

We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,900

Open access books available

186,000

International authors and editors

200M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com



Caffeine and Meniere's Disease

Alleluia Lima Losno Ledesma,
Monique Antunes de Souza Chelminski Barreto and
Carlos Augusto Costa Pires de Oliveira

Additional information is available at the end of the chapter

<http://dx.doi.org/10.5772/intechopen.69667>

Abstract

Meniere's disease is characterized by recurrent vertigo, fluctuating hearing loss, and persistent tinnitus. Caffeine consumption in modern society is a widespread and culturally accepted habit; however, there is no consensus about its mechanism of action in various organs and systems, including the auditory and vestibular. The few clinical studies have shown that abstention from caffeine has little effect in patients with Meniere's disease, both in relation to vertigo, tinnitus and hearing loss.

Keywords: caffeine, vertigo, Meniere's diseases, tinnitus, vestibular disease

1. Introduction

Caffeine consumption in modern society is a widespread and culturally accepted habit and sets up the most widely consumed psychoactive substance in the world. It is found in a variety of products such as coffee, tea, chocolate, soft drinks, mate, guarana powder, slimming drugs, diuretics, stimulants, painkillers, and anti-allergics [1, 2].

The effects of caffeine have been investigated for a long time; however, there is still no consensus on the effect of this substance in the body [1]. Its action and its effect on the body are still controversial in the scientific literature. They are described as benefits the improvement of cognitive and psychomotor performance, alertness, attention span, attention, and memory; enhances visual and auditory vigilance; and decreases sleepiness and fatigue [3]. It also describes that it may cause tachycardia, increased gastric secretion, diuresis, increased levels of fatty acids in the plasma, cerebral vascular constriction, and dilation system of the other vessels of the body when in high doses [1].

Meniere's disease is a clinical syndrome that affects the inner ear, and it is characterized by episodes of spontaneous vertigo, usually associated with unilateral fluctuating sensorineural hearing loss (SNHL), tinnitus, and aural fullness [4]. It is believed that there is an association between the use or caffeine abstinence with complaints of vertigo and tinnitus. However, the evidence supporting this claim is conflicting and sparse [5, 6].

2. Caffeine and its effects on metabolism

Caffeine is the most consumed psychoactive substance in the world and is found in many different products such as coffee, tea, chocolate, soft drinks, mate, guarana powder, diuretics, stimulants, analgesics, and anti-allergic [1].

Caffeine (1, 3, 7-trimethylxanthine) is a stimulant of the central nervous system belonging to the group of methylxanthines [2, 7, 8]. The interaction of caffeine with the organism is difficult to research because factors such as age, presence of chronic diseases, gender, and intake of other substances such as tobacco interfere with this interaction [8].

It is believed that, with regard to pharmacokinetics, caffeine has rapid absorption, 99% absorbed within 45 minutes after its ingestion [9, 10]. It is fat-soluble, being able to overcome all biological barriers [1, 10]. The plasma concentration in humans is achieved between 15 and 120 minutes after intake [11]. In humans, doses below 10 mg/kg have half-life by 2.5–4.5 hours and was not related difference in young and elderly subjects [1, 10].

Caffeine improves cognitive and psychomotor performance, alertness, ability to concentrate, attention, and memory; improves auditory and visual vigilance; and reduces sleepiness and fatigue [3]. Caffeine in high doses can cause tachycardia, increased gastric secretion, diuresis, increased levels of fatty acids in plasma, constriction in the cerebral vascular system, and expansion of other vessels of the body [1].

In otorhinolaryngology (ENT)/audiology, it has been linked to several symptoms and diseases, such as tinnitus, hydrops, dizziness, laryngopharynx acid reflux disease (LPRD), and as a risk factor for head and neck cancer [5, 6].

Caffeine mechanism of action for the production of these effects has not been fully elucidated. However, it is known that the caffeine molecule is chemically similar to other metabolically important compounds such as purines (adenine, guanine), adenosine, xanthine, and uric acid. Due to the structural similarity of caffeine molecule with adenosine, caffeine connects itself to adenosine A1 and A2A receptors, blocking them. Thus, adenosine cannot perform their inhibitory effect, which occurs through the release of several neurotransmitters, such as glutamate, acetylcholine, monoamines, and gamma-aminobutyric acid [8, 12].

Other effects such as the inhibition of phosphodiesterase (cAMP enzyme inactivating) and release of intracellular calcium are also described, however, occur only at high doses of caffeine, which cannot be achieved only with the coffee intake [8, 10]. It is suggested that the mechanisms are unrelated to the central effects of caffeine [13].

