International Journal of Biology and Life Sciences
ISSN: 2957-9511 | Vol. 13, No. 3, 2026

Studies and Applications of Multi-Sensory Integration Abnormalities and Neuroplasticity in PPPD

Zhiqing Ma *

Guangzhou Red Cross Hospital, Guangzhou, Guangdong, 510220, China
* **Corresponding author Email:** MASAYA2399@outlook.com

Abstract: Persistent postural-perceptual dizziness (PPPD) is a vestibular dysfunction disorder characterized by chronic non-rotatory dizziness, postural instability, and excessive sensitivity to complex visual environments. Its pathogenesis is not yet fully understood. Recent studies have shown that PPPD patients have enhanced visual dependence, abnormal vestibular and proprioceptive senses, leading to multimodal perceptual conflicts and forming a vicious cycle of "visual-anxiety-symptom aggravation". At the same time, the structural and functional plasticity of the brain regions in patients is disordered, further solidifying the abnormal perceptual patterns. This review sorts out the related research on the abnormal multisensory integration and neural plasticity changes of PPPD, aiming to reveal its important role in the chronicity of the disease and its precise treatment, with the expectation that in the future, through interdisciplinary research, the dynamic interaction relationship will be revealed, and based on neural plasticity, multi-level and individualized treatment strategies will be developed.

Keywords: Persistent Postural-Perceptual Dizziness; Multi-sensory Integration Abnormalities; Neuroplasticity; Visual Dependence.

1. Introduction

Persistent Postural-Perceptual Dizziness (PPPD) is a vestibular functional disorder characterized by core symptoms of chronic non-spinning vertigo, postural instability, and hypersensitivity to complex visual environments. Patients typically experience symptoms lasting for more than three months, which are significantly exacerbated by an upright posture, active or passive movements, or complex visual stimuli (e.g., moving crowds, rotating scenes) [1, 2]. Current research indicates that patients with PPPD exhibit multimodal sensory conflict; multi-sensory integration abnormalities involving vestibular, proprioceptive, and visual inputs lead to spatial disorientation. Furthermore, approximately 79.3% of patients present with comorbid anxiety or depression, creating a vicious cycle of "dizziness-anxiety-symptom exacerbation" that severely impacts daily life [3]. Although PPPD symptoms are not fatal, their chronic nature significantly reduces patients' quality of life and may even lead to dysfunctional avoidance behaviors. Studies suggest that patients without standardized treatment may develop intractable symptoms due to long-term decompensation, highlighting the importance of early intervention [4].

The pathogenesis of PPPD has not yet been fully elucidated; however, recent studies have revealed that its core pathology involves the interaction between multi-sensory integration abnormalities and maladaptive neuroplasticity [5]. The hyperactivation of the visual cortex, coupled with a decline in vestibular signal processing capacity, creates a compensatory visual dependence in these patients, resulting in abnormal sensory weight allocation. Chronic symptoms are accompanied by gray matter atrophy and functional connectivity reorganization in brain regions such as the superior temporal gyrus and the insula, which further consolidates these abnormal perceptual patterns. In-depth investigation of these mechanisms not only helps to uncover the pathological essence of PPPD but also provides a theoretical basis for optimizing treatments such as vestibular rehabilitation and neuromodulation techniques. This review aims to systematically explore the interaction between multi-sensory integration abnormalities and neuroplasticity alterations in patients with PPPD, elucidate their roles in the onset, progression, and chronification of the disease, and provide a scientific framework for optimizing clinical intervention strategies.

2. Multi-sensory Integration Abnormalities in PPPD

2.1. Normal Physiological Basis of Multi-sensory Integration

Under normal physiological conditions, visual, vestibular, and proprioceptive inputs achieve dynamic integration through complex neural mechanisms to collectively maintain human postural balance and spatial perception. The visual system captures environmental image information via the retina and transmits it through the optic nerve to the occipital visual cortex, providing critical cues such as object position and direction of movement. The vestibular system detects angular acceleration through the semicircular canals and perceives linear acceleration and gravitational pull via the otolith organs, transmitting these signals to the brainstem and cerebellum through the vestibular nerve. Vestibular signals contain not only acceleration and velocity information but also encompass more complex temporal dynamics and directional selectivity [6]. These signals are subsequently integrated with visual and proprioceptive inputs in the parietal cortex to formulate a unified perception of self-motion and spatial orientation[7].

