

## Dizziness, migrainous vertigo and psychiatric disorders

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### Abstract

**Objectives:** This study sought to establish the prevalence of vestibular disorders, migraine and definite migrainous vertigo in patients with psychiatric disorders who were referred for treatment of dizziness, without a lifetime history of vertigo.

**Study design:** Retrospective study.

**Setting:** Out-patients in a university hospital.

**Materials and methods:** Fifty-two dizzy patients with panic disorders and agoraphobia, 30 with panic disorders without agoraphobia, and 20 with depressive disorders underwent otoneurological screening with bithermal caloric stimulation. The prevalence of migraine and migrainous vertigo was assessed. The level of dizziness was evaluated using the Dizziness Handicap Inventory.

**Results:** Dizzy patients with panic disorders and agoraphobia had a significantly  $p = 0.05$  regarding the prevalence of peripheral vestibular abnormalities in the group of subjects with PD and agoraphobia and in those with depressive disorders. Migraine was equally represented in the three groups, but panic disorder patients had a higher prevalence of migrainous vertigo definite migrainous vertigo. Almost all patients with a peripheral vestibular disorder had a final diagnosis of definite migrainous vertigo according to Neuhauser criteria. These patients had higher Dizziness Handicap Inventory scores. The Dizziness Handicap Inventory total score was higher in the subgroup of patients with panic disorders with agoraphobia also presenting unilateral reduced caloric responses or definite migrainous vertigo, compared with the subgroup of remaining subjects with panic disorders with agoraphobia ( $p < 0.001$ ).

**Conclusions:** Our data support the hypothesis that, in patients with panic disorders (and especially those with additional agoraphobia), dizziness may be linked to malfunction of the vestibular system. However, the data are not inconsistent with the hypothesis that migrainous vertigo is the most common pathophysiological mechanism for vestibular disorders.

**Key words:** Vestibular Disorders; Vertigo; Psychiatric Disorders; Migraine

### Introduction

In patients diagnosed with anxiety disorders, panic disorders or depressive disorders, dizziness in the absence of a history of true rotational vertigo has long been considered to be simply a somatoform symptom.<sup>1,2</sup>

Recent studies have focused on a more complex link: after an acute vestibular loss, patients often develop anxiety or depressive disorders.<sup>3,4</sup> There is increasing evidence for an association between vertigo and depression, but the directionality of this association is still unclear.<sup>5,6</sup> A higher rate of vestibular abnormalities has been demonstrated in patients with anxiety disorders, and vestibular dysfunction has been postulated to give rise to situational discomfort in particular surroundings when a sensory conflict arises.<sup>7,8</sup> Moreover, many experimental studies have documented vestibular abnormalities in over 50 per cent of patients

with panic disorders and vertigo-related symptoms.<sup>9–11</sup> Some studies have reported a higher rate of vestibular anomalies in patients with panic disorders and agoraphobia, compared with those with panic disorders without agoraphobia.<sup>12</sup> On the other hand, other authors have reported a higher rate of vestibular abnormalities in patients with panic disorders than in healthy controls, but no difference in patients with panic disorders with versus without agoraphobia.<sup>13</sup>

The lifetime prevalence of psychiatric disorders is increased in migraine patients with vestibular anomalies, compared with those with vestibular anomalies without migraine.<sup>14</sup>

Migraine sufferers frequently report various vestibular symptoms. Various definitions have been used to identify the association between vertigo and migraine, such as ‘migraine-associated vertigo’, ‘migraine related vestibulopathy’ and ‘migrainous vertigo’.<sup>15–17</sup>

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Anxiety and depressive disorders have been observed in both clinic- and community-based populations suffering from migraine.<sup>18,19</sup>

Previous studies proposed the possibility of overlapping comorbidity between psychiatric disorders, vestibular disorders and migraine-anxiety related dizziness.<sup>20</sup>

The purpose of this study was to establish the prevalence of vestibular disorders in three groups of dizzy patients: those with panic disorders and agoraphobia, those with panic disorders without agoraphobia, and those with depressive disorders. Moreover, we aimed to assess the prevalence of migrainous vertigo in these three groups.

