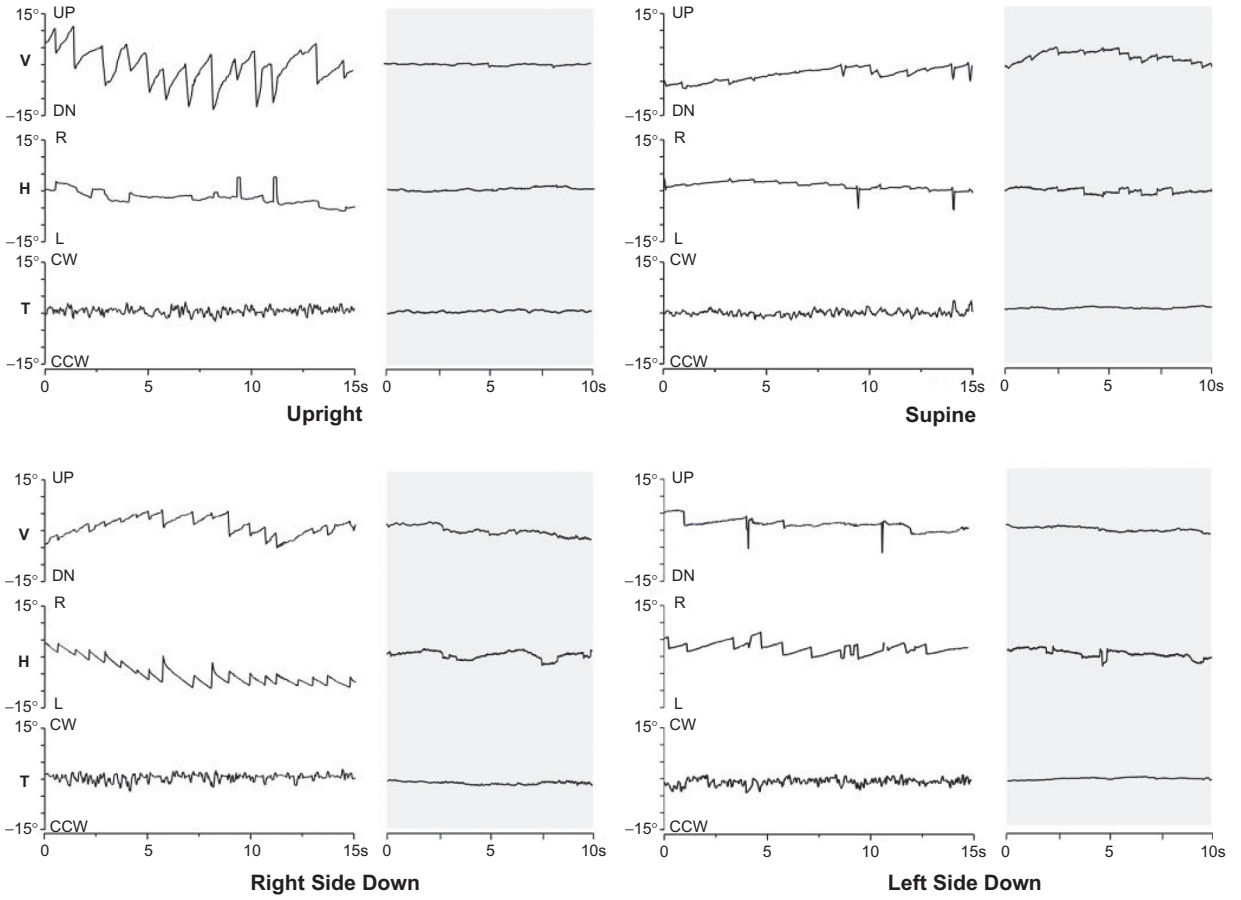

Fig. 22.1. Video-oculographic recording of spontaneous and persistent positional nystagmus in a patient during acute vestibular migraine and during the symptom-free interval (gray shading). Vertical (V), horizontal (H), and torsional (T) eye movement components are shown. Note the downbeating nystagmus in the upright position, which ceases in the supine position. In the lateral positions a predominantly horizontal, geotropic nystagmus appears. (Reproduced from von Brevern et al., 2005.)

inconclusive with regard to the involved structure in 35%. On follow-up vestibular and ocular motor abnormalities had disappeared in almost all patients.

A retrospective study reported on findings in 26 patients presenting with pathologic nystagmus during acute VM (Polensek and Tusa, 2010). All patients had positional nystagmus, mostly of a horizontal, direction-changing type. Furthermore, 19% of patients presented with spontaneous nystagmus and 35% with head-shaking-induced nystagmus, always beating in the horizontal plane. As the intensity of the nystagmus was weak, it could only be observed with fixation blocked. In the interval, nystagmus had dissipated in all patients. Caloric testing was normal in all patients. The authors concluded that findings pointed to a central vestibular dysfunction in all patients. Another retrospective study described transient spontaneous nystagmus in 8 patients with VM examined in the attack, 3 of whom also had severe vertical positional nystagmus (Dieterich and Brandt, 1999).

Findings in the interval

Saccadic pursuit has been reported in 3% (Cass et al., 1997) to 57% (Neugebauer et al., 2013) of adult patients and in 24% of children (Langhagen et al., 2015) with VM. No other ocular motor finding has been reported with such a wide variance in VM, which may be due to the fact that the vast majority of studies assessed smooth pursuit clinically without eye movement recording. Furthermore, assessment of smooth pursuit is problematic as it relies on attention and cooperation of the patient. In most studies, saccadic pursuit has been described in about 10–20% of patients with VM in the interval (Table 22.4). Two case series that described saccadic horizontal smooth pursuit in about half of patients with VM found impaired fixation suppression of the VOR in only 3% of these patients (Dieterich and Brandt, 1999; Neugebauer et al., 2013). These are conflicting findings, as cancellation of the VOR is typically impaired when smooth pursuit is saccadic (Radtke et al., 2012).

Spontaneous nystagmus is rare in the interval, with a prevalence of well below 10% in most case series (Table 22.4). In contrast, positional nystagmus of a central type is not uncommon and has been described in about 10–20% of patients (Table 22.4). Gaze-evoked nystagmus occurred in less than 5% of patients in several case series (Çelebisoy et al., 2007; Casani et al., 2009; Jeong et al., 2010; Radtke et al., 2012; Boldingh et al., 2013), and only Dieterich and Brandt (1999) observed gaze-evoked nystagmus in a large proportion of patients (27%) with VM. Head-shaking nystagmus has been described in 15–50% of patients (Jeong et al., 2010; Radtke et al., 2012; Boldingh et al., 2013; Shin et al., 2013) and can be horizontal or downbeating (Jeong et al., 2010). Vibration-induced nystagmus, typically indicating peripheral vestibular hypofunction (Hamann and Schuster, 1999), has been observed in 32% of patients with VM (Shin et al., 2013).

