RECENT ADVANCES IN THE DIAGNOSIS OF SOME COMMON VESTIBULAR DISORDERS

Mario Milkov

Department of Dental Material Sciences and Propedeutics of Prosthetic Dental Medicine, Faculty of Dental Medicine, Medical University of Varna

ABSTRACT

The interest in the diagnosis of common vestibular disorders in children and adults is permanently increasing. In this survey, the applications of the main diagnostic methods in this interdisciplinary field are briefly discussed. The diagnostic capacities of the caloric test, video head impulse test, cervical and ocular vestibular evoked myogenic potentials, videonystagmography, electrococheography, magnetic resonance imaging, computed tomography, etc. are summarized. Special attention is paid to some common vestibular disorders such as Menière's disease, benign paroxysmal positional vertigo, vestibular migraine, vestibular neuritis, and acute vestibular syndrome. United international efforts will contribute to further improvement of the diagnosis of the vestibular disorders, which warrants their adequate treatment.

Keywords: vestibular disorders, apparatus diagnosis, imaging diagnosis

In the recent years, we have faced a series of considerable advances in the diagnostic capacities for the socially significant vestibular disorders in adulthood and childhood. In this survey, we discuss the application of modern diagnostic methods in patients with Menière's disease, benign paroxysmal positional vertigo, vestibular migraine, vestibular neuritis, and acute vestibular syndrome.

Modern Diagnosis of Menière's Disease

Recently, the video head impulse test assessing the vestibulo-ocular reflex, the electrocochleogra-

Address for correspondence: Mario Milkov Faculty of Dental Medicine Medical University of Varna 84 Tzar Osvoboditel Blvd 9002 Varna e-mail: mario.milkov@gmail.com

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The results from a retrospective case-control study of 52 Ménière disease patients and 99 normal hearing adults prove that absorbance measures at tympanic peak pressure obtained by wide-band tympanometry can reliably distinguish between patients and normal ears within the frequency range of 2000–4000 Hz (2).

At a cost of 2 min extra scanning time compared to a 3 Tesla scanner, endolymphatic hydrops is confidently demonstrated in eight out of nine Menière's disease patients with 1.5 Tesla magnetic resonance imaging using the standard 20-channel head and neck coil and the current standard 4-hour delayed intravenous gadolinium-enhanced three-dimensional fluid-attenuated inversion recovery sequence (3). According to the Bárány Society classification, Menière's disease patients have: i) two or more spontaneous episodes of vertigo with each one lasting 20 min to 12 hours; ii) audiometrically documented low- to medium-frequency sensorineural hearing loss in one ear, defined and located in the affected ear in at least one instance prior, during or after one of the episodes of vertigo; iii) fluctuating aural symptoms such as fullness, hearing and tinnitus located in the affected ear, and iv) not better accounted for by any other vestibular diagnosis (4).

In 38 patients with definite unilateral Ménière's disease, magnetic resonance imaging classification of endolymphatic hydrops with clinical features, audiological and vestibular tests is accomplished (5). Cochlear and vestibular hydrops are visualized in 81.6% and 63.2% of affected ears using the Barath grading system. Sensitivity increases up to 94.7% using Bernaerts modification. There is a significant relationship between the hearing level and the vestibular hydrops degree in the Bernaerts scale.

The results from a prospective study of endolymphatic hydrops in Menière's disease patients demonstrate that magnetic resonance imaging diagnostic sensitivity and specificity are 79.2% and 80.7%, respectively (6). The magnetic resonance imaging with intratympanic gadolinium-based contrast media administration offers reliable radiological diagnostic criteria for Menière's disease.

The ocular vestibular evoked myogenic potentials for 500 Hz and 1000 Hz tone bursts are assessed in individuals from different age groups (7). The inter-frequency amplitude ratio is a sensitive tool in the test battery for the diagnosis of Menière's disease and is affected due to ageing. Its cautious interpretation is recommended in adults >50 years of age with suspicion of this disease.

The application of three-dimensional fluid-attenuated inversion recovery magnetic resonance imaging in 31 patients with definite unilateral Ménière's disease and 20 patients with a probable one reveals a statistically significantly more severe grade of endolymphatic hydrops in the definite than in the probable group (p<0.05) (8). In 22 unilateral Ménière's disease patients at a mean age of 52.1 years with delayed post-gadolinium three-dimensional fluid-attenuated inversion recovery magnetic resonance imaging, inferior axial or sagittal vestibular cross-sections are more accurate for the diagnosis of Ménière's disease ears and have excellent reproducibility (9).