## Materials and methods

### Subjects

We included in the study 52 patients with a psychiatric diagnosis of panic disorders with agoraphobia (38 women and 14 men, mean age  $35.8 \pm 9.2$  years), 30 subjects diagnosed with panic disorders without agoraphobia (21 women and nine men, mean age  $36.5 \pm 8.5$  years) and 20 diagnosed with depressive disorders (12 women and eight men, mean age  $41.3 \pm 6.6$  years). All patients also reported dizziness, defined as persistent (i.e. at least three months) sensations of nonvertiginous dizziness, light-headedness, heavy-headedness or subjective imbalance present on most days. Patients were consecutively recruited from January 2007 to December 2008 at the out-patient facility of the anxiety disorders clinical and research unit at San Raffaele Hospital, Milan. Psychiatric diagnoses were established according to the *Diagnostic and Statistical Manual IV* of mental disorders criteria and were made by a senior psychiatrist, who assessed the patients in a clinical interview using the Mini International Neuropsychiatric Interview Plus system.<sup>21</sup>

Our inclusion criterion was the presence of dizziness not solely during panic attacks.<sup>22</sup>

Our exclusion criteria were: evidence of chronic otitis media; prior use of ototoxic drugs and/or chemotherapy, and a clinical history of true rotational vertigo.

All patients underwent a 14-day period of abstinence from drugs active on the central nervous system, before vestibular testing.

The diagnosis of definite migraine was made by a neurologist according to International Headache Society 2004 criteria.<sup>23</sup>

The diagnosis of migrainous vertigo was based on the criteria of Neuhauser and Lempert.<sup>24</sup> According to these criteria, definite migrainous vertigo was considered to be present if there were: (1) episodic vestibular symptoms of at least moderate severity (i.e. rotational vertigo, other illusory self or object motion, positional vertigo, or head motion intolerance); (2) at least two of the following migrainous symptoms during at least two vertiginous attacks – migrainous headache, photophobia, phonophobia, or visual or other auras; (3) attacks of migraine (not during episodes of vertigo) as defined by International Headache Society criteria; and (4) some

central and/or peripheral vestibular abnormalities found in vertigo-free periods.

Other causes of dizziness were ruled out by history, physical examination and other appropriate investigations.

### Procedure

All patients underwent a full otoneurological examination to detect spontaneous, positional and positioning nystagmus (using Dix–Hallpike and McClure manoeuvres), including the head-shaking and head-thrust tests. Positional nystagmus was recorded in the supine position, with the head straight, head turned to the left and right side, and head hanging down. Nystagmus in darkness with a slow phase velocity of less than  $3^\circ/\text{second}$  was considered insignificant.

Examination of the oculomotor system (i.e. smooth pursuit and saccades) was also performed. In the same session, patients underwent caloric stimulation as proposed by Freyss (i.e. 125 ml of water,  $30^\circ$  and  $44^\circ$  in 30 seconds). Evaluation of the ocular movements was carried out using a videonystagmography (VO25 System, Interacoustics, Assens, Denmark) while bithermal caloric testing was performed with an otocalorimeter (Amplaid, Milan, Italy). We used angular slow phase velocity, as calculated during 10 seconds of culmination, as the single parameter of labyrinthine function. Data were interpreted in terms of directional preponderance and unilateral weakness, which were considered significant when greater than 30 and 25 per cent, respectively. When total slow phase velocity was less than  $20^\circ/\text{second}$ , stimulations were considered hyporesponsive, and hyper-responsive when greater than  $140^\circ/\text{second}$ .<sup>25,26</sup>