The most consistent laboratory finding in VM is a unilaterally reduced caloric response. In most studies, about 10–20% of patients with VM showed a unilateral canal paresis (Table 22.4). The magnitude of caloric asymmetry has been specified in almost none of these studies. Thus, it is unclear whether a complete or almost complete

Table 22.4

Prevalence of ocular motor and vestibular dysfunction in patients with vestibular migraine in the symptom-free interval

Reference	*n*	Spontaneous nystagmus	Central positional nystagmus	Saccadic pursuit	Central ocular motor disorder	Unilateral caloric paresis
Cutrer and Baloh, 1992	91	7%	7%	n.r.	n.r.	21%
Cass et al., 1997	100	7%	13%	3%	n.r.	18%
Dieterich and Brandt, 1999	90	11%	11%	48%	66%	8%
Bir et al., 2003	53	0%	n.r.	24%	n.r.	12%
Çelebisoy et al., 2007	35	0%	n.r.	9%	12%	20%
Wang et al., 2009	62	26%	n.r.	21%	n.r.	21%
Teggi et al., 2009	30	3%	10%	9%	23%	20%
Casani et al., 2009	22	n.r.	9%	14%	18%	18%
Radtke et al., 2012	61	2%	18%	8%	28%	16%
Neugebauer et al., 2013	30	3%	n.r.	57%	63%	7%
Boldingh et al., 2013	38	5%	19%	13%	54%	16%

Reproduced from von Brevern (2014).
n.r., not reported.

canal paresis is compatible with a diagnosis of VM. In two studies, about 25% of patients with a canal paresis had an asymmetry of more than 50% (Radtke et al., 2012; Blödow et al., 2014). The presence of a caloric asymmetry seems to be independent of the stage of the disease (Blödow et al., 2014). Pathologic caloric testing has also been reported in about 20% of children with VM (Marcelli et al., 2010; Langhagen et al., 2015).

Bilateral caloric hyporesponsiveness has been reported in up to 11% (Kayan and Hood, 1984; Olsson, 1991; Maione, 2006), and an isolated directional preponderance of caloric responses in about 10% of patients with VM (Kayan and Hood, 1984; Dieterich and Brandt, 1999; Vitkovic et al., 2008). Interestingly, patients with VM are four times more likely to have an emetic response to caloric stimulation than patients with a vestibular disorder coexisting with migraine (Vitkovic et al., 2008).

A pathologic head impulse test as assessed by bedside testing has been reported in up to 26% of patients with VM (Boldingh et al., 2013), but in most studies it occurred only exceptionally (Neff et al., 2012; Radtke et al., 2012; Mahringer and Rambold, 2014). Video head impulse testing yielded a mildly reduced unilateral gain in 9–11% of patients with VM (Blödow et al., 2014; Mahringer and Rambold, 2014). The video head impulse test seems to be less sensitive for detection of a vestibular deficit in VM than caloric irrigation (Blödow et al., 2014).

Rotatory chair testing revealed an isolated directional preponderance in about 20% of patients (Cass et al., 1997; Dieterich and Brandt, 1999). Some authors reported a reduced gain of the horizontal VOR during rotatory chair testing (Dimitri et al., 2001; Furman et al., 2005b), but this finding was present in only 1% of patients in a large case series (Cass et al., 1997).

Assessment of cervical and ocular vestibular-evoked myogenic potentials (cVEMPs and oVEMPs) in patients with VM has yielded conflicting results. Some studies have described either unilaterally or bilaterally reduced amplitudes as compared to healthy controls in about two-thirds of patients with VM, indicating saccular and utricular dysfunction (Baier and Dieterich, 2009; Zuniga et al., 2012). Another study found a high prevalence of absent cVEMPs (43%) in patients with VM (Boldingh et al., 2011). Cervical recorded VEMPs were also absent in 35% of 20 patients with basilar-type migraine, most of them experiencing vertigo (Liao and Young, 2004). Another study found no differences in cVEMP parameters between patients with VM and controls, but the rate of absent oVEMPs was higher in patients with VM as compared to controls (Zaleski et al., 2015). The latencies of the response were only rarely prolonged in patients with VM (Murofushi et al., 2009), or entirely normal in other studies (Baier and Dieterich, 2009; Boldingh et al., 2011; Zuniga et al., 2012). VEMPs do not seem to be helpful for the differentiation of VM from Menière's disease, where similar results can be found (Baier and Dieterich, 2009). One study elicited VEMPs applying tone bursts of various frequencies and concluded that this method may help to separate VM from Menière's disease, but these results await replication (Taylor et al., 2012).

A large case series of patients with VM yielded normal results of posturography in 74% of patients (Cass et al., 1997). Group analysis of posturography demonstrated excessive reliance on somatosensory cues (Çelebisoy et al., 2007) or on visual cues (Casani et al., 2009; Teggi et al., 2009) in patients with VM as compared to controls.

It is important to notice that these clinical and laboratory findings are not specific to patients with VM but can also be found in migraine patients without a history of vestibular symptoms. Of note, unilateral caloric hyporesponsiveness occurs with similar frequency in migraine patients with and without a history of vestibular symptoms (Dash et al., 2008; Casani et al., 2009; Marcelli et al., 2010; Boldingh et al., 2013). A unilateral canal paresis has been described in up to 35% of migraine patients without vertigo (Toglia et al., 1981; Casani et al., 2009; Boldingh et al., 2013). Likewise, a study comparing cVEMPs between groups of migraineurs with and without vertigo found no difference in amplitudes (Roceanu et al., 2008). While a high frequency of pathologic oculographic findings has been reported by several authors in migraine (Toglia et al., 1981; Ansink et al., 1985; Bir et al., 2003; Harno et al., 2003; Casani et al., 2009), other studies failed to find significant ocular motor abnormalities (Schlake et al., 1989; Wilkinson et al., 2006). Several studies examined the prevalence of vestibular dysfunction in patients with VM as compared to migraine patients without vertigo. In two studies the prevalence of peripheral and central vestibular dysfunction did not differ between both groups (Bir et al., 2003; Casani et al., 2009), whereas another study reported a higher prevalence of central and peripheral vestibular dysfunction in patients with VM (70%) than in migraine patients (38%) (Boldingh et al., 2013). Saccadic pursuit seems to be more frequent in VM as compared to migraine without vertigo (Casani et al., 2009; Boldingh et al., 2013). Clinical examination yielded head-shaking nystagmus in 9–25% of migraine patients without vertigo (Jeong et al., 2010; Boldingh et al., 2013). Central positional nystagmus has been described by means of video-oculography in 28% of patients with migraine without a history of vestibular symptoms (Harno et al., 2003).

Two studies examined the evolution of interictal vestibular and ocular motor dysfunction in patients with VM over time. In a group of 61 patients with VM the prevalence of at least one ocular motor abnormality increased from 15% at initial presentation to 41% after a median follow-up time of 9 years (Radtke et al., 2012). The most frequent abnormalities were positional nystagmus and head-shaking nystagmus (Table 22.5). Positional nystagmus clearly attributable to central vestibular dysfunction was present at follow-up in 18% of patients. Another 8-year-long observational study with 30 patients found that the prevalence of central ocular motor deficits increased from 20% to 63% in VM (Neugebauer et al., 2013). The most common finding in the latter study was saccadic pursuit.

