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Bilateral vestibulopathy: Diagnostic criteria Consensus document of the Classification Committee of the Bárány Society[1]

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Abstract. This paper describes the diagnostic criteria for bilateral vestibulopathy (BVP) by the Classification Committee of the Bárány Society. The diagnosis of BVP is based on the patient history, bedside examination and laboratory evaluation. Bilateral vestibulopathy is a chronic vestibular syndrome which is characterized by unsteadiness when walking or standing, which worsen in darkness and/or on uneven ground, or during head motion. Additionally, patients may describe head or body movement-induced blurred vision or oscillopsia. There are typically no symptoms while sitting or lying down under static conditions.

The diagnosis of BVP requires bilaterally significantly impaired or absent function of the vestibulo-ocular reflex (VOR). This can be diagnosed for the high frequency range of the angular VOR by the head impulse test (HIT), the video-HIT (vHIT) and the scleral coil technique and for the low frequency range by caloric testing. The moderate range can be examined by the sinusoidal or step profile rotational chair test.

For the diagnosis of BVP, the horizontal angular VOR gain on both sides should be <0.6 (angular velocity 150–300°/s) and/or the sum of the maximal peak velocities of the slow phase caloric-induced nystagmus for stimulation with warm and cold water on *each* side <6°/s and/or the horizontal angular VOR gain <0.1 upon sinusoidal stimulation on a rotatory chair (0.1 Hz, Vmax = 50°/sec) and/or a phase lead >68 degrees (time constant of <5 seconds). For the diagnosis of probable BVP the above mentioned symptoms and a bilaterally pathological bedside HIT are required.

Complementary tests that may be used but are currently not included in the definition are: a) dynamic visual acuity (a decrease of ≥0.2 logMAR is considered pathological); b) Romberg (indicating a sensory deficit of the vestibular or somatosensory system and therefore not specific); and c) abnormal cervical and ocular vestibular-evoked myogenic potentials for otolith function.

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At present the scientific basis for further subdivisions into subtypes of BVP is not sufficient to put forward reliable or clinically meaningful definitions. Depending on the affected anatomical structure and frequency range, different subtypes may be better identified in the future: impaired canal function in the low- or high-frequency VOR range only and/or impaired otolith function only; the latter is evidently very rare.

Bilateral vestibulopathy is a clinical syndrome and, if known, the etiology (e.g., due to ototoxicity, bilateral Menière's disease, bilateral vestibular schwannoma) should be added to the diagnosis. Synonyms include bilateral vestibular failure, deficiency, areflexia, hypofunction and loss.

Keywords: Bilateral vestibulopathy, vertigo, dizziness, disequilibrium, vestibular, diagnostic criteria, Bárány Society

1. Introduction

The Bárány Society representing the international community of basic scientists, otolaryngologists and neurologists committed to vestibular research mandated a Classification Committee for an International Classification of Vestibular Disorders (ICVD). Individual disorders are defined by classification panels, which include otolaryngologists and neurologists from at least three continents. The ICVD has already published a consensus on the definitions of vestibular symptoms [1], vestibular migraine [2], Menière's disease [3], benign paroxysmal positional vertigo [4] and vestibular paroxysmia [5].

In 1882 W. James reported on the "sense of dizziness in deaf-mutes" [6]. In 1907 R. Bárány described a bilaterally reduced caloric response also in deaf-mutes [7]. In 1941, Dandy described oscillopsia and postural instability exacerbated by visual deprivation in subjects on whom he had performed bilateral vestibular neurectomy in an effort to treat Menière's disease [8]. Movement-induced oscillopsia was identified as a frequent additional symptom in 1965 [9]; for additional references related to the history of bilateral vestibulopathy (BVP) see [10]. In 1989 this syndrome was more precisely defined in patients presenting with imbalance and oscillopsia, worsening in darkness, without hearing loss or other neurological symptoms and was called "idiopathic bilateral vestibulopathy" [11]. In 2005 it was demonstrated that BVP also leads to impaired spatial memory and hippocampal atrophy [12], later confirmed by other MRI studies [13, 14]. In 2009 a subtype with bilateral absence of vestibular evoked myogenic potentials (VEMP) in the presence of normal caloric response was described [15]. An association between BVP and impaired cerebellar dysfunction has been described in many publications [16–20] with a particular syndrome "Cerebellar Ataxia, Neuropathy and Vestibular Areflexia" (CANVAS), a gangliopathy with cerebellar atrophy, described in 2011 [21].

