**REVIEW ARTICLE**

# Vestibular contribution to memory processing

**Abdollah Moossavi[1], Meymaneh Jafari[2,3*]**

[1]- Department of Otolaryngology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

[2]- Department of Audiology, Faculty of Rehabilitation, Isfahan University of Medical Sciences, Isfahan, Iran

[3]- Department of Audiology, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran

## Abstract

**Background and Aim:** The vestibular system contributes in the stabilization of the head and body, orientation, and gazing through the processing of sensory inputs. A wealth of evidence supports the involvement of vestibular information in higher functions, too.

**Methods:** In this paper, we reviewed the previous studies on the effect of the vestibular system on memory as one of the cognitive functions.

**Results:** Clinical and laboratory findings indicate the association of vestibular inputs (besides postural control and oculomotor) with a variety of higher functions, especially memory function. Because part of the memory function is determined by other cognitive processes i.e. attention capacity, emotional disturbances, and executive functions, the study of the effect of vestibular inputs on these functions provides a more accurate view of how the vestibular inputs affect memory performance.

**Conclusion:** Although our current knowledge on vestibular-memory interaction is increasing, the exact involvement of vestibular signals in memory representations is still unclear and needs further studies to determine the theoretical basis of vestibular involvement in memory processing.

**Keywords:** Vestibular system; vestibular cortex; cognitive function; memory

## Introduction

The vestibular system is one of the oldest sensory systems [1]. This system is enclosed deeply in the inner ear and surrounded by thick temporal bones. This small but complex structure provides sensory information about acceleration and head movement in space [2,3]. Vestibular signals are important in vertebrates, because they provide information of self-movement and the implementation of these moves in any environment [2]. These signals are also important in human embryonic life so that vestibular inputs tend to orient the embryo during delivery [4].

In everyday life, vestibular receptors continuously monitor the movement of the head to help maintain its balance and orientation toward the target. These signals are also important for some autonomic reflexes, which tend to stabilize the gaze (oculomotor) and the posture (muscular) [5]. However, vestibular afferent signals continuously work (even when the person is in a stable position). Usually, the final signal by the vestibular system is ignored unless it receives an unusual stimulus (e.g. a jerky boat)

* **Corresponding author:** Department of Audiology, Faculty of Rehabilitation, Isfahan University of Medical Sciences, Hezarjerib Ave., Isfahan, 8174656831, Iran.
Tel: 0098313-6693089,
E-mail: meymaneh.jafari@gmail.com

or gets damaged. Then, the significant vestibular responses such as vertigo (illusion of rotation or swaying), visual disturbances or instability occur and the vital role of the vestibular system becomes clear [6].

After vestibular dysfunction, besides severe abnormal symptoms of dizziness and imbalance, disabling mental outcomes such as cognitive, psychological, and autonomic impairments occur [7]. These effects are not noticeable in other sensory disturbances (such as vision, olfactory), so it may be a reflection of the wide network of vestibular projection which extends into multiple cortical and subcortical regions such as brain stem, basal ganglia, hippocampus, cerebellum and cerebral cortex –all related to higher functions [2]. This broad network shows multimodal vestibular processing compared to other sensory modalities. Unlike other senses that send their information to a specific area in the cerebral cortex, information of the vestibular system integrates with other sensory inputs (i.e. vision, joints, skin and muscles) throughout the central nervous system (CNS). As a result, there is no central vestibular area (similar to other primary sensory cortex areas), which only responds to vestibular inputs [8].

Considering what was discussed, the unique role of the vestibular system in everyday functions cannot be ignored. Although, the role of the vestibular system in cognitive functions has been previously overlooked, several studies have recently examined the involvement of the vestibular system in motor, cognitive, affective and perceptive functions [9]. Clinical and laboratory evidence indicates the association of vestibular inputs (besides postural control and oculomotor) with a variety of higher functions, especially memory, as one of the cognitive functions [10]. Various studies have investigated the relationship between vestibular system and memory-related processes in different vestibular disturbances; some of these studies have used artificial stimulation of the vestibular system, too. Since part of the memory function is determined by other cognitive processes (i.e. attention, perception, motivation), the study of vestibular inputs on these functions provides a more accurate view of how the vestibular system affect memory performance. In the continuation, after a brief overview of the vestibulo-cortical maps, the involved pathways are explained. Then, we will review the studies of various vestibular disorders as well as those studies that used artificial stimulation of the vestibular system. Finally, the effect of other cognitive functions on the relationship between the vestibular system and the memory processing will be discussed.

## The vestibulo-cortical maps

Sending projections from vestibular signals to cortical and subcortical regions shows how the information of the vestibular system integrates in the central nervous system and participates in a series of reflexive and higher functions [11,12]. By artificial stimulation of the vestibular system (reducing visual and proprioceptive inputs), several important cortical regions activate which represents the neuroanatomical basis for the involvement of vestibular signals in a variety of cognitive processes. These areas include the parietal cortex, the temporo-parieto-insular and retro-insular cortex, the cingulate cortex, the frontal cortex and numerous subcortical structures, including thalamus, basal ganglia, and cerebellum [13].

Based on these extensive projections, it is quite clear that many vestibular regions in the cerebral cortex have not been located in a single region. With the electrical stimulation of the posterior insula, the sense of vestibular stimulation is induced. In addition, the parieto-insular vestibular cortex (PIVC) is associated with other cortical regions related to vestibular processing. Owning to these two features, this region, especially in non-human primates, is suggested as a primary vestibular cortex [13-16]. Of course, the PIVC also receives other sensory inputs, for example, reception of proprioceptive inputs during body movements, when the head is stable. As a result, vestibular signals converge with other sensory modalities along the central nervous system; therefore, the likelihood that PIVC is a distinct primary cortex with topographic organization, like other sensory

modalities, is weak [14].

The current knowledge about the target areas of vestibulo-cortical projections has increased after using various research methods (neurochemical, neuroimaging, brain stimulation, lesion examination). Through this new methods and information, we can show the potential role of vestibular inputs in functions beyond maintaining balance [11,13,17,18]. Most vestibular signals in the cortex are reflected in three main pathways: 1) to the brain stem nuclei (raphe nucleus and locus coeruleus), 2) to subcortical structures or cortical regions of motion and vision (i.e. the cerebellum and occipital lobe) and 3) to the cortical regions related to cognitive processing, autonomic functions, and mental health through several direct, such as parabrachial nucleus (PBN), and indirect, such as the hippocampus, prefrontal cortex, mainly through thalamus [19].

