Vestibular dysfunction leads to cognitive impairments: State of knowledge in the field and clinical perspectives (Review)

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Abstract. The vestibular system may have a critical role in the integration of sensory information and the maintenance of cognitive function. A dysfunction in the vestibular system has a significant impact on quality of life. Recent research has provided evidence of a connection between vestibular information and cognitive functions, such as spatial memory, navigation and attention. Although the exact mechanisms linking the vestibular system to cognition remain elusive, researchers have identified various pathways. Vestibular dysfunction may lead to the degeneration of cortical vestibular network regions and adversely affect synaptic plasticity and neurogenesis in the hippocampus, ultimately contributing to neuronal atrophy and cell death, resulting in memory and visuospatial deficits. Furthermore, the extent of cognitive impairment varies depending on the specific type of vestibular disease. In the present study, the current literature was reviewed, potential causal relationships between vestibular dysfunction and cognitive performance were discussed and directions for future research were proposed.

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1. Introduction

The vestibular system consists of the peripheral vestibular organs in the inner ear and the associated extensive central nervous system projections (1,2). By sensing the position and movement of the head, this system maintains the coordination of the eyes and the balance of the head and body via reflex mechanisms such as the vestibulo-ocular reflex and vestibulo-spinal reflex (2,3).

Epidemiological studies have shown that >35% of individuals aged 40 years and above experience vestibular problems,

with a one-year incidence of 11.9% (4-7). In addition to balance disorders, patients with vestibular dysfunction also suffer from cognitive impairment, including deficits in attention, working memory, executive function and spatial orientation (8-11). These cognitive impairments can persist even after systematic drug treatment and vestibular rehabilitation and may exacerbate patients' disabilities in both the spatial and non-spatial domains (12-15). However, it is unclear how vestibular dysfunction and cognitive dysfunction are related at this time.

Various classification schemes for cognitive functions exist in the literature; however, a predominant approach in the majority of studies encompasses executive function, attention, memory and spatial ability (16). Wherein, spatial cognitive ability refers to the ability to understand and organize information about the environment in the two- and three-dimensional space, which is more closely related to the vestibular system. It includes a variety of skills, such as spatial memory, spatial navigation and mental rotation (14,17). Spatial memory pertains to the recollection of locations, paths and spatial layouts. Navigation involves recognizing and memorizing paths, locations and directions. Mental rotation involves egocentric rotation and object-based transformation. Nonspatial cognitive ability is subdivided into domains such as working memory, attention, concentration and executive function. Working memory pertains to hold memory temporarily, attention and concentration is generally divided into two global subdomains: Selective attention and sustained attention. The domain of executive functioning includes complex tasks including planning, problem solving, manipulating mazes and other tasks requiring the administration of different cognitive capacities. The main cognitive domains are shown in Fig. 1.

The information provided by the vestibular system to the limbic system and neocortex via the ascending pathway is crucial for higher-order cognitive processes, such as spatial memory and navigation (18). The hippocampus is an important component of the limbic system, located in the medial temporal lobe, and is closely associated with encoding, storing and retrieving of memories (19). Bilateral atrophy of the hippocampus was observed in vestibular disorder patients (13), and substantial evidence suggests the hippocampus is the main brain region mediating the cognitive dysfunction brought on by vestibular disorders.

Since the pathologies of most vestibular illnesses remain poorly understood, the cognitive symptoms and etiology of each vestibular disorder may vary (2,20,21), and the present review highlighted the research progress on various types of vestibular disorders and their specific impacts on cognition. In the current study, the recent literature regarding the relationship between vestibular dysfunction and cognitive performance was summarized, and the importance for clinical practitioners to not only assess the vestibular functional status of the diseases themselves but also to comprehensively evaluate their effects on cognitive states was highlighted (22). The review methods are provided in the supplemental information.

2. Relationship between the vestibular system and cognitive function

Evidence for the involvement of the vestibular system in cognitive function. Clinical research observed that patients with vertigo and vestibular disorders often report symptoms of memory loss, such as 'brain fog', mental confusion and difficulties with memory and concentration (14,23). A four-fold increase in cognitive impairment was observed in patients with vestibular disorders, with 12% reporting limited mobility due to memory problems or confusion (24-26).

Since the early 2000s, numerous animal studies have discovered that the thalamus and hippocampus undergo abnormal plasticity following the loss of vestibular function. Multiple studies have consistently shown that, in rodents, vestibular inputs have a more crucial role than visual inputs in navigation. These vestibular inputs provide essential self-movement cues for tracking trajectory (27-29). Spatial memory deficiencies continued and were able to deteriorate even in chronic stages of vestibular injury, where compensatory processes were more likely to be activated. One study, for instance, found that rodents showed more severe deficits in spatial memory tasks 14 months after bilateral vestibular damage in comparison to only 5 months after the insult (30).

Mechanisms of vestibular system involvement in cognitive function. The vestibular signal is sent by four main ascending pathways to the hippocampus and the entorhinal cortex, which are both involved in spatial cognition. These pathways include the thalamo-cortical pathway, theta-generating pathway, cerebello-cortical pathway and head direction pathway. Figs. 2 and S1 offer a comprehensive depiction, presenting both an overview and detailed diagrams illustrating the four proposed pathways responsible for transmitting vestibular information to the cortical centers implicated in cognition. The neural nuclei involved in this process are also exhibited. The thalamic nuclei, specifically the lateral posterior, ventral posterior, medial geniculate and ventrolateral geniculate nuclei, transmit the outputs from the vestibular nucleus complex to several cortical areas, including the visual and parietal cortices. The vestibulo-cerebellar-cortical route also transmits vestibular data to the parietal and retrosplenial cortices, which in turn project to the hippocampus via the entorhinal cortex (31,32). The head-direction cell system is a network of cells distinguished by firing only in response to the head direction. The dorsal tegmental nucleus, which connects to the lateral mammillary nucleus and then to the postsubiculum and anterodorsal thalamic nucleus, two regions that have finely tuned head-direction cells, is where the vestibular nucleus complex fibers first make contact (33). Finally, it has been proposed that the theta wave-generating system, which includes the medial septum, supramammillary nucleus and pedunculopontine tegmental nucleus, transmits vestibular information to the entorhinal cortex and the hippocampus (34). Overall, a significant amount of highly processed vestibular information is received by the entorhinal-hippocampal system, which may be crucial for processing spatial information and navigation.

