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Migraine Features in Patients with Persistent Postural-Perceptual Dizziness

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Abstract

Objectives: To evaluate the presence of migraine features in patients with persistent postural-perceptual dizziness (PPPD).

Methods: In a retrospective survey study, consecutive patients presenting to a tertiary care neurotology clinic during an 18-month period were given questionnaires about headache and dizziness symptoms. The survey responses plus history and examination of the patient were used to diagnose patients with PPPD. The prevalence of migraine headache, vestibular migraine (VM), and migraine characteristics was evaluated.

Results: In total, 36 subjects with PPPD were included in the study. The mean age of the subjects was 56±16 years with a female (72%) predominance. A total of 19 (53%) patients met the International Classification of Headache Disorders criteria for migraine headache, and 6 of those (17%) met the criteria for definite VM. Of the patients who did not meet full migraine headache criteria, 6 (17%) patients met 4 of 5 criteria, and 5 (14%) patients met 3 of 5 criteria. There was no significant difference between PPPD patients who fulfilled full migraine headache criteria and those who did not in sensitivity to light, sound, smells, weather changes, feelings of mental fog/confusion, and sinus pain/facial pressure.

Conclusions: This study demonstrates that a majority of patients with PPPD fulfill the criteria for migraine headache. A large proportion of PPPD patients who do not meet the full criteria for migraine headache still meet a majority of the migraine headache criteria. This suggests an association between the two conditions. PPPD may be a part of the spectrum of otologic migraine, where migraine manifests as otologic symptoms.

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Conflicts of Interest: Hamid R. Djalilian holds equity in MindSet Technologies and Cactus Medical LLC, and is on the advisory board of Novus Therapeutics.

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Keywords

Persistent postural-perceptual dizziness; Migraine; Migraine headache; PPPD; Otologic migraine

Introduction

Persistent postural-perceptual dizziness (PPPD) is a functional vestibular disorder in which maladaptation typically to an inciting event causes a long-lasting sensation of motion, dizziness, and unsteadiness. Though only recently officially defined in 2015 in the International Classification of Diseases (ICD-11), the condition has been previously investigated for decades, and prior labels include phobic postural vertigo, space-motion discomfort, chronic subjective dizziness, and visual vertigo.¹ The condition is characterized by 3 or more months of non-spinning vertigo, dizziness, or unsteadiness that is often initially triggered by an event that involves vestibular symptoms, psychological distress, or heightened awareness of posture (Table 1).² The subsequent maladaptive response results in continued non-spinning vertigo or imbalance symptoms even after the inciting event has concluded. For example, a patient may develop vestibular neuritis and experience a continued sensation of motion even after the neuritis has resolved. Other inciting events include vestibular migraine, panic attacks, head injuries, autonomic dysfunction, and more.³

PPPD has been found in association with migraine headache. A study by Bittar and Lins found that up to 26% of individuals with PPPD also experience migraine headaches.⁴ Episodes of migraine headache or vestibular migraine can additionally act as a trigger for PPPD. When individuals experience features of migraine headache alongside vestibular symptoms, they can be said to have vestibular migraine.⁵ However, PPPD, migraine headache, and vestibular migraine are thought to be distinct entities that can co-exist. Current treatment for PPPD generally consists of vestibular rehabilitation therapy, cognitive behavioral therapy, and medications including selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs).⁶⁻⁸ Interestingly, vestibular ocular reflex exercises may worsen vestibular symptoms or slow improvement in the setting of active migraine,^{9,10} prompting a need to elucidate the presence of migrainous features in those with PPPD in order to facilitate management of the condition. This study aims to determine the prevalence of migraine headache without aura, vestibular migraine, and migrainous features in a study population of PPPD patients. If an association exists between the two conditions, treatments for PPPD may potentially be expanded to include treatments for migraine headache as well.

