

[ORIGINAL ARTICLE]

The Clinical Key Features of Persistent Postural Perceptual Dizziness in the General Medicine Outpatient Setting: A Case Series Study of 33 Patients

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Abstract:

Objective This case series aimed to investigate the clinical and pathological characteristics of persistent postural perceptual dizziness (PPPD).

Methods We retrospectively examined the medical records of patients with chronic dizziness in our department, and tracked the percentage of PPPD, the age and sex, disorder duration, exacerbating factors for dizziness, and duration of momentary worsening dizziness. We also examined the duration of momentary worsening dizziness in cases of depression, anxiety disorder, and somatic symptom disorder.

Results Among 229 patients with chronic dizziness, 14.4% (33/229) met the diagnostic criteria for PPPD. PPPD was the second most common disorder of patients with chronic dizziness after depression. The median age of patients with PPPD was 75 (75.8% female) and the median duration of the disorder was 60 months (range: 3-360 months). The exacerbating factors were motion without regard to direction or position (90.9%), upright posture (66.7%), and exposure to moving visual stimuli or complex visual patterns (30.3%). While the duration of momentary worsening dizziness was less than 10 minutes in 93.9% of patients with PPPD, the duration in patients with depression, anxiety disorder, and somatic symptom disorder were 3.6% (2/55), 16.1% (5/31), and 0% (0/11), respectively. When the duration was less than 10 minutes, the odds ratios of PPPD for depression and anxiety disorder were 46.5 (95% CI: 6.1-362.0) and 40.3 (95% CI: 7.4-219.3), respectively.

Conclusion Short episodes of momentary worsening dizziness constitute a distinctive feature of PPPD that may be useful for differentiating PPPD from other types of psychogenic dizziness.

Key words: chronic dizziness, chronic vertigo, PPPD, psychogenic dizziness, psychogenic vertigo

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Introduction

The chronically occurring functional disorder known as persistent postural perceptual dizziness (PPPD) was defined in 2017 by the International Society for Neuro-otology, the largest international society on dizziness, and in the same year, PPPD was added to the 11th edition of the International Statistical Classification of Diseases and Related Health Problems (ICD-11) (1). Of the 16 dizziness-causing disorders established by the Japan Society for Equilibrium

Research, disorders categorized as PPPD are included in the “vertigo” of unknown origin category. According to Japanese statistics, “vertigo” of unknown origin category occurs in 20-25% of patients who complain of dizziness (2). Although PPPD is thought to account for some portion of chronic dizziness of unknown origin, there is no clear picture of this disorder in general medical practice. In this study, we investigated the state of PPPD in cases with unknown diagnoses gathered from outpatient cases in the Department of General Medicine at Chiba University Hospital (henceforth, “this department”). Furthermore, we investi-

Table 1. Criteria for the Diagnosis of PPPD (The International Society for Neuro-otology) (1).

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
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.

gated that the differences in the clinical features between PPPD and psychogenic dizziness because when considering cases of chronic dizziness, differentiating the diseases is challenging for physicians.

Materials and Methods

Study participants and setting

This study looked at patients with chronic dizziness (a disorder duration of at least three months) who had an initial examination as an outpatient at this department between January 2017, when PPPD was defined by the International Society for Neuro-otology, and September 2019. ICD-11 was used to diagnose the disorder causing chronic dizziness. The selection criteria for PPPD were the fulfillment of the diagnostic criteria (1) from the International Society for Neuro-otology (Table 1), and criterion E (“symptoms are not better accounted for by another disease or disorder”) being satisfied in cases where central vertigo had been ruled out by the Department of Neurology or Department of Neurosurgery and peripheral vertigo had been ruled out by the Department of Otorhinolaryngology. It was confirmed that there were no abnormalities in the cerebellum and brainstem by head magnetic resonance imaging in the previous hospital for the fulfillment of the criterion E. Furthermore, two or more physicians confirmed no abnormal findings on neurological examination including nystagmus testing (positional nystagmus testing, and supine positional testing if there was a clinical history of worsening dizziness with rolling over) at the time of diagnosis of PPPD. ICD-11 was used to diagnose preceding episodes of acute dizziness. The Fifth Edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) of the American Psychiatric Association was used to diagnose coexisting mental illnesses.