Based on the literature on this topic there is evident agreement on

a) the leading symptoms: postural imbalance and unsteadiness of gait, which both worsen in darkness and on uneven ground; head or body movement induced oscillopsia in some patients, in particular during walking, which engenders head movements with high frequency spectral content, particularly during each heel strike [15, 17, 19, 22–26];
b) the bedside diagnosis of a bilaterally deficient angular vestibulo-ocular reflex (aVOR) by the head impulse test (HIT) [27]. It has its limitations [28]: only VOR deficits with a gain <0.4 can be reliably detected by the bedside HIT [29] and in cerebellar disorders its interpretation is often difficult [30];
c) the use of caloric irrigation and/or the video-HIT to diagnose a peripheral vestibular deficit [31–35]. Rotational chair testing is nowadays less often applied;
d) dynamic visual acuity as a complementary test [36];
e) the etiology of BVP: often it remains unclear. Frequent known causes are ototoxic drugs, bilateral Menière's disease, meningitis, genetic mutations and there is an association with cerebellar disorders [17, 19].

Issues that have to be addressed and if possible defined in future updates are: First, what are pathological values for the caloric response and the gain of the angular VOR (aVOR) to qualify for the diagnosis of BVP with a reasonable specificity and sensitivity? Second, what is the role of testing the vertical canals with the HIT [37] and testing the otolith organs with cervical and ocular vestibular evoked myogenic potentials (cVEMP/oVEMP) for BVP? Third, are there different subtypes of BVP in terms of reduced function of the low and high frequency aVOR [35], different canals [37] and/or of otolith function?

2. Methods

The present work forms part of an ongoing multi-year project to develop an ICVD, which uses a structured process for developing international consensus definitions for vestibular symptoms, syndromes, disorders, and diseases. This process, overseen by the Classification Committee of the Bárány Society (CCBS), is based on expert, multi-disciplinary committees with international representation developing diagnostic criteria for subsequent comment and refinement prior to publication. These criteria are built on a critical appraisal of current best scientific evidence. All definitions are supported by notes, comments, and written discussion according to a template established by the CCBS for ICVD. The criteria for BVP were developed iteratively over a three-year period (2014–2017) through discussion, presentation, and refinement. Special care was taken to ensure that the criteria are specific and practical and can be applied in every country all over the world. This is particularly true for the use of certain laboratory examinations not available everywhere.

3. Diagnostic criteria for bilateral vestibulopathy

A. Chronic vestibular syndrome with the following symptoms
   1. Unsteadiness when walking or standing[1] plus at least one of 2 or 3
   2. Movement-induced blurred vision or oscillopsia during walking or quick head/body movements[2] and/or
   3. Worsening of unsteadiness in darkness and/or on uneven ground[3]

B. No symptoms while sitting or lying down under static conditions[4]

C. Bilaterally reduced or absent angular VOR function documented by
   – bilaterally pathological horizontal angular VOR gain <0.6, measured by the video-HIT[5] or scleral-coil technique and/or
   – reduced caloric response[6] (sum of bithermal max. peak SPV on each side <6°/sec[7]) and/or
   – reduced horizontal angular VOR gain <0.1 upon sinusoidal stimulation on a rotatory chair (0.1 Hz, Vmax = 50°/sec) and a phase lead >68 degrees (time constant <5 sec).

D. Not better accounted for by another disease

4. Diagnostic criteria for probable bilateral vestibulopathy

A. Chronic vestibular syndrome with the following symptoms
   1. Unsteadiness when walking or standing[1] plus at least one of 2 or 3
   2. Movement-induced blurred vision or oscillopsia during walking or quick head/body movements[2] and/or
   3. Worsening of unsteadiness in darkness and/or on uneven ground[3]

B. No symptoms while sitting or lying down under static conditions[4]

C. Bilaterally pathological horizontal bedside head impulse test[8]

D. Not better accounted for by another disease

5. Notes

1. These symptoms in BVP are caused by the sensory vestibular deficit leading to impaired vestibulo-spinal reflexes leading to higher body sway and broad-based gait.
2. About 30 to 40% of the patients report oscillopsia during active body movements such as walking and/or passive head movements (e.g., travelling in a vehicle) [19, 23, 38]; in rare cases oscillopsia can even occur in time with the heartbeat. Oscillopsia is caused by head movement induced retinal slip due to the VOR deficit for which other systems cannot fully compensate [26]. It leads to a reduction of dynamic visual acuity (see below). In contrast, for slow and low frequency head movements the smooth pursuit system can stabilize fixation when a visible target is present.
3. When explicitly asked, many patients with BVP report a worsening of postural imbalance and unsteadiness of gait in darkness and on uneven ground [19. 23] because they depend more on visual and somatosensory control. This is also associated with a higher risk of falls in darkness [39]. Imbalance is even worse if there is an additional sensory polyneuropathy [40].
4. Typically there are no symptoms when sitting or lying down under static conditions because

subjects do not rely very much on the vestibular system under these circumstances. Some patients may report oscillopsia while sitting induced, for instance, by heart beats or chewing.