In general, signs of central ocular motor and vestibular dysfunction remain subtle throughout the course (Radtke et al., 2012; Neugebauer et al., 2013). Interestingly, interictal ocular motor abnormalities may show some variation over time and in some patients eye movements may even return to normal at follow-up (Dieterich and Brandt, 1999; Radtke et al., 2012). Ocular motor abnormalities observed in the symptom-free interval may partly reflect delayed recovery of vestibular dysfunction after an acute vertigo attack.

Audiometry revealed sensorineural hearing loss not attributable to any cause in up to 20% of patients (Maione, 2006). A review of audiometric findings in VM summarized results of nine studies and found an average prevalence of unexplained hearing loss of 7.5% (Battista, 2004). Thus, hearing loss is rather unusual, and low-frequency, progressive, or fluctuating hearing loss, typical for Menière's disease, is a rare finding in VM. In a case series of 61 patients with VM, 18% of patients had developed mild bilateral symmetric sensorineural hearing loss with a downsloping pattern involving the low-frequency range to a minor degree after a median of 9 years after initial presentation (Radtke et al., 2012).

In summary, patients with VM may show mild signs of peripheral and central vestibular dysfunction in the symptom-free interval. Although the prevalence of ocular motor abnormalities tends to increase with time, findings in individual patients may fluctuate. These clinical signs and testing results are not specific to VM and may also be found in patients with migraine without vestibular symptoms. Gross ocular motor abnormalities are found infrequently in VM and should raise the suspicion of another disease.

Table 22.5

Interictal ocular motor abnormalities in 61 patients with definite vestibular migraine at initial presentation and after a median follow-up time of 9 years

	Initial presentation	Follow-up
At least one ocular motor abnormality	15%	41%
Positional nystagmus	12%	28%
Head-shaking nystagmus	2%	15%
Gaze-evoked nystagmus	0%	4%
Spontaneous nystagmus	2%	2%
Saccadic pursuit	0%	8%
Deficit of visual vestibulo-ocular reflex suppression	2%	8%
Pathologic saccades	0%	0%
Unilateral deficit on head impulse test	2%	3%

Modified from Radtke et al. (2012).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of VM includes other disorders causing episodes of spontaneous and positional vertigo. Again, history taking provides more valuable clues than technical procedures, which rather serve to provide further evidence for or against a clinical working diagnosis.

Menière's disease

The most challenging differential diagnosis of VM is Menière's disease, particularly in the early course, when permanent hearing loss may not yet be detectable in the latter. Both disorders present similarly in terms of severity and duration of vertigo episodes (Brantberg and Baloh, 2011). Vestibular testing with caloric irrigation, head impulse test, and VEMPs do not reliably discriminate between VM and Menière's disease. Usually, the distinction can be made based on hearing loss, which is only occasional and mild in VM, while it is a typical and more severe accompaniment of Menière's disease. Furthermore, when hearing loss develops in VM, it is often bilateral (Battista, 2004; Radtke et al., 2011), whereas involvement of both ears from the onset has been described in only 2% of Menière patients (Huppert et al., 2010). Tinnitus and aural fullness may also occur during vertigo attacks in VM (Lopez-Escamez et al., 2014). Again, in contrast to Menière's disease, in which these symptoms are typically unilateral, these symptoms are usually bilateral in VM (Cass et al., 1997; Brantberg and Baloh, 2011). Nonetheless, there is a diagnostic overlap between VM and Menière's disease, not only in the early stage (Neff et al., 2012). After a mean follow-up of 9 years in 75 patients with the initial diagnosis of VM, 10% of patients fulfilled diagnostic criteria for both Menière's disease and VM. Yet, these patients had clinical features atypical of

classical Menière's disease, such as symmetric and mostly mild hearing loss and often long duration of vertigo episodes, raising doubts that Menière's disease was the more appropriate diagnosis (Radtke et al., 2011). These findings can be interpreted in two ways: either current diagnostic criteria for Menière's disease and VM are not sufficiently discriminative or both disorders share an underlying mechanism. A genetic link between VM and Menière's disease is supported by familial clustering of migraine, episodic vertigo, and Menière's disease, but this constellation is rather rare (Cha et al., 2007; Hietikko et al., 2011). Alternatively, migraine could damage the inner ear, leading to endolymphatic hydrops (Gürkov et al., 2014). Endolymphatic hydrops has been identified in a minority of patients with VM by means of magnetic resonance imaging (MRI), but most of them also fulfilled criteria for Menière's disease (Gürkov et al., 2014; Nakada et al., 2014). To complicate matters further, migrainous symptoms such as headache and photophobia are also frequent accompaniments in attacks of Menière's disease (Radtke et al., 2002; Brantberg and Baloh, 2011; Shin et al., 2013; Lopez-Escamez et al., 2014). For practical purposes, when patients present with early unilateral hearing loss and vertigo attacks lasting at least 20 minutes and not longer than 12 hours, Menière's disease should be diagnosed, even when migraine symptoms occur during vertigo episodes. In those patients with only minor hearing symptoms and a history compatible with both VM and Menière's disease, medical treatment with a trial of migraine prophylaxis is advisable. Failure of this approach should prompt consideration of treatment for Menière's disease but invasive procedures should be avoided. Only patients who have two different types of attacks, one fulfilling the criteria for VM and the other for Menière's disease, should be diagnosed with the two disorders. A future classification of VM may include a VM/Menière's disease overlap syndrome (Neff et al., 2012).

Benign recurrent vertigo

The term "benign recurrent vertigo" was coined in 1979 by Slater for patients with recurrent attacks of spontaneous vertigo that cannot be explained by other known peripheral or central vestibular disorders. Other authors have used "recurrent vestibulopathy" for similar patients (Leliever and Barber, 1981). To date, this syndrome is ill defined, as some authors include patients with VM (Cha et al., 2009), whereas others exclude patients with a migraine history (van Leeuven and Bruintjes, 2010). There is a large overlap between benign recurrent vertigo and VM. Notably, Slater (1979) speculated that benign recurrent vertigo may be a migraine equivalent. Several large case series endorse the association between benign recurrent vertigo and migraine (Lee et al., 2002; Cha et al., 2009; Brantberg and Baloh, 2011). Besides the increased prevalence of migraine, there are several clinical similarities between benign recurrent vertigo and VM: (1) female preponderance (Cha et al., 2009); (2) family occurrence suggestive of an autosomal-dominant inheritance, with reduced penetrance in some patients (Lee et al., 2006); (3) precipitation by lack of sleep and emotional stress (Slater, 1979); and (4) transition from spontaneous to positional vertigo during an episode (Slater, 1979). As the majority of patients with benign recurrent vertigo can be classified as VM or probable VM, the term benign recurrent vertigo (or recurrent vestibulopathy) should be restricted to patients with episodic spontaneous vertigo of unknown cause and without a history of migraine. The clinical presentation of benign recurrent vertigo is similar to VM and Menière's disease with respect to duration and severity of vertigo (Brantberg and Baloh, 2011). Although cochlear symptoms during episodes of vertigo are not rare, the rate of conversion to Menière's disease is low, ranging between 1% and 7% 3 years after initial diagnosis (Leliever and Barber, 1981; van Leeuven and Bruintjes, 2010).

