Persistent Postural-Perceptual Dizziness

Review and Update on Key Mechanisms of the Most Common Functional Neuro-otologic Disorder

Jeffrey P. Staab, MD, MS[a,b,*]

KEYWORDS

• Functional dizziness • Functional neurological disorder • Locomotion
• Persistent postural-perceptual dizziness • Perception of motion • Postural control
• Spatial orientation

KEY POINTS

- Persistent postural-perceptual dizziness (PPPD) is the most common chronic neuro-otologic disorder in primary care settings, neurologic practices, and specialized dizziness clinics.
- PPPD is a functional neuro-otologic (vestibular) disorder, a recognized subtype of functional neurological disorder. Its primary pathophysiologic processes are alterations in functioning of neurologic systems that manage postural control, locomotion, and spatial orientation.
- PPPD is precipitated by various conditions that cause vestibular symptoms or disrupt balance and promoted by excessive body vigilance, aberrant illness–related beliefs, and overreliance on visual cues for spatial orientation.
- Emerging data suggest that PPPD is perpetuated by misperceptions of motion that shift top-down priorities from controlling fluid locomotion to maintaining postural stability.
- Treatment with individualized vestibular rehabilitation exercises, serotonin reuptake inhibitors, and cognitive behavioral therapy alone or in combination reduces the substantial handicap of PPPD for most patients.

[a] Department of Psychiatry and Psychology, Mayo Clinic, 200 1st Street Southwest, Rochester, MN 55905, USA; [b] Department of Otorhinolaryngology–Head and Neck Surgery, Mayo Clinic, 200 1st Street Southwest, Rochester, MN 55905, USA
* Department of Psychiatry and Psychology, Mayo Clinic, 200 1st Street Southwest, Rochester, MN 55905.
E-mail address: staab.jeffrey@mayo.edu

Neurol Clin 41 (2023) 647–664
https://doi.org/10.1016/j.ncl.2023.04.003 **neurologic.theclinics.com**

INTRODUCTION

Persistent postural-perceptual dizziness (PPPD) was defined as a chronic functional neuro-otologic (vestibular) disorder for the International Classification of Vestibular Disorders in 2017[1] and International Classification of Diseases, 11th edition in 2022.[2] Its core symptoms are nonvertiginous dizziness, unsteadiness, and swaying or rocking (nonspinning) vertigo that are present most hours of the day, most days of the week (**Box 1**, criterion A). Patients describe their dizziness as heavy-, light-, or foggy-headedness and unsteadiness as wobbling, swaying, or rocking, which may not be observable by others. Some patients report subtle illusions that fixed objects in the environment are not quite still. Once PPPD is established, symptoms are exacerbated by upright posture (sitting or standing), active and passive movement, and exposure to environments with complex or moving visual stimuli (see **Box 1**, criterion B). A recent study of patients examined within 90 days of new-onset vestibular symptoms found that 50% experienced difficulties with at least one of these exacerbating factors, but hypersensitivity to all 3 was strongly associated with development of PPPD.[3] PPPD may be precipitated by peripheral or central vestibular disorders, other medical conditions, and periods of psychological distress (see **Box 1**, criterion C) that can cause vestibular symptoms or disrupt balance. The proportions of these precipitants were examined in 2 cross-sectional investigations of patients with chronic subjective dizziness, a predecessor of PPPD,[4,5] and 2 retrospective studies of patients meeting criteria for PPPD.[6,7] Peripheral or central vestibular disorders (eg, benign paroxysmal positional vertigo, unilateral peripheral vestibulopathies, stroke)

Box 1
Diagnostic criteria for persistent postural-perceptual dizziness from the International Classification of Vestibular Disorders

A. One or more symptoms of dizziness, unsteadiness, or nonspinning 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 3 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.

Reprinted from Staab JP, Eckhardt-Henn A, Horii A, Jacob R, Strupp M, Brandt T, Bronstein A (2017) Diagnostic criteria for persistent postural-perceptual dizziness (PPPD): Consensus document of the committee for the Classification of Vestibular Disorders of the Barany Society. J Vestib Res 27(4):191-208 with permission of IOS Press and the authors.

triggered PPPD in 21% to 25% of patients. Neurologic illnesses also triggered about one-quarter of cases, although specific diagnoses varied among studies: vestibular migraine (11%–25% of patients), mild traumatic brain injury (3%–15%), and dysautonomias (1%–7%). Psychiatric disorders, particularly panic and generalized anxiety disorders, were identified in 20% to 25% of patients in 3 studies,[4–6] with a higher rate of 42% in the fourth report.[7] Medical conditions including paroxysmal cardiac dysrhythmias and metabolic illnesses precipitated 3% to 11% of cases. To warrant a diagnosis of PPPD, patients must have distressing or impairing symptoms (see **Box 1**, criterion D). The final criterion (see **Box 1**, criterion E) ensures proper consideration of patients' entire clinical presentations in making final diagnoses by ruling PPPD in (or out), either as a sole diagnosis or coexisting with other illnesses.[1,8,9] A diagnosis of PPPD, similar to diagnoses of other functional neurological disorder subtypes,[10] is made by positively identifying its key features. Criterion E does not mean that PPPD is a diagnosis of exclusion.[1,8,9]

EPIDEMIOLOGY

After PPPD was defined in 2017, 5 studies gave information about its prevalence in clinical settings.[11–15] Among adults in primary care, 14.4% of 229 patients presenting to a general internal medicine clinic with chief complaints of vestibular or balance symptoms were diagnosed with PPPD.[16] Among adults in neurology clinics, studies from 3 countries,[11–13] including 2 that were quite large (N = 9200, N = 21,267),[12,13] found a remarkably consistent point prevalence of 20% (range 19.0%–21.8%) in patients referred for vestibular complaints. Among adults in a dedicated multidisciplinary dizziness clinic, 53.4% of 292 patients with chronic dizziness had PPPD either as their sole diagnosis (9.2%) or more commonly coexisting with other illnesses (44.2%).[14] Among children and adolescents in a tertiary pediatric balance clinic, 7.3% of 1021 patients were diagnosed with PPPD.[15] In a nonclinical study,[17] situations that exacerbate symptoms of PPPD, such as self-motion and exposure to moving visual stimuli (see **Box 1**, criterion B), also bothered substantial portions (10%–50%) of people without neuro-otologic diagnoses (cohorts of research volunteers, students, paid on-line survey participants). To date, no systematic epidemiologic investigations of PPPD have been conducted in the general population.

