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Spatial Memory Deficits in Patients with Meniere's Disease

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Abstract: *Background:* Spatial memory is a cognitive process that allows us to locate ourselves in space based on visual references. Vestibular signals reaching the hippocampus from the vestibular nuclei have an important role in building this process. Vestibular conditions could affect this cognitive process. Meniere's disease is a chronic internal ear disease that causes impairment of hearing and vestibular function *Objective:* To determine the relationship between Meniere's disease and spatial memory in patients who attend the Anglo American clinic between 2016 and 2018. Specific objectives are: 1) identify patients with Meniere's disease and 2) assess spatial memory in these patients. *Design:* It is a cross-sectional correlated analytical study, where two groups were evaluated: a) with Meniere's disease and b) without Meniere's disease, comparable in age and sex. As a student T test statistic for mean difference in independent samples, considering equal variances. *Methodology:* Hearing and vestibular functions were evaluated, and Morris' virtual test was used to measure spatial memory. Four indicators were measured in the latter: time, percentage, distance and angle. *Results:* Group with Meniere's disease: N = 76, 38 males and 38 females, average age of 44.21-10 years; Meniere's disease-free group: N = 76, 38 males and 38 females, average age of 43.85-10. Comparing spatial memory between the two groups found a statistically significant difference ($p < 0.000$) in favor of Meniere's disease-free group in the four indicators. Within the group with Meniere's disease, spatial memory was evaluated according to the stage, without any significant difference between the different stages for the time indicators ($p = 0.334$), percentage ($p = 0.659$), distance ($p = 0.955$) and angle ($p = 0.916$). As for vestibular function, in which there was unilateral vestibular deficit, when compared to the Meniere's disease-free group, there was significant difference ($p < 0.000$) in the four indicators. The worst results were in those who had bilateral vestibular deficits. *Conclusions:* The group with Meniere's disease had poor spatial memory when compared to Meniere's disease-free group. The greatest commitment to space memory was in subjects with bilateral vestibular deficits.

Keywords: Meniere's Disease, Spatial Memory, Spatial Orientation, Hippocampus, Allocentric Memory

1. Introduction

Meniere's disease is a chronic disease of the inner ear, characterized by the presence of auditory symptoms such as fluctuating hearing loss, tinnitus and aural fullness, and vestibular symptoms such as vertigo and instability. The prevalence data are very variable, in Japan the prevalence is from 16 to 17 per 100 000, in Italy 8.2 per 100 000, while in the USA a prevalence of 218 per 100 000 [1]. Has been reported report highly variable prevalence rates, from 3.5 to 513 per 100,000 [2]. In another study the prevalence is 0.2% [3].

Spatial memory is a cognitive process that allows living beings to locate themselves in space and reach a certain destination, allows to encode, store and retrieve learned information about spatial locations. Studies on spatial cognition have a variety of origins, the behavioral psychologist Edward Tolman in 1948 introduced the term "cognitive map" in his publication Cognitive maps in rats and men [4]. Rats with hippocampal damage performed poorly on spatial memory tasks and assumed that it was due to loss of the neural system that provides the animal with a cognitive or spatial map of its environment [5]. It is the hippocampal "place cells" that are part of this integrated neural system for spatial navigation [6]. It was proposed that learning and memory were supported by two systems: a local system dependent on an intact hippocampus that supports cognitive mapping (learning about

the spatial relationships between signals), and a taxonomic system not confined to the hippocampus that supports stimulus-response learning or habitat learning [7].

In humans there is evidence that spatial orientation is linked to the hippocampus. The spatial memory process has three types of activities: guide signals, which depend on visual recognition memory, not location memory; cognitive mapping, which is the internal representation of spatial information which facilitates allocentric memory (the ability to determine spatial location independent of the body axis); and the integration of the pathway, which allows to update the relative position based on the perception of movement [8]. The "place cells" located in the hippocampus, responsible for the spatial location, are fed by vestibular inputs, and when the temporary inactivation of the vestibular system hapens this led to the disruption of the specific localization discharge of the "place cells" of the hippocampus and the head direction cells [9]. The otolytic vestibular and semicircular canal signals are integrated at the central level, modulating the "place cells" and "head direction cells" in the hippocampus, which has an important role in the coding and evocation of spatial memory [10, 11]. Vestibular information is processed in the hippocampus and the loss of vestibular input to the hippocampus interferes with the processing of internal self-movement signals with external ones that occur as a result of body movement [12]. Has been experimentally demonstrated that vestibular information modulates hippocampal activity for spatial processing and place cell discharges, by stimulating with high-frequency electricity specific vestibular sensory regions of the right labyrinth in guinea pigs, which induced evoked potential in bilateral hippocampal formation [13].