Studies suggest that caffeine also has a vasoconstrictor effect, especially when binds to A2 receptors. Functional magnetic resonance demonstrated a reduction in cerebral perfusion after caffeine intake. Nonetheless, this is the predominant effect at high doses [13].

There are over a hundred years had been reported that the abrupt discontinuation of the act of drinking coffee can cause severe headaches [12, 14]. The most common symptoms of the withdrawal of caffeine are headache, fatigue, lethargy, flu-like symptoms, and mood disorders [15]. These effects appear 12–14 hours after discontinuation of caffeine consumption and dissipate between 4 and 7 days after their occurrence [16]. The intensity of the symptoms seems to depend on the dose of caffeine that the individual usually ingest [17], although it has been reported in sporadic consumers [18]. The authors add that, despite a dose-dependent, caffeine is not effective to alleviate the symptoms caused by one's abstinence.

3. Caffeine and Meniere's disease

Meniere's disease is characterized by recurrent vertigo, fluctuating hearing loss, and persistent tinnitus [19]. The traditional treatment for Meniere's disease involves, in addition to medication and surgical procedures when indicated, a diet that restricts sodium, caffeine, and alcohol [20].

Some authors argue that the treatment of Meniere's disease is empirical and propose food restriction as an initial treatment step, not justifying the need to abstain from caffeine [21]. The recommendation of a diet free of caffeine for Meniere's disease is based on the professional's experience, without scientific evidence [22].

It was believed that sodium restriction followed the same idea of the use of diuretics, or reduced fluid retention in the inner ear. However, it was proved that the critical feature is the sodium level constant [20].

The justification for the recommendation given to Meniere's disease patients to avoid salt is the same to avoid caffeine. It is based on the theory that considers Hydrops as a cause, not symptoms of the disease. They believed that this substance causes large fluid shifts through physiologic compartments and hence result in inner ear instability [6]. Nonetheless, a cross-over study did not find significant effect of caffeine on hydration status when body weight and urinary output were measured [23].

Using the keywords "Meniere's disease" and "caffeine," in PubMed, only one clinical study was found seeking to investigate this relationship (see **Table 1**).

Seeking to verify adherence to a diet consisting of control the sodium and caffeine, in patients with Meniere's disease, a retrospective study was conducted. The numbers of crises and the severity of symptoms decrease, as reported by the participants; however, no statistical significance was found when we analyzed only limited caffeine consumption. Fewer participants were able to restrict caffeine intake compared to reducing sodium intake. The authors suggest

Author, origin, and year of publication	Study design	Sample size	Conclusion
Luxford et al., USA, 2013 [22]	Mailed patient retrospective questionnaire and chart review	136	No statistical significance was found when analyzed only limit caffeine consumption in relation to the numbers of crisis and the severity of symptoms

Table 1. Presentation of articles: “Meniere's disease” and “caffeine”.

the need for prospective controlled studies to reduce the variables found, adding up to more conclusive results [22].

Another study aiming to characterize the patients with Meniere's disease found that 30.1% use decaffeinated coffee, higher percentage than the 19% who make use of this type of coffee in the control group. The authors complete that this restriction is based on limited evidence but are extremely well publicized in the media [24].

Caffeine consumption and interruption has been related to the trigger dizziness, tinnitus, and migraine. In clinical practice, discontinuation of caffeine intake is a common recommendation for patients with these symptoms. However, some professionals report that despite well meaning this is a painful recommendation and may aggravate the discomfort reported by the patient as it can add the effects of caffeine withdrawal syndrome [5, 25].

4. Caffeine and vestibular system

Three systems (vestibular, visual, and proprioceptive) interact with each other to ensure the body balance. The vestibular system has three functions: to provide information about body position, correct body movements that deviate from its center of mass, and control eye movement to keep the visual motor while the individual or the environment is in motion [26, 27].

The posterior labyrinth is a highly sensitive organ to changes in other organs and systems, and many of these changes manifest themselves primarily with vestibular symptoms. It is related to cervical problems, cardiovascular problems, migraine, metabolic and/or hormonal changes, psychiatric disorders, neurological diseases, and the use of medications such as antibiotics, anti-inflammatories, diuretics, and psychotropic substances with labyrinthine disorders [28–31].