Methods

Following institutional review board approval from the University of California, Irvine, electronic tablet surveys were administered to consecutive patients who presented to a tertiary care neurotology clinic from July 2018 to January 2020. Patients completed the surveys immediately after their clinical encounters with a neurotologist. The survey was a custom-designed questionnaire that included questions pertaining to the diagnostic criteria of migraine headache, vestibular migraine, and PPPD as defined by the International

Classification of Vestibular Disorders (ICVD)². Data from the completed surveys was uploaded onto a secure, clinical database using electronic data capture software (REDCap, Vanderbilt University, Nashville, TN, USA). Subjects were classified as having PPPD if their survey responses to the PPPD diagnostic criteria questions and combination of history and physical exam by a neurotologist both supported a diagnosis of PPPD and excluded other diagnoses as being more likely. Similarly, a diagnosis of migraine headache and vestibular migraine was made using a combination of responses to survey questions and a thorough history and physical exam by a neurotologist. Migraine headache without aura and vestibular migraine criteria were based on the International Classification of Headache Disorders (ICHD) 3rd edition published by the International Headache Society (IHS) (Table 2).⁵

Demographics and prevalence of migraine headache features were compared between those with PPPD who met full migraine headache criteria and those who did not. Analysis utilizing chi-square or Fisher's exact tests and independent sample *t*-test were performed to compare the variables between the two groups. SPSS 17.0 software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis, with a $P < 0.05$ being considered statistically significant.

Results

Surveys were administered to all patients presenting with dizziness, of which 36 were diagnosed with PPPD. The mean age of PPPD subjects was 56 ± 16 years, with a female (72%) predominance. As outlined in Figure 1, a total of 19 (53%) patients met the ICHD criteria for migraine headache (13 female, 6 male). Of those with migraine headache, 6 (17% of total cohort) met the ICVD criteria for definite vestibular migraine. Of the PPPD patients who did not meet full migraine headache criteria, 6 (17%) patients met 4 of 5 criteria (probable vestibular migraine), and 5 (14%) patients met 3 of 5 criteria, for a total of 11 (31%) patients.

When comparing features of migraine between PPPD patients who fulfilled full migraine headache criteria and PPPD patients who did not, there was no significant difference between the percentage of those who experienced many migraine-related symptoms, such as sensitivity to light (73.7% vs. 41.2%, $P = 0.09$), sound (52.6% vs. 29.4%, $P = 0.19$), smells (26.3% vs. 11.8%, $P = 0.41$), and weather changes (31.6% vs. 5.9%, $P = 0.09$), feelings of sinus pressure or facial pain (57.9% vs. 35.3%, $P = 0.20$), feelings of mental fog or confusion (63.2% vs. 76.5%, $P = 0.48$), and family history of migraine (36.8% vs. 41.2%, $P = 1.00$) (Table 3). There was a significant difference between those who experienced nausea or vomiting during headache (63.2% vs. 11.8%, $P = 0.005$), relief of headaches with medication (68.4% vs. 94.1%, $P = 0.02$), headaches triggered by cold food or liquid (89.5% vs. 52.9%, $P = 0.02$), and ear pain (68.4% vs. 11.8%, $P = 0.002$).

Discussion

Despite PPPD being recently defined as a distinct clinical entity, its pathophysiology remains poorly understood. Nonetheless, data obtained from neuroimaging studies in

patients with related disorders such as phobic postural vertigo and chronic subjective dizziness have provided a number of clues regarding the possible mechanisms underlying the complex disorder. The prevailing hypotheses include stiffened postural control, an imbalance in processing of visual stimuli over vestibular input, and neural dysfunction in regulating these two processes. In healthy individuals, the normal response to the onset of dizziness or vertigo is activation of high-risk postural control strategies such as shorter strides and more rigid stance when exposed to heights and slippery conditions. After the threat has subsided, these controls are abandoned. However, patients with PPPD experience failure to re-adapt quickly following postural imbalances due to deficiencies in higher cortical processes as well a behavioral maladaptation (often anxiety-driven) to natural postural control and spatial orientation.¹¹

Our study found the prevalence of migraine headache in a population with PPPD to be 53%. This is much higher than the prevalence of migraine headache in the general population, which has been estimated to be about 8–13% in adults,¹² and suggests an association between PPPD and migraine headache. This is also higher than the prevalence of migraine headache in those with PPPD investigated in other studies, which have found a prevalence of 26%⁴ and 16.5%.³ Various factors may account for this difference. In the study by Bittar and Lins,⁴ initially only women were treated in the clinic from which they included patient data before men were also included. In the study by Staab and Ruckenstein,³ patients with concomitant migraine headache and vestibular symptoms were excluded. When excluding patients who experienced vestibular migraine, the migraine headache prevalence in our study decreases to 36%; when men with migraine headache are excluded, the prevalence also decreases to 36%. This ultimately greater prevalence may potentially reflect a self-selective and differing patient population that presents to our tertiary care clinic and a comprehensive questionnaire that can assist in the migraine diagnosis.