The vestibular system also influences the ability to perform certain cognitive processes, which can be evidenced in patients with vestibular deficits who have cognitive deficits as a result of this vestibular disorder, such as poor concentration and short-term memory loss [14]. Peripheral vestibular impairment not only compromises the spatial cognitive field, but also other non-spatial skills such as attention, language, immediate memory, late memory [15].

The progressive nature of Meniere's disease causes many patients to have significant vestibular impairment, as well as poor quality of life as a result. The objective of this research is to evaluate spatial memory in patients with Meniere's disease.

2. Materials and Methods

2.1. Study Design

This is a cross-sectional analytical study conducted at the Anglo American Clinic in the city of Lima, Peru, in patients with Meniere's disease treated in the Otolaryngology office in the years 2016 to 2018, and a group of patients who came who did not have Meniere's disease who were the control group. Patients with Meniere's disease and those in the control group were invited to participate, and signed the informed consent. There was authorization from the Ethics Committee of the institution: CIEI-CAA-497/2015.

2.2. Study Subjects

The diagnostic criterion of Meniere's disease formulated by the Classification Committee of the Bárány Society of 2015 [16] was used. We included patients with Meniere's disease of both sexes, aged between 20 and 60 years, with a degree of instruction of at least high school and with basic knowledge of the use of computers. Those who had pathology of the central nervous system such as tumors, degenerative diseases, sequelae of severe infarction, Parkinson's were excluded; cognitive function impairment, such as dementia; history of alcoholism; important visual pathology: monocular or total blindness, glaucoma, retinal detachment and findings of central vestibular involvement in the oculomotor battery of the vestibular test.

2.3. Hearing Assessment

Tonal audiometry was performed with a Madsen Itera II-Otometrics audiometer, with the evaluated one inside an audiometric booth. Pure tones of frequencies 0.25, 0.5, 1, 2, 3, 4, 6 and 8 KHz were administered through two headphones. The evaluated had to identify the sounds he heard and an auditory average was made using the auditory level of the frequencies 0.5, 1, 2 and 3 KHz. With this value, patients with Meniere's disease were grouped into stages: I, ≤ 25 dB; II, 26-40 dB; III, 41-70 dB and IV, > 70 dB. In cases of bilateral Meniere's disease, the higher auditory level of both ears was taken.

2.4. Vestibular Assessment

An Interacoustics videonystagmograph was used. Thermal stimulation in the ears with air at 28°C and 48°C was performed with an air irrigator (AirFx- Interacoustics), postcaloric nystagmus was recorded. This stimulation was alternate, starting with 48°C in the right ear, then in the left at the same temperature, to follow with 28°C in the left ear and ending in the right at 28°C. Three minutes elapsed between each stimulation. The speed of the slow phase of nystagmus was measured, in degrees per second of angular velocity. Vestibular deficit was considered if the sum of the velocity of post-caloric nystagmus per ear, both in stimulation at 28° and 48°C, was ≤5°/second. Values greater than this were considered normal. It was defined as unilateral vestibular deficit if it only occurred in one ear and bilateral if it was in both ears.

2.5. Spatial Memory Assessment

The Virtual Morris Water Maze (VMWM) test was used, in which participants observed a computer environment where they had first-person perspective and could navigate using the right-left-forward keys of the laptop. The virtual environment was designed in such a way that the participant felt immersed in a square-shaped room in the center of which is a circular pool. On each wall was a visual sign that served as a reference. In one of the pool quadrants is a square platform that occupies 2% of the pool area. The task