This department has thus far seen approximately 100 patients with chronic dizziness of unknown origin per year. In this department, each patient is cared for by at least two physicians and sufficient time is spent evaluating biological,

behavioral, and social problems in patients with symptoms or health problems that have not yet been diagnosed. In this study, diagnoses were made by at least two independent physicians and, because it was a retrospective, cross-sectional study based on medical records, we strove to prevent the occurrence of any recall bias and observer bias through double independent evaluations of the medical records.

Procedure

The medical records of patients in the study were examined retrospectively. The study tracked the following items: the percentage of patients with chronic dizziness who had PPPD, age and sex, disorder duration, preceding episodes of acute dizziness, exacerbating factors for dizziness, duration of momentary worsening dizziness, symptom quality, coexisting mental illness, decline in activities of daily living (ADL), treatment, and outcome of patients with PPPD. The study investigated the presence of the following three exacerbating factors for PPPD listed in the PPPD diagnostic criteria from the International Society for Neuro-otology: (1) 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. The duration of momentary worsening dizziness in the following three disorders was also investigated because the disorders are listed in the DSM-5 and they are known to be able to cause or induce psychogenic dizziness: 1. depression (a diagnosis of at least one of the following: depressive episodes, recurrent depressive disorder, or dysthymia), 2. anxiety disorder (one of the following disorders or their comorbidities: panic disorder, a specific phobia, generalized anxiety disorder, social anxiety disorder, agoraphobia, or other unspecified anxiety disorders), and 3. somatic symptom disorder (3). Information on the treatment and outcome was obtained by contacting patients in the study by telephone. All patients received treatment in which their disorder was explained to them using the techniques of cognitive-behavioral therapy. In addition, we also studied whether treatment with selective serotonin

Table 2. Classification of Outcome.

Recovery: No vertigo and no difficulty in daily activities
Improvement: Vertigo is not recognized, but there is a problem in active daily life. Vertigo sometimes appears, but troubles in active daily life are better than at consultation.
No change: Vertigo persists, active daily life problems continue.
Deterioration: Vertigo worsen, increasing difficulty in active daily living.
Discontinuation: Treatment for vertigo was discontinued.

reuptake inhibitors (SSRIs) or serotonin-norepinephrine reuptake inhibitors (SNRIs) had an effect. Five outcome categories were defined according to the presence of vertigo and decline in ADL due to psychosocial issues: recovery, improvement, no change, deterioration, and discontinuation (Table 2). Decline in ADL was defined as a decline in basic activities of daily living (BADL) or in instrumental activities of daily living (IADL).

Ethics approvals

This study was approved by the ethical review board of the Chiba University Graduate School of Medicine. Although informed consent was not necessarily required in this study according to the provisions of Article 12-1(2b) of the Ethical Guidelines for Medical and Health Research Involving Human Subjects, written consent for their anonymized medical information to be used for academic research was obtained from research subjects when they were seen in this department.

Statistical analyses

Statistical analyses were performed by using SPSS Statistics software program for Mac 26.0 (IBM Corporation, Armonk, USA). Targets were limited to those with momentary worsening dizziness and the duration of momentary worsening dizziness of PPPD and psychogenic dizziness were compared with the Fisher's exact test. P values <0.05 were considered to be statistically significant.

Results

The study examined 229 patients with chronic dizziness. Among those patients, 14.4% (33/229) met the diagnostic criteria for PPPD from the International Society for Neurotology, and PPPD was the second most common disorder for patients with chronic dizziness after depression, which was present in 24.0% (55/229) of the cases. The next most common condition was anxiety disorder at 13.5% (31/229), followed by benign senile disequilibrium at 9.2% (21/229) and somatic symptom disorder at 4.8% (11/229). The median age of the patients with PPPD was 75 (range: 33-87 years of age), 75.8% of the patients (25/33) were female, and the median duration of the disorder was 60 months (range: 3-360 months) (Table 3).

The most common preceding episode of acute dizziness was benign paroxysmal positional vertigo (BPPV) at 81.8%

(27/33), and 12.1% of patients (4/33) had a preceding episode whose diagnosis was unknown. Starting with the most common, the exacerbating factors for PPPD were as follows: active or passive motion without regard to direction or position in 90.9% of patients (30/33), upright position in 66.7% (22/33), and exposure to moving visual stimuli or complex visual patterns in 30.3% (10/33). All three were exacerbating factors in 15.2% of patients (5/33). The symptom quality was dizziness in 93.9% of the patients (31/33).