While thought to be distinct disorders, migraine and PPPD share many characteristics that may help explain the high prevalence of migraine in our cohort of patients. Similar to the mechanisms described for PPPD, the pathophysiology of sensory phenomena during migraine auras can likely be attributed to cortical disturbances in the form of cortical spreading depression. Equally significant are the shared clinical features, particularly hypersensitivity to various sensory stimuli (e.g., visual motion, motion, light, sounds, smells) that may potentiate dizziness, motion sickness, and other vestibular symptoms experienced by migraine patients. For patients with concomitant PPPD, these same triggers that are responsible for migraine episodes likely serve to amplify the onset of PPPD and cause the vestibular symptoms to persist for even longer following termination of the inciting event. Given these observations, it appears that migraine itself may be considered a trigger and cause for the persistence of PPPD. For this reason, identification and effective management of underlying migraine disorder in patients can be reasonably attempted to help treat PPPD.

Our study additionally found a female predominance in both the entire cohort (72% female) and of migraine headache subgroup (68% female). Both PPPD and migraine headache tend to have more female sufferers.^{4,13,14} The increased prevalence of migraine headache in women is theorized to be related to the complex interplay of hormones, particularly

estrogen, after menarche, during monthly cycles, and peri-menopause.¹⁵ In terms of PPPD, a personal or family history of anxiety has been identified as one risk factor for development of the condition;^{2,16,17} anxiety has also been found to be more common in women than in men.¹⁸ If an association between PPPD and migraine headache exists, then likely the combination of a higher risk of both migraine headache and of anxiety disorders may contribute to the female predominance of PPPD sufferers.

Interestingly, we identified a large group of individuals (31% of our cohort) who met three or four of the migraine headache criteria, although they did not meet all five criteria necessary to diagnose migraine headache. Similarly, there was no significant difference between the PPPD patients who met full migraine headache criteria and those who did not. This comparison was made for multiple migraine-associated symptoms that are not part of the diagnostic criteria, including sensitivity to smells and weather, feelings of mental fog, and sinus pressure or facial pain.¹⁹ This finding of no difference in migraine characteristics strongly suggests that multiple migraine features may be present in PPPD patients even when they do not fit all criteria for migraine headache or definite vestibular migraine. This may be especially poignant when it comes to management of PPPD.

Current treatments for PPPD include vestibular rehabilitation therapy, cognitive behavioral therapy, and medications including SSRIs and SNRIs.^{6–8} However, each treatment has varying efficacy according to current studies. Customized vestibular rehabilitation and cognitive behavioral therapy have both shown promise for improving and resolving symptoms.^{7,20,21} SSRIs and SNRIs, having previously been shown to help reduce vestibular symptoms in patients with chronic subjective dizziness, can also benefit PPPD patients and even those without psychiatric comorbidities. Unsurprisingly, PPPD patients with concomitant symptoms of depression and anxiety have also reported improvement in multiple open-label clinical trials. However, to date, only one randomized controlled trial has been conducted to study the efficacy of anti-depressants and compare the benefit of sertraline versus verapamil in patients with PPPD and vestibular migraine.¹¹ In clinical practice, it has been recommended for clinicians to start with one SSRI (at half the dosage typically used in the treatment for depression) and to switch to a SNRI if the patient fails to tolerate or exhibit a clinical response even after trial with a second SSRI. Additionally, data from these trials have suggested that these medications take 8–12 weeks to produce the desired effects and patients who experience benefit should remain on treatment for at least 1 year.⁶

We have also found SSRIs and SNRIs to be effective in patients with vestibular migraine. It is possible that the success of these two classes of drugs may be related to its effectiveness in controlling migraine. The efficacy of these drugs may be through control of stress/anxiety/depression and sleep abnormalities which are significant migraine triggers. Although vestibular therapy can be helpful for PPPD, it can also worsen vestibular symptoms or slow improvement in the setting of active migraine.⁹ For this reason, it is imperative to identify PPPD patients who have comorbid migraine (headache or vestibular migraine) in order to implement an effective treatment plan. This is particularly critical because there may be an association between the two conditions, and treatment of migraine may reduce the severity of dizziness symptoms in PPPD.