In studies of adult patients with PPPD, average ages ranged from 53 to 59 years and women outnumbered men by 2:1,[11,13,14] which is consistent with data on patients with phobic postural vertigo[18] and chronic subjective dizziness.[4] In one study of children, adolescents, and young adults, the average age was 14.6 years (range 8–22 years) and women outnumbered men by 5:1.[15]

The incidence of PPPD following precipitating events is unknown but may be estimated from a systematic review of 13 prospective and retrospective investigations predating publication of the definition of PPPD. These studies examined chronic PPPD-like dizziness following acute vestibular syndromes, mostly vestibular neuritis and benign paroxysmal positional vertigo, in 780 patients.[18] The percentage of patients in whom dizziness persisted for at least 3 months after inciting illnesses ranges from 7.5% to 53% (weighted mean of 26.3%). A retrospective review of patients who presented to a tertiary neurotology center within 90 days of new-onset vestibular symptoms suggested that the incidence of PPPD could be at the lower end of that range.[3] In that study, only 8/155 (5.2%) patients developed PPPD over 18 months of follow-up. Seven of eight patients met criteria for PPPD at the time of their initial evaluations except for the 3-month duration of illness, suggesting that PPPD may consolidate within a short period of time after precipitating illnesses for most patients

who develop the disorder. If this finding is verified in future investigations, then it would inform strategies for early identification of patients at risk for PPPD, potentially minimizing long-term disability and secondary psychiatric comorbidity.[19,20]

DIAGNOSTIC CONSIDERATIONS

The initial clinical course of PPPD depends on the nature of precipitating illnesses. When triggered by acute vestibular syndromes (eg, vestibular neuritis), symptoms of PPPD begin to consolidate as the acute illnesses resolve.[1,3] Patients do not have asymptomatic intervals. Instead, their symptoms evolve from acute vertigo of precipitating illnesses into chronic nonvertiginous symptoms and hypersensitivities of PPPD. When precipitants are episodic vestibular syndromes (eg, benign paroxysmal positional vertigo, vestibular migraine, panic disorder), symptoms of PPPD may begin in full after the first attack, such that patients have no symptom-free intervals between attacks, or they may occur transiently at first, and then gradually extend throughout interictal periods until they consolidate into the disorder.[1] The least common cases are precipitated by chronic conditions such as degenerative neurologic or otologic disorders or gradually worsening generalized anxiety disorder or postural orthostatic tachycardia syndrome that often begin insidiously. In such cases, onset of hypersensitivity to complex or moving visual stimuli when patients are stationary may presage PPPD because this clinical feature would not be expected in other chronic disorders that cause persistent vestibular or balance symptoms.[1,8,9] Some investigators have used the term "primary" PPPD to denote its onset in patients without identifiable structural neurologic or otologic precipitants.[6] This unfortunate designation overlooks "other medical illnesses or periods of psychological distress,"[1] especially the latter, as possible triggers. The experience of this investigator's multidisciplinary team composed of otologists, neurologists, audiologists, physical therapists, psychiatrists, and psychologists suggests that specific precipitants of PPPD can be found in more than 90% of cases, with exceptions typically representing patients with unclear early histories and insufficient medical records to identify precipitants with certainty.[5]

Incorporating 2 self-report questionnaires, the well-known Dizziness Handicap Inventory (DHI)[21] and the new Niigata PPPD Questionnaire (NPQ),[22] into initial evaluations of patients with vestibular and balance symptoms may help to identify those with PPPD. In a retrospective study of patients with chronic vestibular symptoms, DHI scores greater than 60 were highly specific (specificity = 0.88) for the presence of functional or psychiatric vestibular disorders, particularly PPPD, whereas scores less than or equal to 30 were highly specific (specificity = 0.98) for their absence.[23] A similarly high specificity for the presence of PPPD with DHI scores greater than 60 was found in data reported by Staibano and colleagues[14] The 12-item NPQ focuses on the 3 exacerbating factors of PPPD (criterion B). In a retrospective study of patients examined within 3 months of new-onset vestibular symptoms, NPQ scores greater than or equal to 27 were highly sensitive (sensitivity = 0.88) but not very specific (specificity = 0.52) for identifying individuals at risk for PPPD.[3] If these results are validated in future studies, then the NPQ could be used as a sensitive screening tool for detecting PPPD among patients with subacute vestibular symptoms, whereas the DHI could aid identification of PPPD with high specificity in patients with chronic vestibular complaints.

DIFFERENTIAL DIAGNOSIS

The defining manuscript for PPPD details its differential diagnosis.[1] Pitfalls include attributing chronic symptoms to previous acute or active episodic vestibular

syndromes and overlooking coexisting PPPD when other chronic illnesses are present. When PPPD is triggered by acute vestibular syndromes, the diagnostic challenge is to determine if the acute syndrome has resolved completely or the patient has compensated fully for residual vestibular deficits. For episodic vestibular syndromes, the challenge is to recognize the pattern of recurrent attacks of vestibular symptoms lasting seconds (benign paroxysmal positional vertigo, vestibular paroxysmia), minutes (panic attacks), hours (Menière disease, vestibular migraine), or days (vestibular migraine) superimposed on PPPD. For chronic triggers, the challenge is to determine if coexisting PPPD has developed.[1,8,9] As noted earlier, the presence of visually induced dizziness when patients are stationary can be helpful.[9] The diagnostic criteria of PPPD do not include symptoms or signs of altered stance or gait, near falls, or falls, so the presence of any of these merits consideration of structural, metabolic, and functional gait disorders.[9]

INVESTIGATIONS OF PERSISTENT POSTURAL-PERCEPTUAL DIZZINESS

Pathophysiologic models of PPPD matured through 3 iterations. Evidence from physiologic, psychological, and neuroimaging investigations of predecessors of PPPD and PPPD itself has converged around 7 processes: (1) possible predisposition by an anxiety diathesis; (2) promotion by anxiety-related responses to precipitating events; (3) altered control of posture, gait, and gaze; (4) visual dependence; (5) poor spatial cognition; (6) altered activity and connectivity in vestibular and visual cortices, hippocampus, and frontal lobes; and most recently, (7) misperception of motion.