Neuroanatomical information plays an important role in providing evidence for vestibular involvement in cognition [7]. One of the strongest anatomical evidence for cognitive vestibular interactions is vestibular projections to memory cortical regions [20]. In the next section, we will review these pathways.

*Vestibular-memory pathways*

Vestibular pathways that reach (indirectly) the hippocampus, memory processing area, are important to create anatomical substrate for the participation of vestibular signals in cognition, especially spatial memory [21]. There are four hypothetical main pathways for sending vestibular signals to hippocampus. Fig. 1 shows an outline of these pathways, including the (a) vestibulo-thalamo-cortical pathway, (b) theta pathway, (c) head direction pathway and (d) the vestibulo-cerebello-cortical pathway [18].

Pathway (a) sends the spatial and self-movement information through the parietal, entorhinal, and perirhinal cortices to the hippocampus. Pathway (b) sends information to the hippocampus via the pontine reticular formation, supramammillary nucleus and medial septum and is responsible for memory processing. Pathway (c) is related to the head orientation and

before the hippocampus, it sends information through the dorsal tegmental nucleus to the lateral mammillary nucleus and anterodorsal thalamic nucleus. Finally, information on spatial learning is probably transmitted through pathway (d), which passes through the cerebellum and ventral lateral nucleus of thalamus [13,18,22]. In addition to hippocampus, basal ganglia is also a key area in spatial recognition. There is probably a fifth hypothetical path that goes through the striatum and plays a role in spatial learning and spatial memory [13].

By considering the pathways and nerve networks that are activated by vestibular signals (including the above paths), it is clear that there are several regions that receive vestibular signals and also play a role in memory processing [23,24]. Table 1 presents the neuroanatomical overlap between main memory centers and vestibulo-cortical pathways.

The temporal region of the brain (especially the hippocampus) is responsible for guiding various aspects of memory, especially spatial memory and navigation and is involved in the vestibular cortical network [23]. In these anatomical models, vestibular signals are not sent directly to memory cortical regions and effect of these signals on memory functions is not shown, but the overlap between different networks indicates the potential association of vestibular signals and memory functions [24].

The effect of vestibular signals on memory is related to cognitive maps formed in the region of hippocampus and parahippocampus (i.e. entorhinal, perirhinal, and postrhinal cortices) [13]. The activity of the place cells (activity in certain places), the border cells (indicating the boundaries of the environment), the head direction cells (activity when the head is directed in a certain direction) and the grid cells (creating information about the variable position of the person in space) combine to represent the inner impression of the environment [25]. These maps represent the spatial characteristics of an event and are probably the first step in the formation of spatial memory [13].

Smith et al. explained how the relationship between cortical overlap and memory processing

**Table 1. Neuroanatomical overlap between vestibulo-cortical pathways and main memory centers**

| Structure | Sub-component of memory | Pathway |
| --- | --- | --- |
| **Frontal cortex** | Working memory | Vestibulo-thalamo-cortical, The anterior cingulate cortex connects vestibular areas (for example, insula) to prefrontal areas [3] |
| **Parietal cortex** | Episodic memory, long-term memory (LTM), spatial representation | Vestibulo-thalamo-cortical & vestibulo-cerebello-cortical pathway (via the ventral lateral nucleus of the thalamus) see Fig. 1 |
| **Hippocampus** | Declarative memory, spatial representation, navigation, autobiographical | See Fig. 1 |
| **Amygdala** | Emotional learning, retention of emotional experiences | Limbic areas have two-way communications with amygdala and vestibular nuclei [11] |
| **Entorhinal cortex** | Acts as a mediator between the hippocampus (new memory encoding) and the neocortex (remote memory), spatial representation | Vestibulo-thalamo-cortical & Head-direction pathway see Fig. 1 |
| **Thalamus** | Declarative memory, Internal representations of reality | Multiple thalamus nuclei receive vestibular inputs and then relay to the cortex [14] |
| **Cingulate cortex** | Primary memory acquisition (anterior part) and episodic memory retrieval (posterior section) | Vestibulo-thalamo-cortical route see Fig. 1 |
| **Cerebellum** | Procedural memory, conditional learning | Various vestibular projections go to the cerebellum; passing otolith signals from the vestibular nuclei, medullary reticular formation, inferior olive and lateral reticular nucleus to the cerebellar nuclei [12] |
| **Basal ganglia** | Procedural memory, working memory, conditional learning, acts as an inhibitory gate keeper [16] | Possible pathway between the vestibular nucleus and striatum |

is. According to them, since the movement is vital for the continuation of life [26], the vestibular system is designed specifically to detect changes in the individual's movement (i.e. is the head upright, is it fixed, what speed/direction do I go?) [27], so probably the vestibular signals somehow show themselves in memory representations [1]. Although some vestibular inputs are expanded in the cortex and converge with other sensory inputs and motor signals, they are not fully isolated in memory functions [8,13]. By providing basic information about the individual's movements (as a reference for other sensory inputs), these inputs provide an unparalleled contribution to memory processing and allow accurate and simultaneous cognitive and motor functions [26]. In addition, the vestibular disorder causes damage to spatial memory and navigation, so the patients with vestibular disorder show spatial memory impairment regardless of having normal cognitive function. Thus, the strong link between vestibular performance and spatial-cognitive-vision skills is confirmed. The role of the vestibular system in spatial perception and spatial memory has been investigated in numerous studies [1]. In this regard,
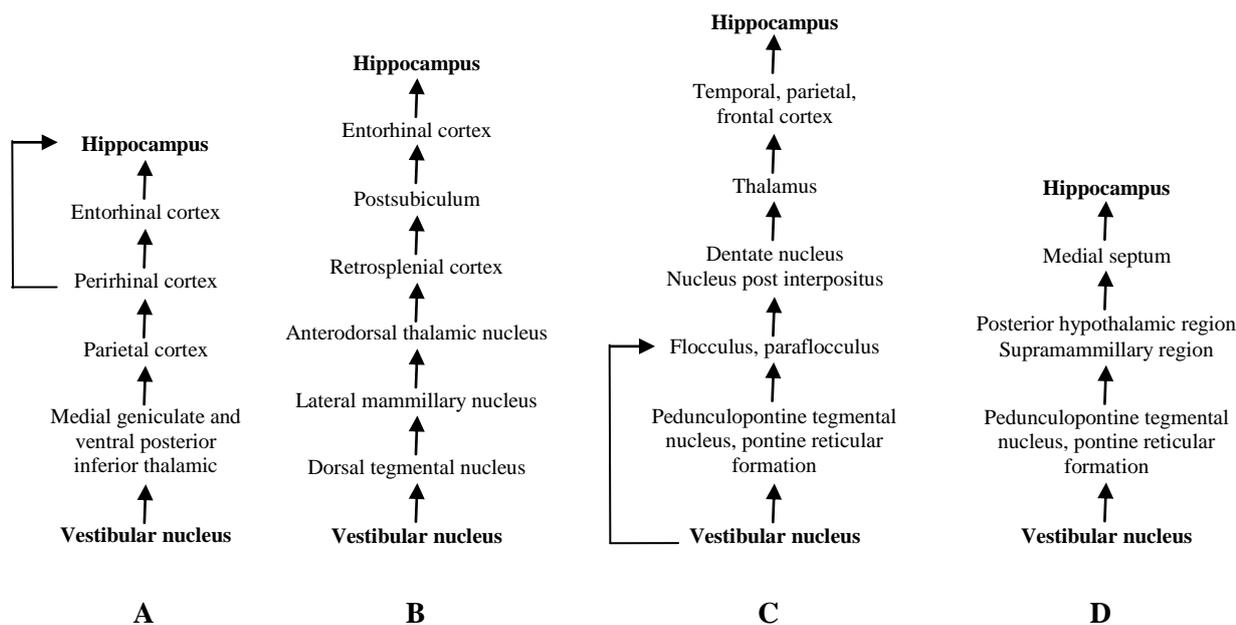
**Fig. 1. Neuroanatomical model of vestibular-hippocampal routes: A) Thalamo-cortical route, B) Head-direction route, C) Vestibulo-cerebello-cortical pathway, D) Theta-generating route (septohippocampal route).**