Tympanic electrocochleography frequencyspecific action potential latency, basilar membrane traveling wave time, and summation to action potential are compared between Ménière's disease and non-Ménière's disease patients (10). There is a statistically significant difference between a 'definite' and an 'unlikely' or 'probable' Ménière's disease diagnosis by an average of 13dB hearing level for the pure-tone thresholds at 250 Hz on the affected side (p=0.006).

The diversity of caloric-video head impulse test response and its related factors is investigated in 98 unilateral Ménière's disease patients within a cross-sectional study (11). There are normal caloric and video head impulse test responses in 35 patients (35.71%), abnormal caloric and normal video head impulse test responses in 57 patients (58.17%) and abnormal caloric and video head impulse test responses in six patients (6.12%).

In 28 suspected Ménière's disease children aged ≤17 years, an inner ear three-dimensional inversionrecovery magnetic resonance imaging sequence with real reconstruction sequence four hours after intravenous gadolinium injection, the contrast agent is distributed in the perilymphatic space with perilymphatic enhancement (12). Endolymphatic hydrops is identified based on perilymph magnetic resonance imaging diagnostic scoring in 18 children (64.29%) in whom the diagnosis of Ménière's disease is confirmed.

In accordance with the Japanese Clinical Practice Guideline of Ménière's disease and delayed endolymphatic hydrops of the Japan Society for Equilibrium Research, the diagnostic criteria are classified into Ménière's disease with typical cochlear and vestibular symptoms and atypical Ménière's disease with either cochlear or vestibular symptoms (13).

The concordance between cervical vestibular evoked myogenic potential tuning property test results (using 500 Hz and 1000 Hz tone bursts) and gadolinium-enhanced 3 Tesla magnetic resonance imaging findings of endolymphatic hydrops is examined in eight patients with unilateral definite and six patients with probable Ménière's disease (14). There is endolymphatic hydrops positivity in the cochlea and vestibule on magnetic resonance imaging in seven affected ears of definite and in three affected ears of probable Ménière's disease. This positivity or no response in cervical vestibular evoked myogenic potential tuning property test is statistically significantly associated with the positivity on magnetic resonance imaging, while the endolymphatic hydrops negativity in this tuning property test is statistically significantly associated with the negativity on magnetic resonance imaging (p=0.0016, Fisher's exact test).

In a retrospective case-control study, three-dimensional fluid-attenuated inversion recovery sequences with delayed acquisition in 31 definite Menière's disease patients and 26 healthy subjects as well as pure-tone audiometry, video head impulse test cervical and ocular vestibular evoked myogenic potential testing are performed (15). Magnetic resonance imaging detects cochlear, saccular, utricular and ampullar hydrops in 88%, 91%, 50% and 8.5% of the cases, respectively.

The endolymphatic hydrops using three-dimenional fluid-attenuated inversion recovery magnetic resonance imaging and extratympanic electrocochleography is evaluated in 51 definite Menière's disease ears of 50 patients and 40 healthy subjects (16). The volume-referencing grading system scores show a better correlation (r=0.88) with the pure tone average, disease duration, and vertigo frequency of Menière's disease than the Bernaerts scores, which grade the cochlea and vestibule separately (r=0.22). The total score of endolymphatic hydrops, vestibular endolymphatic hydrops, and cochlear endolymphatic hydrops correlate with the amplitude ratio of the summating potential to the action potential and the area ratio of the summating potential to the action potential as the strongest correlation is between the area ratio of the summating potential to the action potential and the cochlear endolymphatic hydrops (r=0.60) (16).

The extent of endolymphatic hydrops visualized by gadolinium-enhanced inner ear magnetic resonance imaging, hearing thresholds and the summating potential/action potential ratio of electrocochleography are recorded in 22 patients with intractable Menière's disease (17). There is downgrading of cochlear and/or vestibular hydrops accompanied by the downregulation of the hearing threshold and -summating potential/action potential ratio of electrocochleography, as well as upgrading of cochlear and/or vestibular hydrops tending to upregulate this threshold and this ratio of electrocochleography.