Investigating the vestibulocochlear findings in patients with Type 1 diabetes mellitus was found large percentage of vestibular disorders in these patients (60%). Regarding the complaints and harmful eating habits, caffeine abuse was the most prevalent of them, reported by 20% of patients [32].

The effectiveness of cessation of caffeine consumption in remission of dizziness was investigated previously. For this purpose, patients received this orientation, only being used

drug treatment if symptoms persist 4 weeks after the initiation of restriction. Only 14% of participants reported some improvement in symptoms in the period in which it was only oriented diet. The authors add that patients reported improvement in general had lower consumption of caffeine in the usual diet than those who maintained their complaint after the restriction [25].

In patients with complaints of dizziness is always recommended an evaluation of the vestibular system [33]. To perform these tests, most services suspended the intake of foods high in caffeine, nonessential drugs, tobacco, and alcohol. As for the number of hours of restrictive diet, some authors suggest 72 hours suspension before the exam [27, 34, 35], some 48 hours before [36], and some even 24 hours before the test [28, 37].

Regarding the use of caffeine restriction to conduct vestibular tests, they were found only four studies in the literature. All they found weak relationship between caffeine consumption and changes in the tests, as shown the next.

In 2005, a comparative study was conducted, in which the study group and the control group were formed by the same patients in normal habits and caffeine restriction. Patients received as instruction for the first vestibular test (vectoelectronystagmography): fast 3 hours before the test, suspension of nonessential drugs and alcohol (72 hours before the test), and cigarette and products containing caffeine (24 hours before). The second test had the same guidelines except the restriction of the use of products containing caffeine. Most participants (68.4%) chose to undergo the examination with the habitual intake of caffeine. The most frequent complaints during the examination caffeine abstinence were anxiety (92.3%), headache (69.3%), nausea and/or vomiting (38.5%), and more intense vertigo during the test (38.5%). As the result of the examination, no abnormality was found in the oculomotor tests and there was no statistically significant change between the responses found in the caloric test [38].

A study performed with 30 healthy young individuals aimed to investigate the influence of caffeine on vectoelectronystagmography and VEMP. For this, they performed the tests twice, once with 24-hour restriction of the use of caffeine and other after drinking a cup of coffee. The results showed that moderate caffeine consumption did not influence the test results [17].

A prospective experimental study investigated the influence of caffeine on VEMP. It was recommended, to 25 healthy young, caffeine abstinence for at least 24 hours. They were submitted to the first examination, after given caffeine capsules (420 mg) and performed the second test. There was no caffeine influence on test results [39].

A study aimed to investigate the effect of caffeine on dynamic posturography examination investigating the vestibular-spinal reflex. We investigated 30 healthy young subjects, being conducted a session where they were instructed to abstain from caffeine intake for 24 hours and another where it was offered coffee before the exam. The authors concluded that caffeine did not affect the clinical interpretation of the test in this population [40].

Table 2 summarizes the findings of clinical studies that linked caffeine and the vestibular system.

Author, origin, and year of publication	Study design	Sample size	Conclusion
Felipe et al., Brazil, 2005 [38]	Clinical with transversal cohort	19	The moderate ingestion of coffee was not shown to interfere in the results of the vestibular test
Klagenberg et al., Brazil, 2007 [32]	Cross-sectional study of a contemporary group	30	Significant vestibular system changes were found
Mikulec et al., USA, 2012 [25]	Retrospective chart review	44	Only 14% of participants reported some improvement in symptoms in the period in which it was only oriented diet
McNerney et al., USA, 2014 [17]	Prospective, placebo controlled study	30	Moderate amount of caffeine does not have a clinically significant effect on the results from caloric and cVEMP tests in young healthy adults
McNerney et al., USA, 2014 [40]	Prospective, placebo controlled study	30	The ingestion of caffeine did not produce a clinically significant effect in healthy young control participants
Sousa and Suzuki, Brazil, 2014 [39]	Prospective experimental study	25	The vestibulocollic reflex is not altered by caffeine intake

Table 2. Presentation of articles: “vestibular system” and “caffeine”.

5. Caffeine and tinnitus

Tinnitus is a sound that is perceived in the absence of an external acoustic stimulus. The pathophysiology of this symptom has not been fully elucidated, in part related to the subjective nature of this condition, associated with emotional and psychological factors accompanying its occurrence [41, 42].

A retrospective study was conducted aiming to investigate the correlation of the presence of habits and symptoms with the annoyance of tinnitus. Dizziness, neck pain, headache, and caffeine abuse are prevalent complaints in patients with tinnitus. However, there was no correlation among the degree of annoyance of tinnitus with hearing loss, age, gender, presence of dizziness, neck pain, headache, changes of the temporomandibular joint, and the use of caffeine or excessive intake of carbohydrates [43].