Benign paroxysmal positional vertigo

VM may present with purely positional vertigo, thus mimicking BPPV. Direct nystagmus observation during the acute phase may be required for differentiation. In VM, positional nystagmus is usually persistent and of a central type, i.e., not aligned with a single semicircular canal (von Brevern et al., 2005; Polensek and Tusa, 2010). Symptomatic episodes tend to be shorter with VM (minutes to days rather than weeks) and more frequent (several times per year with VM rather than once every few years with BPPV) (von Brevern et al., 2004). There is epidemiologic evidence for an association between migraine and BPPV. Migraine is three times more common in patients presenting with idiopathic BPPV compared to patients with BPPV secondary to trauma or surgical procedures (Ishiyama et al., 2000). Similarly, the prevalence of migraine was two times higher in patients with idiopathic BPPV compared to age- and sex-matched controls (Lempert et al., 2000). Genetic factors and vascular damage to the labyrinth have been proposed as potential mechanisms linking the two disorders (Ishiyama et al., 2000).

Transient ischemic attacks

Isolated vertigo is the most common manifestation of vertebrobasilar transient ischemic attacks (Paul et al., 2013) and this differential diagnosis should be considered, particularly in elderly patients. Suggestive features include vascular risk factors, coronary or peripheral

atherosclerosis, sudden onset of symptoms, duration of episodes of less than 1 hour, total history of attacks of less than a few months, and angiographic or Doppler ultrasound evidence for vascular pathology of the vertebral or proximal basilar artery (Fife et al., 1994).

Vestibular paroxysmia

Vestibular paroxysmia is a controversial disorder, presumably caused by vascular compression of the vestibular nerve (Hüfner et al., 2008). The presenting feature is brief attacks of vertigo, typically lasting several seconds, which recur many times per day. Successful prevention of attacks with carbamazepine supports the diagnosis.

Episodic ataxia

VM shares some clinical features with episodic ataxia type 2 (EA2). In both disorders, a history of migraine and a positive family history for episodic vertigo are often present. EA2 is a rare autosomal-dominant inherited paroxysmal disorder of early onset characterized by episodes of incoordination and truncal ataxia. Presentation after the age of 20 is exceptional. The attacks are commonly triggered by physical and emotional stress and typically last hours. In about half of the patients at least one of the following can be found: vestibular symptoms with vertigo, nausea, and vomiting during attacks, generalized weakness during attacks, gradually progressive baseline ataxia, and a history of migraine (Jen et al., 2004). Between attacks, the vast majority of patients present with gaze-evoked nystagmus and a third with spontaneous or positional downbeat nystagmus. These interictal ocular motor signs are an important key to differentiate VM from EA2, as they are absent or subtle in the former and prominent in the latter. Other features that may help to distinguish VM from EA2 are the age at onset, triggers, and the striking response to treatment with acetazolamide in EA2. Genetic testing is commercially available for EA2 and identifies a mutation in the CACNA1A gene in about 60% of patients.

Psychiatric dizziness syndromes

There is a complex relationship between vertigo and dizziness, migraine, and some psychiatric disorders. Both panic disorders and major depression are bidirectionally associated with migraine (Breslau et al., 2000, 2001). As with all vestibular disorders, patients with VM are at highest risk of developing comorbid psychiatric disorders, particularly anxiety disorders and depression (Eckhardt-Henn et al., 2008). Because of the frequent association of dizziness, migraine, and anxiety, Furman and coworkers (2005a) have proposed "migraine/anxiety-related dizziness" as a new syndrome on the basis of neuroanatomic links on the brainstem level between the vestibular system and neuronal pathways involved in emotional processing. Besides vestibular episodes, about one-third of patients with VM exhibit chronic subjective dizziness (Neff et al., 2012). Anxiety-related dizziness is characterized by situational worsening, intense autonomic activation, catastrophic thinking, and avoidance behavior, and is not accompanied by severe nausea, vomiting, external vertigo (seeing the world move), and falls. However, in individual patients with co-occurrence of VM and psychogenic dizziness, the differentiation of their relative contribution can be problematic.

PATHOPHYSIOLOGY

The pathophysiology of VM is still a matter of speculation. The vestibular origin has been ascertained by the observation of pathologic nystagmus in the acute phase of VM, indicating central vestibular dysfunction in most patients (von Brevern et al., 2005; Polensek and Tusa, 2010). As the clinical presentation of VM is heterogeneous in terms of duration, type of vestibular symptoms, and nystagmus during the attack, it is likely that migraine interacts with the vestibular system at various levels. Beside central vestibular structures, the labyrinth also seems to be affected, as indicated by an increased prevalence of inner-ear disorders (BPPV and Menière's disease) and unilateral reduced caloric response in patients with migraine.

It remains unclear how migraine affects the vestibular system. Several hypotheses have been proposed; all of them are derived from the presumed pathophysiology of migraine (Furman et al., 2013). Migraine is currently conceptualized as a neurogenic disorder in genetically susceptible individuals that starts in the brain and probably results from dysfunction of brainstem and diencephalic nuclei that activate sensory nerve endings around the extracranial and intracranial arteries of the head (Akerman et al., 2011).

Migraine aura has been associated with a transient and reversible cortical event, spreading depression. Spreading depression is characterized by a short-lasting neuronal depolarization spreading over adjacent areas of the cortex, followed by a longer-lasting inhibition of neuronal activity (Ferrari et al., 2015). This mechanism could lead to vestibular symptoms when the multisensory cortical areas processing vestibular information become involved; these are mainly located in the temporoparietal junction. Alternatively, a spreading depression affecting the brainstem has been proposed to account for short-lasting episodes of VM (Dieterich and Brandt, 1999). Of note, vertigo is the most common aura manifestation in basilar-type migraine/migraine with brainstem aura

(Kirchmann et al., 2006). However, several features of VM, such as the longer duration of most episodes, complex nystagmus pattern, and interictal peripheral vestibular dysfunction, cannot be explained by spreading depression.

Vasospasm of the internal auditory artery has been proposed to cause peripheral vestibular and cochlear dysfunction in migraine with and without vertigo (Baloh, 1997). However, vasospasm can hardly account for episodes lasting hours or days. Furthermore, central vestibular and ocular motor dysfunction in patients with migraine points to another mechanism unrelated to labyrinthine ischemia.

Neuroanatomic studies in animals point to a connection between the vestibular system and nociceptive brainstem structures, such as the noradrenergic locus ceruleus and the serotonergic dorsal raphe nuclei (Schuerger and Balaban, 1999; Halberstadt and Balaban, 2003; Furman et al., 2013). Calcitonin gene-related peptide is another neurotransmitter essential in the cascade leading to a migraine attack and may also modulate the activity of central and peripheral vestibular neurons (Cutrer and Baloh, 1992). When these neurotransmitters are released unilaterally, static vestibular tone imbalance may result, presenting clinically with spontaneous or positional vertigo; when they are released bilaterally, vestibular signal processing in response to head motion may become distorted, presenting with head motion-induced vertigo and dizziness. Reciprocal connections between the vestibular nuclei and the trigeminal system (Buisseret-Delmas et al., 1999) may be the pathophysiologic basis of the observation that vestibular stimulation can trigger migraine headache (Murdin et al., 2009).

