

Brief Insight About Audiovestibular Findings In Multiple Sclerosis

Walid Ibraheem¹, Nadia Elnabtity¹, Eman Shahba²

1. Audio-Vestibular medicine, Otorhinolaryngology Department, Faculty of Medicine- Zagazig University, Egypt.
2. Audio-Vestibular medicine, Otorhinolaryngology Department, Om El Masreyeen General Hospital, Giza, Egypt

Corresponding author: Eman Shahba

Email : eman.gamal136@gmail.com

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Abstract

Multiple sclerosis (MS) is a highly variable disease in its course, site of the lesion and even at the rate of progression. A full picture of the hearing affection cannot be predicted. Most of MS cases start as relapsing-remitting multiple sclerosis (RRMS) then with time it turns into secondary progressive multiple sclerosis (SPMS). Pure tone thresholds may not challenge the auditory system strong enough to detect underlying dysfunction, such as that detected by stimuli varying in the temporal domain. The most common studies of auditory evoked potential (AEP) in MS are the brainstem auditory evoked potential (BAEP), the auditory middle latency response (MLR) and the event related potentials. The most common deficits that were observed in BAEP of MS patients are increased latencies of waves III and V, increased I-III, III-V and I-V interpeaks, the absence of one or more components, and poor reproducibility and morphology of the later components suggesting dyssynchrony. The MLR is considered one of the best tests to evaluate the central auditory nervous system, and it is also a useful tool in the design and monitoring of the therapeutic process. Central auditory processing abnormalities are present in 90% of MS patients. Difficulty in speech perception in background noise was reported by many researchers. Gab in noise (GIN) test is a simple, sensitive test for temporal resolution ability which also affected in MS patients. Patients with MS may develop dizziness or vertigo as the initial disease manifestation or during the course of illness. Many patients experience chronic, intermittent dizziness and ~5 % label dizziness or vertigo as their worst symptom of the disease. The vestibular system function could be evaluated via videonystagmography (VNG), which evaluates peripheral and central vestibular functions.

Keywords: Auditory findings, vestibular , Multiple Sclerosis

INTRODUCTION

MS is a highly variable disease in its course, site of the lesion and even at the rate of progression. A full picture of the hearing affection cannot be predicted. Most of MS cases start as RRMS then with time it turns into SPMS(1).

A person affected with RRMS will have periods of relapse intervened by periods of remission. During the relapse active demyelination and inflammation are the main pathological event that last for weeks; however, axonal loss is partial(2).

If the disease is on its early stage, even if the active lesion is near an important auditory landmark, a silent phase with no hearing complaints may occur. The silent phase is caused by the fact that human CNS has a remarkable ability to compensate for axonal loss(3). As the disease progress, the compensatory mechanisms can't keep up with the increased axonal loss, so the disease may reach a clinical threshold above which the disease manifests. The reported complain in literature in this phase is a sudden transient hearing loss(4).

Suddensorineural hearing loss (SNHL) is reported to occur between relapses or remissions in 4-10% of MS patients. Such complain may occur when MS active lesion oedema overlay the caudal centrally myelinated end of the 8th nerve, cochlear nucleus and pontine trapezoid body(5). With disease progression into SPMS the prominent pathological feature is brain atrophy and the axonal loss becomes extensive. MS turns into a neurodegenerative disease. Some may say it resembles subcortical dementias impairment pattern (6).

1- Auditory findings in MS

A. Pure tone thresholds:

Pure tone thresholds may not challenge the auditory system strong enough to detect underlying dysfunction, such as that detected by stimuli varying in the temporal domain. A well-controlled study observed that pure tone thresholds were not

elevated in chronic MS even if the lesion overlapped the auditory pathway and the pure tone thresholds were not significantly different from the thresholds of MS patients whose lesion did not overlap the auditory pathway (5).

B- Auditory evoked potentials (AEP) in MS:

The most common studies of AEP in MS are the brainstem auditory evoked potential (BAEP), the auditory middle latency response (MLR) and event related potentials(7).