Trait and state anxiety—obsessive compulsive personality traits were part of the definition of phobic postural vertigo.[24] Two cross-sectional studies of patients with chronic subjective dizziness[25,26] and one of patients with PPPD[27] found elevated levels of neurotic personality traits compared with patients with other vestibular disorders,[25,26] healthy volunteers,[26] and population norms.[27] In a complementary prospective study,[28] patients with personality traits opposite of neuroticism, namely higher resilience and sense of coherence, were less likely to develop chronic dizziness following acute or episodic vestibular disorders than those without these protective characteristics. However, unpublished data from a large cohort of patients with PPPD did not find any personality traits outside of population norms (Korean Balance Society Multicenter Working Group 2020. The characteristics of persistent postural perceptual dizziness in Korea. XXXI Bárány Society Congress, Madrid, Spain, May 2022, poster FP1225).

Some investigations predating PPPD found that patients with preexisting personal or family histories of anxiety disorders were at increased risk of developing chronic dizziness after acute vestibular syndromes[29–31] but others did not.[32,33] One observational study suggested that patients with preexisting anxiety disorders had increased risk of prolonged anxiety after experiencing acute vestibular syndromes.[31]

Body vigilance and negative illness perceptions—in studies predating PPPD[30,32,34] and one pilot study of patients with PPPD,[35] heightened body vigilance (ie, conscious attention to sensations of dizziness and unsteadiness) and negative illness perceptions (eg, worrisome thoughts about causes, consequences, and controllability of vestibular symptoms) were the psychological factors most strongly associated with persistence of dizziness following acute or episodic vestibular syndromes. Another study found that these factors were associated with severity of dizziness-related handicap.[36]

Altered control of stance, gait, and gaze—a consistent picture emerged about changes in postural control and gait from studies of patients with PPPD and its

predecessors. Patients with phobic postural vertigo[37] and chronic subjective dizziness[38] stiffened their stance by cocontracting lower leg muscles. Patients with phobic postural vertigo had lower thresholds than normal individuals for engaging closed-loop feedback to control posture.[39] Stiffening the lower body increased sway in the upper body in a portion of patients with chronic subjective dizziness during static posturography[38] and in nearly all patients with PPPD on conditions 5 and 6 of the Sensory Organization Test.[40] Compared with normal individuals, patients with phobic postural vertigo had slower mean gait speed, shorter mean stride length, a wider base of support, and fractional increase in duration of 2-footed support while walking.[41] Their gaze shifts were 25% slower than normal, with end-gaze oscillations indicative of overcontrolled movement.[42]

Visual dependence—visual dependence is the tendency to rely more strongly on visual than vestibular or somatosensory inputs to determine spatial orientation. In a prospective study,[32] the combination of visual dependence and high body vigilance recorded within 48 hours of onset of acute vestibular neuritis predicted persistent PPPD-like chronic dizziness rather than recovery at 6 month. In a cross-sectional study,[43] patients with PPPD performed poorer than healthy controls on a measure of visual dependence.

Cognition—patients with PPPD performed quite poorly on the virtual Morris Water Maze test, which assesses spatial navigation and memory.[44] Their ability to use visual cues to navigate was worse than patients with unilateral vestibular deficits and healthy control volunteers. Patients with PPPD scored worse than patients with vestibular migraine, Menière disease, and benign paroxysmal positional vertigo and poorer than population norms on the Cognitive Failure Questionnaire, a self-report of momentary cognitive slips, absent-mindedness, and inattentiveness,[45] suggesting that patients with PPPD divert cognitive resources from spatial orientation and other valued activities to heightened vigilance about dizziness and conscious control of posture.

Neuroimaging—a recent review summarized results from 13 neuroimaging studies on patients with PPPD and its predecessors.[46] They included 4 resting state and 6 task-related (sound-evoked or caloric vestibular stimulation, virtual reality visual stimulation) functional brain imaging studies. All but one compared patients with healthy controls; the other compared women with PPPD with women who had recovered from acute illnesses that caused dizziness. Three studies investigated brain structure in patients versus healthy controls using surface-based or voxel-based morphometry. Despite differing patient populations and neuroimaging methods, a common pattern of decreased activity and functional connectivity in patients versus controls was found in areas associated with the multimodal vestibular cortex (eg, right posterior insula, parietal operculum, and surrounding regions), with reduced cortical folding and grey-matter volumes in these areas. Hippocampal connectivity to frontal, parietal, and cerebellar regions also was decreased. In contrast, connectivity between the prefrontal cortex and primary visual and motor regions was increased in patients versus controls, modulated by state anxiety and neuroticism. In a task-related functional MRI (fMRI) study comparing women with PPPD to an age-matched cohort that recovered from acute dizziness, standardized pictures designed to evoke negative versus neutral emotions activated brain regions associated with visuospatial processing (parahippocampal gyrus, intraparietal sulcus) rather that emotion processing (amygdala, orbitofrontal cortex) in patients with PPPD. The comparison group showed the expected activation of the amygdala.[47]

Altered perception of motion—patients with PPPD had lower thresholds than normal individuals for perceiving rotation[48] and misperceived (overestimated) both

head tilt[49] and postural sway amplitude, the latter to a greater extent than patients with bilateral vestibulopathy and normal individuals standing on foam.[50]

PATHOPHYSIOLOGIC MODELS

The first pathophysiologic model of PPPD was derived from hypotheses about mechanisms underlying its predecessors.[5,8] It focused on high trait and state anxiety as triggers for a shift to high-risk postural control (stiffened posture and visual dependence). However, PPPD may occur in patients without identifiable anxiety, and the fMRI study using emotional pictures indicated that patients with PPPD may respond more to spatial than emotional aspects of visual stimuli.[47]

Work undertaken after the definition of PPPD was published found that patients had a reduced threshold for detecting motion and misperceived their own motion.[48–50] In addition, physiologic studies identified the importance of interhemispheric processing to resolve spatial and temporal ambiguities in data from peripheral vestibular organs, leading to a second-generation model.[51] It included Bayesian processing, alterations in self-agency, and top-down control of reflexive and overlearned behaviors, which also appeared in models of other functional neurological disorder subtypes.[52] This model brought attentional bias and misperception of motion to the forefront, which was consistent with patients' experiences and research data but left unexplained the curious observation of poor spatial orientation on the virtual Morris Water Maze test[44] and corresponding neuroimaging data showing reduced connectivity in the hippocampus.[46]