Activation of the trigeminovascular reflex during migraine leads to a sterile inflammatory response of intracranial vessels and was shown to affect also the inner ear in animal experiments (Vass et al., 2001; Koo and Balaban, 2006). Electric stimulation of the trigeminal nerve causes plasma extravasation in the murine inner ear (Vass et al., 2001). This mechanism may well explain vestibular and cochlear symptoms due to dysfunction of the inner ear in migraine. This hypothesis is supported by the observation that painful trigeminal stimulation can evoke nystagmus in migraineurs, but not in subjects without a history of migraine (Marano et al., 2005).

Finally, a dysfunction of ion channels expressed in the inner ear or in central vestibular structures could account for vestibular symptoms in VM. This last hypothesis is the only one that was systematically tested thus far. It appears to be promising, since other paroxysmal disorders presenting with migraine and vertigo, such as familial hemiplegic migraine and EA2, have been found to result from dysfunction of the PQ-calcium channel encoded by the CACNA1A gene. However, searching for mutations in this and other candidate genes was negative in patients with VM (Kim et al., 1998; von Brevern et al., 2006).

Recently, cerebral imaging studies have been performed in patients with VM. Fluorodeoxyglucose positron emission tomography examination of 2 patients with VM during an attack has shown increased metabolism of temporoparietoinsular areas and of both thalami, indicating activation of vestibulothalamocortical pathways (Shin et al., 2014). Voxel-based morphometry has shown gray-matter volume reduction in multisensory vestibular processing areas similar to brain changes reported in central vestibular compensation following peripheral vestibular loss (Obermann et al., 2014). Functional imaging with functional MRI during caloric irrigation of the vestibular organ has shown increased thalamic activation in patients with VM as compared to patients with migraine without aura and healthy subjects (Russo et al., 2014). Although these findings may indicate an activation of the central vestibular system in VM, the origin of vestibular dysfunction remains to be elucidated.

TREATMENT

Treatment of VM starts with effective counseling. A thorough explanation of the migrainous origin of the episodes is essential to relieve unnecessary fears of a serious disorder and prepares for adherence to lifestyle changes and medications. At first, many patients are surprised when the diagnosis is explained to them, particularly when the presenting symptom is vertigo and not headache. Nonpharmaceutical approaches to the prophylactic treatment of VM can be as effective as medication. Avoidance of identified triggers, regular sleep and meals, and physical exercise have a firm place in migraine prophylaxis. In migraine headaches, relaxation techniques and biofeedback are as effective as pharmacologic prophylaxis (Holroyd and Penzien, 1990).

Symptomatic treatment during episodes of VM lasting longer than 1 hour can be achieved with vestibular suppressants such as dimenhydrinate. There is anecdotal evidence that triptans may be effective for VM. The only controlled trial on the efficacy of triptans in VM remained inconclusive due to its limited power (Neuhauser et al., 2003). A retrospective study found that the effect of triptans on vertigo was related to its effect on headache (Bikhazi et al., 1997). Interestingly, triptans seem also to reduce motion sickness in migraineurs, possibly by influencing serotonergic vestibuloautonomic projections (Furman et al., 2011). Intravenous methylprednisolone (1000 mg/day for 1–3 days) effectively terminated prolonged attacks or exacerbations with daily recurrences in 4 patients (Prakash and Shah, 2009). In patients with severe nausea or vomiting, the

route of administration of acute medication should be parenteral (i.e., by suppositories, nasal spray, or subcutaneous injection).

In many patients, episodes of VM are severe, long, and frequent enough to warrant prophylactic medication. Unfortunately, there is a lack of solid data derived from placebo-controlled trials. Thus far, there is only one randomized controlled trial of prophylactic treatment of VM, comparing the efficacy of flunarizine over 12 weeks to no prophylactic medical treatment. The frequency and severity of vertiginous episodes decreased with flunarizine, but the study can be criticized for lack of both blinding and application of placebo in the control group (Lepcha et al., 2014). Several retrospective and observational analyses have reported a reduction of intensity and frequency of attacks of VM with prophylactic migraine drugs such as metoprolol, propranolol, flunarizine, topiramate, lamotrigine, valproate, and amitriptyline (Baier et al., 2009; Fotuhi et al., 2009; van Omberg et al., 2015). Furthermore, response to the carbonic anhydrase inhibitor acetazolamide, which is usually not used for migraine prophylaxis, has been reported (Baloh et al., 1996). These results have to be regarded with caution as the clinical course is variable and spontaneous remission is common (Reploeg and Goebel, 2002; Neuhauser et al., 2003; Baier et al., 2009). However, most experts agree that prophylactic drug treatment can be effective in VM. In the absence of evidence for the most effective medication, comorbid conditions and side-effects should be taken into consideration for the choice of drug. In patients with hypertension a beta-blocker is usually the first option. For several drugs, such as flunarizine, valproate, and amitriptyline, weight gain can be a cause for concern. Sedation and other side-effects can be greatly reduced with slow titration of dosage. Treatment efficacy should be evaluated after 3 months on the basis of a diary of events. A realistic goal is a reduction in attack frequency of about 50–70%. Similar to migraine headache, the frequency of episodes of VM varies over time. Thus, the need for prophylactic medical treatment is often only transient.

In patients with constant dizziness, visual dependence, and unsteadiness in addition to episodes of VM, vestibular rehabilitation can be effective (Whitney et al., 2000; Vitkovic et al., 2013). Psychiatric illness often significantly adds to reduction of quality of life and patients with coexisting anxiety disorders or depression may be treated with antidepressants and psychotherapy.

References

Abu-Arafeh I, Russell G (1995). Paroxysmal vertigo as a migraine equivalent in children: a population-based study. Cephalalgia 15: 22–25.

Akdal G, Özge A, Ergör G (2013). The prevalence of vestibular symptoms in migraine or tension-type headache. J Vestib Res 23: 101–106.

Akerman S, Holland PR, Goadsby PJ (2011). Diencephalic and brainstem mechanisms in migraine. Nat Rev Neurosci 12: 570–584.

Ansink BJ, Danby M, Oosterveld WJ et al. (1985). Flunarizine, the vestibuar system and migraine. Cephalalgia 5: 205–210.

Aragones JM, Fortes-Rego J, Fuste J et al. (1993). Migraine: an alternative in the diagnosis of unclassified vertigo. Headache 33: 125–128.

Baier B, Dieterich M (2009). Vestibular-evoked myogenic potentials in "vestibular migraine" and Menière's disease. A sign of electrophysiological link? Ann N Y Acad Sci 1164: 324–327.

Baier B, Winkenwerder E, Dieterich M (2009). "Vestibular migraine": effects of prophylactic therapy with various drugs. A retrospective study. J Neurol 256: 436–442.

Baloh RW (1997). Neurotology of migraine. Headache 37: 615–621.

