

VESTIBOLOGY

Vestibular testing in patients with panic disorder and chronic dizziness

Test di funzionalità vestibolare in pazienti con disturbi di panico e disturbi dell'equilibrio

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SUMMARY

In order to investigate the relationship between chronic dizziness and vestibular function in patients with panic disorder, in the present study neurotologic findings in 15 patients with panic disorder and chronic dizziness were compared with those in 15 patients with chronic dizziness, without panic disorder. All underwent neurotologic screening for spontaneous, positional and positioning nystagmus with head-shaking and head-thrust tests, an audiometric examination and electronystagmography with bithermal stimulation according to Freyss. A significantly higher number of patients with panic disorder and chronic dizziness showed pathological neurotologic findings in comparison to subjects with chronic dizziness only (9 and 2 patients, respectively; $p < 0.05$). Most patients with panic disorder showed signs of peripheral vestibular disorders. These results suggest that the complaint of dizziness in patients with panic disorder may be linked to a malfunction of the vestibular system and vestibular disorders may play a role in the pathophysiology of panic disorder. Possible mechanisms underlying this finding are discussed. In patients with panic disorder and chronic dizziness between panic attacks, a careful neurotologic examination is warranted.

KEY WORDS: Dizziness • Panic disorder • Vestibular function • Electronystagmography

RIASSUNTO

Allo scopo di studiare la relazione esistente tra disturbi dell'equilibrio e funzionalità vestibolare in pazienti con disturbi di panico (PD) abbiamo confrontato i reperti neuro-otologici di 15 pazienti affetti da PD e disturbi dell'equilibrio con quelli di 15 pazienti con disturbi dell'equilibrio senza PD. Tutti i soggetti hanno effettuato un esame otoneurologico comprensivo di rilevazione del nistagmo spontaneo, posizionale e da posizionamento, head-shaking e head-thrust test, esame audiometrico, elettronistagmografia con stimolazione bitermica secondo Freyss. Un numero significativamente più elevato di pazienti affetti anche da PD hanno mostrato anomalie all'esame otoneurologico rispetto al gruppo affetto solo da vertigine (rispettivamente 9 e 2 pazienti, $p < 0,05$). La maggior parte dei pazienti con PD hanno evidenziato segni di sofferenza vestibolare periferica. I nostri risultati suggeriscono che i disturbi di equilibrio nei pazienti con PD possano essere legati a patologie vestibolari e che tali disturbi possano giocare un ruolo nell'evoluzione dei PD. I possibili meccanismi alla base di tali reperti sono discussi. A nostro avviso un esame otovestibolare completo deve essere suggerito a tutti i pazienti con PD e vertigine non concomitante all'attacco di panico.

PAROLE CHIAVE: Disequilibrio • Disturbi di panico • Funzionalità vestibolare • Elettronistagmografia

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Introduction

Several studies have shown an association between panic disorder (PD) and vestibular symptoms. Patients with PD often complain of dizziness and related-sensations, such as light-headedness or instability, and this cluster of symptoms is an important source of functional impairment in these patients^{1,2}. Many experimental studies have investigated whether these symptoms in patients with PD could be linked to a malfunction of the vestibular system, by performing vestibular test battery (e.g. electronystagmography with caloric/rotational stimulation, posturography). Vestibular abnormalities were found in 60-90% of patients with PD, both selected and unselected for dizziness³⁻⁵. Comparison

studies showed more abnormalities in the posturographic parameters of patients with PD and agoraphobia than in those of healthy controls^{6,7} and a higher rate of vestibular abnormalities in patients with PD and agoraphobia than in patients with PD without agoraphobia, patients with anxiety disorders other than PD, patients with depressive disorders or healthy controls². Overall, these studies suggested a significant link between the degree of abnormalities in the balance system and agoraphobia. On the contrary, a recent study showed a higher rate of vestibular abnormalities on electronystagmography in patients with PD than in healthy controls, but no difference was found between patients with PD, with or without agoraphobia⁸. Finally, some studies

suggested that dizziness between panic attacks could be a predictor of vestibular abnormalities in patients with PD²⁻⁸, whereas Swinson et al. found no abnormalities on electronystagmography and caloric testing in patients with PD with prominent dizziness⁹.

In order to clarify the relationship between dizziness and vestibular function in patients with PD, in this study, we compared the otoneurologic findings on electronystagmography and caloric stimulation of patients with PD with chronic dizziness between panic attacks and subjects with chronic dizziness without PD.