A third-generation model (**Fig. 1**) added an element that incorporated findings about spatial orientation. Hierarchical, adaptive systems, such as those supporting spatial orientation and locomotion, require master controllers. In optimal control theory, master controllers contain cost functions that enumerate constraints and prioritize key parameters to optimize performance of specific tasks.[53] **Table 1** compares cost functions for postural stability and fluid locomotion. These cost functions differ substantially, meaning that standing and walking are driven by different sets of top-down commands. Maintaining stance in low- versus high-risk situations also differs in ways that were investigated in healthy volunteers standing at ground level versus on elevated platforms.[54,55] In the optimal control model of **Fig. 1**, misperception of motion breaks the time constraint of using high-risk postural control transiently (ie, only when needed, **Table 1**), thereby limiting normal flexibility in shifting sets. The cost function for high-risk postural control restricts the focus of spatial orientation to immediate surroundings of the support surface because stabilizing stance does not require operations outside this narrow envelope. Patients stuck in high-risk postural control have little need to engage brain networks supporting orientation in a broader environment. Indeed, patients with phobic postural vertigo restricted their gaze to nearby objects when walking,[49,56] indicating that they applied elements of high-risk postural control to locomotion. Persistent application of the cost function for high-risk postural control maintains priorities on postural stability over fluid locomotion. **Table 2** shows how this third-generation model of PPPD aligns symptoms commonly reported by patients with research findings from physiologic, psychological, and neuroimaging investigations.

TREATMENT

Treatment strategies for PPPD were carried over from phobic postural vertigo and chronic subjective dizziness including vestibular rehabilitation, serotonin reuptake inhibitors, and cognitive behavioral therapy, either alone or in combination (see Refs.[5,8,9]

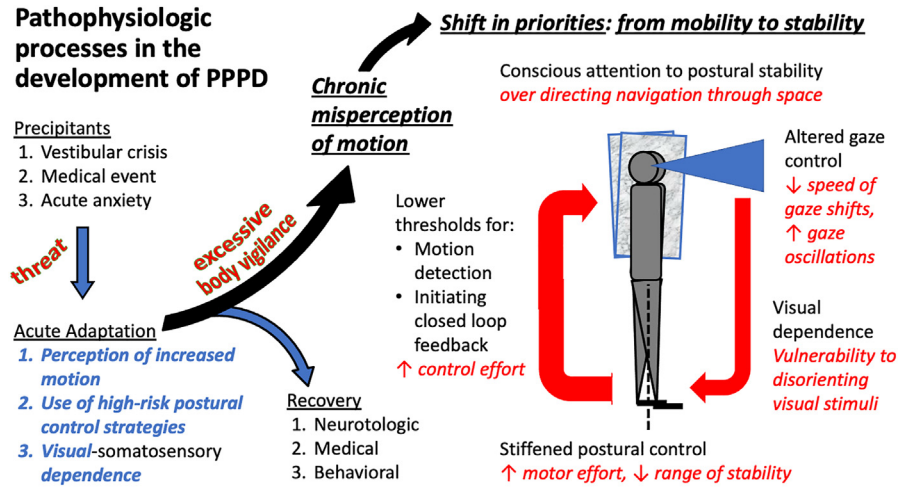

Fig. 1. Model of the pathophysiologic processes presumed to precipitate, provoke, and perpetuate PPPD. Following the arrows from the top left, PPPD may be triggered by any condition that causes vestibular symptoms or disrupts balance. The threat to postural stability inherent in these conditions prompts physiologic shifts that include heightened sensitivity to motion, engagement of high-risk postural control strategies, and preference for visual cues to determine spatial orientation and guide locomotion. Under normal circumstances, these return to normal as the inciting event resolves or remits. In the setting of excessive body vigilance, however, altered sensitivities to self- and object motion become chronic, as patients instinctively shift their priority from fluid locomotion to stabilization of perceived excessive postural sway. With that, as shown around the silhouette, attention to the dynamics of postural stability predominates over a natural focus on spatial orientation and locomotion through the wider world with resultant overcontrol of posture and gaze and continued overreliance on visual inputs.

for detailed reviews). No fully powered, randomized controlled trials have been completed to date, but since 2002 more than 1000 patients have been included in studies of these 3 treatments for PPPD and its predecessors. Studies in patients diagnosed with PPPD are summarized next.

Vestibular rehabilitation—in a retrospective review and telephone follow-up of 26 patients with PPPD, nearly all participants valued the educational component of a single in-person clinic visit and 14 (56%) reported clinically significant benefits from subsequent at-home exercises.[57] Patients improved their tolerance for self-motion more than visual stimuli. A randomized pilot study found no difference between outcomes of 15 patients treated with home-based vestibular exercises versus 15 treated in-clinic.[58] Mean improvements at 12 weeks were just at the minimal clinically important difference (MCID) of 18 points on the DHI. In a prospective study of 6 weeks of therapist-directed vestibular rehabilitation, 60 patients achieved a mean reduction of DHI scores from 55 (high-moderate handicap) to 36 (low-moderate handicap), exceeding the MCID. Twenty-seven patients (45%) achieved final DHI scores less than 30 (mild handicap).[59] In a randomized pilot trial, investigators tested the feasibility of psychologically informed vestibular rehabilitation, which combined cognitive behavior therapy techniques (eg, psychoeducation, relaxation training, reframing of excessive attention to posture and movement), with vestibular exercises targeting maladaptive postural control strategies and motion sensitivity (N = 20) versus standard vestibular

Table 1
Comparison of cost functions for postural stability versus fluid locomotion

Variable	Standing (Low Risk)	Standing (High Risk)	Walking Smoothly
Constraints *(on movement)*	• Sway path constrained at limits of stability. • Specific path not relevant.	• Sway path constrained within narrower (safer) limits. • Specific path not relevant.	Path optimized: • To reach target *or* • Maintain desired trajectory *and* • Avoid obstacles
Set point or target *(spatial orientation)*	• Gravity *(static)*	• Gravity *(static)*	• Trajectory *(dynamic)*
Data streams and weighting *(sensory inputs)*	• Internal data are adequate *(vestibular, proprioceptive)*	• Internal data are adequate *(vestibular, proprioceptive)* • External data are desired *(primarily visual—overweighted)*	• External data are required *(primarily visual)*
Operating envelope *(environment)*	• Support surface *(narrow)*	• Support surface *(narrow)*	• Path and destination *(wide)*
Tolerance for error *(trigger for input from controller)*	• High	• Low	• Variable
Duration	• Not constrained	• Transient *(typically momentary)*	• Not constrained
Energy expenditure	• Minimized	• Not constrained	• Minimized, adjusted to demand • Constrained by physical fitness

Reprinted from J Vestib Res 27(4), Staab JP, Eckhardt-Henn A, Horii A, Jacob R, Strupp M, Brandt T, Bronstein A, Diagnostic criteria for persistent postural-perceptual dizziness (PPPD): Consensus document of the committee for the Classification of Vestibular Disorders of the Barany Society, 191-208, Copyright (2017), with permission from IOS Press. The publication is available at IOS Press through http://dx.doi.org/10.3233/VES-170622.