For cases of PPPD, the duration of momentary worsening dizziness was less than 1 minute in 69.7% of cases (23/33), more than 1 minute but less than 10 in 24.2% (8/33), and more than 10 minutes but less than 60 in 6.1% (2/33). For patients with depression, it was most common to have no momentary worsening (85.5%, 47/55), and none of the patients with somatic symptom disorder (0/11) had momentary worsening (Table 4). In patients with anxiety disorder, the duration was less than 1 minute in 3.2% of cases (1/31), more than 1 minute but less than 10 in 12.9% (4/31), and more than 10 but less than 60 in 6.5% (2/31). There was no momentary worsening in 41.9% of patients (13/31).

Excluding patients with no momentary worsening dizziness, we analyzed the duration of momentary worsening dizziness to differentiate between PPPD and depression, as well as PPPD and anxiety disorder. Youden's index for the discrimination between PPPD and depression or PPPD and anxiety disorder were the highest when the duration of momentary worsening dizziness of less than 10 minutes or not (0.689 and 0.662, respectively). These comparisons between PPPD and depression, as well as PPPD and anxiety disorder with the duration of momentary worsening dizziness of less than 10 minutes or not showed a significant difference ($p < 0.001$) for the groups. The odds ratios were 46.5 [95% Confidence Interval (CI): 6.1-362.0] and 40.3 (95% CI: 7.4-219.3), respectively.

Comorbid mental illness was observed in 63.6% of the patients (21/33), among which anxiety disorder and depression were the most common at 66.7% (14/21) and 57.1% (12/21), respectively, followed by anorexia nervosa at 4.8% (1/21). All of these cases of mental illnesses were mild. A decline in ADL was observed in 81.8% of the cases (27/33).

The telephone response rate for the telephone survey on treatment and outcome was 78.8% (26/33) and the outcomes were as follows: recovery in 5/26 cases (19.2%), improvement in 10/26 (38.5%), and no change in 11/26 (42.3%). In addition to explaining the disorder to patients using the

Table 3. Clinical Features of 33 PPPD Cases.

	Number of patients	33
Age, years (range)		75(33-87)
Gender		
Male, n (%)		8/33(24.2)
Female, n (%)		25/33(75.8)
Median duration of the disorder, months (range)		60(3-360)
Exacerbated factors		
Active or passive motion without regard to direction or position, n(%)		30/33(90.9)
Upright posture, n(%)		22/33(66.7)
Exposure to moving visual stimuli or complex visual patterns, n(%)		10/33(30.3)
Symptom quality		
Dizziness, n(%)		31/33(93.9)
Vertigo, n(%)		2/33(6.1)
The duration of momentary worsening dizziness		
Less than 1 minute, n(%)		23/33(69.7)
More than 1 minute but less than 10, n(%)		8/33(24.2)
More than 10 minutes but less than 60, n(%)		2/33(6.1)
More than 60 minutes, n(%)		0/33(0.0)
No momentary worsening dizziness, n(%)		0/33(0.0)
Comorbid mental illness, n(%)		21/33(63.6)
Anxiety disorder, n(%)		14/21(66.7)
Depression disorder, n(%)		12/21(57.1)
Anorexia nervosa, n(%)		1/21(4.8)
The preceding episode of acute dizziness, n(%)		
BPPV, n(%)		27/33(81.8)
Cerebral infarction, n(%)		1/33(3.0)
Neurally mediated syncope, n(%)		1/33(3.0)
Unknown of the cause, n(%)		4/33(12.1)
Decline in ADL, n(%)		27/33(81.8)

Table 4. The Duration of Momentary Worsening Dizziness.