Meanwhile, the proprioceptive system provides real-time feedback regarding the posture and movement of various body parts via mechanoreceptors located in muscles, tendons, and joints. These signals ascend through the spinal cord to the postcentral gyrus, where they converge with vestibular and visual inputs. Serving as a central hub for multimodal

information, the thalamus receives and relays vestibular, visual, and proprioceptive signals to the cerebral cortex[8]. Multisensory neurons within the parietal cortex facilitate cross-modal integration(e.g., visual-vestibular-proprioceptive) to construct a unified spatial representation. Furthermore, Senkowski et al. [5]discovered that the brain's multi-sensory integration system coordinates efficiently across different time scales through diverse mechanisms, such as cross-frequency coupling and phase resetting. Finally, the vestibulo-ocular reflex (VOR) and vestibulo-spinal pathways correct postural deviations in real time by modulating eye movements and muscle tone, thereby ensuring balance and stability.

2.2. The Importance of Multi-sensory Integration in Adapting to Diverse Environments and Motor States

Multi-sensory integration is the core mechanism by which the human body adapts to complex environments. During simple activities, the visual system processes environmental information, the vestibular system detects head movements, and the proprioceptive system regulates posture; these three systems achieve millisecond-level synchronization through multi-timescale neural oscillations [5].

Zeng et al.[9] demonstrated that when monkeys performed a heading-discrimination task in a virtual reality environment, the congruence of visual and vestibular inputs significantly enhanced decision-making accuracy. Furthermore, the concurrent activation of the dorsal medial superior temporal (MSTd) and ventral intraparietal (VIP) areas reflected this cross-modal integration process.

During more complex activities, particularly motor state transitions, multi-sensory integration achieves adaptive control through the dynamic adjustment of sensory weights (sensory reweighting). For instance, proprioceptive weighting increases when standing with eyes closed, whereas visual weighting predominates in complex visual scenes[10]. This flexibility ensures human stability during the execution of diverse balance tasks. The neural basis of this adaptability involves the synergistic interaction between subcortical structures (e.g., the cerebellum) and cortical regions (e.g., the prefrontal cortex)[7].

2.3. Specific Manifestations of Multi-sensory Integration Abnormalities in Patients with PPPD

2.3.1. Visual Dependence and Increased Sensitivity to Visual Stimuli

Patients with PPPD exhibit a significant phenomenon of excessive visual dependence. De Vestel et al.[11] conducted balance and visual dependence tests on patients with PPPD and other chronic dizziness disorders, finding that visual dependence can serve as a characteristic manifestation of PPPD. However, their static postural balance ability showed no significant difference when compared to other patients with chronic dizziness. Another possible mechanism is that visual discomfort hyperactivates the visual cortex, thereby inducing visual stress[12, 13].

Storm et al.[14]found that in complex visual environments (e.g., moving crowds in shopping malls, rotating visual stimuli), patients' visual motion perception thresholds are elevated. Consequently, they require a higher number of coherent moving dots to identify the overall direction of motion, leading to delayed decision-making and exacerbated anxiety.

Yagi and colleagues [15] designed various moving visual stimuli (e.g., checkerboard patterns, optic flow stimuli, and radial optic flow stimuli) to simulate daily visual scenes that might trigger symptom exacerbation in patients with PPPD. They utilized eye-tracking technology to evaluate patients' gaze stability. The study revealed that, compared to healthy controls, patients with PPPD demonstrated a significant decrease in gaze stability following exposure to moving visual stimuli. This indicates that the multi-sensory integration abnormalities in patients with PPPD render their sensory processing more susceptible to disruption under visual stimulation.

These studies further reveal that in dynamic visual environments, patients with PPPD tend to compensate for perceptual instability by excessively focusing on stationary objects. This behavioral pattern may reinforce the cycle of vision-dominated dependence. Furthermore, gaze fluctuations triggered by complex visual inputs not only impair spatial orientation capabilities but may also indirectly aggravate balance-related anxiety responses by interfering with attention allocation mechanisms.

2.3.2. Vestibular Abnormalities

Vestibular perceptual dysfunction is one of the crucial pathophysiological mechanisms underlying Persistent Postural-Perceptual Dizziness (PPPD). In recent years, numerous studies have delved into the anomalous characteristics of vestibular perception in patients with PPPD using various experimental paradigms. Kobel et al.[16] conducted vestibular threshold tests on patients with PPPD and found that their thresholds for z-axis translation and roll tilt were significantly elevated. This indicates that these patients experience difficulties in processing gravity-related cues.

Helmchen et al. [17] investigated the perception of postural movement in patients with PPPD during Galvanic Vestibular Stimulation (GVS).

The study revealed that the GVS perception threshold in patients with PPPD is generally lower than that of healthy individuals. Furthermore, the lower the patient's GVS perception threshold, the higher their Postural Sway Speed (PSS) when reproducing the perceived sway. This suggests that patients with PPPD are relatively hypersensitive to GVS, and this heightened sensitivity correlates with a higher GVS-induced PSS.