Materials and methods

Study population

Overall, 15 patients with PD with agoraphobia and chronic dizziness between the panic attacks (9 female and 6 male, mean age 36.7 ± 9.4 years) and 15 patients with chronic dizziness without PD (9 female, 6 male, mean age 37.4 ± 9.7 years) were included in the study. The patients with PD were consecutively recruited over 8 months at the outpatient facilities of the Anxiety Disorders Clinical and Research Unit at San Raffaele Hospital in Milan. The diagnoses, according to DSM IV criteria, were obtained by a senior psychiatrist who assessed the patients by means of a clinical interview and the MINI International Neuropsychiatric Interview – Plus¹⁰.

The patients with chronic dizziness and without lifetime diagnoses of PD and/or agoraphobia were retrospectively selected from a database of patients followed in the Vestibular Disorders Unit at San Raffaele Hospital in Milan. These subjects were selected: a) if they had undergone the same vestibular testing as patients with PD and fulfilled the inclusion/exclusion criteria outlined below, and b) if sex distribution, mean age and severity of subjective dizziness overlapped with those of the patients with PD. The severity of dizziness was measured by the 25-item Dizziness Handicap Inventory scale (DHI) obtaining a total score (range 0-100) that indicates the self-perceived level of handicap associated with dizziness¹¹. For each subject, a careful medical history was collected. For both groups, the inclusion criterion was: presence of chronic dizziness, defined as persistent (at least 3 months) sensations of non-vertiginous dizziness, light-headedness, heavy-headedness, or subjective imbalance present on most days¹², without specific lifetime medical/vestibular diagnoses (see exclusion criteria); the exclusion criteria were:

- 1) evidence of chronic otitis media and/or previous surgery on middle ear;
- 2) treatment with ototoxic drugs and/or chemotherapy;
- 3) lifetime neurological diseases, with particular attention on migraine.

All subjects included in the study underwent a 14 days wash-out from drugs active on the central nervous system (CNS) before the vestibular testing.

Procedure

All subjects underwent neurotologic screening for spontaneous, positional and positioning nystagmus with head-shaking and head-thrust tests. Both tests were considered significant for peripheral vestibular dysfunction^{13,14}.

Evaluation of vestibular system function was made by either

Electronystagmography, with an Amplaid MK22 Electronystagmography, and bithermal caloric testing, with an otocalorimeter (Bithermic caloric stimulator McA Biomedica), as proposed by Freyss (125 cc in 30 sec with water at 30° and 44°); the patients wore a pair of Frenzel glasses, with his/her head anteroflexed 30° from the supine position, in a dimly illuminated room. The interval between the stimuli was 5 minutes.

Angular velocity of the slow phase (VSP) of nystagmus was used, calculated during 10 seconds of culmination, as the parameter of labyrinthine function; in accordance with data in the international literature, VSP of $15^\circ/\text{sec} \pm 5^\circ/\text{sec}$ was considered as a normal value. Data were interpreted in terms of directional preponderance (DP) and unilateral weakness (UW) which were considered significant when superior to 25% and 15%, respectively. In a control population of 25 healthy subjects, values of VSP comprised between 12° and $25^\circ/\text{sec}$ were found, with a mean value of $16^\circ/\text{sec}$; no significant DP or LP were found. These results are in agreement with international reports. Stimulation was considered hyporesponsive when VSP was $< 6^\circ/\text{sec}$. with total caloric responses VSPs less than 22° and hyperresponsive when $\geq 35^\circ/\text{sec}$ with total VSP responses exceeding $140^\circ/\text{sec}$. Our data appear to be in agreement with those of Barber and Stockwell (1980) for Dix-Hallpike stimulation, considering as hyperresponsive, a labyrinthine response when exceeding $50^\circ/\text{sec}$ at Dix-Hallpike stimulation¹⁵.

We considered as vestibular central signs at least one of the following findings:

- 1) disorganized pursuit or asymmetrical pursuit gain;
- 2) under or overshoot of saccades or asymmetrical latency or velocity;
- 3) bilateral hyperreflexia;
- 4) rebound nystagmus;
- 5) positional geotropic or apogeotropic nystagmus when bilateral, direction changing, showing no latency, low frequency, lack of fatigability and habituation, without concomitant vertigo.

In condition 5, otolithic input may cause disinhibition of central vestibular responses on perception of eye, head and body position¹⁶.

Statistical analyses

The significance of any difference in continuously distributed variables between the two groups was examined by t test for independent samples. Chi-square test was applied to assess differences for nominal values; when at least 25% of expected cell frequencies were less than 5, Fisher exact test was applied.