ABR:

The most common deficits that were observed in BAEP of MS patients are increased latencies of waves III and V, increased I-III, III-V and I-V interpeaks, the absence of one or more components, and poor reproducibility and morphology of the later components suggesting dyssynchrony(8).

MLR:

The MLR is considered one of the best tests to evaluate the central auditory nervous system, and it is also a useful tool in the design and monitoring of the therapeutic process. The presence of auditory MLR abnormalities in individuals with MS was also evidenced by **Celebisoy et al., (9)**who reported the occurrence of abnormalities in 73.4% of individuals assessed. Auditory MLR abnormalities were also observed in the MS case study presented by **Schochat et al., (10)**thus demonstrating the possibility of involvement of the auditory pathway at the subcortical level.

Event related potentials:

P300:

Studies that compared MS patients with controls in such tests yielded a significant increase in P300 latencies. An example of such a difference was demonstrated by **Magnano et al., (11)**. Moreover, many studies indicate a significant correlation between auditory P300 latency and demyelinating plaques seen on frontal horn and brainstem in MRI (11).

Mismatch negativity (MMN):

Santos et al., (12)use the MMN as an electrophysiological measure for the investigation of the auditory pathway in patients with MS. Moreover, study on forty MS patients found that MMN was absent in 40% of MS individuals using varied duration protocols and in 55% using varying frequency protocol. Moreover, in cases that MMN was present, there were no statistically significant differences in latencies and amplitudes when compared to controls.

Jung et al., (13) study on forty-six MS patients, MMN wave was absent in 6.3% of MS patients that were cognitively intact, and absent in 16.6% of MS patients that were cognitively impaired when tested by paced auditory serial addition task (PASAT). The latencies of MMN were not statistically different between the study and control groups.

C. Central auditory processing in MS patients:

Central auditory pathway abnormalities are present in 90% of MS patients (14). **Elbeltagy et al., (15)** reported that temporal resolution, temporal ordering, dichotic listening and selective attention were affected in MS patients. There for the study considered the assessment of central auditory function is highly recommended for all MS patients as a routine examination and can be used to monitor the effectiveness of medication and related treatment for these patients.

2-Vestibular findings in MS:

Patients with MS may develop dizziness or vertigo as the initial disease manifestation or during the course of illness. Many patients experience chronic, intermittent dizziness and ~5 % label dizziness or vertigo as their worst symptom of the disease(16). It is common for people with MS to have equilibrium disorders caused by involvement of the brainstem and cerebellar structures because they are both functionally linked in the control of sensory inputs and motor output. Furthermore, the brainstem and cerebellum are also linked to the audiovestibular system, which is involved in multisensory integration and coordination of motor responses(17). The impaired balance by people with MS can be caused by weakness in muscle strength and compromised motor control. Cognitive dysfunction in patients with MS may be the underlying risk factor for the increased risk of falls due to altered information processing, attention, decision making, error correction and execution of motor function (18). Acute symptoms of dizziness or vertigo in MS fall into two major categories acute vestibular syndrome (AVS) and positional vertigo. The AVS is a single, prolonged, spontaneous episode of acute vertigo or dizziness lasting days to weeks, coupled with nausea or vomiting, nystagmus, head motion intolerance, and gait disturbance (19).

Videonystagmography (VNG):

The vestibular function could be evaluated via VNG, which evaluates peripheral and central vestibular functions. There are 3 main parts to perform a VNG test. The first part is ocular motor testing. It includes saccade test, smooth pursuit test, optokinetic (OPK) test and gaze test. The common bond of these tests is that each one evaluates eye movements that originate in the cerebellum and abnormalities in these tests are considered signs of neurologic (central) lesion (20). In Saccade test: patients must gaze at a target in front of them rapidly moving in a randomized way horizontally from left to right and from right to left. The same test is then done vertically (21).

While in a smooth pursuit test, the patients must follow a target moving at different frequencies: 0.3 Hz, 0.45 Hz and 0.6 Hz horizontally. In the OPK test, bright spots move from left to right or from right to left and the patient must look straight head. The movement of the bright spots produces the OPK reflex. In central pathologies such as stroke, the patient's OPK reflex gain is reduced (20). The second part of the VNG test is Positioning/Positional testing in which the patient will be asked to move his head and body in a series of positions. During this part of the test, the patient may experience dizziness and/or vertigo. This is more likely to occur if the initial symptoms of dizziness are triggered by movement (22).