Electrophysiologic and neuroimaging studies have determined that multisensory integration occurs at the vestibular thalamus, specifically the ventral posterolateral and ventral posteromedial nuclei, and the vestibular cortex, specifically the insular, parietal operculum, temporoparietal junction, posterior parietal, cingulate, somatosensory and frontal cortices (35). Thalamic nuclei receive vestibular signals from both vestibular
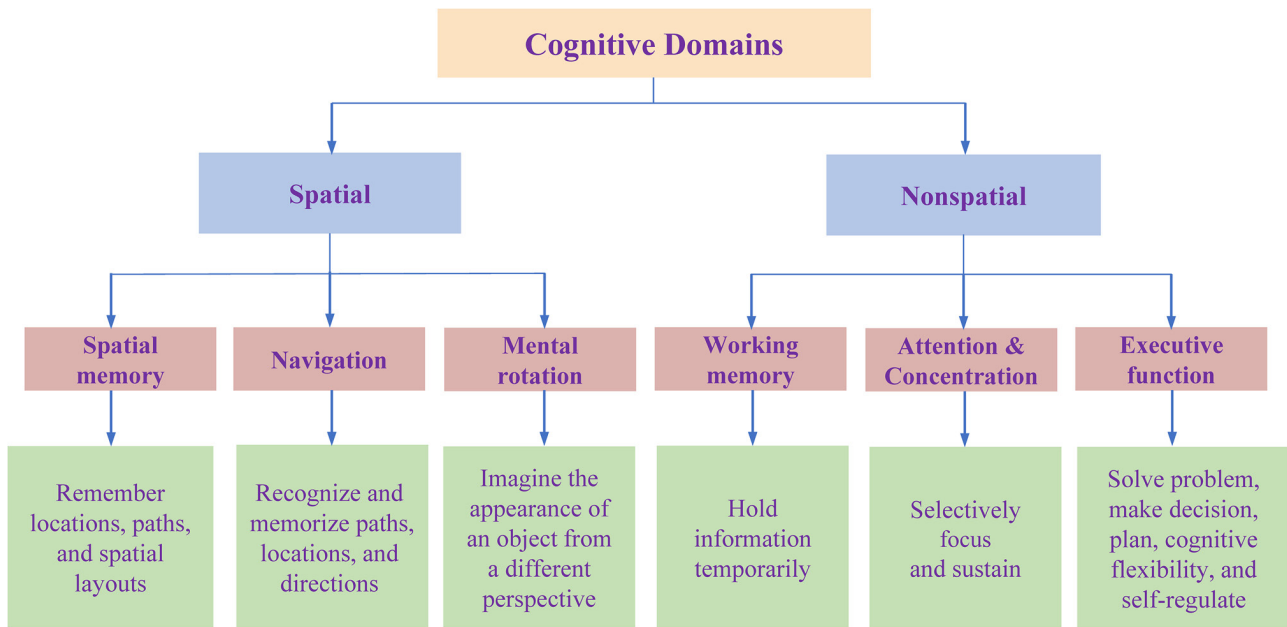
Figure 1. Domains of cognitive function. Cognitive functions can be divided into spatial cognitive functions, including spatial memory, spatial navigation and mental rotation, and non-spatial cognitive functions, including non-spatial memory, attention and executive functions.

and cerebellar nuclei (36); thalamocortical circuits form the canonical building blocks of the brain networks supporting the most complex cognitive functions (33). Sensitization at the level of the thalamus in addition to the convergence of sensory modalities at the cortex level causes perceptual hypersensitivity common in patients with vestibular dysfunction (37). Thus, vestibular dysfunction can be described as central hypersensitization and aberrant sensory integration in vestibulo-thalamic-cortical processing.

Spatial navigation refers to the complex process by which animals construct a navigational map in the brain based on the external environment, and move freely in the spatial environment to perform various tasks (38,39). By recording the firing activity of neuronal cells in the spatial environment of an organism, researchers have identified a series of spatial navigation-related cells, including position cells, grid cells, headward cells, interneurons, boundary cells, integrating cells and motion-sensitive cells. The head direction cell code in the dorsal brainstem tegmentum, anterior thalamus, subiculum and entorhinal cortex, the place cell code in the hippocampus and the grid cell code in the entorhinal cortex are all disrupted in rodents with bilateral vestibular damage, resulting in severe and persistent navigation deficits (40,41).

The vestibular cortical projection areas can be defined as the cortical areas activated during selective stimulation of the vestibular system (e.g., whole body rotation in darkness, excluding visual and proprioceptive stimulation) (42). A total of six cortical regions respond to the movement of the head and simultaneously activate the vestibular nuclei: Dorsal premotor cortex, vestibular related cingulate cortex 23c, somatosensory areas 2v and 3av, parietoinsular vestibular cortex and temporoparietal polysensory cortex (42,43).