We considered central signs to comprise at least one of the following findings: (1) disorganised pursuit and reduction of pursuit gain; (2) saccades dysmetria with undershoot, overshoot, or asymmetrical latency or velocity; (3) rebound nystagmus; (4) visual fixation suppression of nystagmus of less than 60 per cent; (5) pure vertical or torsional spontaneous or positional nystagmus; or (6) positional nystagmus when bilateral, beating to the uppermost or lowermost ear, showing no latency, low frequency, lack of fatigability and habituation, without concomitant vertigo.<sup>27,28</sup>

The severity of dizziness was measured by the 25-item Dizziness Handicap Inventory scale, which generated a total score (range zero to 100) which indicated the patient's self-perceived level of handicap associated with their dizziness. The results of the Dizziness Handicap Inventory scale are divided into emotional, physical and functional subscales.<sup>29</sup>

### Statistical analyses

The significance of any difference in continuously distributed variables between the two groups was examined by *t*-test for independent samples. The chi-square test was used to assess differences for nominal values.

TABLE I  
 PATIENT RESULTS FOR CALORIC TESTS AND CENTRAL SIGNS

Pt Dx	UW	DP	UW & DP	Hyper-reflexic	Hyporeflexic	Central positional	OM alterations
PD + A*	8 (15.3%)	4 (7.7%)	9 (17.3%)	8 (15.3%)	1 (1.9%)	2 (3.8%)	5 (9.6%)
PD <sup>†</sup>	2 (6.6%)	3 (10%)	2 (6.6%)	3 (10%)	1 (3.3%)	2 (6.6%)	1 (3.3%)
DD <sup>‡</sup>		1 (5%)			2 (10%)	1 (5%)	2 (10%)

Data represent patient numbers and percentages. \* $n=52$ ; <sup>†</sup> $n=30$ ; <sup>‡</sup> $n=20$ . Pt Dx = patient psychiatric diagnosis; UW = unilateral weakness; DP = directional preponderance; OM = oculomotor; PD = panic disorders; A = agoraphobia; DD = depressive disorders

## Results

We did not find any patient with spontaneous nystagmus during our examination. Our findings for caloric testing and central signs are summarised in Table I.

Of the 52 patients with panic disorders and agoraphobia, 22 (42.3 per cent) showed normal caloric responses; two of these patients had central positional nystagmus. Seventeen patients (32.6 per cent) showed unilateral weakness with or without directional preponderance, indicating a peripheral vestibular disorder. Four patients showed a pure directional preponderance pattern, three with pursuit or saccadic alterations. The fourth patient with a directional preponderance pattern did not show any other clinical finding which could possibly be related to either a peripheral or central disorder.

Eight subjects showed a hyper-reflexic pattern, but showed no central signs; notably, they showed less than 40 per cent visual fixation. In the absence of any other clinical findings, we considered increased caloric responses to possibly be related to an 'over-anxious pattern'.

Of the 30 patients with panic disorders without agoraphobia, 19 (63.3 per cent) had normal caloric responses. One of these patients showed central positional nystagmus. Four patients (13.3 per cent) showed unilateral weakness with or without directional preponderance. Three patients (10 per cent) showed directional preponderance, one with pursuit abnormalities. Three other patients (10 per cent) had a hyper-reflexic pattern without central signs. One patient had a hyporeflexic pattern and showed central positional nystagmus and pursuit alterations.

None of the patients with depressive disorders showed unilateral weakness. One patient presented directional preponderance and saccadic dysmetria. One other patient with normal caloric responses showed central positional nystagmus and pursuit alterations.

Of the 52 patients with panic disorders and agoraphobia, 24 were diagnosed with migraine (46.6 per cent). In the subgroup of 22 subjects with normal caloric responses only 4 (18.2 per cent) had migraine (two of whom had central positional nystagmus). In the subgroup of 30 subjects with abnormal caloric responses (including unilateral weakness, directional preponderance, hyper or hyporeflexic pattern) 20 also presented migraine (66.6 per cent). In the subgroup of 17 subjects with unilateral weakness with or without directional preponderance 16 (94.1 per cent) also presented migraine. The remaining four subjects with migraine and abnormal caloric tests

had hyperreflexic caloric responses. According to the Neuhauser and Lempert criteria, 18 patients (34.6 per cent) in the group of subjects with panic disorders and agoraphobia had definite migrainous vertigo (16 with unilateral weakness and two with normal caloric responses but central positional nystagmus).