The last part is a caloric test. Caloric testing is a useful clinical tool that can assess the function of the vestibular system. The test utilizes the mechanics of the vestibular-ocular reflex (VOR) to test for a unilateral peripheral deficit. The VOR requires an intact brainstem to function and its purpose is to maintain eye fixation on a stationary target while the head is in motion, thus keeping the object of attention in the center of the visual field(23). Failure of fixation suppression and fixation index (greater than 0.6) is abnormal and indicative of CNS involvement. Hyperactive response which is defined as water responses that exceed 50deg/Sec for cools and 80deg/Sec for warms, usually is due to excellent inner ear function in a nervous young person, in the absence of this, very rarely it is due to a CNS problem (cerebellar lesion). Moreover, caloric inversion and perversion are also indicative of CNS involvement. Caloric inversion which entire caloric response beats in the wrong direction while perversion: vertical or oblique nystagmus in response to caloric stimulation (24).

Bilateral hyperreflexia may be observed in in MS patients. Normally, the cerebellar flocculus inhibits vestibular nucleus neurons. Injury to the cerebellar flocculus affects this inhibitory function, increasing the excitatory state of the vestibular nucleus, resulting in bilateral hyperreflexia(25). No evaluation of a patient either suspected or diagnosed with MS is complete without a systematic examination of their vision and eye movements. The most common eye movement abnormalities in MS patients are saccadic dysmetria, INO, disorders of the VOR, and gaze-evoked nystagmus (26).

Degirmenci et al.,(27) evaluate 30 MS patients compared with 30 healthy individuals using ENG tests. They found 16 of MS patients had impaired smooth pursuit test, 11 patients had abnormalities in saccade test, 5 patients with asymmetry in OPK test, 3 of MS patients with gaze evoked nystagmus, positional test was abnormal in 5 patients and Dix-Hallpike test abnormality was found in 2 patients. 60% of patients had MRI lesions and 40% had a normal MRI, both showing ENG abnormalities, suggesting that evaluation of vestibular symptoms with ENG is more sensitive than clinical examination and MRI.

Video Head impulse test (vHIT):

vHIT is a new objective, quantitative test of vestibular function. It is a video-based equipment test that enables to detect the eye response (VOR) to sudden head impulse stimulations. It is used to measure the gain of the VOR and to detect refixation saccades (overt and covert saccades) which are detected by using head impulses stimulations. It can assess SCCs individually (28). It consists of monitoring eye movements as the patient fixates on a stationary target while the head is moved briskly to the right or left in the plane of the lateral SCCs. Also, the test can be performed in the planes of right anterior-left posterior (RALP) or left anterior-right posterior (LARP) canal pairs (29).

vHIT is the only test that assesses all six SCCs independently and with a physiological stimulus, similar to how the patient uses the VOR system in daily life. The test is essential in determining if the peripheral vestibulopathy affects the superior or inferior branch of the nerve, if the loss is unilateral or bilateral, or only affecting the anterior, posterior or lateral canals. In combination with VEMPs (vestibular evoked myogenic potentials), all 5 end organs for both ears can be assessed(30). Advantages of vHIT over other clinical vestibular measures of canal function (e.g., caloric, rotary chair) are that it provides information regarding individual canal function, is quick to administer, and does not induce dizziness. However, its relationship to other tests of canal function suggests that vHIT is not a replacement to, but adjunctive to other tests of vestibular function (31).

It has been shown that the vHIT is of great importance in evaluating the function of the peripheral vestibular system (31). Although, the primary use of vHIT is to make a distinction between peripheral and central vestibular disorders by detecting peripheral vestibular dysfunction, some researches have shown that VOR can also be impaired when central part of the vestibular system is damaged. With presumption that demyelinating lesions affecting central part of vestibular system could possibly cause impairment in VOR gain (32).