	Less than 1 minute, n(%)	More than 1 minute but less than 10, n(%)	More than 10 minute but less than 60, n(%)	More than 60 minutes, n(%)	No momentary worsening dizziness, n(%)
PPPD (n=33)	23/33(69.7)	8/33(24.2)	2/33(6.1)	0/33(0.0)	0/33(0.0)
Depression (n=55)	0/55(0.0)	2/55(3.6)	2/55(3.6)	4/55(7.3)	47/55(85.5)
Anxiety disorder (n=31)	1/31(3.2)	4/31(12.9)	11/31(35.5)	2/31(6.5)	13/31(41.9)
Somatic symptom disorder (n=11)	0/11(0.0)	0/11(0.0)	0/11(0.0)	0/11(0.0)	11/11(100.0)

PPPD: persistent postural perceptual dizziness

techniques of cognitive-behavioral therapy, we treated 50.0% of patients (13/26) with SSRIs or SNRIs, the effects of which were as follows: recovery in 3/13 cases (23.1%), improvement in 5/13 (38.5%), and no change in 5/13 (38.5%). Patients who only had their disorder explained to them and were not administered SSRIs or SNRIs had the following outcomes: recovery in 2/13 cases (15.4%), improvement in 5/13 (38.5%), and no change in 6/13 (46.2%).

Discussion

Phobic postural vertigo (PPV), a disorder related to PPPD, was proposed in Germany in 1994 and is the second most common disorder in German vertigo statistics, report-

edly accounting for approximately 16% of all cases (4). In this study as well, PPPD accounted for 14% of outpatient cases of chronic dizziness in this department and also accounted for a certain percentage of outpatient cases in general medicine and internal medicine. Furthermore, according to Japanese statistics, vertigo accounts for 20-25% of patients who complain of dizziness (2), and the fact that neither PPV nor PPPD is recognized as a dizziness disorder in Japan may be one reason for the high percentage of cases categorized as “vertigo” of unknown origin category.

In this study, the most common preceding episode of acute dizziness was BPPV at 81.8%. The mechanisms underlying PPPD are believed to be as follows: After an episode of acute dizziness impairs the vestibular apparatus, an

adjustment reaction such as a shift toward prioritizing visual input occurs. As a result, even after the initial acute dizziness disorder has improved, over adjustment in response to visual stimuli or body movement triggers dizziness (5). BPPV is the most common disorder in patients who visit primary care facilities or emergency rooms as outpatients because of dizziness (6). When BPPV is diagnosed, it is important to avoid triggering an over adjustment to visual stimuli and body movement and to prevent a transition to PPPD in advance by providing appropriate treatment and explanations of the symptoms (5).

In this study, PPPD was more common in women, which was similar to the previous report by Adamec et al. (67.9% female) (7). In terms of age, the median age in this study was older than that in the report, 61 years of age (range: 26-87) (7). In addition, the mean age in the previous report by Yagi et al. in Japan was 50 years of age (range: 25-79) (8). In the preceding episode of acute dizziness, BPPV was the most common in this study (81.8%) while vestibular neuritis was most common in the previous reports (39.3% as reported by Adamec et al. and 38.0% as reported by Yagi et al.) (7, 8). Because vestibular neuritis has a younger age of onset compared to BPPV (9, 10), the median age of patients with PPPD in this study may have been higher. In addition, the prognosis of PPPD may be worse if BPPV precedes PPPD because BPPV recurs more frequently than vestibular neuritis. Therefore, the median duration of PPPD in our study (60 months) was longer than the previous report (23 months) (7), and we considered the possibility of some selection bias in the referral of PPPD with a longer duration to our department.

Active or passive motion without regard to direction or position is an exacerbating factor for PPPD in 90.9% of patients, a high percentage. The triggering of symptoms by exposure to moving visual stimuli or complex visual patterns is reported to be a highly specific exacerbating factor that differentiates PPPD from other disorders (8). Although only 15.2% of patients in this study experienced all three factors as exacerbating factors, symptoms were triggered by active or passive motion without regard to direction or position in 90.9% of cases, making this an important factor for PPPD screening.

Chronic dizziness includes dizziness brought on by neurodegenerative diseases and psychogenic dizziness. According to reports, 21% of patients with dizziness who visit primary care facilities as outpatients have psychogenic dizziness (6). Furthermore, when considering cases of chronic dizziness alone, the frequency of psychogenic dizziness is reported to be 93% (11), thus making differentiating between PPPD and psychogenic dizziness a problem. The disorders listed in the DSM-5 that can bring on psychogenic dizziness are depression (a diagnosis of at least one of the following: depressive episodes, recurrent depressive disorder, or dysthymia), anxiety disorder (one of the following disorders or their comorbidities: panic disorder, a specific phobia, generalized anxiety disorder, social anxiety disorder, agora-