This study has limitations that should be taken into consideration when interpreting the results. Its survey-based nature allows for the possibility of self-selection and recall bias. Furthermore, participants may not have full knowledge regarding their own family history. There is no objective diagnostic test for PPPD, and therefore, the amount of false positive diagnoses cannot be accurately quantified. These data were analyzed retrospectively, and randomized controlled trials which identify migraine symptoms and treat them alongside typical vestibular therapies would help elucidate the connection.

Conclusion

This study demonstrates that a majority of patients with PPPD fulfill criteria for migraine headache. A large proportion of PPPD patients who do not meet the full criteria for migraine headache still meet a majority of the migraine headache criteria and display features of migraine. PPPD may be part of the spectrum of otologic migraine, a spectrum of disorders where migraine can present with otologic complaints. This may suggest an association between the two conditions and underscores the importance of identifying when both conditions exist comorbidly, as treatment of only PPPD without addressing migraine may produce suboptimal improvement and treatment of both together may improve outcomes and the overall efficacy of treatment.

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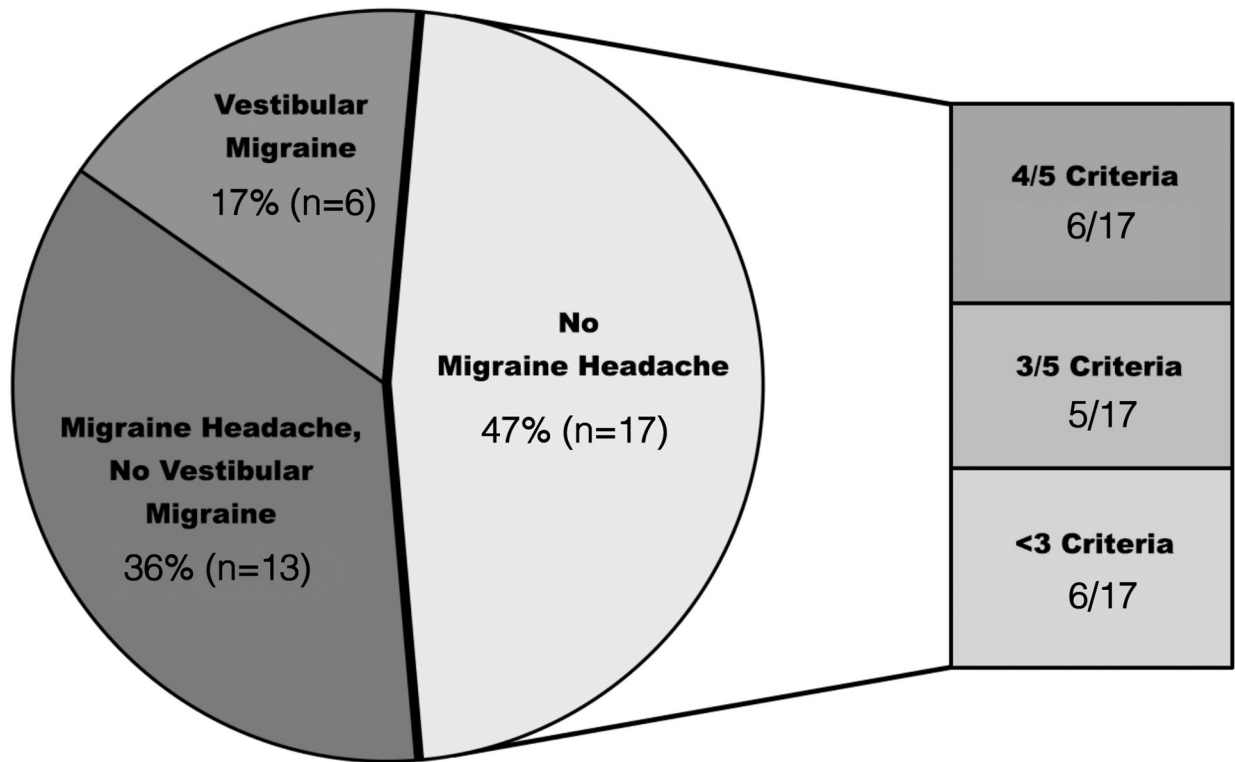


Figure 1. Percentage of persistent postural-perceptual dizziness subjects who met criteria for migraine headache (including vestibular migraine). Both 'Migraine Headache, No Vestibular Migraine' and 'Vestibular Migraine' patients meet full migraine headache criteria.