Results

The two groups did not differ as far as concerns sex distribution, mean age and total scores of DHI scale. The DHI score in patients with PD was 28.4 ± 9.7 and in patients with chronic dizziness was 29.6 ± 5.7 . The patients with PD showed a significantly higher number of pathological otoneurologic findings in comparison to patients with chronic dizziness only. Nine patients with PD (60%) and 2 patients with chronic dizziness (13%) showed abnormal ENG parameters, while 6 patients with PD (40%) and 13

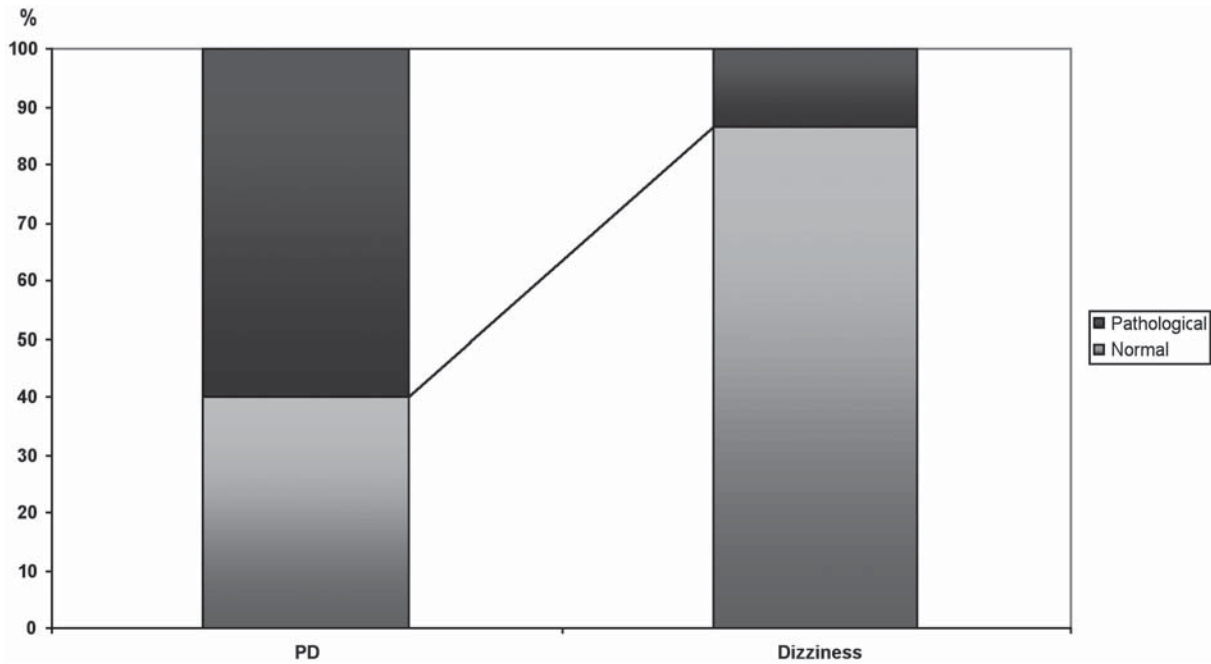


Fig. 1. Rate of normal and pathological neurotological findings in patients with PD and in patients with chronic dizziness only. In PD group, 3 patients showed central signs, two of them also with peripheral damage signs and one without (hyper-responsive pattern); in patients with chronic dizziness only, one patient showed central signs, with also VOR asymmetry.

Table I. Distribution of ENG pattern in the two groups: values are expressed as number of patients.

Patients	Normal	UW	UW + DP	DP	HypoR	HyperR
With PD (n = 15)	6	2	2	2	1	2
With dizziness (n = 15)	13	0	1	1	0	0

UW: unilateral weakness; DP: directional preponderance; HypoR: hypo-responsiveness; HyperR: hyper-responsiveness.

patients with chronic dizziness (87%) did not show any abnormal parameter (Fisher test, $p < 0.05$) (Table I). In the group of patients with PD, two patients presented asymmetry with a UW pattern, two with UW and DP, two with pure DP, one had bilateral hypo-responsiveness and two hyper-responsiveness without asymmetries of oculomotor reflexes. Three patients with PD showed vestibular central signs: one patient with pure DP presented geotropic bilateral low frequency nystagmus, the patient with bilateral hypo-responsiveness had asymmetric gain of pursuit and one patient with hyper-responsiveness had disorganized pursuit. In the group of patients with chronic dizziness only, one patient showed asymmetry with pure DP and one with UW and DP. In this group, the patient with DP pattern showed central signs for disorganized pursuit.