5. Video-HIT: It is possible to quantify the aVOR function by a video-oculography system (video-HIT) that measures head and eye velocity during passive head rotation (150°/s–300°/s), similar to the scleral-coil technique which can, of course, also be used. Thereby, the gain of the aVOR can be determined and catch-up saccades can be detected even if they are of short latency and already occur during the head impulses (covert catch-up saccades) [31, 32, 41]. Horizontal VOR velocity gain is the ratio of angular eye velocity to angular head velocity. It can also be measured as the ratio of the area under curve (AUC) of the angular eye velocity divided by the AUC of angular head velocity. According to a study on 60 healthy subjects [42], the lower limit of the normal horizontal VOR velocity gain (2SD below mean) is 0.79 at 80 ms and 0.75 at 60 ms. The lowest and highest values of the normal horizontal VOR velocity gain are 0.76 and 1.18 at 80 ms and 0.65 and 1.17 at 60 ms. There is a decline of normal horizontal VOR velocity gain at 80 ms with aging by 0.012 per decade with increasing age (95% CI 0.001 to 0.022; $p = 0.028$). Normal horizontal VOR velocity gain at 60 ms also declines with aging. Horizontal VOR velocity gain was found to decline by 0.017 per decade with increasing age (95% CI 0.006 – 0.029; $p = 0.005$). Taking this into account, the authors agreed on a pathological gain of the video-HIT <0.6. The specific role of testing the VOR gain of the vertical canals for the diagnosis of BVP has to be further evaluated. According to a video-HIT study of all three semicircular canals in patients with BVP, the anterior canals seem less often impaired in aminoglycoside vestibulotoxicity, Menière's disease and BVP of unknown etiology [37].
6. Caloric testing: the low frequency aVOR can be tested by bithermal caloric stimulation during 30 seconds with a minimum of 200 ml warm (44°C) and cold (30°C) water and measurement of the peak SPV of caloric induced nystagmus at the culmination phase. The lower threshold applied for the mean SPV is generally lower for the cold than for the warm irrigation. As the response to the cold and warm irrigation can be affected by a spontaneous nystagmus, most laboratories use the sum of absolute values of nystagmus peak SPV to both responses of each ear as a criterion for excitability. In our experience, the lower limit of the normative data applied for the sum of the mean SPV upon cold (30°C) and warm (44°C) irrigation per ear varies among laboratories from 20–25°/sec (personal communication/discussions during conferences and courses of HK). A sum of both responses per ear <6°/sec can therefore be considered a safe criterion to point to BVP. The absence of a VOR to caloric irrigation with ice water also points to BVP. To test for convection-dependent responses to ice water independent of the direct inhibitory effect ice water cooling has on vestibular nerve activity, the subject initially undergoes ice water irrigation while supine with the head of the bed elevated 20 deg. Once the nystagmus starts, the examiner assists the subject in quickly flexing at the hips, pitching the torso and head forward and down so that the nose points toward the floor. If the nystagmus initially observed was due to convection of endolymph, then its direction should reverse; if it does, then at least some vestibular hair cell function is present. If the nystagmus does not reverse, then the initial response can be attributed mainly to direct inhibition of the vestibular nerve, and one can conclude that there is little or no vestibular hair cell function (if central causes of failed vestibular reflexes, including sedating medications, have been excluded).
7. Rotational tests: the low to middle frequency aVOR can be tested using a rotatory chair. The rotatory chair tests are especially useful when the video-HIT or caloric tests cannot be executed or are not tolerated, or appropriate instruction is difficult (e.g. cervical limitations, anxiety, young infants). Although many stimulus profiles are used (e.g., sinusoidal stimulation or velocity steps), a significant disadvantage of rotatory chairs is that rotation tests performed at accelerations less than $\sim 1000°/s^2$ are less sensitive than the video HIT (with high acceleration) and caloric irrigation (stimulating each ear independently) for detection of *unilateral* reduced vestibular function when the opposite labyrinth is normal. Therefore, strict criteria are required for diagnosis of unilateral vestibulopathy with rotary chair stimuli to avoid inclusion of false positives. In contrast, rotatory chairs are useful for diagnosis of BVP