The core vestibular network is structurally (44) and functionally (45) linked to regions involved in visuospatial processing, arousal and attentional modulation [e.g., anterior insula (46-48)], sensory gain control, proprioceptive [supramarginal gyrus (SMG) (49,50)], sensorimotor [SMG and cingulate cortex (51,52)], cognitive-perceptual (53) and affective processes [SMG, subgenual cortex and anterior insula (54-58)]. Furthermore, the 'core' cortical vestibular system's parieto-insular and temporoparietal cortex, along with the cerebellum, frontal-prefrontal, superior parietal and temporal cortices, as well as the posterior fossa, all generate cerebral potentials in response to naturalistic and artificial vestibular stimulation (59). Therefore, the vestibular function may be related to egocentric orientation and motor planning through body ownership and representation (10,60). In addition, it has been demonstrated that the vestibular system substrates are necessary for processing visuospatial memory, navigation, motion perception and even object-based mental picture transformations (53). All of these functions can be interfered with in situations of vestibular dysfunction.

Vestibular dysfunction causes cognitive impairment through the hippocampus. Studies on the neuroanatomical basis of the vestibular system have shown that the vestibular pathway is involved not only in the afferent input of head movement direction information, but also in the transmission of spatial learning and memory information, in which the internal olfactory cortex of the hippocampus is the main integration center of spatial information (61). In a circuit with the hippocampus, head direction and place cells, along with angular head velocity and grid cells, have a role in spatial orientation and navigation (62). They are located across the medial entorhinal cortex's layers, including the parasubiculum and postsubiculum (63,64).

The hippocampus is thought to be important for spatial representation processes that depend on the integration of both self-movement and allocentric cues; it also has significant interactions with areas associated with voluntary motor
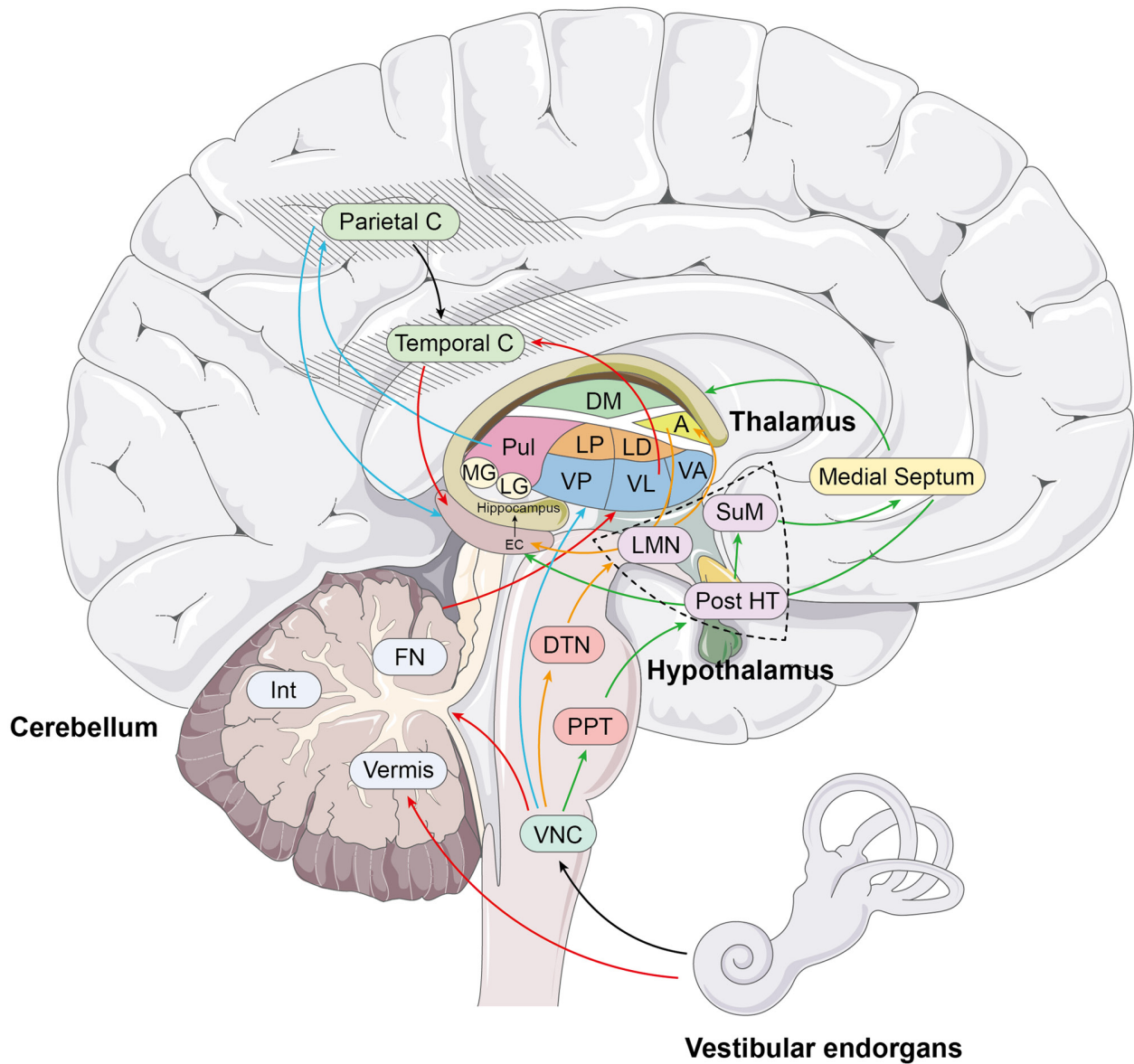
Figure 2. Overview showing the four proposed pathways to transmit vestibular information to cortical centers involved in cognition: i) Thalamo-cortical pathway (blue arrows); ii) theta generating pathway (green arrows); iii) cerebello-cortical pathway (red arrows); and iv) head direction pathway (orange arrows) [reproduced from (178)]. ADN, anterodorsal nucleus of the thalamus; DTN, dorsal tegmental nucleus; Int, interpositus; FN, fastigial nucleus; LMN, lateral mammillary nuclei; EC, entorhinal cortex; MG, medial geniculate nucleus; Parietal C, parietal cortex; Post HT, posterior hypothalamus; PPT, pedunculopontine tegmental nucleus; Pulv, pulvinar; RPO, reticularis pontis oralis; SuM, supramammillary nucleus; VLN, ventral lateral nucleus of the thalamus; VNC, vestibular nucleus complex; VP, ventral posterior nucleus.

control, such as the striatum in the basal ganglia (62,65). The vestibular system has direct connections with the amygdala and hippocampus, both key components of the limbic system involved in emotion and memory processing (65-67). Studies have shown that vestibular input can modulate activity in the amygdala and hippocampus, and that the limbic system can influence vestibular processing (68,69).