Baloh RW, Foster CA, Yue Q et al. (1996). Familial migraine with vertigo and essential tremor. Neurology 46: 458–460.

Basser LS (1964). Benign paroxysmal vertigo of childhood. Brain 87: 141–152.

Battista RA (2004). Audiometric findings of patients with migraine-associated dizziness. Otol Neurotol 25: 987–992.

Behan PO, Carlin J (1982). Benign recurrent vertigo. In: C Rose (Ed.), Advances in migraine research and therapy, Raven Press, New York, pp. 49–55.

Bikhazi P, Jackson C, Ruckenstein MJ (1997). Efficacy of antimigrainous therapy in the treatment of migraine-associated dizziness. Am J Otol 18: 350–354.

Bir LS, Ardic FN, Kara CO et al. (2003). Migraine patients with or without vertigo: comparison of clinical and electronystagmographic findings. J Otolaryngol 32: 234–238.

Blödow A, Heinze M, Bloching MB et al. (2014). Caloric stimulation and video-head impulse testing in Ménière's disease and vestibular migraine. Acta Otolaryngol 134: 1239–1244.

Boenheim F (1917). Über familiäre Hemicrania vestibularis. Neurol Centralbl 36: 226–229.

Boldingh MI, Ljostad U, Mygland A et al. (2011). Vestibular sensitivity in vestibular migraine: VEMPs and motion sickness susceptibility. Cephalalgia 31: 1211–1219.

Boldingh MI, Ljostad U, Mygland A et al. (2013). Comparison of interictal vestibular function in vestibular migraine vs migraine without vertigo. Headache 53: 1123–1133.

Brandt T (1999). Vertigo. Its Multisensory symptoms, Springer, London, p. 23.

Brandt T, Strupp M (2006). Migraine and vertigo: classification, clinical features, and specific treatment considerations. Headache Current 3: 12–19.

Brantberg K, Baloh RW (2011). Similarity of vertigo attacks due to Meniere's disease and benign recurrent vertigo, both with and without migraine. Acta Otolaryngol 131: 722–727.

Breslau N, Schultz LR, Stewart WF et al. (2000). Headache and major depression: is the association specific to migraine? Neurology 54: 308–313.

Breslau N, Schultz LR, Stewart WF et al. (2001). Headache types and panic disorder: directionality and specificity. Neurology 56: 350–354.

Buisseret-Delmas C, Compoint C, Delfini C et al. (1999). Organisation of reciprocal connections between trigeminal and vestibular nuclei in the rat. J Comp Neurol 409: 153–168.

Casani AP, Sellari-Franceschini S, Napolitano A et al. (2009). Otoneurologic dysfunction on migraine patients with or without vertigo. Otol Neurotol 30: 961–967.

Cass SP, Ankerstjerne JKP, Yetiser S et al. (1997). Migraine-related vestibulopathy. Ann Otol Rhinol Laryngol 106: 182–189.

Çelebisoy N, Gökçay F, Şirin H et al. (2007). Migrainous vertigo: clinical, oculographic and posturographic findings. Cephalalgia 28: 72–77.

Cha YH, Kane MJ, Baloh RW (2007). Familial clustering of migraine, episodic vertigo, and Ménière's disease. Otol Neurotol 29: 93–96.

Cha YH, Santell LS, Baloh RW (2009). Association of benign recurrent vertigo and migraine in 208 patients. Cephalalgia 29: 550–555.

Cutrer FM, Baloh RW (1992). Migraine-associated dizziness. Headache 32: 300–304.

Dash AK, Panda N, Khandelwal G et al. (2008). Migraine and audiovestibular dysfunction: is there a correlation? Am J Otolaryngol 29: 295–299.

Dieterich M, Brandt T (1999). Episodic vertigo related to migraine (90 cases): vestibular migraine? J Neurol 246: 883–892.

Dimitri PS, Wall C, Oas JG et al. (2001). Application of multivariate statistics to vestibular testing: discrimination between Menière's disease and migraine associated dizziness. J Vestib Res 11: 53–65.

Eckhardt-Henn A, Best C, Bense S et al. (2008). Psychiatric comorbidity in different organic vertigo syndromes. J Neurol 255: 420–428.

Escat E (1904). De la migraine otique. In: VII. Congr. Internat. d'Otologie; compte rendu, Gounouilhon, Bordeaux, p. 1176.

Ferrari MD, Klever RR, Terwindt GM et al. (2015). Migraine pathophysiology: lessons from mouse models and human genetics. Lancet Neurol 14: 65–80.

Fife TD, Baloh RW, Duckwiler GR (1994). Isolated dizziness in vertebrobasilar insufficiency: clinical features, angiography, and follow-up. J Stroke Cerebrovasc Dis 4: 4–12.

Fotuhi M, Glaun B, Quan SY et al. (2009). Vestibular migraine: a critical review of treatment trials. J Neurol 256: 711–716.

Furman JM, Balaban CD, Jacob RG et al. (2005a). Migraine-anxiety related dizziness (MARD): a new disorder? J Neurol Neurosurg Psychiatry 76: 1–8.

Furman JM, Sparto PJ, Soso M et al. (2005b). Vestibular function in migraine-related dizziness: a pilot study. J Vestib Res 15: 327–332.

Furman JM, Marcus DA, Balaban CD (2011). Rizatriptan reduces vestibular-induced motion sickness in migraineurs. J Headache Pain 12: 81–88.

Furman JM, Marcus DA, Balaban CD (2013). Vestibular migraine: clinical aspects and pathophysiology. Lancet Neurol 12: 706–715.

Geser R, Straumann D (2012). Referral and final diagnoses of patients assessed in an academic vertigo center. Front Neurol 3: 169. Nov 28.

Gürkov R, Kanter C, Strupp M et al. (2014). Endolymphatic hydrops in patients with vestibular migraine and auditory symptoms. Eur Arch Otorhinolaryngol 271: 2661–2667.

Halberstadt AL, Balaban CD (2003). Organisation of projections from the raphe nuclei to the vestibular nuclei in rats. Neuroscience 120: 573–594.

Hamann KF, Schuster EM (1999). Vibration-induced nystagmus – a sign of unilateral vestibular deficit. ORL J Otorhinolaryngol Relat Spec 61: 74–79.

Harno H, Hirvonen T, Kaunisto MA et al. (2003). Subclinical vestibulocerebellar dysfunction in migraine with and without aura. Neurology 61: 1748–1752.

Headache Classification Subcommittee of the International Headache Society (2013). The international classification of headache disorders: 3rd edition. Cephalalgia 33: 629–808.

Hietikko E, Kotimäki J, Kentala E et al. (2011). Finnish familial Meniere disease is not linked to chromosome 12p12.3, and anticipation and consegration with migraine are not common findings. Genet Med 13: 415–420.

Holroyd KA, Penzien DB (1990). Pharmacological versus non-pharmacological prophylaxis of recurrent migraine headaches: a meta-analytic review of clinical trials. Pain 42: 1–13.

Hsu LC, Wang SJ, Fuh JL (2011). Prevalence and impact of migrainous vertigo in midlife women. A community-based study. Cephalalgia 31: 77–83.