Table 2
Effects of shifting control priorities from fluid locomotion to postural stability

Shifts in Functioning	Clinical Symptoms[a]	Physiologic and Psychological Data	Neuroimaging Data[46]
Increased attention to motion	• **Symptoms of dizziness, unsteadiness, and swaying/rocking vertigo** • Mental fatigue—distracting effects of attention to motion	• Increased body vigilance[32,35] • Poor scores on Cognitive Failure Questionnaire[45]	• Reduced *activity* and *connectivity* in regions of the multimodal vestibular cortex[b] in resting state and during vestibular and visual stimulation
Misperception of motion	• **Symptoms exacerbated by active motion** • **Symptoms exacerbated by passive motion**	• Lower threshold for detection of motion of self[48] • Overestimation of head roll[49] • Overestimation of postural sway[50]	• Reduced *activity* in precuneus and cuneus during resting state
Stiffened posture	• **Symptoms exacerbated by upright posture** • Reduced balance confidence	• Smaller static sway area[38] • Reduced limits of dynamic stability[40]	—
Increased postural control effort	• Physical fatigue – increased effort of standing	• Lower threshold for engaging closed loop feedback control[39]	—
Altered gait "walking on ice"	• Physical fatigue—increased effort of walking	• Shorter stride length[41] • Wider base of support[41] • Increased fraction of stride with 2-footed support[41]	—
Visual dependence	• **Symptoms exacerbated by exposure to moving visual stimuli or complex visual patterns**	• Impaired performance on functional head impulse test[43] • Increased deviation of subjective visual vertical[32]	• Increased *activity* in the primary visual cortex (V1, V2, V3) in proportion to symptom severity during visual motion stimulation • Increased *connectivity* between frontal regulatory regions[c] and visual association (V3, V4) cortices modulated by anxiety and neuroticism • Increased *connectivity* between sensorimotor network[d] and occipital visual network[e]

Altered gaze control	• Inertial illusions with gaze shifts • Sensations of stationary objects oscillating slightly in space	• Reduced speed of gaze shifts with end-gaze oscillations[42] • Narrowed gaze range during ambulation[56]	—
Impaired spatial navigation	• Uneasiness in challenging environments	• Impaired performance on virtual Morris Water Maze test[44]	• Decreased *activity* and *connectivity* of hippocampi (L > R) to multiple brain regions

[a] Symptoms in *bold* are included in the diagnostic criteria of PPPD. Others are commonly reported by patients with PPPD.
[b] The multimodal vestibular cortical network includes the right middle and posterior insula, parietal operculum, and posterior perisylvian regions of the temporal and parietal lobes.
[c] Frontal regulatory regions include the inferior frontal gyrus, anterior cingulate gyrus, and anterior insula.
[d] The sensorimotor network includes sensorimotor cortex, supplementary motor area, and secondary somatosensory cortex.
[e] The occipital visual network includes primarily the occipital poles.
Please see the text for additional information on these references.[32,35,38–46,48–50,56]

rehabilitation (N = 20).[60] Acceptability of the enhanced approach was good. Treatment outcomes favored it on cognitive and behavioral variables, although not strongly on vestibular symptoms.

Medication—a retrospective review[61] of 197 patients with PPPD treated with selective serotonin reuptake inhibitors (SSRIs), mostly escitalopram, with or without adjunctive benzodiazepines, mostly clonazepam, found that outcomes mirrored results of older studies,[5,8,9] with 65% of all patients being much improved or very much improved on medication. An 8-week prospective, 2-arm comparison trial of sertraline alone (N = 45) versus sertraline plus cognitive behavioral therapy (CBT) (N = 46) (no inactive control) showed that sertraline alone decreased mean DHI scores from 54 (moderate) to 26 (mild), similar to older studies, whereas sertraline plus CBT decreased mean DHI scores from 54 (moderate) to 15 (mild), a significant improvement over sertraline alone, despite using lower doses of medication.[62] **Table 3** lists dosing strategies for 2 commonly used SSRIs, sertraline and escitalopram, and one commonly used serotonin norepinephrine reuptake inhibitor (SNRI), venlafaxine.

Psychotherapy—Waterston and colleagues[7] conducted a retrospective review of 150 patients with PPPD treated with CBT over a 5-year period, finding a reduction in mean DHI scores from 50 (moderate) to 24 (mild). In a prospective study of 6 weeks of acceptance and commitment therapy (which stems from CBT) plus vestibular rehabilitation, 27 patients with PPPD had a reduction in mean DHI scores from 49 (moderate) to 26 (mild) at 6-month follow-up.[63] **Table 4** lists key principals for vestibular rehabilitation and psychotherapy.

These investigations of patients with PPPD produced results consistent with treatment studies of its predecessors[5,8,9] in finding that vestibular rehabilitation, pharmacotherapy with SSRIs/SNRIs, and psychotherapy with cognitive behavioral techniques reduced mean dizziness-related handicap from moderate (ie, interfering with daily activities) to mild (ie, nagging but not impairing) levels. These treatments may be combined based on clinical circumstances and patients' preferences. Axer and colleagues[64] reported that treatment using individualized combinations started during a week-long intensive outpatient program produced sustained benefits for 305 patients with PPPD at 6-month follow-up.