after the vestibular disorder, damage to the short-term memory capacity, in addition to spatial memory, are discussed [28].

**Effect of vestibular dysfunction on memory**
In the 1960s, it was first shown that, animals for navigation and remembering paths, in addition to the visual signs, use other idiothetic and non-visual signs such as atrial info and deep sense [26,29]. The first clinical evidence of the impact of vestibular disorders on spatial memory impairment was presented in 1989 by Grimm et al. [30]. In the following decades, various studies have shown that abnormalities in one or both vestibular labyrinths lead to non-orientation of animals in memory exercises (searching or navigating paths learned) and there is no possibility of learning new spatial locations for them [31]. The obtained data from individuals with vestibular disorders such as perilymph fistula syndrome [30], bilateral vestibular neuroectomy [22,32], bilateral partial vestibular disorder [33] and unilateral compensated labyrinthine impairment (non-vertigo) [34] also confirm these findings. Of course, it should be

noted that perilymph fistula syndrome also causes hearing impairment, which can be a reason for other cognitive impairments [30]. However, a new epidemiological study on the impact of vestibular disorder on age-related cognitive functions (with control of auditory and visual impairments) has been shown that declining vestibular function is associated with worsening of cognitive function in visuospatial tests (including visual memory), but does not affect executive function or verbal memory [35]. In these studies, after the vestibular disorder, damage to spatial memory, delay in spatial learning and navigating and damage to spatial short-term memory capabilities have been seen [22,30,32-34] which does not correlate with the normal cognitive, perceptive, and movement capacities (including non-spatial memory) or other standard assessments [36]. With regard to this information, if there is a disturbance in the vestibular system, at least some of memory functions are damaged. Thus, normal vestibular function is essential for some memory processes, especially for visuospatial information [10,26].

Hippocampus plays a key role in the study of how to store and represent spatial information; therefore, following a vestibular dysfunction, neuroanatomical effects are likely to be expected in addition to behavioral changes [7]. Damage to spatial memory that occurs following vestibular impairment is probably related to dysfunction of hippocampus, because both the place cell responses [37] and theta rhythm [38-40] become abnormal. In contrast, the field potentials of CA1 and dentate gyrus and long-term potentiation (LTP) are not significantly affected by bilateral vestibular impairment [41]. Lack of vestibular inputs changes the functions of the hippocampus [22]. Along with this theory, studies on the hippocampal morphology following bilateral vestibular impairment have shown numerous and different results, such as bilateral hippocampal atrophy (approximately 17%) about 5 to 10 years after surgery [22] to no significant changes after a shorter period [42-44]. In patients with unilateral vestibular neurectomy, no results of hippocampal atrophy has been observed [18]. In patients with unilateral Meniere disorder, bilateral hippocampal atrophy has been reported with a further reduction on the left side [45]. It has also been observed that bilateral vestibular impairment leads to a bilateral reduction in the gray matter of the CA3 region of the hippocampus, and the rate of reduction is consistent with the degree of clinical vestibular impairment [46]. In addition, bilateral vestibular disorders leads to morphological changes in the hippocampus, in the form of decrease in the number of basal dendrites (not apical) of CA1 [47] and N-Methyl-D-Aspartate (NMDA) receptors in the hippocampus [43]. There is a hypothesis that vestibular dysfunction also contributes in the development of the Alzheimer disease by affecting the hippocampus and other regions of the medial temporal lobe [48]. Such changes in the hippocampal atrophy have not been observed in rats with bilateral vestibular disorders [43,44]. One possible explanation for this observation is that in rats with bilateral vestibular disorders, locomotor hyperactivity is observed, which may neutralize the effects of vestibular impairment

on hippocampus [37,43,49].

In a study by Kremmydal et al., significant atrophy was observed in the mid-hippocampus and posterior parahippocampus areas in patients with bilateral reduced vestibular function. Moreover, the atrophy of the hippocampus structure has been observed in partial bilateral [33] and complete unilateral vestibular disorders [50]. A number of researchers have reported similar results, the most structural changes observed between patients with bilateral damage and less changes after unilateral/partial damage, because in these cases, there is still enough information from the remaining healthy labyrinth for compensation [18,45,50-52]. In healthy subjects with unusual memory experiences, changes in the hippocampus are also seen in response to vestibular inputs. For example, Hüfner et al. observed changes such as reduction in the size of the anterior portions and the enlargement of the posterior sections of the hippocampus in professional slack liners [53]. Considering the results of these findings, the change in vestibular inputs affect the morphology of the hippocampus. This effect is complex and in different vestibular syndromes, it will be different according to the latest posture/spatial experience [7].

Numerous animal studies demonstrate that temporary or permanent vestibular impairment leads to a disturbance in the selective firing of place cells of the hippocampus in rats [37,54]. In addition, the effect of bilateral vestibular degeneration has also been seen in the hippocampal theta rhythm, a large-amplitude electroencephalography oscillation; this rhythm is created by coordinating and combining the firings of the hippocampal place cells during motion and navigating [40,55]. In a study, the researcher reported that after the vestibular damage in rodents, firing of the head-direction cells in the postsubiculum and the anterior thalamus decreases [54,56]. With the temporary removal of theta oscillations in the medial entorhinal cortex (using an intratympanic injection), the firing of the grid cells disappears. The results of animal studies on the effect of the vestibular system on the firing characteristics of cells indicate the active and strong support of these signals by

spatial coding and navigating [57].