The application of videooculography, video head impulse test, and cervical vestibular evoked myogenic potentials in 77 definite unilateral Ménière's disease patients identifies pure or predominant spontaneous ictal downbeat nystagmus in seven patients (9.09%) (18). This nystagmus is without visual fixation and with a slow-phase velocity ranging from 1.5 to 11.2°/sec. Four patients show transiently decreased head impulse vestibulo-ocular reflex gains for the posterior canals in both ears, while three patients do in the affected ear only. Cervical vestibular evoked myogenic potentials are decreased in the affected ear in two patients and in both ears in another two patients when evaluated during the attacks.

Modern Diagnosis of Benign Paroxysmal Positional Vertigo

Benign paroxysmal positional vertigo presents with a specific paroxysmal positional nystagmus, which can be identified by using the appropriate diagnostic positional test (19). Its prevalence is higher in older than in younger patients.

In a newly published review, recent advances in the diagnosis of benign paroxysmal positional vertigo including the use of web-based technology and artificial intelligence are considered (20). By virtue of both recent developments in information and biology technology using artificial intelligence and a deep-learning model, this approach is applied to determine the underlying disorders causing dizziness and vertigo with the subtype of benign paroxysmal positional vertigo (21). Nystagmus recording during vertigo attacks may become feasible in near future using various portable devices (22).

Among a total of 122 screened articles investigating the effect of cupula deflection in benign paroxysmal positional vertigo through the measured vestibulo-ocular reflex gain in individual semicircular canals and retrieved from *PubMed*, *Scopus*, *Web of Science*, and the *Cochrane Library* databases, five original articles for meta-analysis are selected (23). There are 123 patients with posterior canal, 28 patients with lateral canal, and 17 patients with anterior canal benign paroxysmal positional vertigo. The video head impulse test is valuable as a supporting test in the diagnosis of this disorder, especially in cases with posterior canal benign paroxysmal positional vertigo.

Using three-dimensional computed tomography with several different computed tomography window values, ten benign paroxysmal positional vertigo patients are diagnosed with distinct disease, canalolithiasis and cupulolithiasis of the horizontal canal based on the criteria of the Bárány Society (24). The horizontal canals are clearly visualized and the luminal aspects show differences among ears with cupulolithiasis and canalolithiasis.

The diverse nystagmus patterns during the simple bedside Dix-Hallpike test are identified and their clinical significance is analyzed in 128 patients with geotropic horizontal canal benign paroxysmal positional vertigo (25). There is a direction-changing positional nystagmus on both sides in 48 patients (37.50%), a horizontal beating nystagmus towards one side in 25 patients (19.53%) and no nystagmus at all in 55 patients (42.97%). Among 144 patients with apogeotropic horizontal canal benign paroxysmal positional vertigo, 54 patients (37.50%) present with direction-changing positional nystagmus on both sides, 27 patients (18.75%) present with horizontal beating nystagmus towards one side while 63 patients (43.75%) do not show any nystagmus at all (25). Horizontal beating nystagmus direction provoked by the Dix-Hallpike test correlates statistically significantly with the affected side in the geotropic type (p=0.049) and the apogeotropic type (p=0.040) of the horizontal canal benign paroxysmal positional vertigo.

A real-time virtual simulation system is used to observe otolith movement during a posterior semicircular canal benign paroxysmal positional vertigo diagnostic test and to analyze the diagnostic mechanisms (26). The visual cluster analysis of otolith position and the analysis of otolith movement time in the standard Dix-Hallpike test demonstrates that otolith positions are relatively scattered, especially on the z-axis (z1=10.67±3.98) and the fall time of otoliths at different positions has relatively large changes (t1=22.21±1.40). In a multicenter study of 134 consecutive patients with lateral semicircular canal-benign paroxysmal positional vertigo, the diagnostic feasibility of the upright benign paroxysmal positional vertigo protocol is determined (27). A correct diagnosis of this verstibular disorder is achieved in 95.5% of the cases using exclusively this protocol with a highly significant concordance with the complete diagnostic protocol (p<0.0001; Cohen's kappa = 0.94) including the evaluation of pseudo-spontaneous nystagmus and data resulting from head pitch test, upright head roll test, seated-supine positioning test, and supine head yaw test.