Storm et al. [14] found that the perceptual performance of patients with PPPD is inconsistent across different vestibular stimuli. While these patients exhibit a decreased perception threshold for GVS—indicating hypersensitivity to certain vestibular stimuli—their threshold for perceiving self-rotation in a passive rotation chair test shows no significant difference from that of healthy controls. This discrepancy further underscores the complexity and the presence of multi-sensory integration abnormalities in this patient population.

2.3.3. Proprioceptive Abnormalities

Patients with PPPD frequently exhibit abnormal proprioceptive processing, which exerts a significant impact on their postural balance and motor functions. Jáuregui-Renaud et al. [18]discovered that patients with PPPD demonstrate a higher degree of variability in estimating the Subjective Visual Vertical (SVV). This imprecision in gravity perception may precipitate difficulties in postural control and spatial orientation among these patients. Moreover, patients

with PPPD present with heightened levels of spatial anxiety, particularly anxiety associated with navigation.

Utilizing the Head Tilt Subjective Visual Vertical (HT-SVV) test, Yagi et al.[19] further revealed that patients with PPPD exhibit an augmented perceptual gain for head tilt; specifically, they perceive the degree of head tilt to be greater than the actual physical angle, thereby leading to spatial orientation errors. Patients with PPPD manifest anomalous proprioceptive processing characterized by reduced flexibility in postural control, with their postural sway demonstrating greater regularity and predictability in its temporal structure[20].

Ichijo[21] conducted foam posturography testing on 53 patients with PPPD, finding that during quiet stance, these patients may rely more heavily on visual input and rely less on somatosensory input compared to healthy individuals. This pattern—characterized by high dependence on visual cues and low dependence on somatosensory inputs—may constitute a core feature of multi-sensory integration abnormalities in PPPD, independent of vestibular function. During the Sensory Organization Test (SOT), under conditions favoring visual dependence or presenting low sensory demands, patients with PPPD exhibited greater peak-to-peak sway displacement in both the anteroposterior and mediolateral directions. Furthermore, their scores on the Functional Reach Test and the Dynamic Gait Index were significantly lower than those of healthy controls. These impairments affect not only the patients' postural control but also their motor and gait control capabilities, reflecting a compromised capacity for proprioceptively-driven balance regulation [10].

2.3.4. Multisensory Integration Abnormalities in PPPD

Visual dependence, vestibular abnormalities, and proprioceptive deficits interact to form a vicious cycle in patients with Persistent Postural-Perceptual Dizziness. When visual inputs are unstable or proprioceptive cues are ambiguous, patients exhibit an excessive reliance on residual vestibular signals, leading to an exacerbation of perceptual conflict [22]. For instance, navigating an uneven walking surface triggers a proprioceptive error, which subsequently instigates an anxious response. This anxiety then amplifies visual search behaviors, effectively establishing a positive feedback loop of "vision—proprioception—anxiety"[12].

Such multisensory integration abnormalities are further manifested in gait asymmetries that deteriorate notably under visual stimulation. This pattern strongly indicates the additive and disruptive effect of multimodal interference on motor control and stability [23]

3. The Role of Neuroplasticity in PPPD

3.1. Neuroplasticity

Vestibular neuroplasticity achieves functional compensation and adaptation through multi-tiered dynamic mechanisms. At the central level, vestibular nuclear neurons display short-term rapid adjustments and long-term structural remodeling. Short-term rapid adjustments are primarily realized through excitability changes mediated by neuromodulators such as norepinephrine and acetylcholine. Conversely, long-term structural remodeling, triggered by unilateral injury, initiates resting membrane potential depolarization, neural network reorganization, and the redistribution of synaptic weights, driving a compensatory process that shifts from behavioral substitution to intrinsic changes in synaptic properties[24].Studies in rat models have further elucidated the multi-layered characteristics of vestibular neuroplasticity. At the cellular level, this involves enhanced GABAergic inhibition and glial cell activation. At the whole-brain metabolic network level, cross-hemispheric functional clusters form during the early post-injury phase, such as the activation of the contralateral vestibular-thalamocortical pathway and brainstem-cerebellar reorganization. In the later stages, the system returns to foundational connectivity by optimizing synaptic efficacy, reflecting the synergy of multisensory integration and structural remodeling[25].