Twenty nine MS patients (58 ears) were investigated using the vHIT comparing them with 39 controls (78 ears). In MS group 16 ears had abnormal in horizontal canals, 11 ears had abnormal in anterior canals and 11 ears had abnormal in posterior canals. The mean gain of the horizontal canals was significantly reduced in MS group, but a mean gain of anterior and posterior canals were not significantly reduced in MS. There was statistically significant association between the presence of brainstem MRI lesions and bilateral pathology on vHIT for lateral SSC. So, these results indicate that vHIT can detect brainstem dysfunction in patients with MS (33).

VEMPs:

VEMPs, are electro-myographic responses derived from the vestibular labyrinth evoked by sound, vibration, or electrical stimulation. VEMP is a clinical test of the otolith organs, sensors of linear acceleration and related reflex pathways. The otolith organs in human are consisted of the saccule and the utricle. VEMP was first reported by **Colebatch and Halmagyi**,(34).

The cervical VEMP (cVEMP) pathway is believed to originate in the saccular macula and continues through the vestibular nerve and nucleus, the vestibulospinal tracts, spinal motor nucleus and sternocleidomastoid (SCM) muscles. cVEMP responses are characterized by biphasic waves with initial positivity (p13) followed by a negative wave (n23). Recently, the myogenic response recorded from contralateral extraocular muscles in response to acoustic stimuli has been reported to be a manifestation of crossed VOR and named "ocular VEMP" (oVEMP). The oVEMP pathway is thought to travel through the MLF, the

oculomotor nuclei and nerves and the extraocular muscles after the activation of the vestibular nerve and nucleus. oVEMP responses are characterized by biphasic waves with an initial negative peak (n10) followed by a positive peak (p15) (35). The cVEMP test has become an important diagnostic tool, particularly in the evaluation of peripheral vestibular disorders. Moreover, VEMPs are thought to provide useful information about brainstem functions, as the neural pathway of both VEMPs passes through the brainstem. While cVEMP descends via the vestibulospinal tract through the lower brainstem, oVEMP ascends via the MLF through the upper brainstem (35).

Colebatch and Halmagyi, (34) reported that the test is not suitable for subjects with neck spasm or cervical spine problems. Also, testing VEMPs in children are difficult especially in very young subjects as it needs sustained tonic contraction of the muscle from which the response will be recorded.

Shimizu et al., (36) investigated VEMPs in patients with MS and reported that the latencies of VEMPs can be prolonged in patients with MS. Prolonged VEMPs latencies could be due to demyelination from either of primary afferent axons at the root entry zone or secondary vestibulospinal tract axons rather than to lesions involving vestibular nucleus. Severe demyelinating lesions accompanied with axonal loss will result in a total conduction block with absence of responses. Measurement of VEMPs is therefore helpful in detecting subclinical vestibulospinal lesions in suspected MS (37).

Crnosija et al., (38) examined 121 MS patients using oVEMP. Patients who presented with brainstem symptoms had a higher oVEMP abnormality. Patients with signs of brainstem involvement during the neurological examination had a higher oVEMP abnormality compared to patients with no signs of brainstem involvement, while they found no difference in oVEMP abnormality regarding the presence of brainstem MRI lesions. There was significant correlation between prolonged latencies and/or absent oVEMP response and the presence of pontine and medulla oblongata lesions. This study had confirmed the oVEMP abnormalities as a valid tool for detection of brainstem dysfunction in patients with MS.

Posturography:

The evaluation of the body balance consists of tests that either determine diagnostic values or inform the ability of the individual in remaining in a static posture. One of these tests is the computerized dynamic posturography (CDP). It evaluates the body oscillation by recording patient's foot pressure on a platform (force plate) and it also allows us to analyze the secondary posture reaction towards the central displacement of the body mass(39).The CDP is a method of quantity and quality evaluation. It is performed with a computed-system that analyses the participation of the vestibular, sensory, visual and somatosensory information in the body balance in a global and isolated way and also analyses the central integration of these systems (40).