consisted of moving along the pool until you find the platform, which at the time of the test is invisible, for this it is necessary to make use of the visual signals that serve as a reference. Ten trials were conducted each with four repetitions, six of these trials were with non-visible platform and in four yes. Each test lasts up to one minute and ends when the platform is found, once found, the process is restarted, but with the start at another point in the environment. The platform was always in the same place. The participant had to remember the location of the platform not visible. The whole test takes about thirty minutes. Four spatial memory indicators were measured: (1) "time", this is the time it took to find the platform, (2) "distance" is the distance traveled to find the platform, (3) the "angle" is the angular deviation of the straight-line path to the platform measured one second after the movement has begun, and (4) the "percentage" is the percentage of the total path that passes in the quadrant of the platform. The "time" was expressed in seconds, the "distance" traveled was measured as the ratio of the route between the diameter of the pool, the "angle" in degrees and the "percentage" as the percentage of the time that the evaluated remained in the quadrant where the platform was located. In this test, the ability to remember the location of a platform in a pool was evaluated. In a good spatial memory there is less "time", less "distance", smaller "angle" and greater "percentage".

2.6. Statistical Analysis

The Kolmogorov-Smirnov normality test was applied to verify if the data presented a normal distribution, in case of normal distribution "t" test will be used for independent samples considering equal variances, otherwise the Wilcoxon test. Descriptive statistics were performed for the presentation of the characteristics of the two groups applying summary measures: Mean and standard deviation or median and interquartile range if the distribution is not normal. With a $\alpha = 0.05$.

3. Results

In order to evaluate the relationship between spatial memory and Meniere's disease, two groups were studied: 1) Group with Meniere's disease, N = 76, 38 women and 38 men, aged 44.21±10 and 2) Group without Meniere's disease, N = 76, 38 women and 38 men, aged 43.85±10. There was no significant difference in age in both groups (t=0.2219, p=0.8247) (Table 1).

In the group with Meniere's disease, the following were evaluated: a) auditory function, in which the auditory average was determined and grouped into stages; b) vestibular function, in which patients with vestibular function deficit were identified as those in whom the rate of post-caloric bitermal nystagmus ≤ 5°/second (Tables 2 y 3).

When comparing the means of the four indicators between the groups with Meniere's disease and without Meniere's disease, a statistically significant difference was found in these indicators (Table 4).

The stages of Meniere's disease were grouped into two groups, which were compared with each other, without finding a statistically significant difference between them (Table 5), but when compared independently with the group without Meniere's disease there was a difference (Tables 6 y 7).

Regarding spatial memory and unilateral vestibular deficit, there was a significant difference when compared with the group without Meniere's disease (Table 8). Because only 8 patients with Meniere's disease had bilateral vestibular deficit, which does not allow a statistical analysis, but the values of the indicators are different: "time"=25.41±7.66, "percentage"=43.29±7.98, "distance"=1.69±0.63 and "angle"=30.50±12.37.

Table 1. *Characteristics of groups with Meniere's disease and without Meniere's disease according to age and sex. Anglo American Clinic, 2016-2018.*

Age	Meniere's disease		Non-Meniere's disease	
	Men	Women	Men	Women
20 - 30	6	4	6	5
31 - 40	7	11	8	11
41 - 50	13	10	12	10
51 - 60	12	13	12	12
	38	38	38	38
X ± SD	44.21±10		43.85±10	

Table 2. *Stage of Meniere's disease. Anglo American Clinic.2016-2018.*

Meniere's Disease		
Stage	**n**	**%**
I	2	3
II	17	22
III	42	55
IV	15	20
	76	100

Table 3. *Vestibular Function in Meniere's Disease Group. Anglo American. Clinic. 2016-2018.*

Meniere's Disease		
Vestibular Function	**n**	**%**
Unilateral vestibular deficit	30	39
Bilateral vestibular deficit	8	11
Non-vestibular deficit	38	50
	76	100

Table 4. *Spatial Memory Between Meniere's Disease and Non-Meniere´s Disease Groups. Anglo American Clinica. 2016-2018.*

Spatial Memory	Meniere´s Disease		Non-Meniere´s Disease		T-test			
Indicators	**Mean**	**SD**	**Mean**	**SD**	**Mean Difference**	**t-test**	**gl**	**Sig (bilateral)**
Time[1]	25.19	9.41	18.06	6.89	7.13	5.335	150	0.000
Percentage	46.25	8.66	57.62	8.72	-11.38	-8.07	150	0.000
Distance	1.42	0.44	1.12	0.35	0.30	4.642	150	0.000
Angle[2]	25.02	9.34	15.09	7.31	9.93	7.295	150	0.000

SD: Standar deviation 1: Time in seconds 2: Angle in grades.