Research by Faralli et al.[26] on Bral2 knockout mice demonstrated that compensation is accelerated by releasing axonal growth restrictions, revealing the dual role of the extracellular matrix in regulating the plasticity window—promoting remodeling during the injury phase while maintaining stability post-repair. Moreover, Perineuronal Nets (PNNs) play a dynamic regulatory role in post-injury remodeling. Their transient degradation facilitates excitatory synaptic regeneration and the reorganization of inhibitory afferents. Upon functional recovery, PNNs reconstruct to stabilize these new connections. Progressing from synaptic dynamics and neural network reorganization to extracellular matrix regulation, these mechanisms construct a multi-scale plasticity framework, ultimately achieving a dynamic balance between vestibular functional compensation and long-term stability.

3.2. Neuroplasticity

Neuroplasticity plays a central role in postural and motor control by dynamically adjusting sensory integration and neural circuit reorganization. During normal motor learning, cerebellar Purkinje cells (PCs) optimize the encoding efficiency of sensory feedback through plasticity mechanisms: when rats undergo balance training, the linear encoding ability of their Simple Spikes (SS) for head movement angle (θ) and angular velocity (ω) is significantly diminished. However, this capacity is restored during unexpected perturbations or under anesthesia. This implies that the cerebellum actively filters out sensory feedback generated by self-motion during active movement. Simultaneously, the cerebellum dynamically adjusts sensory weights by strengthening the negative correlation between SS and Complex Spikes (CS)[27]. This plasticity integrates motor commands with external sensory inputs to form a dynamic equilibrium within dual-sensory maps, thereby improving the precision of motor control. On the other hand, following an acute vestibular injury, the central nervous system achieves functional compensation via multimodal plasticity. For example, the vestibular nuclei undergo remodeling, specifically manifested by adjusting neuronal thresholds; cervical proprioception becomes integrated; visual and proprioceptive inputs exhibit compensatory enhancement; and motor strategies are optimized, prioritizing the stabilization of truncal tilt during gait. The temporal discrepancy in recovery and the low correlation between the Vestibulospinal Reflex (VSR) and the Vestibulo-ocular Reflex (VOR) suggest reorganization mechanisms within independent neural pathways[28]. Collectively, these findings reveal that neuroplasticity maintains the adaptability and precision of postural and motor control under both physiological and pathological conditions through cerebellar regulation of sensory feedback, remodeling of vestibular

nuclear circuits, and the dynamic allocation of sensory weights.

4. Conclusion

This paper has reviewed the multi-sensory integration abnormalities and neuroplastic alterations in PPPD, shedding light on the critical roles of visual dependence, vestibular and proprioceptive aberrations, and the dysregulation of neuroplasticity in this condition. Research demonstrates that multi-sensory integration abnormalities in patients with PPPD originate from maladaptive multi-level neuroplasticity, which gives rise to elevated visual weighting, mismatches in sensory prediction, and cerebellar dysregulation. Various therapeutic interventions have shown favorable clinical efficacy by activating mechanisms of neuroplasticity to rectify these anomalous patterns of multi-sensory integration. Future research needs to further elucidate the molecular mechanisms underlying neuroplasticity and leverage multimodal imaging techniques to uncover its dynamic relationship with multi-sensory integration abnormalities. Concurrently, efforts should be made to develop personalized treatment protocols, conduct long-term follow-up studies, and strengthen interdisciplinary collaboration to drive research progress in this field and enhance the quality of life for patients.

References

[1] Tang Yong, Yan Zhihui, Xue Hui, et al. Expert Consensus on Persistent Postural-Perceptual Dizziness [J]. Chinese Journal of Otolaryngology, 2021, 19(06): 992-996.

[2] Staab J P, 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 Bárány Society [J]. J Vestib Res, 2017, 27(4): 191-208.

[3] 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 [J]. Intern Med, 2020, 59(22): 2857-62.

[4] Popkirov S, Staab J P, Stone J. Persistent postural-perceptual dizziness (PPPD): a common, characteristic and treatable cause of chronic dizziness [J]. Pract Neurol, 2018, 18(1): 5-13.

[5] Senkowski D, Engel A K. Multi-timescale neural dynamics for multisensory integration [J]. Nat Rev Neurosci, 2024, 25(9): 625-42.

[6] Liu B, Shan J, Gu Y. Temporal and spatial properties of vestibular signals for perception of self-motion [J]. Front Neurol, 2023, 14: 1266513.

[7] Keshavarzi S, Velez-Fort M, Margrie T W. Cortical Integration of Vestibular and Visual Cues for Navigation, Visual Processing, and Perception [J]. Annu Rev Neurosci, 2023, 46: 301-20.

[8] Smith L J, Wilkinson D, Bodani M, et al. Cognition in vestibular disorders: state of the field, challenges, and priorities for the future [J]. Front Neurol, 2024, 15: 1159174.