The deficit of postural control observed in patients with MS, who have a widespread, varied and sometimes extensive damage into the CNS, may be due to multifactorial causes that differ from person to person. Therefore, the postural balance deficit has been generally interpreted as a result of an impaired central integration of visual, vestibular and somatosensory inputs(41). However, it is also possible that damage in specific locations of CNS is the primary contributor to MS-related balance deficit, as suggested by MRI studies. One preliminary study found that the presence of a greater lesion volume (as seen on T2-weighted images) at the brainstem level might be considered as a risk factor for multiple accidental falls (collected in a time frame of 6 months), regardless of the patient's disability level. Indeed, impaired postural control is often observed in MS, with approximately two-thirds of these patients reporting lack of balance and coordination as the main symptom affecting their mobility in daily living (42).

The balance deficit reduces mobility and independence, leads to falls and injuries, and impacts upon the overall quality of life. Fatigue, muscle weakness and spasticity further contribute to compromising adequate balance and predispose patients to accidental falls.Observational studies conducted on young and middle aged MS sample also showed that the proportion of fallers may range from 30% to 63% in a time frame of 1–12 months, with about 29%–45% being recurrent fallers(43). Reliability is a principal psychometric property of tests and outcome measures. The CDP is a statistically significantly reliable test of balance of central sensory integration (CSI) in people with MS. The test-retest reliability coefficients, ranging from 0.70 to 0.90 and the composite score for individuals with MS are consistent with individuals with transtibial amputation (range 0.67–0.90) (44).

Furthermore, the reliability coefficients for people with MS have a narrower range compared with findings from a study of individuals with chronic low back pain (range, 0.26–0.89), and a greater coefficient than that reported in a sample of individuals with a stroke (composite score–only coefficient, 0.81)(45). The reliability of the CDP composite score was excellent (0.90). This is similar to the test-retest reliability of the summary scores from other performance-based clinic tests of balance for people with MS, such as the Berg Balance Scale (range, 0.85–0.96), and the Dynamic Gait Index (0.85) (46).

Hebert and Mangano, (47) studied 30 individuals with MS from age 18 to 60 years to perform the CDP with a two week interval, repeated measures (sessions 1 and 2) design was implemented to investigate, test-retest reliability of the CDP and the ability of the CDP to discriminate between participants with lower versus higher disability. The CDP had good-to-excellent reliability and excellent reliability of composite scores. Composite scores were significantly greater in the lower disability group versus the higher disability group at session 1 and session 2. The CDP is a reliable measure of balance and accurately differentiates disability status in people with MS.

Rotational chair test:

The primary purpose of rotational chair testing is to assess the integrity of the VOR reflex. There are multiple tests that can be performed using the rotational chair, each of which is designed to analyze vestibular responses by observation of eye movements. The most frequently used rotational chair tests are: Sinusoidal Harmonic Acceleration (SHA), Velocity Step (step rotation), and VOR Suppression tests(48). Rotary chair testing is complementary to the caloric test for evaluation of peripheral vestibular function. Rotary chair testing provides an assessment of the VOR over a wider range of head movement frequencies than caloric testing, more closely approximating those found under physiologic conditions (0.01-2.0 Hz). Therefore, it is possible that a subject may have a normal caloric test, but manifest a VOR deficit during head movements within a higher frequency range (49).

Eza-Nuñez et al.,(50) compared the results of the rotary chair test, caloric test, and the vHIT in patients with dizziness. The diagnostic agreement between the 3 tests to identify the subjects as having abnormal or normal vestibular function were low, each test measures the VOR with a unique velocity range. Therefore, while complementary, the caloric test measures the VOR function using a very low analog of head velocity as estimated from the eye movement responses (0.003 Hz). The rotary chair test measures the VOR over a moderate range of head velocities and in the case of SHA head frequencies, while the vHIT measures the VOR with rapid, impulsive head rotations. Gain is an essential measure for validating rotational responses, whether the corresponding phase and asymmetry values for a particular trial are clinically meaningful, if gain at 0.8 Hz is ignored, asymmetry will appear as a "gunshot" pattern, a label that has been adopted by some SHA users indicating central vestibular dysfunction (51).