Eight of the 30 (26.6 per cent) patients with panic disorders without agoraphobia had migraine. Four of these eight showed unilateral weakness with or without directional preponderance, while three showed a caloric hyper-reflexic pattern and one had normal otoneurological findings. Migrainous vertigo was diagnosed in four panic disorder without agoraphobia patients (13.3 per cent), all of whom showed unilateral weakness on caloric testing.

Of the 20 patients with depressive disorders, six (30 per cent) had migraine, one showed a hyporeflexic caloric response, and three had normal caloric responses. In two of the 20 depressive disorder patients (10 per cent; one hyporeflexic patient and another with central positional nystagmus), we made a final diagnosis of definite migrainous vertigo.

A higher rate of abnormal caloric test results (especially unilateral reduced response) was found in patients with panic disorders and agoraphobia, compared with patients with panic disorders alone; a statistical significance between the two groups has been detected in the rate of unilateral reduced responses (chi square = 3.74,  $p = 0.05$ ) but not in the total number of abnormal caloric responses (chi square = 2.06,  $p = 0.15$ ).

Patients with panic disorders and agoraphobia showed a higher rate of vestibular abnormalities (chi-square = 4.17,  $p = 0.04$ ) and unilateral reduced caloric responses (chi-square = 5.34,  $p = 0.02$ ), compared with patients with depressive disorders.

Migraine was not significantly more prevalent in patients with panic disorders and agoraphobia, compared with patients with panic disorders alone (chi-square = 3.04,  $p = 0.08$ ) and with patients with depressive disorders (chi-square = 1.56,  $p = 0.21$ ), although there was a trend towards higher prevalence in patients with panic disorders plus agoraphobia. In patients with panic disorders and agoraphobia, migraine was significantly more prevalent in the subgroup with unilateral weakness (chi-square = 18,  $p < 0.001$ ).

Definite migrainous vertigo was significantly more prevalent in patients with panic disorders and agoraphobia, compared with patients with panic disorders

TABLE II  
PATIENTS' DIZZINESS HANDICAP INVENTORY SCORES

Pt Dx	DHI total	DHI subscale		
		Emotional	Physical	Functional
PD + A*	30.3 ± 13	7.6 ± 3.1	8.1 ± 3.8	14.5 ± 6.4
PD <sup>†</sup>	28.1 ± 8.6	8 ± 3.0	6.2 ± 1.9	13.9 ± 4.1
DD <sup>‡</sup>	27.8 ± 7.6	16.2 ± 4.2	2 ± 1.2	9.7 ± 3.8

Data are expressed as mean ± standard deviation. \**n* = 52; <sup>†</sup>*n* = 30; <sup>‡</sup>*n* = 20. Pt Dx = patient psychiatric diagnosis; DHI = Dizziness Handicap Inventory; PD = panic disorders; A = agoraphobia; DD = depressive disorders

TABLE III

DIZZINESS HANDICAP INVENTORY SCORES FOR PATIENTS WITH PANIC DISORDERS AND AGORAPHOBIA, BY PRESENCE OF UNILATERAL WEAKNESS ON CALORIC STIMULATION

UW?	DHI total	DHI subscale		
		Emotional	Physical	Functional
Yes*	42.1 ± 11.5	9.9 ± 2.7	11.8 ± 3.4	19.9 ± 6.0
No <sup>†</sup>	24.7 ± 9.4	6.4 ± 2.7	6.3 ± 2.6	11.9 ± 4.8

Data are expressed as mean ± standard deviation. \**n* = 17; <sup>†</sup>*n* = 35. UW = unilateral weakness; DHI = Dizziness Handicap Inventory

alone (chi-square = 4.39, *p* = 0.036) and patients with depressive disorders (chi-square = 4.36, *p* = 0.036).