The hippocampus is essential for spatial navigation and memory, suggesting a potential interaction with the vestibular system. Spatial memory deficits observed in the virtual Morris Water Maze (vMWM) task correlate with a bilateral atrophy of the hippocampus of patients with bilateral vestibular loss, as reported originally (61,70). Interestingly, in cases of acute and chronic unilateral vestibular dysfunction, a reduced volume was observed in the right presubiculum of the hippocampus

and the left supramarginal gyrus, while the total hippocampal volume remained similar to that of healthy controls (71).

Vestibular disorders may cause cognitive impairment through the hypothalamic-pituitary-adrenal (HPA) axis. Vestibular deafferentation could be responsible for the HPA axis activation (72,73). Anatomical evidence of vestibular nucleus complex projections to the paraventricular nucleus (PVN) in rats and cats has supported the idea that the HPA axis is influenced by vestibular inputs (74,75). Empirical evidence for a significant increase in Fos-like immunoreactive neurons in the hypothalamic PVN of unilaterally vagotomized rats (76) and unilaterally vestibular neurectomized cats suggests neuroendocrine plasticity in response to the stress induced by vestibular deafferentation. Falls and continued postural

instability for the mammals are presumably stressful events that keep the HPA axis chronically activated.

Alterations in neurochemicals, cytoarchitecture remodeling, synaptic plasticity, neural activity and neurogenesis take place in the hippocampus as the severity, intensity and duration of stress increases, and these changes can have an impact on subsequent cognitive processes, such as learning and memory, and contribute to psychopathologies (77,78). According to results of rat research, the glucocorticoid-induced changes in synaptic plasticity, neurogenesis, neuronal atrophy and cell death cause the cognitive impairments brought on by excessive hippocampal exposure to glucocorticoids. The 'glucocorticoid cascade hypothesis' states that the hippocampal damage brought on by excessive glucocorticoid exposure should result in a decrease in the feedback inhibition mediated by cortisol, via the hippocampus, on corticotropin-releasing hormone secretion, leading to further excessive cortisol secretion and creating a cascade of hippocampal damage (79). This theory, which was first proposed in 1986, is now widely recognized as a pathophysiological route leading to alterations in the brain that are connected to intense and prolonged stress. Under the influence of glucocorticoids, cellular cytokines and macrophage migration inhibitory factors (MIF) within the immune system increase, thereby activating the HPA axis. Elevated leukocyte-derived MIF levels in the peripheral circulation can promote the onset of depression, while MIF from the central nervous system has a crucial role in neurogenesis, mood modulation and cognitive functions such as learning and memory (80). However, only a small number of studies have examined the neuroendocrine response following vestibular deafferentation and during the vestibular compensatory process.

On the other hand, brain-derived neurotrophic factor (BDNF) has crucial roles in the development and survival of auditory and vestibular ganglion neurons through signaling via neurotrophic tyrosine kinase receptors type 2 and 3 (81). In the developing mouse brain, BDNF protein is expressed in the piriform cortex and hippocampus (82). Some research underscores the pivotal role of BDNF in long-term potentiation in the hippocampus, a process fundamental to memory and learning (83,84). Furthermore, a clear link exists between reduced BDNF levels and acute stress responses (85-87). One research found that mice undergoing unilateral labyrinthectomy exhibited a decline in spatial cognitive abilities, attributing this to a decrease in BDNF (86). However, the link between the decrease in BDNF and cognitive impairment caused by vestibular dysfunction still lacks strong evidence and requires further research.

Potential relationship between vestibular compensation and cognitive function. Vestibular compensation is a remarkable process wherein the central nervous system adjusts to changes in vestibular input. However, this adaptation is not always complete and the degree of recovery differs among individuals (88).

In animal studies, functional compensation after unilateral labyrinthectomy has been studied in guinea pigs in both postural and locomotor behavior and in squirrel monkeys (89,90). Vestibular information contributes to dead reckoning and suggests possible recovery of function over time after the lesion (91,92). The impact of unilateral labyrinthectomy on the angular orientation task is evident. While this effect diminishes over time, there is considerable variability among animals, with some exhibiting notable recovery in task performance (93).

Evidence indicated that patients with vestibular loss have a significant impairment in spatial memory and navigation (20,94). According to human studies, numerous individuals undergo substantial recovery in cognitive functions related to spatial orientation and balance following vestibular compensation (95-97). However, the extent of recovery may vary, particularly in challenging or dynamic environments (98,99). The success of compensation is contingent on various factors, including the nature and severity of vestibular dysfunction, overall health and the efficacy of interventions or rehabilitation strategies employed.

Of note, patients may allocate cognitive resources to compensate for vestibular pathology. Research emphasizes a finite quantity of cognitive resources available for tasks during compensation stages (100). These attentional limitations contribute to diverse compensation profiles in patients, regardless of the presence of cognitive dysfunction, depending on the compensation stage.

Following vestibular compensation, there appears to be a potential for improved long-term spatial memory recovery, while less consistent evidence was obtained for working memory recovery (20,91,98). However, there is no robust evidence to support these observations and the underlying mechanisms remain unclear. In short, the impact of vestibular compensation on cognitive function in humans remains inconclusive. The lack of a definitive conclusion may be attributed to variations in detection methods.