Emerging treatments (neuromodulation)—the first studies using neuromodulation therapies for PPPD were completed with mixed results. Eren and colleagues[65] treated 16 patients for 4 weeks with noninvasive vagal nerve stimulation scheduled twice daily and when needed for symptom flares. Participants experienced statistically significant improvements in quality of life and coexisting depressive symptoms (reduced from mild at baseline) but had limited improvement in PPPD symptoms (only 1 of 3 metrics

Table 3
Dosing strategies for selected serotonergic medications for persistent postural-perceptual dizziness

Medication	Initial Dose[a]	Titration Schedule	Maintenance Dose[b]
Sertraline	12.5–25 mg daily	25 mg every 2 wk	50–200 mg daily
Escitalopram	2.5–5 mg daily	5 mg every 2 wk	10–20 mg daily
Venlafaxine XR	37.5 mg daily	37.5 mg every 2 wk	75–225 mg daily

[a] Lower starting doses may be needed for patients who report sensitivity to medications.
[b] Continue maintenance medication for a minimum of 1 year (see text for details). Higher maintenance doses may be needed for patients with comorbid anxiety or depressive disorders.

Table 4
Targets for physical and psychological rehabilitation for persistent postural-perceptual dizziness

Symptom	Intervention
Conscious attention to posture and motion (excessive body vigilance)	• Cognitive reframing • Mental relaxation (eg, imagery)
Stiffened postural control (usually present) Functional stance abnormalities (may coexist)	• Muscle relaxation or distraction (eg, simple mental tasks) while standing • Normalize natural sway and weight distribution
Altered gait and gaze (when present)	• Muscle relaxation or distraction (eg, simple mental tasks) while walking • Normalize natural gait with and without head and eye movements, to include balance confidence exercises when needed
Visually induced dizziness	• Habituation exercises—exposure to increasingly complex or moving visual stimuli (in vivo and virtual reality options) and performance of tasks requiring precise visual focus (reading printed materials, use of devices with electronic screens)
Reduced involvement in activities (usually present)	• Exposure schedule—gradually restore engagement in necessary and valued activities

reached statistical significance), although 1 of 2 measures of postural sway improved significantly. Im and colleagues[66] treated 12 patients with PPPD using transcranial direct current stimulation (tDCS) applied to the left dorsolateral prefrontal cortex (lDLPFC) for 20 minutes, 5 times per week, for 3 weeks. When compared with 12 patients randomized to the same course of sham treatments, active tDCS produced no differences in dizziness handicap, balance confidence, anxiety, or depressive symptoms posttreatment or at 1- or 3-month follow-ups. As of this writing, one small trial of repetitive transcranial magnetic stimulation of the lDLPFC was completed with results forthcoming.

The pathophysiologic model of **Fig. 1** offers insights for advancing treatment of PPPD. It suggests that patients may need specific interventions (physiotherapy or psychotherapy) to counter misperceptions of motion. San Pedro Murillo and colleagues[50] reported anecdotal benefits from showing patients video feedback of their perceived versus observed sway. The model also offers a framework for hypothesizing about bottom-up and top-down sites of action of SSRIs/SNRIs, given studies finding that serotonin modulated gains of second-order neurons in the vestibular nuclei,[67] serotonin 2A receptors are present in pathways linking vestibular inputs to the amygdala via the parabrachial nuclei,[68] and that administration of SSRIs may influence spatial working memory,[69] sustained attention,[70] and choices about gathering data versus taking action.[68,71]

SUMMARY

Formal diagnostic criteria for PPPD were included in the International Classification of Vestibular Disorders and the International Classification of Diseases, 11th edition.

Clinical epidemiologic studies found PPPD to be the most common cause of chronic dizziness in primary care (14% of all patients with chief complaints of vestibular symptoms), neurologic clinics (20% of all patients with chief complaints of vestibular symptoms), and specialized dizziness centers (>50% of all patients). Physiologic studies identified multiple alterations in functioning of postural control and spatial orientation systems, and neuroimaging investigations found changes in activity and connectivity in brain regions associated with these crucial components of locomotion. Conceptual models of PPPD continue to evolve in sophistication, now offering better insights into pathophysiologic mechanisms that may lead to refinements in physical therapy, psychotherapy, medication management, and neuromodulation.

CLINICS CARE POINTS

- PPPD is the most common cause of chronic vestibular symptoms in medical settings from primary care to subspecialty clinics. It should be at the top of the differential diagnosis for patients with persistent vestibular and balance complaints.
- PPPD must be ruled in using its diagnostic criteria. It is not a diagnosis of exclusion. Guidance for working through the differential diagnosis of potential precipitants and coexisting conditions may be found in the open access (free) manuscript that defined PPPD, available at https://content.iospress.com/articles/journal-of-vestibular-research/ves622.
- Treatment with individualized vestibular rehabilitation, a moderate dose of an SSRI or SNRI, and cognitive behavioral therapy, alone or in combination, reduces symptom severity by greater than 50% in most patients, although it may take 3 to 6 months to achieve that improvement.

DISCLOSURE

Dr J.P. Staab was supported by grant W81XWH1810760 from the US Army Medical Research and Materiel Command via the Congressionally Directed Medical Research Program. He had no commercial or financial conflicts of interest.

REFERENCES

1. Staab JP, Eckhardt-Henn A, Horii A, et al. Diagnostic criteria for persistent postural-perceptual dizziness (PPPD): Consensus document of the committee for the Classification of Vestibular Disorders of the Barany Society. J Vestib Res 2017;27(4):191-208. Available at https://content.iospress.com/articles/journal-of-vestibular-research/ves622 and can be downloaded free of charge. Accessed March 26, 2023.
2. World Health Organization. AB32.0 Persistent Postural-Perceptual Dizziness. In: ICD-11 for Mortality and Morbidity Statistics (Version: 01/2023). Available at: https://icd.who.int/browse11/l-m/en#/http://id.who.int/icd/entity/2005792829 Accessed March 26, 2023.
3. Kabaya K, Tamai H, Okajima A, et al. Presence of exacerbating factors of persistent perceptual-postural dizziness in patients with vestibular symptoms at initial presentation. Laryngoscope Investig Otolaryngol 2022;7(2):499–505.
4. Staab JP, Ruckenstein MJ. Expanding the differential diagnosis of dizziness. Arch Otolaryngol Head Neck Surg 2007;133:170–6.
5. Staab JP. Behavioural neuro-otology. In: Bronstein AM, editor. Oxford textbook of vertigo and imbalance. Oxford, UK: Oxford University Press; 2013. p. 333–46.