The parameters of positional nystagmus, observed by videooculography in the Dix-Hallpike test as prognostic factors for unilateral posterior semicircular canal-benign paroxysmal positional vertigo, are investigated in 357 patients after a computercontrolled canalith repositioning procedure within a case-control study (28). The results from univariate and multivariate analyses during slow phase of nystagmus recording demonstrate a statistically significantly decreased vertical time course on the affected side (p=0.011 and p=0.027, respectively) and an increased vertical velocity amplitude in the Dix-Hallpike test (p=0.029 versus p=0.035) remaining an associated factor of maneuver resistance.

Positional nystagmus of benign paroxysmal positional vertigo is prospectively evaluated in 129 patients using electrooculography tracings of polysomnography (29). In 19 patients (14.73%), there are positional nystagmus patterns typically appearing a few seconds after changes in head position as in nine of them, the nystagmus is also provoked by the positioning maneuvers. Nystagmus occurs during wakefulness only. Nocturnal positional nystagmus is independently associated with positive positioning maneuvers.

Between October 2016 and March 2019, upright positioning-related reverse nystagmus is determined using videonystagmography in 273 out of 312 patients with posterior canal-benign paroxysmal positional vertigo (85.05%) (30).

The sensitivity of video head impulse test in detecting the canal involvement in 59 consecutive patients with peripheral positional downbeat nystagmus due to vertical canal-benign paroxysmal positional vertigo is determined (31). The benign paroxysmal positional vertigo involving the non-ampullary tract of posterior semicircular canal is diagnosed in 78%, while the contralateral anterior canal-benign paroxysmal positional vertigo is detected in 11.9% of the cases. The overall video head impulse test sensitivity in detecting the affected semicircular canal is 72.9% and increases up to 88.6% when considering only cases with persistent positional downbeat nystagmus where an incomplete canal plug is more likely.

In a unique case of a normally sighted patient with a windmill nystagmus triggered by an episode of benign paroxysmal positional vertigo due to bilateral posterior canalolithiasis, videonystagmography reveals an anticlockwise upbeat nystagmus followed by a clockwise downbeat nystagmus with a cycle lasting two minutes and by a brief burst of horizontal left-beating nystagmus (32).

In 40 posterior canal-benign paroxysmal positional vertigo undergoing cervical vestibular evoked myogenic potential testing, p13 and n23 latencies of the affected side are significantly longer than in 40 healthy controls (33). There is a more delayed p13 latency on the affected than on the non-affected side, too. These results indicate a saccular dysfunction accompanying utricular dysfunction confined to the symptomatic side at least in the early stage of the disease.

Several precise training activities for the application of specific diagnostic maneuvers such as Dix-Hallpike test and the supine head yaw test for algorithm decisions are evaluated during a six-month observation period in the Emergency Department of the Cardarelli Hospital of Naples, Italy, and the advantages in terms of costs, time and number of benign paroxysmal positional vertigo diagnoses are identified (34).

A new diagnostic test for lateral semicircular canal-benign paroxysmal positional vertigo, complementary to the head pitch test in upright position, the upright head roll test, the seated-supine test, and the head yaw test in supine position, is proposed in order to easily determine the affected ear and the involved arm in the sitting position (35). The upright head roll test can increase the sensitivity of the minimum stimulus strategy without resorting to the the head yaw test and reduce the patient's discomfort.

Cervical vestibular evoked myogenic potential recordings with stimulus intensity of 95 dB and 105 dB hearing levels and different stimuli (toneburst and click) are evaluated in 34 patients with unilateral posterior canal-benign paroxysmal positional vertigo (36). There are differences between click and tone-burst cervical vestibular evoked myogenic potential only in peak-to-peak p1-n1 amplitude values when 95 dB stimulus is measured. Both p1 and n1 latencies are longer and peak-to-peak p1-n1 amplitudes are higher in tone-burst than in click cervical vestibular evoked myogenic potential measurements with 105 dB stimulus.

The results from a meta-analysis of English language articles abstracted in *PubMed* and *Scopus* databases and dealing with the clinical significance of cervical and ocular vestibular evoked myogenic potentials in benign paroxysmal positional vertigo indicate that the p13 latency in cervical and n1 latency in ocular vestibular evoked myogenic potentials are slightly but significantly prolonged in benign paroxysmal positional vertigo patients than in controls (37). Asymmetry ratio in ocular vestibular evoked myogenic potentials shows a higher value in patients than in control subjects, too.

