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Study of Vestibular Evoked Myogenic Potentials in Unilateral Vestibulopathy: Otolithic Versus Canal Function Testing

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Objective: The study provides a qualitative evaluation of unilateral vestibulopathy by comparing otolithic and canal function, to establish possible relationships between the type of dysfunction observed and the evolving clinical pictures associated with it.
Study Design: Retrospective study of a series of cases.
Setting: Department of Medical-Surgical Specialization, Otolaryngology and Cervicofacial Surgery Division, University of Perugia, Perugia, Italy.
Patients: Twenty patients whose medical history showed at least one episode corresponding to the clinical parameters of acute vestibulopathy.
Interventions: Study of vestibular function by recording VEMPs and repeating canal function testing at least 6 months after the first episode of vertigo.
Main Outcome Measures: Relationship between the type of vestibulopathy (canal and otolithic) and the clinical pictures observed.
Results: Paroxysmal positional vertigo, observed in 4 patients, was correlated with the presence of vestibular evoked myogenic potentials (VEMPs) and the absence of an ipsilateral canal response in all cases (100%). Persistent dizziness was observed in nine patients, and VEMPs were absent in all of them (100%); three (33.3%) showed the recovery of previously absent canal function. Comparison of responses in six patients with recurrent acute vestibulopathy showed persistent and complete loss of canal function in five cases (83.3%), whereas impairment of otolithic response was less constant (40%).
Conclusion: The combined VEMPs-canal test study shows predictive value regarding certain evolving clinical pictures of vestibulopathy. The absence of VEMPs confirms the role of otolithic dysfunction in the onset of dizziness. Likewise, it suggests that a vestibular origin of these disorders should be considered in cases that have shown aspecific symptoms since onset, without frank vertigo and with normal vestibular response to canal function testing. **Key Words:** Caloric test—Dizziness—Vertigo—Vestibular evoked myogenic potentials.
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Investigation of vestibular function is generally based on stimulation of the ampullary receptors and testing of vestibulo-ocular pathways. It has been acknowledged that studies relying on well-established methods such as caloric and rotational-acceleration tests are influenced by a conceptual exemplification of the function of the posterior labyrinth, whose overall response is assumed to depend on individual stimulation of the ampullary receptors of the horizontal semicircular canal. Consequently, vestibular normoreflexia is defined based on the interpretation of quantitative and qualitative parameters obtained from responses to caloric and/or rotational-acceleration stimulation. Nevertheless, the observation of paroxysmal positional vertigo (PPV) in patients with consensual vestibular areflexia on the side of the triggering position (1) suggests that there are vestibular compartments which are relatively independent from an anatomic and functional standpoint. At the same time, it confirms the fact that complete and unequivocal investigation of vestibular function is impossible using the above-mentioned methods. The introduction of vestibular evoked myogenic potentials (VEMPs) (2,3) in clinical practice offers the opportunity to clarify several aspects of vestibular function that are still unclear, particularly the function of macular receptors and vestibulospinal pathways: associated with traditional methods, VEMPs permit more complete investigation of vestibular function.

What we mean by unilateral acute vestibulopathy (AV) is a sudden loss of vestibular function. From a functional standpoint, this means an asymmetrical vestibular response that, on an objective level, is responsible for spontaneous nystagmus, mainly on the horizontal plane and with high-frequency oscillations. On a subjective level, it triggers violent rotatory vertigo, often accompanied by

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TABLE 1. *Acute vestibulopathy diagnostic criteria*

□ Acute attack of vertigo with sudden and spontaneous onset, lasting more than 24 hours, and accompanied by nausea and vomiting.
□ Serious difficulty in maintaining orthostatic position (early phase) and ataxic gait.
□ Presence of spontaneous unidirectional nystagmus lasting for more than 24 hours.
□ Presence of significant unilateral canal dysfunction, ascertained via head-impulse and caloric testing. The dysfunction can be transitory or persistent.
□ Otoscopic and auditory examination within normal range.
□ No other neurological deficits.

neurovegetative symptoms that can last from 36 to 48 hours (4,5). Recent studies have found the DNA of the herpes simplex Type 1 virus in the vestibular nuclei of subjects with acute peripheral disorders of the labyrinth (6), supporting the theory of a viral pathogenesis. In short, the functional changes that emerge with conventional vestibular studies (caloric and rotational-acceleration tests) designed to stimulate the ampullary receptors mainly involve the vestibulo-ocular reflex and undoubtedly play a fundamental role as far as symptoms are concerned. Instead, determining the importance of otolithic input in vestibulopathy is more complex not only because of the objective study limitations seen so far but also because its symptoms are less evident in the acute phase of the disorder.