Table 5. *Spatial memory between stages I-II and III-IV in Meniere's Disease Group. Anglo American Clinic. 2016-2018.*

Spatial Memory	Stage I-II (N=19)		Stage III-IV (N=57)		T-test			
Indicators	Mean	SD	Mean	SD	Mean Difference	t-test	gl	Sig (bilateral)
Time[1]	23.37	9.52	25.80	23.37	-2.42	-0.972	74	0.334
Percentege	45.48	9.82	46.50	45.48	-1.02	-0.443	74	0.659
Distance	1.41	0.40	1.42	1.41	-0.01	-0.057	74	0.955
Angle[2]	25.22	9.35	24.95	25.22	0.26	0.105	74	0.916

SD: Standar deviation 1: Time in seconds 2: Angle in grades.

Table 6. *Spatial Memory between stages I-II and Non-Meniere´s Disease Group. Anglo American Clinic. 2016-2018.*

Spatial Memory	Stage I-II (N=19)		Non-Meniere's Disease		T-test			
Indicators	Mean	SD	Mean	SD	Mean Difference	t-test	gl	Sig (bilateral)
Time[1]	23.37	9.52	18.06	6.89	5.32	2.776	93	0.007
Percentege	45.48	9.82	57.62	8.72	-12.14	-5.292	93	0.000
Distance	1.41	0.40	1.12	0.35	0.29	3.180	93	0.002
Angle[2]	25.22	9.35	15.09	7.31	10.12	5.017	93	0.000

SD: Standar deviation 1: Time in seconds 2: Angle in grades.

Table 7. *Spatial Memory between stages III-IV and Non-Meniere´s Disease Group. Anglo American Clinic. 2016-2018.*

Spatial Memory	Stage III-IV (N=57)		Non-Meniere´s Disease (N=76)		T-test			
Indicators	Mean	SD	Mean	SD	Mean Difference	t-test	gl	Sig (bilateral)
Time[1]	25.80	9.37	18.06	6.89	7.74	5.491	131	0.000
Percentege	46.50	8.31	57.62	8.72	-11.12	-7.423	131	0.000
Distance	1.42	0.45	1.12	0.35	0.30	4.314	131	0.000
Angle[2]	24.95	9.26	15.09	7.31	9.86	6.863	131	0.000

SD: Standar deviation 1: Time in seconds 2: Angle in grades.

Table 8. *Spatial Memory between Unilateral Vestibular Deficit in Meniere´s Disease Group and Non-Menere´s Disease Group. Anglo American Clinic. 2016-2018.*

Spatial Memory	Unilateral Vestibular Deficit (N=30)		Non-Meniere´s Disease (N=76)		T-test			
Indicators	Mean	SD	Mean	SD	Mean Difference	t-test	gl	Sig (bilateral)
Time[1]	27.76	11.14	18.06	6.89	9.71	5.426	104	0.000
Percentege	46.01	8.86	57.62	8.72	-11.61	-6.14	104	0.000
Distance	1.51	0.49	1.12	0.35	0.40	4.703	104	0.000
Angle[2]	25.90	8.81	15.09	7.31	10.84	6.480	104	0.000

SD: Standar deviation 1: Time in seconds 2: Angle in grades.

4. Discussion

The objective of the present research was to determine the spatial memory in patients with Meniere's disease. Two groups were compared, with Meniere's disease and without Meniere's disease; both groups are comparable in age and sex. A quarter of the patients with Meniere's disease were in the first two stages, while the rest had more advanced stages of this disease. In a retrospective study in 89 patients, found figures similar to ours [17]. This in general, because the initial stages of the disease are usually underdiagnosed, for several reasons, among them, because the initial symptoms of the disease are usually auditory and are overlooked by patients who do not come in a timely manner to medical attention. However, in a prospective study conducted in Japan in 90 patients, had different figures in different stages and, in stage I, had proportionally more patients than in this study; this difference may perhaps be due to the fact that the health system in Japan allows early diagnosis [18].