Hüfner K, Barresi D, Glaser M et al. (2008). Vestibular paroxysmia. Diagnostic features and medical treatment. Neurology 71: 1006–1014.

Huppert D, Strupp M, Brandt T (2010). Long-term course of Menière's disease revisted. Acta Otolaryngol 130: 644–651.

Ishiyama A, Jacobson KM, Baloh RW (2000). Migraine and benign positional vertigo. Ann Otol Rhinol Laryngol 109: 377–380.

Jahn K, Langhagen T, Schroeder AS et al. (2011). Vertigo and dizziness in childhood – update on diagnosis and treatment. Neuropediatrics 42: 129–134.

Jen J, Kim GW, Baloh RW (2004). Clinical spectrum of episodic ataxia type 2. Neurology 62: 17–22.

Jensen R, Stovner LJ (2008). Epidemiology and comorbidity of headache. Lancet Neurol 7: 354–361.

Jeong SH, Oh SY, Kim HJ et al. (2010). Vestibular dysfunction in migraine: effects of associated vertigo and motion sickness. J Neurol 257: 905–912.

Johnson GD (1998). Medical management of Migraine-related dizziness and vertigo. Laryngoscope 108 (Suppl. 85): 1–28.

Kayan A, Hood JD (1984). Neuro-otological manifestations of migraine. Brain 107: 1123–1142.

Kim JS, Yue Q, Jen JC et al. (1998). Familial migraine with vertigo: no mutation found in CACNA1A. Am J Med Genet 79: 148–151.

Kirchmann M, Thomsen LL, Olesen J (2006). Basilar-type migraine: clinical, epidemiological, and genetic features. Neurology 28: 880–886.

Koo JW, Balaban CD (2006). Serotonin-induced plasma extravasation in the murine inner ear: possible mechanism of migraine-associated inner ear dysfunction. Cephalalgia 26: 1310–1319.

Krams B, Echenne B, Leydet J et al. (2011). Benign paroxysmal vertigo of childhood: long-term outcome. Cephalalgia 31: 439–443.

Kuritzky A, Ziegler DK, Hassanein R (1981). Vertigo, motion sickness and migraine. Headache 21: 227–231.

Lahmann C, Henningsen P, Brandt T et al. (2015). Psychiatric comorbidity and psychosocial impairment among patients with vertigo and dizziness. J Neurol Neurosurg Psychiatry 86: 302–308.

Langhagen T, Lehrer N, Borggraefe I et al. (2015). Vestibular migraine in children and adolescents: clinical findings and laboratory tests. Front Neurol 5: 292. Jan 26.

Lee H, Sohn SI, Jung DK et al. (2002). Migraine and isolated recurrent vertigo of unknown cause. Neurol Res 24: 663–665.

Lee H, Jen JC, Wang H et al. (2006). A genome-wide linkage scan of familial benign recurrent vertigo: linkage to 22q12 with evidence of heterogeneity. Hum Mol Genet 15: 251–258.

Leliever WC, Barber HO (1981). Recurrent vestibulopathy. Laryngoscope 91: 1–6.

Lempert T, Neuhauser H (2009). Epidemiology of vertigo, migraine, and vestibular migraine. J Neurol 256: 333–338.

Lempert T, Leopold M, von Brevern M et al. (2000). Migraine and benign positional vertigo. Ann Otol Rhinol Laryngol 109: 1176.

Lempert T, Olesen J, Furman J et al. (2012). Vestibular migraine: Diagnostic criteria. Consensus document of the Bárány Society and the International Headache Society. J Vestib Res 22: 167–172.

Lepcha A, Amalanathan S, Augustine AM et al. (2014). Flunarizine in the prophylaxis of migrainous vertigo: a randomized controlled trial. Eur Arch Otorhinolaryngol 271: 2931–2936.

Liao LJ, Young YH (2004). Vestibular evoked myogenic potentials in basilar artery migraine. Laryngoscope 114: 1305–1309.

Liveing E (1873). On megrim, sick-headache and some allied health disorders: a contribution to the pathology of nerve storms, Churchill, London, pp. 129–148.

Lopez-Escamez A, Dlugaiczyk J, Jacobs J et al. (2014). Accompanying symptoms overlap during attacks in Menière's disease and vestibular migraine. Front Neurol 5: 265. Dec 15.

Mahringer A, Rambold HA (2014). Caloric test and video-head-impulse: a study of vertigo/dizziness patients in a community hospital. Eur Arch Otorhinolaryngol 271: 463–472.

Maione A (2006). Migraine-related vertigo: diagnostic criteria and prophylactic treatment. Laryngoscope 116: 1782–1786.

Marano E, Marcelli V, Di Stasio E et al. (2005). Trigeminal stimulation elicits a peripheral vestibular imbalance in migraine patients. Headache 45: 325–331.

Marcelli V, Furia T, Marciano E (2010). Vestibular pathways involvement in children with migraine: a neuro-otological study. Headache 50: 71–76.

Murdin L, Davies RA, Bronstein AM (2009). Vertigo as a migraine trigger. Neurology 73: 638–642.

Murofushi T, Ozeki H, Inoue A et al. (2009). Does migraine-associated vertigo share a common pathophysiology with Meniere's disease? Study with vestibular-evoked myogenic potentials. Cephalalgia 29: 1259–1266.

Nakada T, Yoshida T, Suga K et al. (2014). Endolymphatic space size in patients with vestibular migraine and Menière's disease. J Neurol 261: 2079–2084.

Neff BA, Staab JP, Eggers SD et al. (2012). Auditory and vestibular symptoms and chronic subjective dizziness in patients with Ménière's disease, vestibular migraine, and Ménière's disease with concomitant vestibular migraine. Otol Neurotol 33: 1235–1244.

Neugebauer H, Adrion C, Glaser M et al. (2013). Long-term changes of central ocular motor signs in patients with vestibular migraine. Eur Neurol 69: 102–107.

Neuhauser H, Leopold M, von Brevern M et al. (2001). The interrelations of migraine, vertigo, and migrainous vertigo. Neurology 56: 436–441.

Neuhauser H, Radtke A, von Brevern M et al. (2003). Zolmitriptan for treatment of migrainous vertigo: a pilot randomized placebo-controlled trial. Neurology 60: 882–883.

Neuhauser HK, von Brevern M, Radtke A et al. (2005). Epidemiology of vestibular vertigo: a neurotological survey of the general population. Neurology 65: 898–904.

Neuhauser HK, Radtke A, von Brevern M et al. (2006). Migrainous vertigo. Prevalence and impact on quality of life. Neurology 67: 1028–1033.

Obermann M, Wurthmann S, Schulte B et al. (2014). Central vestibular system modulation in vestibular migraine. Cephalalgia 34: 1053–1061.

Oh AK, Lee H, Jen JC et al. (2001). Familial benign recurrent vertigo. Am J Med Genet 100: 287–291.

Olsson J (1991). Neurotologic findings in basilar migraine. Laryngoscope 101: 1–41.

Park JH, Viirre E (2010). Vestibular migraine may be an important cause of dizziness/vertigo in perimenopausal period. Med Hypotheses 75: 409–414.