The purpose of this study was to evaluate the status of the vestibulospinal pathway by recording VEMPs and associating this with traditional methods to determine the overall dysfunction of the posterior labyrinth. Moreover, by comparing responses, this analysis also permitted qualitative evaluation of vestibular damage, identifying cases with "associated" dysfunctions and those with isolated macular or canal dysfunction. By comparing these two functions, it was also possible to ascertain any relationships between the type of dysfunction that emerged and commonly observed clinical pictures such as recurrent vertigo, instability or dizziness, and PPV.

MATERIALS AND METHODS

The study was conducted on 20 subjects (40 ears) (12 women and 8 men; mean age, 26 yr) with peripheral vestibular disorders that were not associated with hearing loss or neurological disorders. All the patients we examined had a medical history of at least one documented episode of vertigo corresponding to clinical parameters of unilateral AV (Table 1) first occurring at least 6 months before this study. Specifically, 14 patients reported a single episode, and 6 complained of recurrent vertigo; persistent dizziness was reported by 9 patients, 6 of whom with a single episode of AV, and 3 with recurrent AV. PPV of the posterior semicircular canal (PSC), arising after the diagnosis of vestibulopathy, was documented in four cases (Table 2).

TABLE 2. *Medical history of the 20 patients with unilateral acute vestibulopathy*

Clinical pictures	No. of patients
Single AV episode	6
Recurrent AV	1
Single AV episode–PPV	2
Recurrent AV-PPV	2
Single AV episode–dizziness	6
Recurrent AV–dizziness	3

AV, acute vestibulopathy; PPV, paroxysmal positional vertigo.

TABLE 3. *Methodological criteria*

Pregelled sponge electrodes with adhesive pad
Two separate electrodes per side + ground (n = 5)
Acoustic stimulation with logon 500 Hz pol−, 130 dBpeSPL, 04 Hz, right monaural, left monaural, and binaural
Symmetrical head flexion
Routine use of binaural stimulation

dBpeSPL, decibels peak sound pressure level.

Before VEMPs were tested, all the patients underwent the following checkups:

- *otolaryngology examination* to evaluate the condition of the tympanic membrane and exclude the presence of earwax;
- *audiometric examination* to evaluate thresholds and exclude the possibility of hearing loss;
- *impedance measurement* to evaluate the conditions of the middle ear;
- *auditory evoked potentials* to exclude damage along the auditory pathways;
- *vestibular tests*, including caloric stimulation using the Fitzgerald-Hallpike method, head-shaking test (HST), and vibration test (VT), to verify the persistence of canal dysfunction (persistent canal dysfunction) or the recovery of function (prior canal dysfunction); and
- *stabilometry/posturography* according to the standards of the French Association of Posturology (S.Ve.P. Amplifon system). For each patient, we conducted a test and a retest (each one lasted 25.6 seconds; 10 Hz) while the patient's eyes were closed (EC) because in this condition, vestibular function is more important in postural control. The evaluation parameter was the surface (S), expressed in mm^2, occupied by the center of pressure for 90% of the testing time. For each patient, the overall S value was obtained from the mean of the S values in the two tests that were performed.

VEMPs were recorded based on the criteria suggested by Valli et al. (7) (Table 3). The study of electrophysiological data involved the P1/N1 waveform and the P2/N2 waveform. The results were compared with the ones obtained from the VEMPs recorded in 15 healthy subjects (30 ears) without hearing loss or lack of vestibular response to canal function tests. The results of this study were evaluated based on the number of ears. Therefore, we considered the following:

healthy ears;
ears with persistent canal dysfunction; and
ears with prior canal dysfunction.

RESULTS

At the time VEMPs were recorded, 14 of the 20 vertiginous patients enrolled in our study presented a unilateral deficit in all the canal function tests that were performed. Four patients with previously documented unilateral

TABLE 4. *Patient behavior at canal function testing (prevestibular evoked myogenic potentials)*

Clinical pictures	Normoreflexia (prior canal dysfunction)	Hyporeflexia/ areflexia (persistent canal dysfunction)	No. of totals
Single AV episode	1	5	6
Recurrent AV	0	1	1
Single AV episode–PPV	0	2	2
Single AV episode–dizziness	3	3	6
Recurrent AV–PPV	0	2	2
Recurrent AV–dizziness	0	3	3
Patients	4	16	20

AV, acute vestibulopathy; PPV, paroxysmal positional vertigo.