REFERENCES

- 1- **Faguy, K. (2016):** Multiple sclerosis: An update. *Radiologic technology*; 87(5): 529-550.
- 2- **Mahad, D.H., Trapp, B.D. and Lassmann, H. (2015):** Pathological mechanisms in progressive multiple sclerosis. *The Lancet Neurology*; 14(2): 183-193.
- 3- **Bjartmar, C., Kidd, G., Mörk, S., Rudick, R. and Trapp, B.D. (2000):** Neurological disability correlates with spinal cord axonal loss and reduced N-acetyl aspartate in chronic multiple sclerosis patients. *Annals of Neurology*; 48(6): 893-901.
- 4- **Hellmann, M.A., Steiner, I. and Mosberg-Galili, R. (2011):** Sudden sensorineural hearing loss in multiple sclerosis: Clinical course and possible pathogenesis. *Acta Neurologica Scandinavica*; 124(4): 245-249.
- 5- **Doty, R.L., Tourbier, I., Davis, S., Rotz, J., Cuzzocreo, J.L., Treem, J. and Pham, D.L. (2012):** Pure-tone auditory thresholds are not chronically elevated in multiple sclerosis. *Behavioral Neuroscience*; 126(2): 314-324.
- 6- **Beatty, W.W. and Squire, L.R.B.N. (1992):** A strategy for studying memory disorders in multiple sclerosis. *Neuropsychology of Memory (2nd Ed.)*: 285-289.
- 7- **Furst, M. and Levine, R.A. (2015):** Hearing disorders in multiple sclerosis. In *Handbook of clinical neurology*; 129: 649-665. Elsevier.
- 8- **Lima, T.M.A., Crato, A.N., Mancini, P.C., Simoes, L.C. and Goncalves, D.U. (2009):** Alterations in early auditory evoked potentials in multiple sclerosis patients. *Brazilian Journal of Otorhinolaryngology*; 75(2): 177-181.
- 9- **Celebisoy, N., Aydo, I., Ekmekçi, Ö. and Akürekli, Ö. (1996):** Middle latency auditory evoked potentials (MLAEPs) in (MS). *Acta neurologica scandinavica*; 93(5): 318-321.
- 10- **Schochat, E., Matas, C.G., Sanches, S.G., Carvalho, R.M. and Matas, S. (2006):** Central auditory evaluation in multiple sclerosis: case report. *ArqNeuropsiquiatr*; 64(3B): 872-876.
- 11- **Magnano, L., Aiello, I. and Piras, M.R. (2006):** Cognitive impairment and neurophysiological correlates in MS. *Journal of the Neurological Sciences*; 245(1-2): 117-122.
- 12- **Santos, M.A.R., Munhoz, M.S.L., Peixoto, M.A.L., Haase, V.G., Rodrigues, J.L. and Resende, L.M. (2006):** Mismatch Negativity contribution in multiple sclerosis patients. *Brazilian Journal of Otorhinolaryngology*; 72(6): 800-808.
- 13- **Jung, J., Morlet, D., Mercier, B., Confavreux, C. and Fischer, C. (2006):** Mismatch negativity (MMN) in multiple sclerosis: An event-related potentials study in 46 patients. *Clinical Neurophysiology*; 117(1): 85-93.
- 14- **Oh, Y.M., Oh, D.H., Jeong, S.H., Koo, J.W. and Kim, J.S. (2008):** Sequential bilateral hearing loss in multiple sclerosis. *Annals of Otolaryngology, Rhinology and Laryngology*; 117(3): 186-191.