## Effect of artificial vestibular stimulation on memory

Information from the vestibular system for self-movement is essential for the growth of normal spatial memory. For this purpose, various studies have examined the effect of changing or enhancing the signals of the vestibular system on memory [26]. Astronauts' findings in space have created a unique opportunity for temporary changes in vestibular inputs, because in weightlessness status, the participation of the otolithic sense in gravity is eliminated [10]. Although microgravity cognitive effects (conditions where no otolithic inputs exist) varies, the impairment of visuospatial functions (for example, referring to memorized places with closed eyes) has been considered in various studies [10,58,59]. The results of these studies, besides confirming previous findings, suggest that temporary reduction in memory performance in healthy subjects is similar to those who have recently had an experience of vestibular disorder (without any specific symptoms, such as hearing loss or prolonged dizziness). Of course, in healthy people, non-vestibular factors such as anxiety and sleep deprivation can also lead to cognitive impairment [58].

Laboratory methods are used to study the effect of increased vestibular stimulation. These practices, besides clinical applications, can be used in research because of their low cost, non-invasiveness, safety and easy to use implementation [60-62]. In some studies, the effect of vestibular stimulation on memory has been studied. Extra-threshold electrical currents in galvanic vestibular stimulation (GVS) induce a similar effect to mild vestibular impairment [63]. GVS activates vestibular nerve by inducing a small flow through the mastoid prominent skin to the vestibular system. GVS activates the discharge zone of primary vestibular afferents and by producing irregular firings of vestibular afferents, leading to depolarization (cathodic stimulation) or hyperpolarization (anodic stimulation) of vestibular nerve [64,65]. Functional imaging studies in humans show that using galvanic

atrium stimulation, a network of multimodal cortical regions (including insular cortex, superior temporal gyrus, temporo-parietal cortex, basal ganglia and anterior cingulate gyrus [66], PIVC, temporo-parietal joint [67] and hippocampus [64] are activated. Therefore, GVS may have a positive effect on the activation of memory-related brain regions [68]. Stimulation with more GVS intensity can sometimes lead to disturbances in the vestibular system and will have a positive effect when less stimulation occurs [26,31]. This stimulation method has led to a shift in the behavior of normal individuals in the practice of short-term visuospatial memory [63]. Therefore, there is probably a close connection between GVS, vestibular system, the memory [68]. However, the reason for memory impairment with extra-threshold GVS is unknown, this may be due to indirect relation to visual impairment (i.e. oscillopsia or nystagmus), or direct relation to cognitive resource conflicts due to inappropriate inputs of vestibular, visual and proprioceptive systems [10]. To avoid these limitations, Wilkinson et al. used small sub-sensory GVS [69]. GVS leads to improved visual memory recall, speed and accuracy [68,69]. Although several studies have shown improvement in cognitive performance after a session of using noisy or stochastic GVS in healthy people, there is little information on the efficacy of repeated GVS in pathologic conditions. In a study with presentation of low frequency noisy GVS presentation during learning and recall stages, spatial memory function improved in rats with cognitive impairment. This effect may be related to the effective and frequent activity of vestibular neurons and the hippocampal regions of the vestibular system. The study results have shown the potential benefits of this approach in encountering the cognitive decline caused by sporadic AD [64].

It has also been observed that caloric vestibular stimulation (CVS) using water improves visual memory [70]. In CVS, with warm stimulation, the ipsilateral hemisphere and with cold stimulation, the contralateral hemisphere is activated [71]. By stimulation of the left ear with cold

water, increased spatial memory for visual places is observed and by stimulation of the right ear, increased verbal memory in visually presented words is observed. Thus, as a result of CVS, facilitating cerebral blood flow in the opposite brain structures, which is needed for verbal and spatial cognitive processing, leads to improved visual memory [70]. Of course, during interpreting the results, attention should be paid to the complications of CVS, such as nausea and visual disturbances (nystagmus), as it may lead to impaired vestibular influences on cognitive functions [72]. Considering the results of various studies, memory functions are affected by increased activity of the vestibule after artificial stimulation and this effect is likely to be positive and beneficial. These methods stimulate different parts of the vestibular system and have different applications; therefore, before drawing any conclusions regarding the stability and mechanism of the effect, more explanations and studies are needed [10].

**Related vestibular-cognitive effects**
Evidence from various studies suggests that other cognitive processes may also be affected by changes in vestibular inputs. Therefore, in order to investigate the relationship between vestibular signals and memory, their effects on cognitive functions should be considered regardless of reflexive functions [73].
Since part of the memory function is determined by other cognitive processes (attention capacities, emotional disturbances, executive function), the study of the effect of vestibular inputs on these functions provides a more accurate view of how the vestibular inputs affect memory performance [10]. In this section, we will review the available evidence for various functional interactions.

*Visuospatial abilities*
The results of various studies indicate that the vestibular system is likely to have a specific and significant contribution to the organization of the representation of two or three-dimensional spaces. Therefore, the stimulation of the vestibular system or its impairment affects cognitive

processes such as spatial memory and navigating (which are used to determine the position of an individual or an external goal in a three dimensional space and rely on these mental representations) [10]. Because there are several brain regions that respond both to vestibular inputs and to visuospatial processing (e.g. the hippocampus, insula, superior temporal gyrus, inferior parietal lobe, temporo-parietal joint, ventral intraparietal cortex and posterior parietal cortex), these effects can be interpreted by considering cortical networks activated by stimulation of the vestibular system [10,62,74,75]. Therefore, when the vestibular system is impaired, a cascade of neurological changes (through the vestibulo-cortical network) is likely to occur, which will damage the cognitive aspects of spatial vision, such as navigation, mental imagery, and memory [26].