During a prospective study of 50 patients aged between 20 and 60 years with complaints of benign paroxysmal positional vertigo, a positive Dix-Hallpike test is established in 38 patients (76%) and cervical vestibular evoked myogenic potentials are with abnormal latencies and amplitudes suggesting abnormal saccular functioning on affected side in 15 patients (30%) (38). There is a positive correlation between the cervical vestibular evoked myogenic potentials and the Dix-Hallpike test.

Modern Diagnosis of Vestibular Migraine

In 27 patients with vestibular migraine and 74 patients with probable vestibular migraine, ictal and interictal videooculography, vestibular evoked myogenic potential testing as well as caloric and video head impulse tests are performed (39). There are normal lateral video head impulse test gains in 97.8% (mean gain 0.95 ± 0.12) and symmetric caloric test results in 84.2% (mean canal paresis of $7.0\pm23.3\%$) of the cases. Air- and bone-conducted cervical vestib-

ular evoked myogenic potential amplitudes are symmetric in 88.4% and 93.4% of the cases (mean corrected amplitude of 1.6 ± 0.7 and 1.6 ± 0.8) with mean asymmetry ratios of 13.0% and 9.0%. Air- and bone-conducted ocular-vestibular evoked myogenic potentials are symmetric in 67.7% and 97.2% of the cases (mean amplitude of 9.2 ± 6.4 and $20.3\pm12.8\,\mu\text{V}$) with mean asymmetry ratios of 15.7% and 9.9% (39).

The vestibulo-ocular reflex of 21 vestibular migraine children aged 11–16 years is assessed using the video head impulse test by EyeSeeCam[®] (Interacoustics, Denmark) within a prospective multicentric study (40). These patients have higher values of video head impulse test gain than asymptomatic controls.

The evaluation of body balance using virtual reality posturography in 26 patients during the intercritical period of vestibular migraine and 30 ageand gender-matched controls identifies statistically significant differences (p<0.05) in the values of sway velocity (cm/sec) in nine out of ten evaluated sensory conditions and in the pressure center displacement area (cm²) values in eight out of those ten sensory conditions between both groups (41).

Modern Diagnosis of Vestibular Neuritis

The results from the systematic review and meta-analysis of 16 studies including 474 patients devoted to the clinical application potential of the video head impulse test in vestibular neuritis diagnosis and retrieved from *EMBASE*, *MEDLINE*, *ScienceDirect*, *Google Scholar*, and the *Cochrane Database of Systematic Reviews* databases indicate a high diagnostic value of the video head impulse test for this vestibular disorder (42). This test is a useful complement or alternative to caloric and rotational tests as an indicator of damaged vestibular canal function, especially at the time of onset.

A total of 49 patients with unilateral acute vestibular neuronitis are assessed using high frequency semicircular canal function tests such as video head impulse test and vestibular autorotation test (43). The video head impulse test displays in all the patients a lower lateral horizontal semicircular canal gain, in 93.88% of the cases—a lower anterior semicircular canal gain, and in 22.45% of the cases—a lower posterior semicircular canal gain than in normal controls. The vestibular autorotation test shows a decline of horizonal vestibular autorotation test gain in 40 patients (81.63%), an abnormal horizonal phase shift in 41 patients (83.67%), and an abnormal horizontal symmetry in 31 patients (63.27%).

In 29 newly diagnosed vestibular neuritis patients, an abnormal horizontal semicircular canal in 89.7%, an abnormal anterior semicircular canal in 86.2%, and an abnormal posterior semicircular canal in 44.8% of the cases can be diagnosed by means of video head impulse test (44).

In 22 vestibular neuritis and 22 posterior circulation stroke patients, video head impulse tests are used to assess all three semicircular canal pairs, while cervical and ocular vestibular evoked myogenic potentials are applied to assess otolith function (45). Abnormality rates for the cervical and ocular vestibular evoked myogenic potentials are 38% and 9% for the stroke and 43% and 50% for the vestibular neuritis. A gain \leq 0.68, refixation-saccade prevalence of \geq 135% and cumulative-saccade amplitudes \geq 5.3° separate vestibular neuritis from stroke with sensitivities of 95.5%, 95.5%, and 81.8% and specificities of 68.2%, 86.4%, and 95.5%, respectively. The combination of vestibulo-ocular reflex gain and saccade prevalence distinguishes vestibular neuritis from stroke with a sensitivity and specificity of 90.9%, while abnormal ocular vestibular evoked myogenic potential asymmetry ratios are of the same high specificity only (45).