because they enable delivery of en bloc, passive whole-body rotations in darkness, which can identify BVP in subjects for whom bedside HIT or vHIT responses are augmented by cervico-ocular reflexes, anticipatory saccades, and other non-labyrinthine visual stabilizing systems. A gain of the aVOR of less than 0.15 upon sinusoidal stimulation in the range from 0.05 to 0.1 Hz at a maximum angular velocity of 60°/sec suggests BVP, as does a short time constant of VOR responses during constant-velocity step rotations (typically less than 5 sec).

8. Bedside HIT: The patient is asked to look at the tip of the examiner's nose. The examiner, in turn, holds the head of the patient firmly and delivers impulses with high acceleration, but limited amplitudes (<15°), in the horizontal plane to each side in pseudo-random order. After each impulse, the head is held in the eccentric position and the eyes are carefully observed for catch-up saccades that bring the eyes back on the visual target, i.e. the tip of the examiner's nose, which indicates a deficient VOR [27]. In patients with BVP with complete or almost complete loss of VOR, catch-up saccades are elicited by head impulses to both sides yip [29]. Sometimes the catch-up saccades have a very short latency and therefore occur already during the head impulse. Such covert catch-up saccades cannot be seen clinically, which results in a false-negative bedside HIT [33]. Finally, using the bedside HIT only severe deficits of the angular VOR below 0.4 can be reliably detected yip [29].

6. Comments

6.1. Epidemiology

The prevalence of BVP in the US adult population was estimated to be 28 per 100,000 in 2008 [43]. The relative incidence of BVP was estimated to be 4 to 7% in various reports [17, 19, 23]. The age distribution of patients with BVP ranges from youth to old age depending on the etiology. The mean age at which the diagnosis of acquired BVP is established is given as around 50–60 years [11, 17, 19, 23, 35].

6.2. Natural course of the disease

In about 60% of patients the disease develops slowly and progressively. Forty percent of the patients have a course of events marked by episodes of dizziness leading incrementally to bilateral loss of function, again depending on the etiology [19]. Some patients could have a progressive course after recurrent attacks with spinning vertigo [19, 44, 45] (in these cases an autoimmune or vascular or rarely infectious process should be considered). Bilateral vestibulopathy causes an impairment of the health-related quality of life in 90% of the patients [46, 47]. In follow-up studies on patients with BVP the clinical findings, especially in terms of caloric responses showed a slight worsening over time [47, 48].

6.3. Pathophysiology

Bilateral impairment or loss of peripheral vestibular input causes deficits of vestibulo-ocular and vestibulo-spinal reflexes, orientation, navigation, and spatial memory: (1) As a result of a reduced gain of the aVOR, the visual world cannot be stabilized on the retina during high-acceleration head movements, which leads to head-movement induced oscillopsia [9] and reduced dynamic visual acuity [49]. (2) Balance during standing and locomotion is impeded due to insufficient vestibulo-spinal reflexes [50], especially if postural control cannot appropriately rely on proprioceptive (e.g. on soft or uneven ground) or visual input (e.g. in darkness). (3) In the absence of visual and proprioceptive cues, patients with BVP lose their sense of earth-verticality and become disoriented (e.g. when trying to dive). (4) Spatial learning performance is delayed as a consequence of anatomical and functional changes in the hippocampal formation [12, 13].

6.4. Bedside examination

a) Bedside HIT: HIT is a simple bedside test for high-frequency VOR function [27]. The examiner gives a subject high-acceleration head rotation with small amplitudes. The subject is asked to fixate the examiner's nose. Corrective saccades after head rotation (catch-up saccades) imply impaired angular VOR. Although it is applicable for diagnosis of BVP, bedside HIT could overlook patients with covert catch-up saccade [33, 51]. It is evidently only reliable in patients with a severe aVOR deficit with a gain <0.4 [29].
b) Dynamic visual acuity test: The examiner shakes the head of a subject rapidly (dis-

placement of 10–15° at approx. 2 Hz) in the horizontal plane. Impaired aVOR results in a drop of visual acuity. A decrease of ≥0.2 LogMAR units is pathological.

c) Romberg test: This is a test of static balance. A subject is asked to stand on a firm, earth-horizontal surface with the feet together with eyes open and then closed. When the subject shows obvious sway or fall with eyes closed despite no sway or fall with eyes open, the Romberg test is regarded as pathological. A pathological Romberg test implies vision-dependency for maintenance of body balance. While patients with BVP show a positive Romberg test (preferably tandem Romberg with the eyes open and closed), patients with severe proprioceptive loss could also show a positive Romberg test.