6. Habs M, Strobl R, Grill E, et al. Primary or secondary chronic functional dizziness: Does it make a difference? A DizzyReg study in 356 patients. J Neurol 2020;267:212–22.
7. Waterston J, Chen L, Mahony K, et al. Persistent postural-perceptual dizziness: Precipitating conditions, co-morbidities and treatment with cognitive behavioral therapy. Front Neurol 2021;12:795516.
8. Dieterich M, Staab JP. Functional dizziness: from phobic postural vertigo and chronic subjective dizziness to persistent postural-perceptual dizziness. Curr Opin Neurol 2017;30(1):107–13.
9. Staab JP. Persistent postural-perceptual dizziness. Semin Neurol 2020;40(1):130–7.
10. Hallett M, Aybek S, Dworetzky BA, et al. Functional neurological disorder: new subtypes and shared mechanisms. Lancet Neurol 2022;21(6):537–50.
11. Adamec I, Meaški SJ, Skorić MK, et al. Persistent postural-perceptual dizziness: Clinical and neurophysiological study. J Clin Neurosci 2020;72:26–30.
12. Xue H, Chong Y, Jiang ZD, et al. Etiological analysis on patients with vertigo or dizziness. Zhonghua Yixue Zazhi 2018;98(16):1227–30.
13. Kim HJ, Lee JO, Choi JY, et al. Etiologic distribution of dizziness and vertigo in a referral-based dizziness clinic in South Korea. J Neurol 2020;267:2252–9.
14. Staibano P, Lelli D, Tse D. A retrospective analysis of two tertiary care dizziness clinics: a multidisciplinary chronic dizziness clinic and an acute dizziness clinic. J Otolaryngol Head Neck Surg 2019;48:11.
15. Wang A, Fleischman KM, Kawai K, et al. Persistent postural-perceptual dizziness in children and adolescents. Otol Neurotol 2021;42(8):e1093–100.
16. Ishizuka K, Shikino K, Yamauchi Y, et al. The clinical key features of persistent postural perceptual dizziness in the general medicine outpatient setting: A case series study of 33 patients. Intern Med 2020;59(22):2857–62.
17. Powell G, Derry-Sumner H, Rajenderkumar D, et al. Persistent postural perceptual dizziness is on a spectrum in the general population. Neurology 2020;94(18):e1929–38.
18. Trinidade A, Cabreira V, Goebel JA, et al. Predictors of persistent postural-perceptual dizziness (PPPD) and similar forms of chronic dizziness precipitated by peripheral vestibular disorders: a systematic review. J Neurol Neurosurg Psychiatry 2023. https://doi.org/10.1136/jnnp-2022-330196.
19. Huppert D, Strupp M, Rettinger N, et al. Phobic postural vertigo – a long-term follow-up (5 to 15 years) of 106 patients. J Neurol 2005;252:564–9.
20. Staab JP. Chronic subjective dizziness. Continuum: Lifelong Learning in Neurology (Minneap Minn) 2012;18:1118–41.
21. Jacobson GP, Newman CW. The development of the Dizziness Handicap Inventory. JAMA Otolaryngol Head Neck Surg 1990;116:424–7.
22. Yagi C, Morita Y, Kitazawa M, et al. A validated questionnaire to assess the severity of persistent postural-perceptual dizziness (PPPD): The Niigata PPPD Questionnaire (NPQ). Otol Neurotol 2019;40:e747–52.
23. Graham MK, Staab JP, Lohse CM, et al. A comparison of dizziness handicap inventory scores by categories of vestibular diagnoses. Otol Neurotol 2021;42(1):129–36.
24. Brandt T, Dieterich M. Phobischer Attacken Schwankschwindel, ein neues Syndrom? Munch Med Wschr 1986;28:247–50.
25. Staab JP, Rohe DE, Eggers SD, et al. Anxious, introverted personality traits in patients with chronic subjective dizziness. J Psychosom Res 2014;76(1):80–3.

26. Chiarella G, Petrolo C, Riccelli R, et al. Chronic subjective dizziness: Analysis of underlying personality factors. J Vestib Res 2016;26(4):403–8.
27. Yan Z, Cui L, Yu T, et al. Analysis of the characteristics of persistent postural-perceptual dizziness: A clinical-based study in China. Int J Audiol 2016;56:1–5.
28. Tschan R, Best C, Beutel ME, et al. Patients' psychological well-being and resilient coping protect from secondary somatoform vertigo and dizziness (SVD) 1 year after vestibular disease. J Neurol 2011;258:104–12.
29. Best C, Tschan R, Eckhardt-Henn A, et al. Who is at risk for ongoing dizziness and psychological strain after a vestibular disorder? Neuroscience 2019;164:1579–87.
30. Heinrichs N, Edler C, Eskens S, et al. Predicting continued dizziness after an acute peripheral vestibular disorder. Psychosom Med 2017;69:700–7.
31. Staab JP, Ruckenstein MJ. Chronic dizziness and anxiety: Effect of course of illness on treatment outcome. Arch Otolaryngol Head Neck Surg 2005;131(8):675–9.
32. Cousins S, Kaski D, Cutfield N, et al. Predictors of clinical recovery from vestibular neuritis: A prospective study. Ann Clin Transl Neurol 2017;4:340–6.
33. Godemann F, Koffroth C, Neu P, et al. Why does vertigo become chronic after neuropathia vestibularis? Psychosom Med 2004;66(5):783–7.
34. Godemann F, Siefert K, Hantschke-Bruggemann M, et al. What accounts for vertigo one year after neuritis vestibularis—anxiety or a dysfunctional vestibular organ? J Psychiatr Res 2005;39:529–34.
35. Trinidade A, Harman P, Stone J, et al. Assessment of potential risk factors for the development of persistent postural-perceptual dizziness: A case-control pilot study. Front Neurol 2021;11:601883.
36. Wolf J, Sattel H, Limburg K, et al. From illness perceptions to illness reality? Perceived consequences and emotional representations relate to handicap in patients with vertigo and dizziness. J Psychosom Res 2020;130:109934.
37. Krafczyk S, Schlamp V, Dieterich M, et al. Increased body sway at 3.5–8 Hz in patients with phobic postural vertigo. Neurosci Lett 1999;259:149–52.
38. Ödman M, Maire R. Chronic subjective dizziness. Acta Otolaryngol 2018;128:1085–8.
39. Wuehr M, Pradhan C, Novozhilov S, et al. Inadequate interaction between open- and closed-loop postural control in phobic postural vertigo. J Neurol 2013;260(5):1314–23.
40. McCaslin DL, Shepard NT, Hollman JH, et al. Characterization of postural sway in patients with persistent postural-perceptual dizziness (PPPD) using wearable motion sensors. Otol Neurotol 2022;43(2):e243–51.
41. Schniepp R, Wuehr M, Huth S, et al. Gait characteristics of patients with phobic postural vertigo: Effects of fear of falling, attention, and visual input. J Neurol 2014;261:738–46.
42. Schröder L, von Werder D, Ramaioli C, et al. Unstable gaze in functional dizziness: A contribution to understanding the pathophysiology of functional disorders. Front Neurosci 2021;15:685590.
43. Teggi R, Gatti O, Cangiano J, et al. Functional head impulse test with and without optokinetic stimulation in subjects with persistent postural perceptual dizziness (PPPD): Preliminary report. Otol Neurotol 2020;41:e70–5.
44. Breinbauer HA, Contreras MD, Lira JP, et al. Spatial navigation is distinctively impaired in persistent postural perceptual dizziness. Frontiers Neurol 2020;10:1361.