- 15- **Elbeltagy, R., Gad, N.H. and Ismail, M.H. (2019):** Central Auditory Function in Multiple Sclerosis Patients; *Indian Journal of Otolaryngology*; 25(2): 90-96.
- 16- **Rae-Grant, D.A., Eckert, N.J., Bartz, S. and Reed, J.F. (1999):** Sensory symptoms of multiple sclerosis: a hidden reservoir of morbidity. *Multiple Sclerosis Journal*; 5: 179-183.
- 17- **Alpini, D., Caputo, D., Pugnetti, L., Giuliano, D.A. and Cesarani, A. (2001):** Vertigo and multiple sclerosis: aspects of differential diagnosis. *NeuroSci Journal*; 22: 84-87.
- 18- **Feinstein, A., Kartsounis, L.D., Miller, D.H., Youl, B.D. and Ron, M.A. (1992):** Clinically isolated lesions of the type seen in multiple sclerosis: a cognitive, psychiatric, and MRI follow up study. *J NeurolNeurosurg Psychiatry*; 55: 869-876.
- 19- **Tarnutzer, A.A., Berkowitz, A.L., Robinson, K.A., Hsieh, Y.H. and Newman-Toker, D.E. (2011):** Does my dizzy patient have a stroke? a systematic review of bedside diagnosis in acute vestibular syndrome. *Croatian Medical Journal*; 183: 571-592.
- 20- **Bhattacharyya, N., Baugh, R., Orvidas, L., Barrs, D., Bronston, L., Cass, S. and Haidari, J. (2008):** Clinical practice guideline: Benign paroxysmal positional vertigo. *Otolaryngology - Head & Neck Surgery*; 139 (4-5): 47-81.
- 21- **Junicho, M., Fushiki, H., Aso, S. and Yukio, W. (2008):** Prognostic value of initial electronystagmography findings in idiopathic sudden sensorineural hearing loss without vertigo. *OtolNeurotol*; 29: 905-909.
- 22- **McCaslin, D. and Jacobson, G. (2009):** Current role of the videonystagmography examination in the context of the multidimensional balance function test battery. *Sem Hear*; 30 (4): 242-253.
- 23- **Shepard, N. and Jacobson, G. (2016):** The caloric irrigation test. *HandbClinNeurol*; 137: 119-31.
- 24- **Janky, K. and Shepard, N. (2009):** "Vestibular evoked myogenic potential (VEMP) testing: normative threshold response curves and effects of age," *Journal of the American Academy of Audiology*; 20(8): 514-522.
- 25- **Tomaz, A., Borges, F.N., Ganança, C.F., Campos, C.A. and Tilbery, C.P. (2005):** Signs and symptoms associated to otoneurologic alterations diagnosed on computerized vestibular exam of patients with multiple sclerosis. *ArqNeuropsiquiatr Journal*; 63: 837-842.
- 26- **Derwenskus, J., Rucker, J.C., Serra, A., Stahl, J.S., Downey, D.L., Adams, N.L. and Leigh, R.J. (2005):** Abnormal eye movements predict disability in MS: two-year follow-up. *Annals of New York Academy of Science*; 1039: 521-523.