6.5. Laboratory examinations

During head movements, efficient stabilization of the image on the retina is necessary to preserve visual acuity. In patients with BVP, gaze stabilization fails and can lead to significant deterioration in visual acuity during head movements. Visual acuity in dynamic conditions can be assessed by testing for dynamic visual acuity (DVA). Dynamic visual acuity testing can be performed in many ways: the patient has to read letters from a visual acuity chart or a computer screen during active or passive, vertical or horizontal head movements, or while walking on a treadmill at different velocities [52]. A decline of more than 2 lines on the optotype chart is considered abnormal [53], although a loss of 2 lines (0.2 logMAR) is not unusual for healthy subjects. In order to trade sensitivity for specificity, 4 lines may be required [54]. Moreover, DVA may show false negative results due to mechanisms that at least partially compensate for the retinal instability during head movements [49]. However, in subjects with unilateral and bilateral vestibular loss, computerized DVA testing reached a sensitivity of 94.5% and a specificity of 95.2% [55]. In another group of BVP patients, DVA was impaired in 96% of the cases [23]. To conclude, DVA can help to establish the diagnosis of BVP, but a normal DVA does not definitely rule out BVP, and an impaired DVA does not imply vestibular hypofunction per se. It is still not understood by which specific vestibular deficits (which semicircular canal, which otolith organs and which frequencies) DVA decreases.

6.6. Caloric testing

The caloric test, first described by Bárány, is believed to evaluate the low-frequency part (∼0.01 Hz) of the horizontal semicircular canal function, which is much lower than the frequency spectrum of most natural head movements relevant to normal function of the vestibular labyrinths. This, together with the fact that the caloric stimulus is monaural, is why the caloric test is considered a non-physiological vestibular test [7, 56]. On the other hand, the caloric test is the only widely used clinical test that exclusively stimulates only one side, in contrast to HIT and all other head rotation tests. Based on extensive research in the twentieth century, the caloric response is believed to be predominantly induced by convection [57], non-specific thermic stimulation of hair cells [56] and endolymph expansion [58]. Many challenges are met when using the caloric test for diagnosing BVP. Further, putting Reid's horizontal plane 20° off vertical, not 30°, is the optimum pitch for orienting the horizontal canals in an earth-vertical plane [59]. A 5-minute stimulus interval should be maintained between successive irrigations to reduce the residual effects of the previous irrigation. During each caloric irrigation of 30 seconds duration the stimulus must have the same characteristics: the same total volume of at least 200 ml water and the same temperatures for cold and warm irrigations (30 and 44°C, respectively) [60, 61]. A 1-degree variation in temperature from the intended 30 or 44°C can already result in a 14% difference in stimulation magnitude [62]. The required thermic stimulus is best achieved by the use of water and not by air [61]. Statistically higher slow-component values of the VOR are obtained for water than for air, and evidence shows that air has poorer test-retest reliability and greater inter-subject variability (for reference see [61]). Based on our extensive clinical experience in comparing air calorics to water calorics in many hundreds of patients, we advise using water calorics. However, responses to water calorics also show considerable test-retest variation and variability between healthy subjects [61]. In the past, responses were quantified by SPV (in the culmination phase) of the caloric nystagmus, the maximum nystagmus frequency and the total number of nystagmus beats. The maximum SPV at the time of maximum response (culmination phase) occurs generally about 50–60 s after the start of irrigation and is the preferred parameter to be determined. Ice water calorics are not preferred, since they can induce a pseudo-caloric