3. Cognitive impairment in different vestibular disorders

Persistent postural-perceptual dizziness (PPPD). PPPD is one of the most common causes of chronic dizziness, characterized by non-spinning vertigo and perceived unsteadiness (101-103). According to an epidemiologic study, PPPD accounts for 15-20% of the cases encountered at the clinical centers for vertigo (104). The newest study showed that the prevalence of PPPD in patients with dizziness was 19% (105).

PPPD, often triggered by a peripheral or central vestibular disorder, was indicated to be associated with dysfunctional visual and visuospatial processing (106,107). Patients frequently report feeling disconnected from themselves and their surroundings (mild depersonalization and derealization) (108-110). Dissociative symptoms are characterized by a sense of brain fog or non-specific sensations of disorientation, as well as a variety of more specific cognitive symptoms, such as short-term memory loss, difficulty concentrating and impairments in multitasking (108). Adaptation abilities to dizzying trigger events, including high-risk postural control strategy, increased vigilance awareness of imbalance and dizziness, and visual dependency in processing spatial orientation, are persistently impaired in patients with PPPD. Patients with PPPD performed significantly worse in the vMWM spatial navigation test (111). Neuroimaging techniques have identified differences in brain activity and connectivity within the visual-vestibular networks of individuals with PPPD compared

to healthy individuals (112-114). It has been observed that traits such as neuroticism and introversion, which are associated with agoraphobia and PPPD, can influence how the brain responds to vestibular and visual motion stimuli in patients with PPPD (112).

Currently, the pathogenesis of PPPD remains a hot debate. The research on the pathogenesis of PPPD included structural and functional neuroimaging. Using sound-evoked vestibular stimulation, one study examined changes in brain activation and connectivity in patients with PPPD (115). Patients with PPPD displayed lower activity than healthy controls in the parieto-insular vestibular cortex (PIVC), hippocampus, inferior frontal gyrus, the posterior and the anterior insula, and the anterior cingulate cortex. The primary innervation of the vestibular cortex, or PIVC, is responsible for processing vestibular inputs, self-motion perception, verticality estimation and processing of visual motion, particularly motion coherent with gravity (116-119). Additional research revealed decreased functional connectivity between PIVC with the hippocampus, inferior frontal gyrus and anterior cingulate cortex. In addition, hippocampal hypofunction in subjects with chronic subjective dizziness may make it harder for them to put space-motion stimuli in the correct context while also making it harder for them to judge the importance of this information due to decreased activity in the anterior insula and anterior cingulate cortex (115). The frontal operculum and anterior tissues play a part in determining the prominence of sensory stimuli (120).

In conclusion, the vestibular-cognitive network combines knowledge of the space-motion context in which people live and work with vestibular inputs, which are largely processed in the PIVC at the cortical level (primarily dependent on hippocampal function). The lower cortical activation and poor cortical connectivity may account for cognitive symptoms in patients with PPPD.

Bilateral vestibulopathy (BVP). BVP is a chronic vestibular syndrome characterized by impairment or complete loss of function of the peripheral labyrinths or the eighth cranial nerve. Patients with BVP suffer frequent falls, dizziness, oscillopsia and vertigo, resulting in high disability and affecting the quality of life. The prevalence of BVP is 280 per 100,000 individuals and about half of the cases are idiopathic, together with other causes, including ototoxic medications, brain injury, Meniere's disease and vestibular neuritis (121).

The increasing evidence of cognitive impairment in patients with BVP has fueled concern regarding a possible link between peripheral vestibular loss and dementia (122-126). Although still controversial clinical studies have found that, compared to controls, patients with bilateral vestibulopathy show poorer spatial learning and navigation ability and more severe spatial anxiety in the vMWM accompanied by a significant hippocampal volume loss (61,70,127,128). Additional studies have shown that patients with BVP have difficulty completing mental rotation tasks (11,129). Patients with BVP performed worse compared to the cognitive performance of subjects without vestibular loss, with poorer average performance in immediate memory, attention, language and visuospatial abilities (130). Furthermore, patients with bilateral vestibular loss exhibited more pronounced cognitive impairments compared to those with unilateral vestibular loss (131),

and heterocentric strategic ability was decreased in patients with BVP and egocentric strategic ability was decreased in subjects with unilateral vestibular loss (132,133). Unilateral vestibular loss causes spatial disturbance and the extent of vestibular impairment showed a direct correlation with the magnitude of deficits in visuospatial abilities (134). A recent study found that patients with BVP performed worse than healthy controls when a new route needed to be reorganized, and their difficulty in building a mental model of a novel environment was consistent with the navigation-induced brain activation pattern in BVP (135).

Vestibular migraine (VM). VM is considered the most common cause of recurrent spontaneous vertigo attacks lasting minutes to days (136). It has a lifetime prevalence of ~1% and a 1-year prevalence of 0.9% (137,138). The diagnosis of VM is based on recurrent vestibular symptoms, a history of migraine, the temporary association between vestibular symptoms and migraine symptoms, and elimination of other causes of vestibular symptoms (136,139).

Unlike simple migraine, patients with VM have obvious cognitive impairment and a decline in life quality (140). A common complaint in VM is 'brain fog', described as difficulty in thinking, attention and memory (140-146).

Research in animals and humans has revealed the effect of the vestibular system in cognition (147), which concerns self-motion perception, bodily self-consciousness, spatial navigation, spatial learning, spatial memory and object recognition memory (30,148,149).