45. Rizk HG, Sharon JD, Lee JA, et al. Cross-sectional analysis of cognitive dysfunction in patients with vestibular disorders. Ear Hear 2020;41:1020–7.
46. Indovina I, Passamonti L, Mucci V, et al. Brain correlates of persistent postural-perceptual dizziness: A review of neuroimaging studies. J Clin Med 2021; 10(18):4274.
47. von Sohsten Lins EMD, Bittar RSM, Bazan PR, et al. Cerebral responses to stationary emotional stimuli measured by fMRI in women with persistent postural-perceptual dizziness. Int Arch Otorhinolaryngol 2021;25(3):e355–64.
48. Wurthmann S, Holle D, Obermann M, et al. Reduced vestibular perception thresholds in persistent postural-perceptual dizziness - a cross-sectional study. BMC Neurol 2021;21:394.
49. Yagi C, Morita Y, Kitazawa M, et al. Head roll-tilt subjective visual vertical test in the diagnosis of persistent postural-perceptual dizziness. Otol Neurotol 2021; 42(10):e1618–24.
50. San Pedro Murillo E, Bancroft MJ, Koohi N, et al. Postural misperception: a biomarker for persistent postural-perceptual dizziness. J Neurol Neurosurg Psychiatry 2023;94(2):165–6.
51. Arshad Q, Saman Y, Sharif M, et al. Magnitude estimates orchestrate hierarchal construction of context-dependent representational maps for vestibular space and time: Theoretical implications for functional dizziness. Front Integr Neurosci 2022;15:806940.
52. Edwards MJ, Bhatia KP. Functional (psychogenic) movement disorders: merging mind and brain. Lancet Neurol 2012;11:250–60.
53. VanLandingham HF. Introduction to digital control systems. New York, NY: MacMillan Publishing Company; 1985. p. 347–91.
54. Cleworth TW, Adkin AL, Allum JHJ, et al. Postural threat modulates perceptions of balance-related movement during support surface rotations. Neuroscience 2019; 404:413–22.
55. Cleworth TW, Inglis JT, Carpenter MG. Postural threat influences the conscious perception of body position during voluntary leaning. Gait Posture 2018;66:21–5.
56. Penkava J, Bardins S, Brandt T, et al. Spontaneous visual exploration during locomotion in patients with phobic postural vertigo. J Neurol 2020;267(Suppl 1): 223–30.
57. Thompson KJ, Goetting JC, Staab JP, et al. Retrospective review and telephone follow-up to evaluate a physical therapy protocol for treating persistent postural-perceptual dizziness: A pilot study. J Vestib Res 2015;25(2):97–103.
58. Teh CS, Abdullah NA, Kamaruddin NR, et al. Home-based vestibular rehabilitation: A feasible and effective therapy for persistent postural perceptual dizziness (a pilot study). Ann Otol Rhinol Laryngol 2023;132(5):566–77.
59. Nada EH, Ibraheem OA, Hassaan MR. Vestibular rehabilitation therapy outcomes in patients with persistent postural-perceptual dizziness. Ann Otol Rhinol Laryngol 2019;128(4):323–9.
60. Herdman D, Norton S, Murdin L, et al. The INVEST trial: a randomised feasibility trial of psychologically informed vestibular rehabilitation versus current gold standard physiotherapy for people with persistent postural perceptual dizziness. J Neurol 2022;269(9):4753–63.
61. Min S, Kim JS, Park HY. Predictors of treatment response to pharmacotherapy in patients with persistent postural-perceptual dizziness. J Neurol 2021;268(7): 2523–32.

62. Yu Y-C, Xue H, Zhang Y-X, et al. Cognitive behavior therapy as augmentation for sertraline in treating patients with persistent postural-perceptual dizziness. BioMed Res Int 2018. Article ID 8518631.
63. Kuwabara J, Kondo M, Kabaya K, et al. Acceptance and commitment therapy combined with vestibular rehabilitation for persistent postural-perceptual dizziness: A pilot study. Am J Otolaryngol 2020;41(6):102609.
64. Axer H, Finn S, Wasserman A, et al. Multimodal treatment of persistent postural–perceptual dizziness. Brain Behav 2020;10(12):e01864.
65. Eren OE, Filippopulos F, Sönmez K, et al. Non-invasive vagus nerve stimulation significantly improves quality of life in patients with persistent postural-perceptual dizziness. J Neurol 2018;265(Suppl 1):63–9.
66. Im JJ, Na S, Kang S, et al. A randomized, double-blind, sham-controlled trial of transcranial direct current stimulation for the treatment of persistent postural-perceptual dizziness (PPPD). Front Neurol 2022;13:868976.
67. Licata F, Li Volsi G, Maugeri G, et al. Serotonin-evoked modifications of the neuronal firing rate in the superior vestibular nucleus: A microiontophoretic study in the rat. Neuroscience 1993;52:941–9.
68. Balaban CD. Neural substrates linking balance control and anxiety. Physiol Behav 2002;77:469–75.
69. Cano-Colino M, Almeida R, Compte A. Serotonergic modulation of spatial working memory: predictions from a computational network model. Front Integr Neurosci 2013;7:71.
70. Wingen M, Kuypers KP, van de Ven V, et al. Sustained attention and serotonin: a pharmaco-fMRI study. Hum Psychopharmacol 2008 Apr;23(3):221–30.
71. Livermore JJA, Holmes CL, Cutler J, et al. Selective effects of serotonin on choices to gather more information. J Psychopharmacol 2021;35(6):631–40.