nystagmus by activating a latent spontaneous nystagmus [23], and the absence of an ice water response does not prove a complete vestibular areflexia, as was thought in the past. The average maximum SPV varies between laboratories from 14.9 to 29.7°/s for cold irrigations and from 12.1 to 30.9°/s for warm irrigations [60, 63, 64]. These normative data will probably reveal a high variability among values. For example, in one vestibular laboratory, the 95% prediction interval of the average maximum SPV may vary from 3.4 to 32.9°/s for cold irrigations and from 6.9 to 55.0°/s for warm irrigations. There is as yet no consensus among investigators about correcting values for age [64–66]. Also, the asymmetry between labyrinths may be up to 19% and still considered be within the normal range [60]. This variability may partly be due to uncontrollable factors such as differences in anatomy of the temporal bone (differences in temperature conduction), blood flow and middle ear fluids – all the more reason to have controllable factors such as stimulus parameters and technical skills optimized and to absolutely avoid any visual suppression [60]. A criterion often suggested for diagnosing BVP is to have a sum of 4 irrigations that is less than 20°/s [23, 24, 60, 61, 67]. While this is sensitive, it could still lead to false-positive results (partly due to the anatomical variations mentioned above) and also to false-negative results. Other parts of the vestibular system, such as the remaining semicircular canals and the otolith organs, are not tested.

To summarize, using the caloric test to diagnose BVP is challenging, due to the high standards necessary for testing and difficult interpretation as a result of inter- and intra-subject variation for which the present diagnostic criteria for BVP are not always sufficient. When the high testing standards are not adhered to, and inter- and intra-subject variability is not taken into account, this leads to unnecessary false-positive and false-negative diagnoses of BVP.

6.7. Rotatory chair tests

Rotatory chair tests can demonstrate residual horizontal semicircular canal vestibular function in patients with severe BVP, when (almost) no vestibular response is measured with the caloric test [68–70]. They can also provide additional data about central processing of vestibular input from both labyrinths [60]. Two frequently used algorithms are the sinusoidal harmonic acceleration test and the velocity step test (VST) [71]. The sinusoidal harmonic acceleration test is often promoted as a real multi-frequency rotation test. However, compared to the optimum frequency sensitivity of the semicircular canals (ranging from about 0.1 to 10 Hz), the sinusoidal harmonic acceleration test uses only low-frequency stimuli ranging from 0.005 to a maximum of 0.64 Hz. Another complicating factor is that the total sinusoidal harmonic acceleration test takes considerable time. Therefore, the frequency response might be affected by changes in alertness of the patient during the test. The VST involves more high-frequency components compared to the sinusoidal harmonic acceleration test (step function) and comes closer to HIT. The first challenge when performing rotatory chair testing is to conduct it in a standardized way. The patient must be alert, since alertness during rotation increases the gain of the measured VOR [60]. Many vestibular laboratories prefer to have the eyes of the patient open during testing in complete darkness, since closing the eyes decreases gain of the VOR [72]. For the VST, it is preferred to use the first rotation for familiarization with the test to get responses that are as accurate as possible [71]. The second challenge is to have the right frame of reference for the rotatory tests. Regarding gain of the VOR, its values differ considerably between vestibular laboratories for the sinusoidal harmonic acceleration test as well as for the VST. It is therefore common sense for many vestibular laboratories to have their own normative data wall [73]. Furthermore, in the sinusoidal harmonic acceleration test and the VST, gain is considered to be the most variable parameter between and within subjects, probably as a consequence of factors such as fatigue, alertness, stress and habituation [71, 74, 75]. Gain is also reduced by the test itself; rotating in the dark is an artificial condition that reduces VOR gain [76]. Moreover, gain is frequency-dependent: it increases to a certain extent with an increasing modulation frequency [74]. Taking all these facts into account, normative data for a vestibular laboratory can vary widely: for the sinusoidal harmonic acceleration test, a mean gain of 58.77% with a standard deviation of 13.98% (0.1 Hz, 50°/s peak velocity), and for the VST, a mean gain of 67.66% with a standard deviation of 18.14% (200°/s deceleration after a continuous velocity of 100°/s rotating to the right). However, it has been indicated that the sinusoidal harmonic acceleration test and VST gain parameters can be highly consistent, despite the fact that they are influenced by many other factors [71]. Regarding other parameters, directional preponderance can vary widely within one vestibular laboratory, up to a 95% prediction interval of 26% (0.05 Hz, 50°/s peak

velocity) [60]. Parameters believed to be more consistent and reproducible are the phase in the sinusoidal harmonic acceleration test and the time constant in the VST [71, 75, 77]. The time constant refers to the duration in seconds that an induced nystagmus persists related to the chair (head) rotation. When the sinusoidal harmonic profile is used, the time constant is calculated at 0.01 Hz and is expressed as an abnormal phase lead; when the VST profile is used, the time constant is determined as the duration at which the nystagmus has reduced to 37% of its peak velocity. The time constant is considered abnormal when it is less than 10 s, and it is often less than 5 s in BVP [78]. All these facts show that interpreting the results correctly is a last challenge when using the rotatory chair to diagnose BVP. Some authors suggest that rotatory chair tests should be the gold standard [34, 54]. If any abnormalities are found in BVP patients, the strongest effects are often found at low frequencies, with a decrease in gain and an increase in phase [54]. However, depending on the criteria, only 53% of BVP patients show abnormal responses on the rotatory chair. This emphasizes the need for establishing a standardized protocol for the diagnosis of BVP patients. So far, the modulation frequencies to be tested and the cut-off criteria have not been established [23, 79]. To summarize, use of the rotatory chair is challenging. In order to get reproducible and consistent results, a high standard for testing is necessary.