Dizziness Handicap Inventory scores (total and subscale) are summarised in Table II.

Dizziness Handicap Inventory scores are also shown for the subgroup of 17 patients with unilateral peripheral vestibular disorder (i.e. unilateral weakness with or without directional preponderance), versus the remaining 35 patients (Table III).

The Dizziness Handicap Inventory total score did not differ significantly, comparing patients with panic disorders and agoraphobia versus those with panic disorders alone (*p* = 0.47) or those with depressive disorders (*p* = 0.52), and comparing patients with panic disorders alone versus those with depressive disorders (*p* = 0.93).

Comparison of Dizziness Handicap Inventory results for patients with panic disorders and agoraphobia versus panic disorders alone showed no significant difference regarding the emotional (*p* = 0.60) or functional (*p* = 0.70) subscales; however, physical subscale scores were lower in patients with panic disorders alone (*p* = 0.03).

Comparison of Dizziness Handicap Inventory results for patients with panic disorders and agoraphobia versus depressive disorders showed significantly lower emotional subscale scores (*p* < 0.001), but significantly higher physical (*p* < 0.001) and functional (*p* = 0.014) subscale scores.

The Dizziness Handicap Inventory total score was significantly higher in panic disorder plus agoraphobia patients with unilateral reduced caloric responses, compared with panic disorder plus agoraphobia patients without unilateral caloric reduced responses (*p* < 0.001).

TABLE IV

DIZZINESS HANDICAP INVENTORY SCORES FOR PATIENTS WITH PANIC DISORDERS AND AGORAPHOBIA, BY PRESENCE OF MIGRAINOUS VERTIGO\*

MV?	DHI total	DHI subscale		
		Emotional	Physical	Functional
Yes <sup>†</sup>	43.4 ± 10.4	10.2 ± 2.4	11.6 ± 3.4	20.9 ± 4.9
No <sup>‡</sup>	23.1 ± 9.4	6 ± 2.7	5.9 ± 2.6	11.1 ± 4.7

Data are expressed as mean ± standard deviation. \*15 patients with peripheral and two with central vestibular disorder. <sup>†</sup>*n* = 15; <sup>‡</sup>*n* = 37. MV = migrainous vertigo; DHI = Dizziness Handicap Inventory

Dizziness Handicap Inventory results for panic disorder plus agoraphobia patients with and without migrainous vertigo are shown in Table IV; a statistically significant difference was detected between these two groups (*p* < 0.001).

## Discussion

In this study, a trend towards higher prevalence of vestibular disorders (especially unilateral reduced caloric responses) was observed in dizzy patients with panic disorders and agoraphobia, compared with dizzy patients with panic disorders alone; a statistical significance between the two groups has been detected in the rate of unilateral reduced responses (chi square = 3.74, *p* = 0.05) but not in the total number of abnormal caloric responses (chi square = 2.06, *p* = 0.15). Dizzy patients with depressive disorders showed a lower prevalence of vestibular disorders.

In dizzy patients with panic disorders and agoraphobia, 32.6 per cent showed unilateral reduced vestibular responses; these data are similar to other recent reports.<sup>30</sup>

Amongst the three psychiatric diagnostic groups, 20 patients showed unilateral reduced caloric responses, and 18 (90 per cent) fulfilled Neuhauser and Lemper's criteria for diagnosis of definite migrainous vertigo. Migrainous vertigo was more prevalent in patients with panic disorders and agoraphobia, compared with those with panic disorders alone.