The pathophysiology of VM is not fully known. However, the growing body of knowledge regarding migraine in general points to possible central as well as peripheral mechanisms (150). The dorsal raphe nuclei, locus coeruleus and lateral tegmentum, which have tight inter-neural connections with the vestibular system, as well as the connections between the inferior, medial and lateral vestibular nuclei and the caudal trigeminal nucleus, strongly suggest that the nociceptive and vestibular systems interact at the brain stem level (150). The brainstem auditory evoked potential (BAEP) reflects the degree of auditory pathway and brainstem ischemia, and is highly sensitive to synaptic dysfunction. BAEP is widely used to evaluate functional impairment of brainstem auditory pathway and auditory system diseases in the central nervous system. Using BAEP examinations and Addenbrooke's cognitive examination-revised scale, researchers found that patients with VM have more severe brainstem dysfunction and cognitive impairment than patients with migraine, suggesting that patients with VM have central nervous system damage (151).

Meniere's disease (MD). MD is a chronic condition with a prevalence of 200-500 per 100,000 in population-based studies and characterized by episodic vertigo, fluctuating or progressive sensorineural hearing loss and aural fullness (152,153). Despite the vertigo attacks initially progressing in the early stage, they typically diminish gradually over the years, while the hearing loss worsens (154).

Clinically, there were deficits in attention, recognition and recall in verbal memory, recall in visual memory, visual spatial construction, planning skills and executive functions in patients with Meniere's disease (155,156). A study revealed

that individuals with MD and right-sided hearing loss exhibited more prominent memory and concentration difficulties than those with left-sided hearing loss (157). Previous research has indicated that individuals with MD display signs of hippocampal atrophy, which could potentially contribute to their cognitive decline (158,159). A recent study found that patients with MD were more likely to have cognitive deficits than benign paroxysmal positional vertigo (160). Furthermore, the improvement of vertigo and cognitive function of patients were partially correlated before and after treatments (155,161). Specific physical and emotional subscales may help understand changes/improvements in cognitive dysfunction after treatment.

While the relationship between vestibular dysfunction and cognitive impairment was increasingly supported by evidence, the complexity increased due to the separate recognition of hearing loss as an independent risk factor for dementia (123,162). Furthermore, the unpredictability of vertigo attacks, chronic dizziness and hearing loss may increase complexity to clarify the correlation between cognitive performance and multiple clinical features of MD.

Benign paroxysmal positional vertigo (BPPV). BPPV is the most common peripheral origin of vertigo (163,164), characterized by head position shift-induced rotatory vertigo and nystagmus, with a lifetime prevalence of 2.4% and a one-year prevalence of 1.6% (165).

A population-based cohort study (166) identified the relationships between BPPV and subsequent dementia; the risk of dementia was 1.24 times higher in patients with BPPV than in the controls. Although BPPV shares similar risk factors with cognitive impairment, such as cardiovascular disorder and head trauma, it has not been determined whether BPPV is the original cause or comorbidity of dementia.

Vestibular schwannoma (VS). VS, benign tumors originating from the myelin-forming Schwann cells within the vestibular segment of the vestibulocochlear nerve, constitute ~8% of intracranial tumors and account for ~80% of tumors located in the cerebellopontine angle (167). The estimated occurrence rate ranges from 3 to 5 cases per 100,000 individuals annually (168).

Patients with VS often experience cognitive problems (169-171). Clinical researches discovered that patients with VS exhibited impaired general cognitive function, memory, psychomotor speed, visuospatial ability, attention and processing speed, and executive function, compared with the matched controls (169,172,173). Another clinical study performed neuropsychological examination within 57 months of post-surgical follow-up and determined that 32% of the patients with VS experienced cognitive disturbance after transtemporal removal of acoustic neuromas. This could be attributed to the temporal lobe lesion (170).

Surgery for neurinomas may lead to vestibular deficits, resulting in volume reductions in critical brain regions and decreased functional connectivity for cognitive processing (170,174). A significant decrease in functional connectivity between the default mode network (DMN) and auditory cortical subregions was observed in patients with VS after surgery (175). Given that internalized cognitive processes linked to planning, encoding and memory functions are associated with the DMN, researchers hypothesize that the disruption of the DMN may contribute to the cognitive deterioration in patients with VS (169,175). Another study demonstrated a significant increase in regional homogeneity in the right anterior insular cortex in patients with VS compared to controls through whole-brain regional homogeneity analysis (176). The insula cortex, a vital node in the central executive network, is closely linked to various cognitive functions, including executive function, attention and working memory (169,177).

Table I provides a comprehensive summary of major studies investigating cognitive function in patients with vestibular disorders. The majority of these studies consistently indicate that individuals with vestibular disorders experience declines in both spatial and non-spatial cognitive abilities. However, the extent of cognitive impairment varies depending on the specific type of vestibular disease. This variation highlights the importance of understanding the nuances of different disease types and their impact on cognitive function.

4. Conclusions

This review highlights that individuals with vestibular disorders may exhibit deficits in various cognitive domains, such as spatial navigation, memory and attention. The underlying mechanisms behind these cognitive deficits are not yet fully understood, although several assumptions and hypotheses have been made. One possible explanation is that vestibular dysfunction leads to disrupted networks responsible for transmitting vestibular information to the hippocampus, particularly information associated with spatial learning and memory. The high comorbidity of affective disorders in individuals with vestibular dysfunction may additionally have a role in the development of cognitive dysfunction. Increased gaze and postural instability linked to vestibular loss may demand an elevated allocation of attentional resources for balance maintenance, leading to a reduction in resources available for cognitive tasks. The mechanism by which vestibular dysfunction is associated with cognitive impairment is still unclear. However, existing research suggests four potential pathways, namely the thalamo-cortical pathway, theta generating pathway, cerebello-cortical pathway and head direction pathway, as illustrated in Fig. 3. The findings underscore the importance of recognizing and addressing potential cognitive impacts in patients with vestibular dysfunction, with the hope that future research will contribute to improved management and interventions for these individuals.

5. Future direction

The vestibular system can serve as a promising area to investigate brain function beyond balance maintenance, extending into realms of cognition, emotion and psychiatric symptoms. With a global aging population, the prevalence of age-related vestibular dysfunction is expected to rise. More research is required to further elucidate the link between vestibular dysfunction and cognitive impairment.