Due to inter- and intra-subject variations in some parameters, interpretation of the results often remains difficult. Despite all these critical considerations, the sinusoidal rotatory test is a potentially useful tool to augment the diagnosis of BVP in patients where video-HIT or caloric test are impossible to perform. This holds, for example, in individual cases of anxiety or anatomical restrictions or infants (calorics) or patients who fail to follow the instructions for the video-HIT.

6.8. Vestibular evoked myogenic potential

Vestibular evoked myogenic potential (VEMP) testing provides useful information about the otolith organs. The air-conducted sound-evoked cVEMP tests predominantly saccular function and the bone-conducted vibration-evoked oVEMP tests predominantly utricular function. There have been several small case series and two larger studies of cVEMP in patients with BVP showing that cVEMPs are smaller than normal on average and are often absent, suggesting saccular damage [15, 67, 80, 81]. Likewise, oVEMP are also often abnormal in BVP, indicating utricular damage [15, 80, 82]. Utricular function is correlated with horizontal canal function in BVP [15]. However, as VEMP remain intact in a significant number of patients, the degree of otolith dysfunction appears to be less than that of canal dysfunction, though this may differ depending upon the underlying cause of BVP. VEMP therefore provide only supporting information and are not used in the diagnosis of BVP.

Vestibular evoked myogenic potentials can provide information about the extent of disease and involvement of the otolith organs in BVP. They can also be used to monitor disease progression or track the response to any treatment. However, abnormal VEMP should be interpreted carefully in light of other test results because of the following limitations. The range of normal VEMP amplitudes is large, positively skewed and, in older people (above about 60 yrs), extends down to an absent response. The range is large because factors other than otolith function contribute to reflex amplitude: including the intensity of sound or vibration reaching the otoliths (which is never known), placement of recording electrodes, strength of underlying muscle contraction (cVEMP) or angle of vertical gaze (oVEMP). The large normal range makes it difficult to define a meaningful lower limit of normal VEMP amplitude, especially in older populations. Bilaterally small (or even absent) cVEMP or oVEMP responses are therefore often a normal finding in older patients. This is in contrast to a VEMP asymmetry, which can be more confidently interpreted as unilateral otolith dysfunction. Isolated bilateral otolith abnormalities have been reported ([15]; for references [83]), and examination of canal function without otolith function may overlook these rare cases of BVP. But isolated VEMP abnormalities need to be carefully distinguished from false positive (abnormal) responses.

6.9. Etiology of BVP

A broad spectrum of etiologies has been shown to be important causes of BVP. In a case series of 255 patients reported in 2007, the etiology of BVP was ascertained in approximately 30% of the patients, with the remainder thought to be idiopathic and degenerative in nature [19]. The three most frequently identifiable causes of BVP include: ototoxic drugs (13%; gentamicin and other ototoxic antibiotics, anticancer chemotherapy, loop diuretics,

aspirin in very high dosages [84] or styrenes [85]), bilateral Menière's disease (7%), and meningitis (5%). Other causes are a) tumors: bilateral vestibular schwannoma in neurofibromatosis type 2, meningeal carcinomatosis, infiltration of the skull base or due to tumor irradiation; b) autoimmune diseases [86] like Cogan syndrome [87], neurosarcoidosis, Behçet's disease, cerebral vasculitis, systemic lupus erythematosus, granulomatous polyangiitis (Wegener's granulomatosis); c) rarer causes such as bilateral labyrinth concussion or superficial siderosis [88, 89]. In another case series of 154 patients with BVP, Menière's disease and ototoxic exposure were the most common definite etiologies, followed by infectious and genetic causes [90]. Indeed, recent advances in human genetics have led to the identification of firm genetic causes in 15% of one BVP cohort, with another 10% suspected to have a probable genetic cause [90]. The proportion of patients with a definite etiology was 47% in that study. Some patients with BVP could have a cerebellar syndrome with downbeat nystagmus [18–20, 91]. Such cases probably involve a neurodegenerative illness that affects the vestibular ganglia cells and the cerebellum; it often occurs with an additional neuropathy: cerebellar ataxia with neuropathy and vestibular areflexia syndrome (CANVAS). This combination of symptoms occurs in up to 10%–20% of patients with BVP in some case series [21, 92, 93].