Regarding vestibular function, 50% of patients with Meniere's disease had vestibular deficit, either unilateral or bilateral, determined in this study by caloric test. This test is the most sensitive to detect canal paresis in Meniere's disease (19). Taking as a reference the asymmetries ≥ 25%, in different studies the percentages of canal paresis vary from 45% to 76% [17-22]. Fukushima [18] reported the lowest percentage of vestibular deficit and this may be because in its sample a significant percentage of patients were in the early stages of the disease (I-II). As can be seen from the studies mentioned, there is variability in the percentages of vestibular deficit found. This study reports vestibular deficit in 50%, because a significant percentage of patients are in an advanced stage of the disease.

To evaluate the impact of peripheral vestibular pathology on spatial memory, the means of these indicators of the group with Meniere's disease were compared with the group without Meniere's disease, finding a statistically significant difference in the means of the values of the four indicators between both groups. In a study made in Germany where was used the Morrris Water Maze virtual test to assess spatial memory showed evidence of deficit in memory and spatial

learning in chronic bilateral vestibulopathy [23]; this work is mentioned, despite being more than fifteen years old, because it is one of the first to address this topic and because the same spatial memory test has been used, which allows comparison. Brandt et al [24] evaluated the same population in order to determine if there was variation in hippocampal volume, finding that in patients with bilateral vestibulopathy the volume of the hippocampus was lower than in the controls. Using the same spatial memory measurement instrument as in this study, the controls performed better on spatial memory indicators without becoming statistically significant and no found changes in hippocampal gray matter volumen [25]. Has been found that reduction in hippocampal gray matter volume was related to the severity of bilateral vestibulopathy and that reduction in hippocampal volume was related to peripheral vestibular impairment [26]. In this study measuring hippocampal volume was not a goal, however, this is mentioned to reinforce the concept of the hippocampus as the axis of spatial memory.

In the relationship between meniere's disease and spatial memory, patients were gathered into two groups, stages I-II and stages III-IV. When comparing both groups individually with the group without Meniere's disease, statistically significant difference was found in all indicators (tables 6 y 7). When both groups were compared with each other, there was no statistically significant difference in the four indicators, but there was a difference in the mean of the time indicator between stages I-II and III-IV (Table 5). In an experimental study in rats that were exposed to noise, in order to produce sensorineural hearing loss, who were evaluated spatial memory with the Morris pool test found that sensorineural hearing loss significantly reduced spatial learning at various stages of hippocampal neurogénesis [27]. Although patients in stages III-IV should be more compromised and therefore more impaired spatial memory compared to the stage I-II group except for the mean of the time indicator, this is not decisive in the deterioration of spatial memory in this study.

Because the bilateral vestibular deficit group consisted of only eight patients, it is not possible to draw exact conclusions, but when comparing the means of the indicators "percentage", "distance" and "angle", with the unilateral vestibular deficit group, greater commitment of the bilateral vestibular deficit group was observed, especially in the "angle" indicator. Vestibular deficit, especially bilateral deficit, was a determining factor in spatial memory impairment in this population of patients with Meniere's disease studied. Spatial memory indicators in this study showed greater engagement than in previous similar studies [23, 24]; this may be due to the fact that the population of those investigations was formed by patients who had undergone bilateral neurectomy for neurofibromatosis type 2 between five to ten years before their study and the protocol in these surgeries has the obligation to perform vestibular rehabilitation therapy after the surgical procedure, so as a result of rehabilitation therapy, compensation occurs at the central level that provides 60% of the improvement of the vestibule-ocular reflex [28], and vestibular rehabilitation therapy improves visuo-spatial work; therefore, patients with neurofibromatosis type 2 mentioned in these studies, reached after several years a state of functional stability [29].

Regarding the relationship of vestibular function and spatial memory, when comparing the unilateral deficit group in Meniere's disease, with the group without Meniere's disease, the difference was statistically significant in the four indicators (table 8). In Meniere's disease the vestibular compensation is never completed completely, it is a progressive, unstable disease, with periods of transient compensation and decompensation, so the spatial memory is more impaired generating greater spatial cognitive impairment. In a computational model showed that the neural substrate that underpins spatial memory is transient and synaptic connections in the hippocampus never stop forming and deteriorating at a rapid rate [30]. Seo et al [31] in a study conducted to establish the relationship between Meniere's disease and hippocampal volume, found that this was lower than in healthy controls ($p<0.001$); his explanation goes beyond the already established fact that vestibular afferences that start from the vestibular nuclei feed the hippocampus, since he claimed that chronic stress due to the unpredictability of vertigo and fluctuating hearing loss caused stress-related hormones to increase and this causes atrophy of the hippocampus. This work opens another possible explanation for the deterioration of spatial memory in patients with Meniere's disease, chronic stress; both explanations, the deficit of vestibular signals and chronic stress go through a common point, the functional deterioration of the hippocampus.