phobia, or other unspecified anxiety disorders), and somatic symptom disorder (3). According to diagnostic criteria from the International Society for Neuro-otology, the following points are crucial for differentiating PPPD from other psychogenic disorders: 1. some type of preceding episode of acute dizziness, and 2. clear exacerbating factors (3). Furthermore, momentary worsening and symptoms that come in waves are also distinctive characteristics of PPPD (3), and episodes of PPV, a related disorder, last for seconds or minutes (12). The results of this study show that PPPD is distinctive in that the duration of momentary worsening dizziness is less than 1 minute in 69.7% of cases and less than 10 minutes in 93.9% of cases. Meanwhile, dizziness in cases of depression and somatic symptom disorder is differentiated by the fact that there is no momentary worsening, and in cases of anxiety disorder, the duration of momentary worsening dizziness was less than 10 minutes in only 16.1% of patients (5/31), suggesting that the duration may be useful in differentiating these conditions from PPPD. When there is momentary worsening dizziness, it is important for physicians to differentiate PPPD from depression or anxiety disorder. The comparisons between the PPPD and depression, as well as PPPD and anxiety disorder with the duration of momentary worsening dizziness of less than 10 minutes or not showed a significant difference ($p < 0.001$) for the groups and the odds ratios were 46.5 (95% CI: 6.1-362.0) and 40.3 (95% CI: 7.4-219.3), respectively. These results suggest that in chronic dizziness patients, the duration of momentary worsening dizziness, less than 10 minutes, can be useful clinical information for differentiating between PPPD and psychogenic dizziness.

While the definition of PPV includes comorbid conditions such as anxiety disorder, phobias, and depression, the definition of PPPD does not include organic vestibular disease or mental illnesses despite the fact that these conditions sometimes accompany PPPD. In this study, there were no coexisting mental illnesses in 36.4% of cases. Because PPPD symptoms can bring on significant distress and functional impairment even without any coexisting mental illness (5), any accompanying avoidant behavior or limitations on ADL should be taken into consideration, even in the absence of anxiety disorder or adjustment disorder.

Treatments that have been reported to be effective for PPPD are drug therapy with SSRIs or SNRIs (even without comorbid depression or anxiety), vestibular rehabilitation, and psychotherapy such as cognitive-behavioral therapy (13, 14). In terms of the outcomes in this study, we observed no difference in the treatment effects between the patients administered SSRIs or SNRIs and the patients not administered these medications. However, more than 50% of the patients in the study either recovered or saw an improvement, and psychotherapy, such as cognitive-behavioral therapy including an explanation of the condition, may have alleviated the symptoms. Accordingly, if some cases of vertigo of unknown origin could be diagnosed as PPPD, it would be possible to produce detailed treatment plans for them.

This study is associated with several limitations. First, this study is a retrospective, observational study, and has not been validated at other clinical settings. Considering the limitation, we need to obtain prospective external validations in other multicenter settings. Second, BPPV and vestibular dysfunction must be strictly excluded. However, there is a possibility that BPPV could not be completely excluded because we could not check the positional nystagmus testing and supine positional testing using a CCD camera with infrared illumination over Frenzel glasses at the time that PPPD was diagnosed (15, 16). In addition, vestibular dysfunction cannot be completely excluded because we could not check the quantifiable video-head impulse test or caloric test by at the time of diagnosis of PPPD (17, 18). Third, the telephone interviews used to determine outcomes had a response rate of 78.8%, and it is possible that there was some sampling bias for the treatment outcomes. Fourth, because all patients were provided with cognitive-behavioral therapy that included reassurance, we were unable to evaluate the independent treatment effects of SSRIs/SNRIs.

Conclusion

PPPD accounted for 14% of the outpatient cases of chronic dizziness in this department. These results suggest that short episodes of momentary worsening dizziness (69.7% lasting less than 1 minute, 93.9% lasting less than 10 minutes). Regarding the comparison of PPPD and depression or anxiety disorder, less than 10 minutes momentary worsening dizziness, a distinctive feature of PPPD, may be useful for differentiating PPPD from other types of psychogenic dizziness. The results also suggest that carefully explaining this disorder to patients may lead to an improvement in symptoms.

The authors state that they have no Conflict of Interest (COI).

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