vestibulopathy instead showed complete recovery of canal function when VEMPs were tested. In two cases, canal dysfunction persisted at medium-high frequencies (HST and VT), with a normalized response to caloric tests. Therefore, the vestibular tests showed canal dysfunction in 16 patients, with complete dysfunction in 14 cases (Fitzgerald-Hallpike, HST, and VT) and partial dysfunction in the other 2 (HST and VT). The four cases of PPV of the PSC, which were diagnosed and treated at our Vestibulogical Department, involved patients who, when VEMPs were recorded, showed dysfunctions on all tests on the side affected with canalolithiasis-cupulolithiasis. The six patients with recurrent vertigo presented persistent canal dysfunction, complete in five cases and partial in one. Of the nine patients with dizziness, three recovered completely from the previously documented canal dysfunction, whereas persistent dysfunction was noted in the remaining six when VEMPs were recorded (Table 4).

Stabilometry showed pathological S values in 12 cases, including the 9 patients with dizziness. A comparison between the two groups (patients with dizziness versus patients without dizziness) showed significantly higher S values ($p = 0.003$) in the group with dizziness, which presented a mean of 672 ± 206, as opposed to 405 ± 178 for the group of patients without this symptom.

TABLE 5. *Behavior of P1/N1 and P2/N2 waveforms in patients with persistent canal dysfunction*

Clinical pictures associated with persistent dysfunction	N°	P1/N1 present	P1/N1 absent	P2/N2 present	P2/N2 absent
Single AV episode	5	2	3	2	3
Recurrent AV	1	1	0	0	1
Single AV episode–PPV	2	2	0	2	0
Recurrent AV-PPV	2	2	0	2	0
Single AV episode–dizziness	3	0	3	0	3
Recurrent AV–dizziness	3	0	3	0	3
Patients	16	7	9	6	10

AV, acute vestibulopathy; PPV, paroxysmal positional vertigo; N°, number of patients.

TABLE 6. *Behavior of P1/N1 and P2/N2 waveforms in patients with prior canal dysfunction*

Clinical pictures associated with prior dysfunction	N°	P1/N1 present	P1/N1 absent	P2/N2 present	P2/N2 absent
Single AV episode	1	1	0	1	0
Recurrent AV	0	0	0	0	0
Single AV episode–PPV	0	0	0	0	0
Recurrent AV-PPV	0	0	0	0	0
Single AV episode–dizziness	3	0	3	0	3
Recurrent AV–dizziness	0	0	0	0	0
Patients	4	1	3	1	3

AV, acute vestibulopathy; PPV, paroxysmal positional vertigo; N°, number of patients.

Evaluation of the First P1/N1 Waveform

Analysis of VEMPs response rate showed that the P1/N1 waveform was present bilaterally in all 15 healthy subjects (30 ears) from the control group, as it was in the 16 healthy ears of patients with persistent contralateral canal dysfunction and in the 4 healthy ears of patients with prior contralateral canal dysfunction. In short, the initial biphasic component, composed of the sequence of P1/N1 waves, was present in all 50 healthy ears (100%) of the 35 subjects who were examined (15 healthy and 20 dysfunctional).

The P1/N1 component was also present in 1 of the 2 ears with persistent canal dysfunction and in 6 of the 15 ears showing dysfunction on all canal tests conducted when VEMPs were recorded; the latter included the 4 patients (100%) who developed ipsilateral PPV of the posterior semicircular canal after the initial diagnosis of AV. In the six patients with recurrent vertigo (five with complete canal dysfunction and one with partial dysfunction), the P1/N1 wave was identified in three cases, whereas none of the six cases of persistent canal dysfunction with dizziness showed a P1/N1 component that was worthy of note in terms of morphology and latency (Table 5).

Lastly, in the four ears with prior AV and a normal canal response to testing, the P1/N1 waveform was present in one case and absent in three; the latter involved three ears with prior AV in patients prevalently experiencing dizziness (Table 6).

Evaluation of the Second P2/N2 Waveform

The P2/N2 waveform was present in 17 of the 30 healthy ears of the control group (15 healthy subjects), in 8 of the 14 healthy ears of patients with contralateral dysfunction on all canal tests, and in the 1 of the 2 healthy ears of patients with partial contralateral dysfunction. The P2/N2 component was also observed in two of the four healthy ears of patients with prior contralateral canal dysfunction. On the whole, the sequence of P2/N2 waves was present in 28 (56%) of the 50 healthy ears of the 35 subjects who were examined (15 healthy and 20 dysfunctional).