Dix-Hallpike and McClure manoeuvres for VPPB were negative in all subjects of the 2 groups. Three patients with PD and one patient with only dizziness reported motion sickness; this difference was not statistically significant.

In the group of patients with PD, a significantly higher number of patients showed a positive head-thrust test, indicating a peripheral vestibular disorder, in comparison to the group of patients with only chronic dizziness, respectively 4 patients (27%, all patients with UW with and without DP) and 0 (Fisher test, $p < 0.05$).

Head-shaking test was positive in 5 PD patients (the 4 patients with UW and 1 of the PD patients) and in only 1 patient in the control group, showing DP pattern (Fisher test, $p < 0.05$).

Audiometric exams did not show any significant sensorineural hearing gap between the two thresholds, in either group.

Discussion

The results of this study show a significantly higher prevalence of vestibular abnormalities in patients with PD with chronic dizziness between the panic attacks than in patients with chronic dizziness only. The finding of vestibular abnormalities in patients with PD is in agreement with other studies²⁻⁸, but, to our knowledge, this is the first study in which the comparison group is composed of patients without PD and with chronic dizziness. In this study, we performed the caloric testing because it is considered the gold standard to investigate labyrinthine asymmetries. We applied the stimulation procedure developed by Freyss, instead of that by Dix-Hallpike, since the former allows an adequate stimulation with lower risk of nausea, vomiting and anxiety. Nonetheless, it should be noted that the outcome of caloric testing could be affected by individual

variables not linked to the vestibular function, such as the volume of the external ear canal, the thickness and blood flow of the temporal bone. Thus, we cannot exclude a possible effect of these factors on our results. Patients were told not to hyperventilate. Moreover, we cannot exclude a possible influence of anxiety or emotional state on the outcome of the vestibular tests in patients with PD, even though it seems unlikely that anxiety levels could affect the finding of labyrinthine asymmetry. Finally, the size of the samples is small and the results should be confirmed on larger samples. Bearing in mind these shortcomings, our findings indicate that most patients with PD have vestibular abnormalities, mainly of the peripheral type; moreover, most of these patients (6 out of 9) showed impaired Vestibulo-Oculomotor Reflexes, indication of previous peripheral damage. Thus, at least in a subgroup of these patients, the complaint of dizziness may not be a "functional" symptom related to anxiety state but be linked to a malfunction of the vestibular system. On the contrary, most of the patients with chronic dizziness without PD did not show vestibular abnormalities; similar findings have been reported in previous studies showing rates of non-otologic dizziness between 60 and 70%¹⁷. To investigate the sources of dizziness other than vestibular disorders was beyond the aims of this study; we cannot, however, exclude a possible influence of different psychiatric disorders, other than PD, such as Somatoform Disorders or other Anxiety Disorders, on the complaint of dizziness in this group of patients. Overall, our results support the idea that the vestibular system may be involved in the pathophysiology of PD. The source of this relationship is still unclear and could arise from multiple mechanisms:

1) primary vestibular disorders may have an impact on subjects vulnerable to PD. Patients with PD showed signs of a malfunction of homeostatic systems, such as decreased

global heart rate variability¹⁸ and irregularity in their respiratory patterns^{19,20}; thus, pathologies of the vestibular system, that is widely connected to the cardiovascular and respiratory systems, might act as "disrupting" factors on the homeostatic instability of patients with PD, possibly influencing the onset and/or the maintenance of the disorder. Moreover, since the serotonergic system is involved in the pathophysiology both of PD and vestibular disorders^{21,22} vestibular loadings might influence PD also by affecting the serotonergic system function in these patients;

2) vestibular abnormalities might be a consequence of PD, for instance by hyperventilation-increased vestibular responses, possibly influencing the symptomatological features of the patients;

3) vestibular abnormalities might influence the subsequent development of agoraphobia in patients with PD, rather than to be involved in the pathophysiology of PD *per se*².

The data so far available are not sufficient to clarify these issues; moreover, different mechanisms might be involved in different subgroups of patients with PD. Finally, even though a bidirectional relationship between dizziness, neurotologic conditions and PD has been reported²¹, the temporal relationship between PD and vestibular abnormalities has not yet been exhaustively investigated. Further studies on the vestibular function, under different experimental manipulations, and the lifetime temporal relationship between PD and vestibular disorders might help to clarify these open matters.

In conclusion, our study suggests that in patients with PD and chronic dizziness a careful neurotologic examination is warranted. In the presence of laboratory evidence of vestibular function abnormalities, the treatment approach of PD could consider including vestibular rehabilitation and use of specific therapies focusing on vestibular symptoms.

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