*Attention capacities*
Studies in normal people have shown that cognitive functions decrease with increasing need for preservation of the posture [10,29]. Thus, maintaining the balance is a complex process and extends beyond a simple reflex performance. It uses different cognitive resources when needed and weakens processes such as memory activities. This effect is especially noticeable in the elderly, because they are at risk of vestibular dysfunction and cognitive impairment [76].
There is empirical evidence of a functional relationship between vestibular and memory systems, for example, in people with vestibular dysfunction, the balance and functions of cognitive domains do not work individually [21]. The studies conducted on using dual tasks indicate that in situations where there is a disturbance of balance, attentional capacities is dedicated to balance. On the other hand, in difficult mental exercises, attentional resources are taken from equilibrium exercises, resulting in symptoms like dizziness. It should be noted, on the other hand, that dizziness can disrupt attention to mental exercises. The underlying mechanisms of these findings are still unclear. However, there are two possible

causes: limited overall capacity (i.e. reduction of attention resources due to postural instability and widespread cognitive damage after that), or competition in the use of specific spatial processing resources (disturbance in spatial reference detection after vestibular disorder or direct effect of postural disturbance on specific spatial cognitive exercises) [77]. The results of various studies indicate that postural function is associated with limited capacity and increased attention needs in equilibrium exercises. If this relationship exists, vestibular involvement in the process of memory processing may indicate a widespread effect of vestibular stimulation or the general discharge of attentional resources due to a vestibular dysfunction that extends to multiple cognitive functions, for example, attention and information processing, and it is not just limited to the functions of spatial memory [20].

*Executive function*
Sensory stimulation during physical exercises is effective on the proliferation and neurogenesis of the cells in the hippocampus. Therefore, vestibular stimulation during physical exercises may cause neurogenesis of the cell in the dentate gyrus [78]. Equilibrium exercises increase memory performance and spatial recognition in people with a healthy vestibular system [79].
Moderate physical exercises for at least 20−30 minutes, two or three times a week, improve cognitive performance in the elderly [80] and reduces the risk of developing AD [81]. This effect has been seen even with the control of vascular disorders, locomotor disorders and other risk factors for AD, which can be related to exercise. The beneficial effects of exercises on delaying and preventing AD are parallel to increasing blood flow in vestibular nucleus and higher vestibular centers, but such an effect was not observed in cochlear nuclei and other hearing centers [82]. Physical exercise results in improved vestibulospinal and vestibulo-ocular reflexes [83]. Physical exercise affects the volume of the anterior hippocampus (the entry of vestibular inputs) in AD but has no effect on the caudate core or volume of thalamus [84].

*Psychiatric disorders*
In addition to the vestibular-cognitive communication described above, clinical reports show a clear relationship between vestibular dysfunction and psychiatric symptoms like panic, anxiety, and depression. Patients with vestibular dysfunction suffer from emotional disturbances and depression [11,58,86] and people with psychiatric conditions often complain of feelings of dizziness and instability [87]. The emotional state of individuals is a factor in changing learning and memory abilities [88]. Animals with high levels of anxiety usually have poor learning and memory functions [89]. Anxious people tend to scan the environment more in comparison with relaxed people (regardless of the existence of intimidating stimuli or threats), with more head movements and different orientations [90]. Such a tedious scan causes conflicts in their capacity with environmental events and reflects the general inability to keep their attention focused on targeted stimuli, which, in turn, affects the information needed to learn and memory [89].
When vestibular involvement is considered in memory function, this two-way communication should also be taken into account; because mental problems can lead to cognitive impairment (such as damage to attention and working memory in schizophrenia or excessive attention to threatening triggers in panic disorder) [91]. In fact, PBN creates a direct link between the vestibular system and the limbic system (including amygdala, locus coeruleus, hypothalamus and prefrontal cortex) that are involved in emotional processing and mental disorders [11]. Vestibulo-hippocampal interactions can also cause psychological symptoms, as this area is involved in both spatial and emotional processing [29]. In other words, any cognitive disorder can potentially have a psychological and or vestibular origin [7,21,29].

**Conclusion**
In this paper, clinical and laboratory evidence was presented about the association of vestibular inputs (besides postural control and oculomotor) with a variety of higher functions,

especially memory. Ascending vestibular pathways send vast projections to areas involved in spatial memory and navigation, such as hippocampus, entorhinal cortex, and thalamus. Therefore, damage to the vestibular system causes spatial memory disturbance and results in structural changes in the hippocampus. In addition, various studies in healthy adults indicate that microgravity conditions lead to memory errors, while artificial stimulation of the vestibular system with temperature or electrical flow facilitates memory function.

Although, the two systems are connected and our current knowledge about vestibule-memory interactions is increasing, the involvement of atrial signals in memory representations are still unclear. It seems that balance is a complex process based on cognitive resources and factors. Therefore, further studies are needed to diagnose the relationship between vestibular and memory systems and to determine the theoretical basis of vestibular involvement in memory processing.

## Conflict of interest
The authors declared no conflicts of interest.

### References
1. Smith PF, Darlington CL, Zheng Y. Move it or lose it--is stimulation of the vestibular system necessary for normal spatial memory? Hippocampus. 2010;20(1):36-43. doi: 10.1002/hipo.2058
2. Highstein SM. Anatomy and physiology of the central and peripheral vestibular system: overview. In: Highstein SM, Fay RR, Popper AN, editors. Springer handbook of auditory research. New York: Springer; 2004. p. 1-10.
3. Preuss N, Hasler G, Mast FW. Caloric vestibular stimulation modulates affective control and mood. Brain Stimul. 2014;7(1):133-40. doi: 10.1016/j.brs.2013.09.003
4. Eliot L. What's going on in there? How the brain and mind develop in the first five years of life. 1st ed. New York: Bantam; 1999.
5. Holstein GR, Friedrich VL Jr, Martinelli GP, Ogorodnikov D, Yakushin SB, Cohen B. Fos expression in neurons of the rat vestibulo-autonomic pathway activated by sinusoidal galvanic vestibular stimulation. Front Neurol. 2012;3:4. doi: 10.3389/fneur.2012.00004
6. Khan S, Chang R. Anatomy of the vestibular system: A review. NeuroRehabilitation. 2013;32(3):437-43. doi: 10.3233/NRE-130866
7. Smith PF. The vestibular system and cognition. Current opinion in neurology. 2017;30(1):84-9. doi: 10.1097/WCO.0000000000000403