The P2/N2 component was also present in 1 of the 2 ears with partial dysfunction, and in 5 of the 14 ears with complete canal dysfunction; the latter included the 4 patients who developed ipsilateral PPV of the CSP. In several cases, the P2/N2 component was present in six ears (five with complete dysfunction and one with partial dysfunction) of patients with recurrent vertigo, whereas the P2/N2 component was not appreciable in any of the patients with dizziness (Table 5).

In the four ears with prior AV and a normalized canal response to testing, the P2/N2 component was present in one case and absent in three, reflecting results essentially comparable with those of the P1/N1 component (Table 6).

DISCUSSION

The data reveal that AV is often characterized by the complete loss of vestibular function on both a macular and canal level. Quite often, however, the latter is also impaired in an isolated manner, confirming the fact that the inferior vestibular nerve is less vulnerable to viral inflammation (8). Consequently, there is the possibility of a dissociated macular or canal dysfunction from the very beginning, but there may also be secondary dissociation in cases in which one of the two functions is recovered.

Some of the evolving clinical aspects of this dysfunction seem to be associated with, or even conditioned by, the type of vestibular damage. These include recurrent vertigo, dizziness, and paroxysmal positional vertigo.

Concurring with the literature, which indicates that 20 to 30% of the subjects involved can present at least one relapse (9), this study also confirms the high probability of recurrent vertigo (30% of the patients examined). In our study, the presence of several episodes of vertigo corresponding to AV parameters in the patient's medical history seems to be related mainly to persistent canal dysfunction. A comparison of the two functions demonstrates that canal function is always impaired, whereas the absence of VEMPs seems to be a variable element (40%). Several histopathologic aspects attributable to viral damage have recently been documented in the temporal bone of subjects with recurrent vertigo (10). In these cases, it is possible to theorize that after entering the neural structures of the vestibular ganglion, neurotropic viruses can remain latent and be reactivated periodically as a result of various factors (10,11). Recurring episodes would thus lead to irreversible cell damage that, from a clinical standpoint, leads to persistent canal dysfunction. This theory is supported by the fact that most of the patients with recurrent vertigo and persistent canal dysfunction also had a medical history of more than three relapses.

Dizziness was observed in nearly half of the vertiginous patients who were studied. This subjective element was confirmed by stabilometry, which revealed an increase in postural sway in all these cases. Generally reported as a sensation of instability, lack of balance or oscillopsy, it represents a subcontinuous condition that is not very intense, and it is not accompanied by neurovegetative symptoms. According to the patients, it "feels different" from the episodes of frank vertigo characterizing AV. In this case, the absence of VEMPs in all nine patients with dizziness not only represents the electrophysiological marker of impaired otolithic function, but it also provides fascinating food for thought regarding the true importance of a disturbance of the vestibulospinal pathway in the onset of this disorder, above all in cases of selective dysfunction with recovery of canal function. Furthermore, the close correlation between dizziness and the absence of VEMPs suggests that a vestibular origin of these disorders should also be considered in cases that have shown aspecific symptoms since onset, without episodes of frank vertigo and with normal vestibular response to canal function testing.

Starting with the earliest description of these cases by Lindsay and Hemenway (1) (1954), it has been evident that the evolution of unilateral vestibulopathy is often, but not always, complicated by PPV of the PSC. In 1996, Murofushi et al. (12) demonstrated that, after vestibular neurolabyrinthitis, the persistence of VEMPs activity was correlated with the subsequent development of PPV, whereas cases in which VEMPs were absent were never complicated by PPV of the PSC. The data from our study unequivocally agree with the observations of these authors. Therefore, the use of VEMPs to predict potential PPV after selective vestibulopathy involving the canal represents a very interesting application. In this case, the presence of VEMPs demonstrates the integrity of the inferior vestibular nerve that innervates the saccule and PSC. The presence of "extraneous" endolymphatic material inside the latter could thus trigger vertiginous symptoms, initially through excitation of the ampullary crest, followed by the conduction of impulses along the inferior vestibular nerve. The absence of VEMPs instead seems to confirm reduced function of the nerve, which would thus be unable to respond adequately to cupular and canal excitation from the PSC.

From an electrophysiological standpoint, the P1/N1 component represents the most stable and repeatable pattern (13,14), which can constantly be evoked in all the healthy ears of healthy subjects and in dysfunctional ones with contralateral vestibulopathy. Consequently, its absence is a sure indication of impaired otolithic function. Instead, the P2/N2 component is far less repeatable and stable in terms of morphology and latency, and it is absent in a substantial number of cases, even in healthy ears without any dysfunctions.

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