Table 1.

Diagnostic criteria for persistent postural-perceptual dizziness (PPPD) as defined by the International Classification of Vestibular Disorders (ICVD).

All five criteria (A-E) must be fulfilled to make the diagnosis:

- A.** One or more symptoms of dizziness, unsteadiness, or non-spinning vertigo are present on most days for 3 months or more.
 - 1.** Symptoms last for prolonged (hours-long) periods of time, but may wax and wane in severity.
 - 2.** Symptoms need not be present continuously throughout the entire day.
- B.** Persistent symptoms occur without specific provocation, but are exacerbated by three factors:
 - 1.** Upright posture,
 - 2.** Active or passive motion without regard to direction or position, and
 - 3.** Exposure to moving visual stimuli or complex visual patterns.
- C.** The disorder is precipitated by conditions that cause vertigo, unsteadiness, dizziness, or problems with balance including acute, episodic, or chronic vestibular syndromes, other neurologic or medical illnesses, or psychological distress.
 - 1.** When the precipitant is an acute or episodic condition, symptoms settle into the pattern of criterion A as the precipitant resolves, but they may occur intermittently at first, and then consolidate into a persistent course.
 - 2.** When the precipitant is a chronic syndrome, symptoms may develop slowly at first and worsen gradually.
- D.** Symptoms cause significant distress or functional impairment.
- E.** Symptoms are not better accounted for by another disease or disorder.

Table 2.

Diagnostic criteria for migraine headache without aura and vestibular migraine as defined by the International Classification of Headache Disorders, 3rd edition (ICHD).

Migraine headache without aura	
A.	At least five attacks fulfilling criteria B-D
B.	Headache attacks lasting 4–72 hours (untreated or unsuccessfully treated)
C.	Headache has at least two of the following four characteristics: <ol style="list-style-type: none"> 1. unilateral location 2. pulsating quality 3. moderate or severe pain intensity 4. aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs)
D.	During headache at least one of the following: <ol style="list-style-type: none"> 1. nausea and/or vomiting 2. photophobia and phonophobia
E.	Not better accounted for by another ICHD-3 diagnosis.
Vestibular migraine	
All five criteria (A-E) must be fulfilled to make the diagnosis:	
A.	At least five episodes fulfilling criteria C and D
B.	A current or past history of migraine without aura or migraine with aura
C.	Vestibular symptoms of moderate or severe intensity, lasting between 5 minutes and 72 hours.
D.	At least half of episodes are associated with at least one of the following three migrainous features: <ol style="list-style-type: none"> 1. headache with at least two of the following four characteristics: <ol style="list-style-type: none"> a. unilateral location b. pulsating quality c. moderate or severe intensity d. aggravation by routine physical activity 2. photophobia and phonophobia 3. visual aura
E.	Not better accounted for by another ICHD-3 diagnosis or by another vestibular disorder.

Table 3.

Comparison of migraine features between persistent perceptual-postural dizziness (PPPD) patients who met full migraine headache criteria and those who did not meet full migraine headache criteria. A $P < 0.05$ was considered statistically significant.

Feature	PPPD patients fulfilling migraine headache criteria (N=19)	PPPD patients not fulfilling migraine headache criteria (N=17)	P value
Sensitivity to light	14 (73.7%)	7 (41.2%)	0.09
Sensitivity to sound	10 (52.6%)	5 (29.4%)	0.19
Sensitivity to smells	5 (26.3%)	2 (11.8%)	0.41
Sensitivity to weather changes	6 (31.6%)	1 (5.9%)	0.09
Sinus pressure/facial pain	11 (57.9%)	6 (35.3%)	0.20
Mental fog/confusion	12 (63.2%)	13 (76.5%)	0.48
Family history of migraine	7 (36.8%)	7 (41.2%)	1.00
Family history of Meniere's disease	4 (21.1%)	1 (5.9%)	0.34
Family history of motion sickness	7 (36.8%)	5 (29.4%)	0.73
Nausea/vomiting during headache	12 (63.2%)	2 (11.8%)	0.005*
Relief of any headache with medications	13 (68.4%)	16 (94.1%)	0.02*
Headache triggered by cold food or liquid	17 (89.5%)	9 (52.9%)	0.02*
Ear pain	13 (68.4%)	2 (11.8%)	0.002*