8. Angelaki DE, Cullen KE. Vestibular system: the many facets of a multimodal sense. Annu Rev Neurosci. 2008;31:125-50. doi: 10.1146/annurev.neuro.31.060407.125555
9. Grabherr L, Macauda G, Lenggenhager B. The moving history of vestibular stimulation as a therapeutic intervention. Multisens Res. 2015;28(5-6):653-87.
10. Bigelow RT, Agrawal Y. Vestibular involvement in cognition: Visuospatial ability, attention, executive function, and memory. J Vestib Res. 2015;25(2):73-89. doi: 10.3233/VES-150544
11. Gurvich C, Maller JJ, Lithgow B, Haghgooie S, Kulkarni J. Vestibular insights into cognition and psychiatry. Brain Res. 2013;1537:244-59. doi: 10.1016/j.brainres.2013.08.058
12. Büttner-Ennever JA. A review of otolith pathways to brainstem and cerebellum. Ann N Y Acad Sci. 1999;871:51-64.
13. Hitier M, Besnard S, Smith PF. Vestibular pathways involved in cognition. Front Integr Neurosci. 2014;8:59. doi: 10.3389/fnint.2014.00059
14. Lopez C, Blanke O. The thalamocortical vestibular system in animals and humans. Brain Res Rev. 2011;67(1-2):119-46. doi: 10.1016/j.brainresrev.2010.12.002
15. Mazzola L, Lopez C, Faillenot I, Chouchou F, Mauguière F, Isnard J. Vestibular responses to direct stimulation of the human insular cortex. Ann Neurol. 2014;76(4):609-19. doi: 10.1002/ana.24252
16. Baier B, Karnath HO, Dieterich M, Birklein F, Heinze C. Keeping memory clear and stable--the contribution of human basal ganglia and prefrontal cortex to working memory. J Neurosci. 2010;30(29):9788-92. doi: 10.1523/JNEUROSCI.1513-10.2010
17. Shinder ME, Taube JS. Differentiating ascending vestibular pathways to the cortex involved in spatial cognition. J Vestib Res. 2010;20(1):3-23. doi: 10.3233/VES-2010-0344
18. Hüfner K, Hamilton DA, Kalla R, Stephan T, Glasauer S, Ma J, et al. Spatial memory and hippocampal volume in humans with unilateral vestibular deafferentation. Hippocampus. 2007;17(6):471-85. doi: 10.1002/hipo.20283
19. Lopez C. A neuroscientific account of how vestibular disorders impair bodily self-consciousness. Front Integr Neurosci. 2013;7:91. doi: 10.3389/fnint.2013.00091
20. Besnard S, Lopez C, Brandt T, Denise P, Smith PF. Editorial: the vestibular system in cognitive and memory processes in mammalians. Front Integr Neurosci. 2015;9:55. doi: 10.3389/fnint.2015.00055
21. Hanes DA, McCollum G. Cognitive-vestibular interactions: a review of patient difficulties and possible mechanisms. J Vestib Res. 2006;16(3):75-91.
22. Brandt T, Schautzer F, Hamilton DA, Brüning R, Markowitsch HJ, Kalla R, et al. Vestibular loss causes hippocampal atrophy and impaired spatial memory in humans. Brain. 2005;128(Pt 11):2732-41. doi: 10.1093/brain/awh617
23. Glikmann-Johnston Y, Saling MM, Reutens DC, Stout JC. Hippocampal 5-HT1A receptor and spatial learning and memory. Front Pharmacol. 2015;6:289. doi: 10.3389/fphar.2015.00289
24. Squire LR. Memory and brain systems: 1969-2009. J Neurosci. 2009;29(41):12711-6. doi:

10.1523/JNEUROSCI.3575-09.2009

25. Moser EI, Kropff E, Moser MB. Place cells, grid cells, and the brain's spatial representation system. Annu Rev Neurosci. 2008;31:69-89. doi: 10.1146/annurev.neuro.31.061307.090723

26. Smith PF, Geddes LH, Baek JH, Darlington CL, Zheng Y. Modulation of memory by vestibular lesions and galvanic vestibular stimulation. Front Neurol. 2010;1:141. doi: 10.3389/fneur.2010.00141

27. Wilkinson D, Morris R, Milberg W, Sakel M. Caloric vestibular stimulation in aphasic syndrome. Front Integr Neurosci. 2013;7:99. doi: 10.3389/fnint.2013.00099

28. Popp P, Wulff M, Finke K, Rühl M, Brandt T, Dieterich M. Cognitive deficits in patients with a chronic vestibular failure. J Neurol. 2017;264(3):554-563. doi: 10.1007/s00415-016-8386-7

29. Smith PF, Zheng Y. From ear to uncertainty: vestibular contributions to cognitive function. Front Integr Neurosci. 2013;7:84. doi: 10.3389/fnint.2013.00084

30. Grimm RJ, Hemenway WG, Lebray PR, Black FO. The perilymph fistula syndrome defined in mild head trauma. Acta Otolaryngol Suppl. 1989;464:1-40.

31. Ghaheri F, Adel Ghahraman M, Jarollahi F, Jalaie S. [Visuo-spatial memory enhancement by galvanic vestibular stimulation: A preliminary report]. Audiol. 2014;23(1):50-61. Persian.

32. Schautzer F, Hamilton D, Kalla R, Strupp M, Brandt T. Spatial memory deficits in patients with chronic bilateral vestibular failure. Ann N Y Acad Sci. 2003;1004:316-24.

33. Kremmyda O, Hüfner K, Flanagin VL, Hamilton DA, Linn J, Strupp M, et al. Beyond dizziness: virtual navigation, spatial anxiety and hippocampal volume in bilateral vestibulopathy. Front Hum Neurosci. 2016;10:139. doi: 10.3389/fnhum.2016.00139

34. Guidetti G, Monzani D, Trebbi M, Rovatti V. Impaired navigation skills in patients with psychological distress and chronic peripheral vestibular hypofunction without vertigo. Acta Otorhinolaryngol Ital. 2008;28(1):21-5.

35. Bigelow RT, Semenov YR, Trevino C, Ferrucci L, Resnick SM, Simonsick EM, et al. Association between visuospatial ability and vestibular function in the baltimore longitudinal study of aging. J Am Geriatr Soc. 2015;63(9):1837-44. doi: 10.1111/jgs.13609

36. Wiener-Vacher SR, Hamilton DA, Wiener SI. Vestibular activity and cognitive development in children: perspectives. Front Integr Neurosci. 2013;7:92. doi: 10.3389/fnint.2013.00092

37. Russell NA, Horii A, Smith PF, Darlington CL, Bilkey DK. Long-term effects of permanent vestibular lesions on hippocampal spatial firing. J Neurosci. 2003;23(16):6490-8.