- 27- **Degirmenci, E., Bir, L.S. and Ardic, F.N. (2010):** Clinical and electronystagmographical evaluation of vestibular symptoms in relapsing remitting multiple sclerosis. *Neurol Res*; 32(9): 986-991.
- 28- **Bartl, K., Lahnen, N., Kohlbecher, S. and Schneider, E. (2009):** Basics and clinical aspects of vertigo and dizziness: Head impulse test using video-oculography. *Annals of the New York Academy of Sciences*; 1164: 331-333.
- 29- **Curthoys, S. (2012):** The interpretation of clinical tests of peripheral vestibular function. *Laryngoscope*; 122: 1342-1352.
- 30- **Olszewski, J., Pietkiewicz, P., Milon, J. and Bielin, M. (2010):** The use of VHIT (videonystagmography head impulse test) in the diagnostics of semicircular canal injuries. *Otolaryngol*; 64: 32-35.
- 31- **MacDougall, H.G., Weber, K.P., McGarvie, L.A., Halmagyi, G.M. and Curthoys, I.S. (2009):** The video head impulse test: diagnostic accuracy in peripheral vestibulopathy. *Neurology*; 73: 1134-1141.
- 32- **Barkhof, F. (2002):** The clinico-radiological paradox in multiple sclerosis revisited. *CurrOpinNeurol*; 15: 239-245.
- 33- **Pavlović, I., Ruška, B., Pavičić, T., KrbotSkorić, M., Crnošija, L., Adamec, I. and Habek, M. (2017):** Video head impulse test can detect brainstem dysfunction in multiple sclerosis. *Multiple Sclerosis Related Disorders*; 14: 68-71.
- 34- **Colebatch, J. and Halmagyi, G. (1992):** Vestibular evoked potentials in human neck muscles before and after unilateral vestibular deafferentation. *Neurology*; 42: 259.
- 35- **Rosengren, S.M., Welgampola, M.S. and Colebatch, J.G. (2010):** Vestibular evoked myogenic potentials: past, present and future. *ClinNeurophysiol*; 121: 636-651.
- 36- **Shimizu, K., Murofushi, T., Sakurai, M. and Halmagyi, G. (2000):** Vestibular evoked myogenic potentials in multiple sclerosis. *J. Neurol. Neurosurg. Psychiatry*; 69: 276-277.
- 37- **Young, Y. (2004):** Audiovestibular evolution in a patient with multiple sclerosis. *Ann. Otol. Rhinol. Laryngol*; 113: 726-729.
- 38- **Crnošija, L., KrbotSkorić, M., Gabelić, T., Adamec, I. and Habek, M. (2017):** Vestibular evoked myogenic potentials and MRI in early multiple sclerosis: Validation of the VEMP score. *Journal of the Neurological Sciences*; 372: 28-32.
- 39- **Novalo, E.S., Pedalini, M.E.B., Bittar, R.S.M., Lorenzi, M.C. and Bottino, M.A. (2008):** Posturografia dinamic computadorizada: avaliação quantitativa de pacientes com vestibulopatia tratados por meio de reabilitação vestibular. *ArqIntOtorrinolaringol*; 12(2): 253-257.
- 40- **Black, F.O. (2001):** What can posturography tell us about vestibular function. *Annals of the New York Academy of Sciences*; 942: 446-64.
- 41- **Jackson, R.T., Epstein, C.M. and Del Aune, W.R. (1995):** Abnormalities in posturography and estimations of visual vertical and horizontal in multiple sclerosis. *Am J Otol*; 16(1): 88-93.
- 42- **Van Asch, P. (2011):** Impact of mobility impairment in multiple sclerosis 2—patients' perspectives. *EurNeurol Rev*; 6: 115-120.
- 43- **Gianni, C., Proserini, L., Jonsdottir, J. and Cattaneo, D. (2014):** A systematic review of factors associated with accidental falls in people with multiple sclerosis: a meta-analytic approach. *ClinRehabil*; 28(7): 704-716.
- 44- **Jayakaran, P., Johnson, G.M. and Sullivan, S.J. (2011):** Test-retest reliability of the Sensory Organization Test in older persons with a transtibial amputation. *PMR*; 3(8): 723-729.
- 45- **Chien, C.W., Hu, M.H., Tang, P.F., Sheu, C.F. and Hsieh, C.L. (2007):** A comparison of psychometric properties of the smart balance master system and the postural assessment scale for stroke in people who have had mild stroke. *Arch Phys Med Rehabil*; 88: 374-380.
- 46- **Cattaneo, D., Jonsdottir, J. and Repetti, S. (2007):** Reliability of four scales on balance disorders in persons with multiple sclerosis. *DisabilRehabil*; 29: 1920-1925.
- 47- **Hebert, J.R. and Manago, M.M. (2017):** Reliability and Validity of the Computerized Dynamic Posturography Sensory Organization Test in People with Multiple Sclerosis. *International Journal of MS Care*; 19(3): 151-157.
- 48- **Smith, A., Petrak, M. and Bahner, C. (2013):** Balance and Dizziness Introduction to the Rotational Chair Test Battery. Info @ interacoustics.com.
- 49- **Blatt, P.J., Schubert, M.C., Roach, K.E. and Tusa, R.J. (2008):** The Reliability of the Vestibular Autorotation Test (VAT) in Patients with Dizziness. *J NeurolPhysTher*; 32(2): 70-79.
- 50- **Eza-Núñez, P., Fariñas-Alvarez, C. and Fernandez, N.P. (2016):** Comparison of three diagnostic tests in detecting vestibular deficit in patients with peripheral vestibulopathy. *J LaryngolOtol*; 130: 145-150.
- 51- **Rubin, W. (1981):** Sinusoidal harmonic test in clinical practice. *Ann OtolRhinolLaryngol*; 90(4 _suppl2): 18-25