5. Conclusion

Meniere's disease is a disease of the inner ear in which there is progressive auditory and vestibular involvement. In this study most patients were in advanced stages of the disease. Half had impaired vestibular function. Spatial memory was impaired in patients with Meniere's disease, related to the compromise of vestibular function, especially in bilateral vestibular deficits, and not to the auditory level. Due to the unstable and progressive nature of this disease for which adequate vestibular compensation is not achieved, an important compromise of spatial memory indicators was evidenced.

6. Recommendations

Investigate the effect of vestibular system conditions on cognitive processes. Incorporate cognitive rehabilitation therapy into vestibular rehabilitation therapy to achieve a comprehensive recovery of patients with vestibular impairment.

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References

[1] Kotimäki J (2003). Meniere's disease in Finland. An epidemiological and clinical study on occurrence, clinical picture and policy. Academic Dissertation presented with the assent of the Faculty of Medicine, University of Oulu. October 17th.

[2] Tassinari MT, Mandrioli D, Gaglioli N, Di Sarsina PR (2015). Meniere's disease treatment; A patient-centered systematic review. Audiol Neurotol; 20: 153-165.

[3] Neuhauser HK, Lempert T (2009). Vertigo: epidemiologic aspects. Seminars in Neurology. 29 (5): 473-481.

[4] Tolman EC. Cognitive maps in rats and men (1948). Phychological Review. 55: 189-208.

[5] O'Keefe J, Dostrovsky J [1971). The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat. Brain Research. 34: 171-175.

[6] Poucet B, Lenck-Santini PP, Hok V, Lave E, Banquet JP, Gaussier P, Muller RU (2004). Spatial navigation and hippocampal place cell firing: The problem of goal encoding. Reviews in The Neuroscience. 15: 89-107.

[7] Good M (2002). Spatial memory and hippocampal function: where are we now? Psicologica. 23: 109-138.

[8] Allen GL (2004) Human spatial memory. Remembering where (XIII-XVIII). London: Lawrence Erlbaum Associates, Publishers. 368.

[9] Stackman RW, Clark As, Taube JS (2002). Hippocampal spatial representations require vestibular input. Hippocampus. 12: 291-303.

[10] Medendorp WP, Selen LJP (2017): Vestibular contribution to high-level sensorimotor functions. Neuropsychologia. 105: 144-152.

[11] Brandt T, Zwergal A and Glasauer S (2017): 3-D spatial memory and navigation: functions and disorders. Curr Opin Neurol. 30: 000-000. DOI: 10.1097/WCO.0000000000000415.

[12] Russell NA, Horii A, Smith PF, Darlington CL, Bilkey DK (2003). Long-term effects of permanent vestibular lesions on hippocampal spatial firing. Journal of Neuroscience. 23 (16): 6490-6498.

[13] Cuthbert PC, Gilchrist DP, Hicks SL, Mac Dougall HG, Curthoys IS (2000). Electrophysiological evidence for vestibular activation of the guinea pig hippocampus. NeuroReport. 11: 1443-1447.

[14] Hanes DA, McCollum G (2006). Cognitive-vestibular interactions: A review of patient's difficulties and possible mechanisms. Journal of Vestibular Research. 16: 75-91.

[15] Dobbels B, Mertens G, Gilles A, Claes A, Moyaert J, Raymond Van den Berg et al (2019). Cognitive Function in Acquired Bilateral Vestibulopathy: A Cross-sectional Study on Cognition, Hearing, And Vestibular Loss. Front Neurosci. 13: 340. DOI: 10.3389/fnins.2019.00340.

[16] Lopez-Escamez JA, Carey J, Chung WH Goebel JA, Magnusson M, Mandalá M et al (2015). Classification comittee of the Barany Society; Japan Society for Equilibrium Research: European Academy of Otology and Neurotology (EAONO); Equilibrium Committe of the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS); Korean Balance Society Diagnostic criterio for Meniere's disease. J Vestib Res. 25 (1): 1-7. DOI: 10.3233/VES-150549. PMID: 25882471.