38. Russell NA, Horii A, Smith PF, Darlington CL, Bilkey DK. Lesions of the vestibular system disrupt hippocampal theta rhythm in the rat. J Neurophysiol. 2006;96(1):4-14. doi: 10.1152/jn.00953.2005

39. Tai SK, Ma J, Ossenkopp KP, Leung LS. Activation of immobility-related hippocampal theta by cholinergic septohippocampal neurons during vestibular stimulation. Hippocampus. 2012;22(4):914-25. doi: 10.1002/hipo.20955

40. Neo P, Carter D, Zheng Y, Smith P, Darlington C, McNaughton N. Septal elicitation of hippocampal theta rhythm did not repair cognitive and emotional deficits resulting from vestibular lesions. Hippocampus. 2012;22(5):1176-87. doi: 10.1002/hipo.20963

41. Zheng Y, Mason-Parker SE, Logan B, Darlington CL, Smith PF, Abraham WC. Hippocampal synaptic transmission and LTP in vivo are intact following bilateral vestibular deafferentation in the rat. Hippocampus. 2010;20(4):461-8. doi: 10.1002/hipo.20645

42. Cutfield NJ, Scott G, Waldman AD, Sharp DJ, Bronstein AM. Visual and proprioceptive interaction in patients with bilateral vestibular loss. Neuroimage Clin. 2014;4:274-82. doi: 10.1016/j.nicl.2013.12.013

43. Besnard S, Machado ML, Vignaux G, Boulouard M, Coquerel A, Bouet V, et al. Influence of vestibular input on spatial and nonspatial memory and on hippocampal NMDA receptors. Hippocampus. 2012;22(4):814-26. doi: 10.1002/hipo.20942

44. Zheng Y, Balabhadrapatruni S, Baek JH, Chung P, Gliddon C, Zhang M, et al. The effects of bilateral vestibular loss on hippocampal volume, neuronal number, and cell proliferation in rats. Front Neurol. 2012;3:20. doi: 10.3389/fneur.2012.00020

45. Seo YJ, Kim J, Kim SH. The change of hippocampal volume and its relevance with inner ear function in Meniere's disease patients. Auris Nasus Larynx. 2016;43(6):620-5. doi: 10.1016/j.anl.2016.01.006

46. Göttlich M, Jandl NM, Sprenger A, Wojak JF, Münte TF, Krämer UM, et al. Hippocampal gray matter volume in bilateral vestibular failure. Hum Brain Mapp. 2016;37(5):1998-2006. doi: 10.1002/hbm.23152

47. Balabhadrapatruni S, Zheng Y, Napper R, Smith PF. Basal dendritic length is reduced in the rat hippocampus following bilateral vestibular deafferentation. Neurobiol Learn Mem. 2016;131:56-60. doi: 10.1016/j.nlm.2016.03.009

48. Previc FH. Vestibular loss as a contributor to Alzheimer's disease. Med Hypotheses. 2013;80(4):360-7. doi: 10.1016/j.mehy.2012.12.023

49. Aitken P, Zheng Y, Smith PF. Ethovision™ analysis of open field behaviour in rats following bilateral vestibular loss. J Vestib Res. 2017;27(2-3):89-101. doi: 10.3233/VES-170612

50. zu Eulenburg P, Stoeter P, Dieterich M. Voxel-based morphometry depicts central compensation after vestibular neuritis. Ann Neurol. 2010;68(2):241-9. doi: 10.1002/ana.22063

51. Brandt T, Zwergal A, Glasauer S. 3-D spatial memory and navigation: functions and disorders. Curr Opin Neurol. 2017;30(1):90-97. doi: 10.1097/WCO.0000000000000415

52. Helmchen C, Ye Z, Sprenger A, Münte TF. Changes in resting-state fMRI in vestibular neuritis. Brain Struct Funct. 2014;219(6):1889-900. doi: 10.1007/s00429-013-0608-5

53. Hüfner K, Binetti C, Hamilton DA, Stephan T, Flanagin VL, Linn J, et al. Structural and functional plasticity of the hippocampal formation in professional dancers and slackliners. Hippocampus. 2011;21(8):855-65. doi: 10.1002/hipo.20801

54. Stackman RW, Clark AS, Taube JS. Hippocampal spatial representations require vestibular input. Hippocampus. 2002;12(3):291-303. doi: 10.1002/hipo.1112

55. Buzsáki G. Theta rhythm of navigation: link between

path integration and landmark navigation, episodic and semantic memory. Hippocampus. 2005;15(7):827-40. doi: 10.1002/hipo.20113

56. Yoder RM, Taube JS. Head direction cell activity in mice: robust directional signal depends on intact otolith organs. J Neurosci. 2009;29(4):1061-76. doi: 10.1523/JNEUROSCI.1679-08.2009

57. Jacob PY, Poucet B, Liberge M, Save E, Sargolini F. Vestibular control of entorhinal cortex activity in spatial navigation. Front Integr Neurosci. 2014;8:38. doi: 10.3389/fnint.2014.00038

58. Grabherr L, Mast FW. Effects of microgravity on cognition: The case of mental imagery. J Vestib Res. 2010;20(1-2):53-60. doi: 10.3233/VES-2010-0364

59. Oman C. Spatial orientation and navigation in microgravity. In: Mast FW, Jäncke L, editors. Spatial processing in navigation, imagery and perception. New York: Springer; 2007. p. 209-48.

60. Fitzpatrick RC, Day BL. Probing the human vestibular system with galvanic stimulation. J Appl Physiol. 2004;96(6):2301-16. doi: 10.1152/japplphysiol.00008.2004

61. Palla A, Lenggenhager B. Ways to investigate vestibular contributions to cognitive processes. Front Integr Neurosci. 2014;8:40. doi: 10.3389/fnint.2014.00040

62. Lopez C, Blanke O, Mast FW. The human vestibular cortex revealed by coordinate-based activation likelihood estimation meta-analysis. Neuroscience. 2012;212:159-79. doi: 10.1016/j.neuroscience.2012.03.028

63. Dilda V, MacDougall HG, Curthoys IS, Moore ST. Effects of galvanic vestibular stimulation on cognitive function. Exp Brain Res. 2012;216(2):275-85. doi: 10.1007/s00221-011-2929-z

64. Adel Ghahraman M, Zahmatkesh M, Pourbakht A, Seifi B, Jalaie S, Adeli S, et al. Noisy galvanic vestibular stimulation enhances spatial memory in cognitive impairment-induced by intracerebroventricular-streptozotocin administration. Physiol Behav. 2016;157:217-24. doi: 10.1016/j.physbeh.2016.02.021

65. Cheng YY, Kuo CH, Hsieh WL, Lee SD, Lee WJ, Chen LK, et al. Anxiety, depression and quality of life (QoL) in patients with chronic dizziness. Arch Gerontol Geriatr. 2012;54(1):131-5. doi: 10.1016/j.archger.2011.04.007

66. Utz KS, Dimova V, Oppenländer K, Kerkhoff G. Electrified minds: transcranial direct current stimulation (tDCS) and galvanic vestibular stimulation (GVS) as methods of non-invasive brain stimulation in neuropsychology--a review of current data and future implications. Neuropsychologia. 2010;48(10):2789-810. doi: 10.1016/j.neuropsychologia.2010.06.002