Predisposing genetic factors are suspected but poorly understood for patients with idiopathic loss of vestibular function. Genetic factors for susceptibility of toxic damage have been proposed on the basis of familial cases with BVP with exquisite sensitivity to aminoglycosides, yet no mitochondrial abnormality or mutations have been demonstrated [91]. Similar to Menière's disease, familial BVP is commonly found in the setting of migraine, raising the possibility of selective vulnerability of the inner ear to migraine-related damage [90]. Linkage analysis in a handful of families with BVP suggested a locus on chromosome 6q [94]. Thus far, no mutations have been identified in BVP with normal hearing, in contrast with an ever increasing number of genetic loci for hearing loss [95, 96]. In conclusion, BVP has been proposed to be a monogenic disorder with different modes of inheritance including autosomal dominant, autosomal recessive, sex-linked or mitochondrial [97, 98]. BVP related to migraine could be a complex trait, as migraine itself is complex. There is continuing effort to characterize the genetic basis of BVP.

In children, the underlying diseases leading to BVP are different: for instance, various congenital malformations, such as inner ear dysplasia, Waardenburg or Usher syndrome, which are often associated with deafness, or embryopathic infections (e.g., rubella) or bacterial meningitis.

6.10. Differential diagnosis

Clinically relevant differential diagnoses are summarized in Table 1.

6.11. Limitations, areas of uncertainties and deficits in current knowledge

There are several areas of uncertainty in the classification:

1) There has been much discussion about the terminology of the entity. Terms suggested by the authors in addition to BVP were bilateral vestibular hypofunction, bilateral peripheral vestibular hypofunction, bilateral vestibular hyopreflexia/areflexia, and bilateral vestibular deficiency. To come to an agreement on this important issue, a transparent democratic approach was used with two rounds of voting: firstly, every author could list three terms in order of preference. Secondly, there was a vote with points for the three favourite terms with the following results: 21 points for BVP, 11 points for a combined term BVP/bilateral vestibular hypofunction, 9 points for bilateral vestibular hypofunction only.
2) A major challenge in the classification is that no single test can fully characterize the functional integrity of the vestibular apparatus.

Table 1
Differential diagnosis of bilateral vestibulopathy

• Cerebellar ataxias without bilateral vestibulopathy
• Downbeat nystagmus syndrome
• Functional dizziness: persistent postural-perceptual dizziness, phobic postural dizziness, visual induced dizziness
• Unilateral vestibular deficit
• Intoxications
• Vestibular suppressant medications
• Orthostatic tremor
• Visual disorders (if oscillopsia is prominent)
• Peripheral neuropathies
• Movement disorders: Parkinson's disease, atypical Parkinson's syndromes, multiple system atrophies
• Central gait disorders due to normal pressure hydrocephalus, frontal gait disorders, lower-body Parkinson, subcortical vascular encephalopathy or multiple sclerosis

3) The panel discussed the clinical utility of distinguishing BVP from "probable BVP" as well as "complete" or "incomplete" BVP based on quantitative measurement from caloric testing, video-HIT of horizontal and vertical canals, cVEMP and oVEMP and rotational testing, keeping in mind that the latter is used less and less often. "Probable BVP" is a working diagnosis for clinical practice in primary care and quantitative measurement of the vestibular function is required for BVP.
4) A corollary to the definition of BVP is whether there is clinical utility for the sub-classification of reduced/absent low- vs. high-frequency canal function, horizontal and/or vertical canal function vs. otolith function. This means partial or complete loss of sensory function in any subset of the 10 vestibular endorgans on both sides.
5) It has to be kept in mind that VOR responses in some or all tests commonly used to examine labyrinthine function are used under the assumption that all downstream aspects of the reflex pathways are normal.
6) The proposed pathological values of reduced peripheral vestibular function as measured by video-HIT and peak SPV in response to caloric irrigation are a conservative consensus by the panel to enhance the stringency of the diagnostic criteria. They can therefore be considered criteria for "profound" BVP, whereas "severe" BVP could be diagnosed in the setting of less dramatically reduced function on video-HIT and caloric testing.

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