[9] Zeng Z, Zhang C, Gu Y. Visuo-vestibular heading perception: a model system to study multi-sensory decision making [J]. Philos Trans R Soc Lond B Biol Sci, 2023, 378 (1886): 20220334.

[10] Mccaslin D L, Shepard N T, Hollman J H, et al. Characterization of Postural Sway in Patients With Persistent Postural-Perceptual Dizziness (PPPD) Using Wearable Motion Sensors [J]. Otol Neurotol, 2022, 43(2): e243-e51.

[11] De Vestel C, De Hertogh W, Van Rompaey V, et al. Comparison of Clinical Balance and Visual Dependence Tests in Patients With Chronic Dizziness With and Without Persistent Postural-Perceptual Dizziness: A Cross-Sectional Study [J]. Front Neurol, 2022, 13: 880714.

[12] Powell G, Penacchio O, Derry-Sumner H, et al. Visual stress responses to static images are associated with symptoms of Persistent Postural Perceptual Dizziness (PPPD) [J]. J Vestib Res, 2022, 32(1): 69-78.

[13] Chang T P, Hong Y C, Schubert M C. Visual vertigo and motion sickness is different between persistent postural-perceptual dizziness and vestibular migraine [J]. Am J Otolaryngol, 2024, 45(4): 104321.

[14] Storm R, Krause J, Blüm S K, et al. Visual and vestibular motion perception in persistent postural-perceptual dizziness (PPPD) [J]. J Neurol, 2024, 271(6): 3227-38.

[15] Yagi C, Morita Y, Yamagishi T, et al. Gaze instability after exposure to moving visual stimuli in patients with persistent postural-perceptual dizziness [J]. Front Hum Neurosci, 2022, 16: 1056556.

[16] Kobel M J, Wagner A R, Oas J G, et al. Characterization of Vestibular Perception in Patients with Persistent Postural-Perceptual Dizziness [J]. Otol Neurotol, 2024, 45(1): 75-82.

[17] Helmchen C, Blüm S K, Storm R, et al. Postural motion perception during vestibular stimulation depends on the motion perception threshold in persistent postural-perceptual dizziness [J]. J Neurol, 2024, 271(8): 4909-24.

[18] Jáuregui-Renaud K, Cabrera-Pereyra R, Miguel-Puga J A, et al. Graviception Uncertainty, Spatial Anxiety, and Derealization in Patients with Persistent Postural-Perceptual Dizziness [J]. J Clin Med, 2024, 13(22).

[19] Yagi C, Morita Y, Kitazawa M, et al. Head Roll-Tilt Subjective Visual Vertical Test in the Diagnosis of Persistent Postural-Perceptual Dizziness [J]. Otol Neurotol, 2021, 42(10): e1618-e24.

[20] Kobel M J, Wagner A R, Merfeld D M. Recurrence quantification analysis of postural sway in patients with persistent postural perceptual dizziness [J]. Front Rehabil Sci, 2023, 4: 1142018.

[21] Ichijo K, Oka M, Koda K, et al. Analysis of postural stability using foam posturography in patients with persistent postural-perceptual dizziness [J]. J Vestib Res, 2024, 34(2-3): 133-44.

[22] Varangot-Reille C, Pezzulo G, Thacker M. The fear-avoidance model as an embodied prediction of threat [J]. Cogn Affect Behav Neurosci, 2024, 24(5): 781-92.

[23] Tramontano M, Paolocci G, Piatti D, et al. Dynamic postural stability, symmetry, and smoothness of gait in patients with persistent postural-perceptual dizziness [J]. J Vestib Res, 2024: 9574271241295615.

[24] Shibata D, Namiki T, Higuchi R. Identification of a mislabeled fixed specimen by DNA analysis [J]. Am J Surg Pathol, 1990, 14(11): 1076-8.

[25] Grosch M, Lindner M, Bartenstein P, et al. Dynamic whole-brain metabolic connectivity during vestibular compensation in the rat [J]. Neuroimage, 2021, 226: 117588.

[26] Faralli A, Dagna F, Albera A, et al. Modifications of perineuronal nets and remodelling of excitatory and inhibitory afferents during vestibular compensation in the adult mouse [J]. Brain Struct Funct, 2016, 221(6): 3193-209.

[27] Lee R X, Huang J J, Huang C, et al. Plasticity of cerebellar Purkinje cells in behavioral training of body balance control [J]. Front Syst Neurosci, 2015, 9: 113.

[28] Allum J H, Honegger F. Recovery times of stance and gait balance control after an acute unilateral peripheral vestibular deficit [J]. J Vestib Res, 2016, 25(5-6): 219-31.