67. Fink GR, Marshall JC, Weiss PH, Stephan T, Grefkes C, Shah NJ, et al. Performing allocentric visuospatial judgments with induced distortion of the egocentric reference frame: an fMRI study with clinical implications. Neuroimage. 2003;20(3):1505-17. doi: 10.1016/j.neuroimage.2003.07.006

68. Lee JW, Lee GE, An JH, Yoon SW, Heo M, Kim HY. Effects of galvanic vestibular stimulation on visual memory recall and EEG. J Phys Ther Sci. 2014;26(9):1333-6. doi: 10.1589/jpts.26.1333

69. Wilkinson D, Nicholls S, Pattenden C, Kilduff P, Milberg W. Galvanic vestibular stimulation speeds

visual memory recall. Exp Brain Res. 2008;189(2):243-8. doi: 10.1007/s00221-008-1463-0

70. Bächtold D, Baumann T, Sándor PS, Kritos M, Regard M, Brugger P. Spatial- and verbal-memory improvement by cold-water caloric stimulation in healthy subjects. Exp Brain Res. 2001;136(1):128-32.

71. Miller SM, Ngo TT. Studies of caloric vestibular stimulation: implications for the cognitive neuro-sciences, the clinical neurosciences and neurophi-losophy. Acta Neuropsychiatr. 2007;19(3):183-203. doi: 10.1111/j.1601-5215.2007.00208.x

72. Gopinath A, Archana R, Sailesh KS, Mukkadan JK. Effect of caloric vestibular stimulation on memory. Int J Pharm Bio Sci. 2015;6(3):(B)453-59.

73. Deroualle D, Lopez C. Toward a vestibular contribution to social cognition. Front Integr Neurosci. 2014;8:16. doi: 10.3389/fnint.2014.00016

74. Blanke O, Mohr C, Michel CM, Pascual-Leone A, Brugger P, Seeck M, et al. Linking out-of-body experience and self processing to mental own-body imagery at the temporoparietal junction. J Neurosci. 2005;25(3):550-7. doi: 10.1523/JNEUROSCI.2612-04.2005

75. Smith PF. Dyscalculia and vestibular function. Med Hypotheses. 2012;79(4):493-6. doi: 10.1016/j.mehy.2012.06.032

76. Redfern MS, Müller ML, Jennings JR, Furman JM. Attentional dynamics in postural control during perturbations in young and older adults. J Gerontol A Biol Sci Med Sci. 2002;57(8):B298-303.

77. Yardley L, Papo D, Bronstein A, Gresty M, Gardner M, Lavie N, et al. Attentional demands of continuously monitoring orientation using vestibular information. Neuropsychologia. 2002;40(4):373-83. doi: 10.1016/S0028-3932(01)00113-0

78. Smith PF. Is hippocampal neurogenesis modulated by the sensation of self-motion encoded by the vestibular system? Neurosci Biobehav Rev. 2017;83:489-495. doi: 10.1016/j.neubiorev.2017.09.013

79. Rogge AK, Röder B, Zech A, Nagel V, Hollander K, Braumann KM, et al. Balance training improves memory and spatial cognition in healthy adults. Sci Rep. 2017;7(1):5661. doi: 10.1038/s41598-017-06071-9

80. Hindin SB, Zelinski EM. Extended practice and aerobic exercise interventions benefit untrained cognitive outcomes in older adults: a meta-analysis. J Am Geriatr Soc. 2012;60(1):136-41. doi: 10.1111/j.1532-5415.2011.03761.x

81. Rovio S, Kåreholt I, Helkala EL, Viitanen M, Winblad B, Tuomilehto J, et al. Leisure-time physical activity at midlife and the risk of dementia and Alzheimer's disease. Lancet Neurol. 2005;4(11):705-11. doi: 10.1016/S1474-4422(05)70198-8

82. Delp MD, Armstrong RB, Godfrey DA, Laughlin MH, Ross CD, Wilkerson MK. Exercise increases blood flow to locomotor, vestibular, cardiorespiratory and visual regions of the brain in miniature swine. J Physiol. 2001;533(Pt 3):849-59.

83. Gauchard GC, Gangloff P, Jeandel C, Perrin PP. Physical activity improves gaze and posture control in the elderly. Neurosci Res. 2003;45(4):409-17. doi: 10.1016/S0168-0102(03)00008-7

84. Erickson KI, Voss MW, Prakash RS, Basak C, Szabo A, Chaddock L, et al. Exercise training increases size of

hippocampus and improves memory. Proceedings of the National Academy of Sciences. 2011;108(7):3017-22. doi: 10.1073/pnas.1015950108

85.     Lahmann C, Henningsen P, Brandt T, Strupp M, Jahn K, Dieterich M, et al. Psychiatric comorbidity and psychosocial impairment among patients with vertigo and dizziness. J Neurol Neurosurg Psychiatry. 2015;86(3):302-8. doi: 10.1136/jnnp-2014-307601

86.     Balaban CD, Thayer JF. Neurological bases for balance-anxiety links. Journal of anxiety disorders. 2001;15(1-2):53-79. doi: 10.1016/S0887-6185(00)00042-6

87.     Eagger S, Luxon LM, Davies RA, Coelho A, Ron MA. Psychiatric morbidity in patients with peripheral vestibular disorder: a clinical and neuro-otological study. J Neurol Neurosurg Psychiatry. 1992;55(5):383-7.

88.     Hariri AR, Goldberg TE, Mattay VS, Kolachana BS, Callicott JH, Egan MF, et al. Brain-derived neurotrophic factor val66met polymorphism affects human memory-related hippocampal activity and predicts memory performance. J Neurosci. 2003;23(17):6690-4.

89.     Herrero AI, Sandi C, Venero C. Individual differences in anxiety trait are related to spatial learning abilities and hippocampal expression of mineralocorticoid receptors. Neurobiol Learn Mem. 2006;86(2):150-9. doi: 10.1016/j.nlm.2006.02.001

90.     Mathews A, May J, Mogg K, Eysenck M. Attentional bias in anxiety: selective search or defective filtering? J Abnorm Psychol. 1990;99(2):166-73. doi: 10.1037/0021-843X.99.2.166

91.     Millan MJ, Agid Y, Brüne M, Bullmore ET, Carter CS, Clayton NS, et al. Cognitive dysfunction in psychiatric disorders: characteristics, causes and the quest for improved therapy. Nat Rev Drug Discov. 2012;11(2):141-68. doi: 10.1038/nrd3628