Some authors believe that the Dizziness Handicap Inventory total and subscale scores represent the most important information for the management of dizzy patients.<sup>31</sup> The current study demonstrated some interesting results for this inventory. Firstly, no difference in Dizziness Handicap Inventory total score was found between the three psychiatric diagnostic groups, while patients with panic disorders and agoraphobia had a higher physical subscale score. Secondly, in patients with panic disorders and agoraphobia, Dizziness Handicap Inventory scores were higher in those with unilateral reduced caloric responses and also in those with a final diagnosis of migrainous vertigo.

Our data support the hypothesis that, in patients with panic disorders, the symptom of dizziness may not be a 'functional' symptom related to an anxiety state but may instead be linked to malfunction of



the vestibular system. Moreover, our data are not inconsistent with the possibility that migrainous vertigo may be the main aetiological factor for vestibular disorders in such patients. Conversely, in dizzy patients with depressive disorders we found a lower prevalence of vestibular abnormalities; these data support the hypothesis that dizziness in depressive subjects may be a somatoform symptom.

- **The association between psychiatric and vestibular disorders is still under debate. A higher prevalence of vestibular disorders has been reported in patients with panic disorders and agoraphobia, psychiatric patients often complain of migraine, and migraine sufferers often report various vestibular symptoms**
- **This study found a higher prevalence of vestibular disorders in dizzy patients with panic disorders and agoraphobia, compared with those with panic disorders alone and those with depressive disorders**
- **Migrainous vertigo was the most common causal factor for vestibular disorders**

We were unable to assess the relationship between panic disorders and vestibular disorders. However, we consider it significant that peripheral vestibular disorders were more prevalent in dizzy patients with panic disorders and agoraphobia (a space-related, situational psychiatric disorder), compared with patients with panic disorders alone.

It has been theorised that a primitive vestibular disorder may act as a disruptive factor on the homeostatic stability of patients with panic disorders, possibly influencing the onset and/or maintenance of the disorder. Moreover, vestibular loadings may also influence panic disorders by affecting the function of the serotonergic system.<sup>32,33</sup> On the other hand, it may be supposed that vestibular abnormalities might influence the subsequent development of agoraphobia in patients with panic disorders.

The Dizziness Handicap Inventory total score did not vary for the three psychiatric diagnosis groups. However, depressive disorder patients had higher scores for the emotional subscale. Moreover, the Dizziness Handicap Inventory total score was higher in those dizzy patients with panic disorders and agoraphobia who had peripheral vestibular disorders or definite migrainous vertigo.

Our dizzy patients with psychiatric disorders had a higher prevalence of migraine than that reported for the normal population (estimated at approximately 10 per cent).

In our patients, migrainous vertigo was the most important causal factor for vestibular disorders. Overlapping neural circuits may explain the concurrence of panic disorders, migraine and vertigo. However, the pathophysiology of migrainous vertigo is not well understood and is still a matter of speculation.

As the vestibular nuclei receive noradrenergic fibres from the locus coeruleus and serotonergic

afferents from the dorsal raphe nucleus, it is likely that activation of these pathways during migraine could also activate central vestibular processing.<sup>34–36</sup> Moreover, the reciprocal connection of the vestibular nuclei and trigeminal nucleus caudalis may provide a tight linkage between vestibular and vascular–trigeminal processing during migraine attacks.<sup>37</sup>

Serotonergic pathways departing from the nucleus raphe have been demonstrated to play an important role in anxiety processing in rats.<sup>38</sup> Moreover, clinical and pathophysiological studies underline the importance of the amygdala in migraine generation.<sup>39</sup> The amygdala and periaqueductal grey circuit also play a crucial role in the expression of conditioned fear and avoidance, and there is increasing evidence of possible activation of these circuits in panic disorders with agoraphobia.<sup>40</sup>

Finally, a tight link has been demonstrated between the trigeminal nucleus caudalis and the periaqueductal grey circuits.<sup>41</sup>

## Conclusion

Our data are not inconsistent with the hypothesis that migrainous vertigo may be the most frequent causal factor for vestibular disorders in patients with panic disorders and agoraphobia.

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