Clinically, researchers should shift their focus towards delineating the distinct cognitive impairments that are responsible for each specific type of vestibular ailment.

Table I. Clinical investigation on cognitive function in patients with vestibular diseases.

Author, year	Patients	Cognitive domain/measurements	Main findings	(Refs.)
Breinbauer, 2020	PPPD (n=19)	Spatial navigation-virtual T-maze	Significant impairment in spatial navigational abilities	(111)
Donaldson, 2021	VM (n=44)	CFQ	Moderate cognitive dysfunction in patients with VM	(146)
Zhang, 2020	VM (n=78); Migraine (n=76); Control (n=79)	Addenbrooke's cognitive examination-revised	Patients with VM performed worse than Migraine group in verbal fluency, language and visuospatial ability	(151)
Balci, 2018	VM (n=32); Migraine (n=32); Control (n=31)	Stroop test	Patients with VM performed worse than migraine group	(143)
Wang, 2016	VM (n=40); Migraine (n=40); Control (n=40)	i) MMSE; ii) The Rey-Osterrieth complex figure test & tracing score - accuracy and visuospatial abilities; iii) Recall score - mnemonic ability; iv) TMT - perception and motion rates (processing speed) and attention; v) verbal fluency test-language competence	Patients with VM performed worse than migraine group in general cognitive ability, tracing and memorizing, but better in perception, motion rates (processing speed) and attention	(140)
Eraslan Boz, 2023	MD (n=18)	MMSE, digit span test and TMT, phonemic and semantic fluency test, Stroop test, Wisconsin card sorting test, Oktem verbal memory processes, Rey complex figure test, Benton judgment of line orientation	Patients with MD performed worse than healthy controls in Memory, recognition and verbal fluency	(155)
Dornhoffer, 2021	MD (n=29)	CFQ, DHI	Cognitive ability of patients with MD positively correlates with the degree of vertigo	(161)
Demirhan, 2023	VM (n=19); MD (n=19)	i) MMSE; ii) Reading span test and Stroop test (working memory, cognitive processing, reading; comprehension and attention); iii) TMT and Benton's judgment of line orientation test (visual processing, visuospatial skills, processing speed)	No statistically significant difference	(162)
Liu, 2019	BPPV (n=13); VM (n=11); MD (n=20)	Neuropsychiatric inventory questionnaire; CFQ	Patients with VM or MD performed worse than BPPV in general cognitive ability and patients with MD performed worse than VM in attention and emotion	(159)
Rizk, 2020	VM (n=45); MD (n=32); VMMD (n=13); BPPV (n=82); PPPD (n=14)	CFQ	General cognitive ability: PPPD had the lowest cognitive ability, followed by VMMD, VM and MD with the highest cognitive ability	(160)

Table I. Continued.

Author, year	Patients	Cognitive domain/measurements	Main findings	(Refs.)
Gommeren, 2023	BV (n=38)	Immediate and delayed memory, visuospatial/constructional, language and attention. Repeatable battery for the assessment of neuropsychological status for hearing impaired individuals	Patients with BVP performed worse than healthy controls in immediate memory	(124)
Dobbels, 2020	BVP (n=64)	Visuospatial, vMWM	Patients with BVP performed worse than healthy controls, though not statistically significant	(127)
Dobbels, 2019	BVP (n=64)	Repeatable battery for the assessment of neuropsychological status for hearing-impaired individuals	Patients with BVP performed worse than healthy controls in immediate memory/attention/language/visuospatial ability, but better in delayed memory	(130)
Ahmad, 2022	BVL (n=25); UVL (n=14)	CFQ; neuropsychiatric inventory questionnaire; Neuro-QoL	Patients with BVL performed worse than UVL in visuospatial ability	(131)
Gammeri, 2022	UVL (n=23); BVL (n=23)	Spatial navigation - virtual T-maze	Heterocentric strategic ability was decreased in patients with BVP and egocentric strategic ability was decreased in UVL	(132)
Saj, 2021	VL (n=21)	Subjective straight-ahead direction	UVL causes spatial disturbance, which manifests as a right-leaning of the body representation	(133)
Ayar, 2020	Acute UVL (n=21)	Bento's judgment of line, orientation test, verbal and non-verbal, cancellation tests, Rey-Osterrieth complex figure test, MMSE, Oktem verbal memory process test, forward and backward digit span	BVL typically have visuospatial impairment as their primary cognitive weakness	(134)
Popp, 2017	BVL (n=18); UVL (n=16)	Visuospatial tasks measuring working memory; executive function, processing speed	All cognitive domains were impaired in BVLs; visuospatial cognitive domains were impaired in UVLs	(125)
Brandt, 2005	BVL (n=10)	Spatial memory; vMWM	Spatial memory was significantly impaired in BVLs	(61)
Caixeta, 2012	Chronic peripheral vestibular dysfunction (n=76)	MMSE; clock test and verbal fluency test	Patients with vestibular dysfunction had cognitive impairment and there was a low but significant negative correlation between cognitive function and body balance disorders	(126)
Fan, 2023	VS (n=75)	MMSE, memory and executive screening, auditory verbal learning test, adaptive digit ordering test, Boston naming test, grooved pegboard test, judgment of line orientation, Stroop color-naming test, Stroop word-reading test, Stroop color-word interference test, TMT-A, TMT-B, symbol digit modalities test and digit span test	Patients with VS exhibited impaired general cognitive function, memory, psychomotor speed, visuospatial ability, attention and processing speed, and executive function	(169)

Table I. Continued.