Between January 2011 and February 2020, the potential clinical application of the suppression head impulse paradigm in evaluating the vestibulo-saccadic interaction in 15 unilateral vestibular neuritis patients at a mean age of 58.73 ± 10.73 years is assessed (46). There are statistically significant differences in the within-subject analysis of vestibulo-ocular reflex gain (p<0.005) and in the percentages of impulses containing a suppression head impulse paradigm saccade when the head is passively turned towards the affected side (p=0.001).

In 21 acute vestibular neuritis patients, vestibulo-ocular reflex gains demonstrate a statistically significant correlation (R=0.926; p<0.001) between the suppression head impulse paradigm and head impulse paradigm and are slightly lower in the suppression head impulse paradigm than in the head impulse paradigm (mean difference of 0.07 ± 0.09 ; p<0.001) as this difference is slightly larger on the affected (0.10 ± 0.09) than on the healthy side (0.03 ± 0.09) (47). The peak saccade velocity of the suppression head impulse paradigm significantly correlates with head impulse paradigm gain and canal paresis.

A delayed fluid-attenuated inversion recovery sequence with a double dose of gadolinium on a 1.5 Tesla magnetic resonance imaging is applied in 33 patients with a superior unilateral vestibular neuritis (48). There is a strong enhancement intensity of this neuritis on the pathological side in 85% of the patients. The average signal intensity of this pathological superior vestibular neuritis (139±44 units) is more than two times higher than that in the control group (58.5±5 units). A delayed enhancement >71.5 units has a sensitivity of 96% and a specificity of 100% for the diagnosis of superior unilateral vestibular neuritis.

The implementation of cervical and ocular vestibular evoked myogenic potential as well as that of video head impulse test in vestibular function testing enables the diagnosis of the selective damage of the vestibular nerves in vestibular neuritis patients (49).

Modern Diagnosis of Acute Vestibular Syndrome

A three-category differential diagnosis approach based on timing and triggers includes acute vestibular syndrome where bedside physical examination differentiates vestibular neuritis from stroke, spontaneous episodic vestibular syndrome where associated symptoms help differentiate vestibular migraine from transient ischemic attack-triggered episodic vestibular syndrome where the Dix-Hallpike and supine roll test help differentiate benign paroxysmal positional vertigo from posterior fossa structural lesions (50).

Two patients of acute central vestibular syndrome in whom bedside videoophthalmoscopy in the form of magnified fundoscopy aids the precise anatomical diagnosis are presented (51).

During a retrospective descriptive observational study, an unclear origin vertigo protocol is applied in 97 acute vestibular syndrome patients at a mean age of 61.46 years classified as peripheral, central, and other origin (52). There are 26 patients in the peripheral group (26.80%), 33 patients in the central group (34.02%), and 38 patients in the other-origin group (39.18%). This protocol differentiates a possible acute vestibular syndrome of central origin from a peripheral one, thus avoiding unnecessary imaging tests.

One patient with acute vestibular syndrome and another one with superior semicircular canal dehiscence syndrome are reported (53). They undergo delayed inner ear magnetic resonance imaging performed four hours after contrast media administration. The marked enhancement of the superior semicircular canal in both patients rules out the co-existing superior semicircular canal dehiscence syndrome on temporal bone computed tomography, particularly if the patient reports cochlear symptoms such as pulsatile tinnitus and/or autophony.

In a retrospective cohort study, among all the patients with acute vestibular syndrome or episodic vestibular syndrome, 68 patients have diffusionweighted imaging-positive and 113 patients have diffusion-weighted imaging-negative ischemic events (54). Among the patients in the first group, there are acute infarctions in the anterior circulation in 42.6% and in the posterior circulation in 41.2% of the cases. Large vessel stenosis/occlusion and focal neurological symptoms/signs are significantly associated with the risk of acute vestibular syndrome or episodic vestibular syndrome in acute ischemic stroke patients.

We can draw the conclusion that the complex issues of the timely and precise vestibular disorder diagnosis could be successfully solved thanks to the united efforts of the international interdisciplinary scientific community, which warrants the adequate treatment of these patients.

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