[17] Van Esch BF, Abolhosseini K, Masius-Olthof S, Van Der Zaag-Loonen HJ, Van Benthem PPG, Bruintjes TJD (2019). Video-Head Impulse Test Results in Patients with Meniere's Disease Related to Duration and Stage of Disease. Journal of Vestibular Disease Research. DOI: 10.3233/VES.190654.

[18] Fukushima M, Oya R, Nozaki K, Eguchi H, Akahani S, Inohara H et al (2019). Vertical Head Impulse and Caloric Are Complementary but React Opposite to Meniere's Disease Hydrops. Laryngoscope 00: 1-7. DOI: 10.1002/lary.27580.

[19] Blodow A, Heinze M, Bloching MB, Von Brevern M, Radtke A, Lempert T (2014). Caloric Stimulation and Video. Head Impulse Testing in Meniere's Disease and Vestibular Migraine. Acta Oto-Laryngologica. 134: 1239-1244.

[20] Limviriyakul S, Luangsawang Ch, Suvansit K, Prakairugthong, Thongyai K, Atipas S (2019). Video head impulse test and caloric test in definite Meniere's disease. European Archives of Oto-Rhino-Laryngology. DOI: 10.1007/s00405-019-05735-8.

[21] Mc Mullen KP, Lin Ch, Harris MS, Adunka OF (2017). Correlation Of Objetive Audiometric and Caloric Function in Meniere's Disease. Otolaryngology-Head and Neck Surgery. DOI: 10.1177/0194599817690103.

[22] Cordero-Yanza JA, Arrieta Vásquez EV, Hernaiz Leonardo JC, Mancera Sánchez J, Hernández Palestina MS, Pérez-Fernández N (2017). Comparative Study Between the Caloric Vestibular and The Video- Head Impulse Tests in Unilateral Meniere's Disease. Acta Oto-Laryngologica. DOI: 10.1080/00016489.2017.1354395.

[23] Schautzer F, Hamilton D, Kalla R, Strupp M, Brandt T (2003). Spatial memory deficits in patients with chronic bilateral vestibular failure. Ann. N. Y. Acad. Sci. 1004: 316-324.

[24] Brandt T, Schautzer F, Hamilton DA, Brüning R, Markowitsch HJ, Kalla R et al (2005). Vestibular loss causes hippocampal atrophy and impaired spatial memory in humans. Brain. 128: 2732-2741.

[25] Kremmyda O, Hüfner K, Flanagin VL, Hamilton DA, Linn J, Strupp M et al (2016). Beyond Dizzines: Virtual Navigation, Spatial Anxiety and Hippocampal Volume in Bilateral Vestibulopath. Front Hum Neurosci. 10: 139. DOI: 10.3389/fnhum.2016.00139.

[26] Göttlich M, Jandl NM, Sprenger A, Wojak JF, Münte TF, Krämer UM et al (2016). Hippocampal Gray Matter Volume in Bilateral Vestibular Failure. Hum Brain Mapp. 37: 1998-2006.

[27] Liu L, Xuan Ch, Shen P, He T, Chang Y, Shi L et al (2018). Hippocampal mechanisms underlying impairment in spatial learning long after establishment of noise-induced hearing loss in CBA mice. Front Syst Neurosci 12: 35. DOI: 10.3389/fnsys.2018.00035.

[28] Allum JHJ, Scheltinga A, Honegger F (2017). The effect of peripheral vestibular recovery on improvements in vestibulo-ocular reflexes and balance control after acute unilateral peripheral vestibular loss. Otol Neurotol. 38: e531-e538.

[29] Guidetti G, Guidetti R, Manfredi M (2019). Vestibular Pathology and Spatial Working Memory. Acta Otorhinolaryngol Ital. Jul 31. DOI: 10.14639/0392-100X-2189.

[30] Babichev A, Morozov D, Dabaghian Y (2018). Robust spatial memory maps encoded by networks with transient connections. PLoS Comput Biol. 14 (9): e1006433. DOI: 10.1371/journal.pcbi.1006433.

[31] Seo YJ, Kim J, Kim SH (2016). The Change of Hypocampal Volume and its Relevance with inner ear Function in Meniere's Disease Patients. Auris Nasus Larynx. DOI: 10.1016/j.anl.2016.01.006.