Author, year	Patients	Cognitive domain/measurements	Main findings	(Refs.)
Deng, 2022	VS (n=69)	MoCA, Rey auditory verbal learning test immediate memory and delayed memory, Stroop color-word test A, B and C, symbol digit modalities test, TMT-A and B, Hamilton depression scale and Hamilton anxiety scale	Both Left-VS and Right-VS patients developed cognitive dysfunction such as memory, attention, executive function, movement speed and information processing speed	(172)
Deng, 2022	VS (n=64)	fMRI	Cognitive dysfunction occurs in patients with VS. Cognitive decline in patients with VS activates functional activity in some brain regions, thereby compensating for cognition decline	(173)
Goebel, 2018	VS (n=27)	Visuo-construction: Rey-Osterrieth complex figure test; Visuo-perception: Visual object and space perception battery; Attention and visuo-motor speed: Wechsler memory scale, TMT, Testbatterie zur Aufmerksamkeitsprüfung; Executive functions: Digit span backwards, controlled oral word administration test, five-point test; memory: Rey auditory verbal learning test; language: Aachener aphasie test	69% of patients showed impairment in at least one neuropsychological test	(171)

PPPD, persistent postural-perceptual dizziness; VM, vestibular migraine; MD, Meniere's disease; BPPV, benign paroxysmal positional vertigo; BVP, bilateral vestibulopathy; VS, vestibular schwannoma; CFQ, cognitive failure questionnaire; MMSE, mini-mental state examination; DHI, dizziness disorder scale; UVL, unilateral vestibular loss; BVL, bilateral vestibular loss; SCWT, Stroop color-word interference test; SDMT, symbol digit modalities test; TMT-A, trail making test part A.
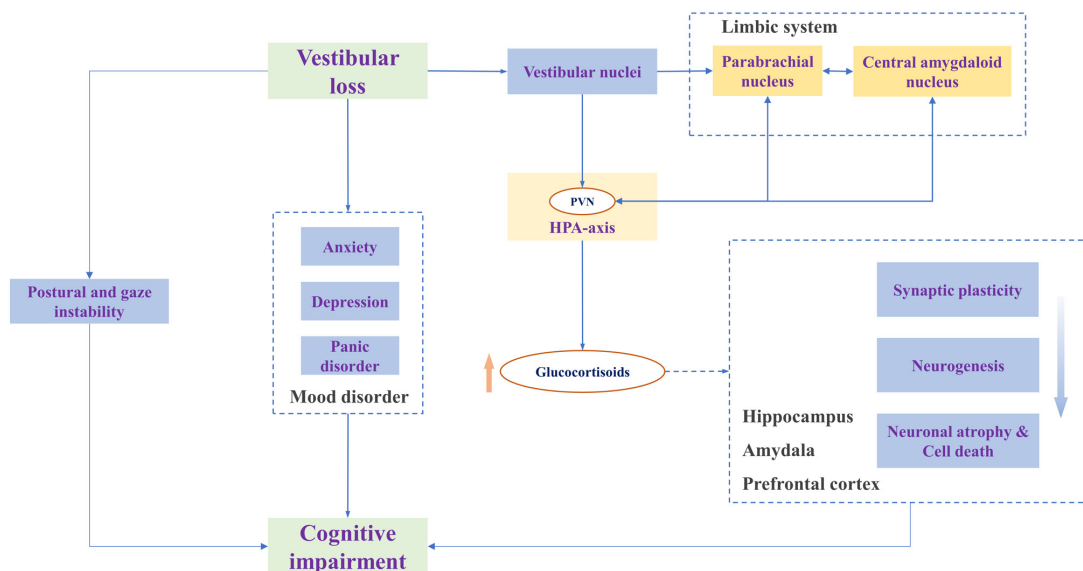

Figure 3. Conceptual model outlining the proposed mechanism by which cognitive impairment may arise from disturbances in the vestibular system. PVN, paraventricular nucleus; HPA, hypothalamic-pituitary-adrenal.

Larger studies with well-matched controls, along with prospective investigations tracking the temporal progression of vestibular disorders and cognitive function, would yield valuable insight. Furthermore, objective and comprehensive evaluations are essential. This may involve assessing factors such as the number, duration and frequency of vertigo attacks and exploring cognitive tasks across various subdomains. Incorporating neuro-electrophysiological indexes, such as electroencephalogram or functional magnetic resonance imaging, in a larger sample of patients may offer a more nuanced understanding of the neural correlates of vestibular dysfunction and cognitive impairment. Lastly, healthcare professionals should be vigilant about the potential cognitive impacts of vestibular disorders. Integrating neuropsychological evaluations into routine clinical assessments can enhance diagnostic accuracy and guide personalized treatment plans. For instance, cognitive rehabilitation tailored to the specific cognitive deficits associated with vestibular dysfunction could significantly improve patient outcomes and quality of life.

From a foundational research perspective, the application of advanced techniques such as single-cell sequencing could shed light on cellular changes in key brain regions and circuits associated with vestibular processing. This could pave the way for targeted interventions, potentially identifying specific cell types or molecular pathways that can be modulated to mitigate cognitive impairments associated with vestibular dysfunction.

In conclusion, by employing a multifaceted approach in clinical and basic research domains, we aspire to gain a more comprehensive understanding of the interplay between vestibular dysfunction and cognitive impairments. The integration of such knowledge with specific diagnostic and therapeutic strategies holds the potential to fundamentally transform management and intervention approaches, ultimately enhancing the quality of life of individuals affected.

Availability of data and materials

Not applicable.

Authors' contributions

SZ and JW conceived and designed the study. JG contributed to the conceptual framework, collected information from the literature and drafted the manuscript. ET, DL and YZ were involved in figure preparation. PL, DCC and WK provided a brief introduction to the article and revised the manuscript. ZG and JC prepared the table. ZZ collected information from the literature. YL reviewed and edited the manuscript and was involved in the conception and design of the study. All co-authors contributed to the final version and have read and approved the submitted version. Data authentication is not applicable.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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