Parker W (1991). Migraine and the vestibular system in adults. Am J Otol 12: 25–34.

Paul NL, Simoni M, Rothwell PM et al. (2013). Transient isolated brainstem symptoms preceding posterior circulation stroke: a population-based study. Lancet Neurol 12: 65–71.

Phillips J, Longridge N, Mallinson A et al. (2010). Migraine and vertigo: a marriage of convenience? Headache 50: 1362–1365.

Polensek SH, Tusa RJ (2010). Nystagmus during attacks of vestibular migraine: an aid in diagnosis. Audiol Neurootol 15: 241–246.

Prakash S, Shah ND (2009). Migrainous vertigo responsive to intravenous methylprednisolone: case reports. Headache 49: 1235–1239.

Radtke A, Lempert T, Gresty MA et al. (2002). Migraine and Menière's disease – is there a link? Neurology 59: 1700–1704.

Radtke A, Neuhauser H, von Brevern M et al. (2011). Vestibular migraine – validity of clinical diagnostic criteria. Cephalalgia 31: 906–913.

Radtke A, von Brevern M, Neuhauser H et al. (2012). Vestibular migraine. Long-term follow-up of clinical symptoms and vestibulo-cochlear findings. Neurology 79: 1607–1614.

Rassekh CH, Harker LA (1992). The prevalence of migraine in Meniere's disease. Laryngoscope 102: 135–138.

Reploeg MD, Goebel JA (2002). Migraine-associated dizziness: patient characteristics and management options. Otol Neurotol 23: 364–371.

Riina N, Ilmari P, Kentala E (2005). Vertigo and imbalance in children. A retrospective study in a Helsinki university otolaryngology clinic. Arch Otolaryngol Head Neck Surg 131: 996–1000.

Roceanu A, Allena M, de Pasqua V et al. (2008). Abnormalities of the vestibulo-collic reflex are similar in migraineurs with and without vertigo. Cephalalgia 28: 988–990.

Russo A, Marcelli V, Esposito F et al. (2014). Abnormal thalamic function in patients with vestibular migraine. Neurology 82: 2120–2126.

Savundra PA, Carroll JD, Davies RA et al. (1997). Migraine-associated vertigo. Cephalalgia 17: 505–510.

Schlake HP, Hofferberth B, Grotemeyer KH et al. (1989). Electronystagmographic investigations in migraine and cluster headache during the pain-free interval. Cephalalgia 9: 271–275.

Schuerger RJ, Balaban CD (1999). Organisation of the coeruleo-vestibular pathway in rats, rabbits and monkeys. Brain Res Rev 30: 189–217.

Shin JE, Kim CH, Park HJ (2013). Vestibular abnormalities in patients with Meniere's disease and vestibular migraine. Acta Otolaryngol 133: 154–158.

Shin JE, Kim YK, Kim HJ et al. (2014). Altered brain metabolism in vestibular migraine: comparison of interictal and ictal findings. Cephalalgia 34: 58–67.

Slater R (1979). Benign recurrent vertigo. J Neurol Neurosurg Psychiatry 42: 363–367.

Sturzenegger MH, Meienberg O (1985). Basilar artery migraine: a follow-up study of 82 cases. Headache 25: 408–415.

Szirmai A (2010). Vestibular disorders in childhood and adolescents. Eur Arch Otorhinolaryngol 267: 1801–1804.

Taylor RL, Zagami AS, Gibson WP et al. (2012). Vestibular evoked myogenic potentials to sound and vibration: characteristics in vestibular migraine that enable separation from Menière's disease. Cephalalgia 32: 213–225.

Teggi R, Colombo B, Bernasconi L et al. (2009). Migrainous vertigo: results of caloric testing and stabilometric findings. Headache 49: 435–444.

Toglia JU, Thomas D, Kuritzky A (1981). Common migraine and vestibular function. Ann Otol 90: 267–271.

van Leeuven RB, Bruintjes TD (2010). Recurrent vestibulopathy: natural course and prognostic factors. J Laryngol Otol 124: 19–22.

van Omberg A, van Rompaey, van der Heyning P et al. (2015). Vestibular migraine in an otolaryngology clinic: prevalence, associated sympoms and prophylactic medication effectiveness. Otol Neurotol 36: 133–138.

Vass Z, Steyger PS, Hordichok AJ et al. (2001). Capsaicin stimulation of the cochlear and electric stimulation of the trigeminal ganglion mediate vascular permeability in cochlear and vertebro-basilar arteries: a potential cause of inner ear dysfunction in headache. Neuroscience 103: 189–201.

Vitkovic J, Paine M, Rance G (2008). Neuro-otological findings in patients with migraine- and nonmigraine-related dizziness. Audiol Neurootol 13: 113–122.

Vitkovic J, Winoto A, Rance G et al. (2013). Vestibular rehabilitation outcomes in patients with and without vestibular migraine. J Neurol 260: 3039–3048.

Von Brevern M (2014). Vestibular migraine: vestibular testing and pathophysiology. In: B Colombo, R Teggi (Eds.), Vestibular migraine and related syndromes, Springer, Switzerland, pp. 83–90.

von Brevern M, Radtke A, Clarke AH et al. (2004). Migrainous vertigo presenting as episodic positional vertigo. Neurology 62: 469–472.

von Brevern M, Zeise D, Neuhauser H et al. (2005). Acute migrainous vertigo: clinical and oculographic findings. Brain 128: 365–374.

von Brevern M, Ta N, Shankar A et al. (2006). Migrainous vertigo: mutation analysis of the candidate genes CACNA1A, ATP1A2, SCN1A, and CACNB4. Headache 46: 1136–1141.

von Brevern M, Baloh RW, Bisdorff A et al. (2011). Response to: migraine and vertigo: a marriage of convenience? Headache 51: 308–309.

Vukovic V, Plavec D, Galinovic I et al. (2007). Prevalence of vertigo, dizziness, and migrainous vertigo in patients with migraine. Headache 47: 1427–1435.

Wang CT, Lai MS, Young YH (2009). Relationship between basilar-type migraine and migrainous vertigo. Headache 49: 426–434.

Waterston J (2004). Chronic migrainous vertigo. J Clin Neurosci 11: 384–388.

Whitney SL, Wrisley DM, Brown KE et al. (2000). Physical therapy for migraine-related vestibulopathy and vestibular dysfunction with history of migraine. Laryngoscope 110: 1528–1534.

Wilkinson F, Karanovic O, Ross EC et al. (2006). Ocular motor measures in migraine with and without aura. Cephalalgia 26: 660–671.

Yacovino DA, Hain TC (2013). Clinical characteristics of cervicogenic-related dizziness and vertigo. Semin Neurol 33: 244–255.

Zaleski A, Bogle J, Starling A et al. (2015). Vestibular evoked myogenic potentials in patients with vestibular migraine. Otol Neurotol 36: 295–302.

Zuniga MG, Janky KL, Schubert MC et al. (2012). Can vestibular-evoked myogenic potentials help differentiate Ménière disease from vestibular migraine? Otolaryngol Head Neck Surg 146: 788–796.