It is observed in clinical practice, including being reported in the literature, the recommendation of discontinuation of caffeine as additional treatment for tinnitus. This recommendation is based on the theoretical deduction that if caffeine has stimulating action on the central

nervous system, it can play a role in the excitability of the auditory pathways and, therefore, can modify some clinical aspects of tinnitus [13].

There was not, however, scientific evidence for this recommendation. Recently, the search for scientific evidence of this recommendation was prospectively investigated in three studies presented in **Table 3**. In none of them significant improvement in annoyance was observed due to tinnitus only with the reduction of caffeine consumption.

A phase 2, pseudo-randomized, double-blind, placebo-controlled cross-over trial was conducted to test the causal relationship between caffeine consumption and tinnitus severity. Specific questionnaires were applied to investigate the annoyance due to tinnitus and visual analogue scale at base line and on days 1, 15, and 30. The groups, study, and placebo were matched. Authors concluded that caffeine content had no effect on tinnitus severity and increase headaches and nausea [5].

Using the answers from the Nurses' Health Study II, a series of questionnaires applied in women aged 25–42 years, the authors sought to examine the association between caffeine intake and the risk of incident tinnitus. After analyzing the data, the study concluded that after adjusting age and potential confounders there was a significant inverse association between caffeine intake and the incidence of tinnitus [44].

Seeking to assess whether tinnitus patients can obtain some benefit from the reduction of caffeine intake, 26 patients with tinnitus were advised to reduce caffeine consumption by 50% of regular consumption. Audiometry being carried out and applied the tinnitus handicap inventory (THI) and visual analogic scale (VAS) before and after reduction consumption. The authors argue that despite the statistical significance of data found, clinical improvement was small. Adds that the greater the amount of caffeine consumed, the greater the impact caused by the reduction of intake, which could be responsible for a possible worsening of tinnitus, related to caffeine withdrawal. The fact indicates that there is no justification for the universal restriction of caffeine intake as a treatment for all patients with tinnitus; however, some groups are more likely to improve [13].

Author, origin and year of publication	Study design	Sample size	Conclusion
Claire et al., UK, 2010 [5]	A phase 2, pseudo-randomized, double-blind, placebo-controlled cross-over trial	66	Caffeine content had no effect on tinnitus severity and increase headaches and nausea
Glicksman et al., USA, 2014 [44]	Longitudinal and prospective study	5289	Higher caffeine intake was associated with a lower risk of incident tinnitus in women
Figueiredo et al., Brazil, 2014 [13]	Contemporary longitudinal cohort study	26	There is no justification for the universal restriction of caffeine intake as a treatment for all patients with tinnitus

Table 3. Presentation of articles: "tinnitus" and "caffeine".

6. Caffeine and auditory system

A larger number of studies have been found attempting to investigate the effects of caffeine in the auditory system. It is believed that caffeine affected the peripheral and central auditory pathways [45]. As the inner ear is the site of lesion for this clinical syndrome, we direct our efforts in presenting the effects of caffeine on the peripheral auditory system [46].

Regard to the effects of caffeine on the peripheral auditory system, it was demonstrated that caffeine induced shortening of outer hair cells, increasing the excitability of the peripheral auditory pathways [47]. The mechanism of action that provides this shortening has not been fully elucidated [13]. It was suggested that caffeine induced contraction by activating the ryanodine receptor, by potassium channel blockage or by creating osmotic imbalance across the cell membrane [47–49].

No clinical studies in humans to investigate the relationship of caffeine to the peripheral auditory system were found.

7. Conclusion

Caffeine despite being widely consumed has no mechanism of action fully elucidated. The vestibular and auditory systems may be influenced by substances that alter the homeostasis of the organism. Thus, while the interaction of caffeine with cochlea and the posterior labyrinth is not better elucidated, the diet recommendations for evaluation and therapy of patients with vertigo and tinnitus remain based on clinical experience. It will be finally necessary more studies to elucidate these questions aiding in driving the most effective treatment for the patient with Meniere's disease.

Author details

Alleluia Lima Losno Ledesma*, Monique Antunes de Souza Chelminski Barreto and Carlos Augusto Costa Pires de Oliveira

*Address all correspondence to: luafono@yahoo.com.br

University of Brasília, Brazil

References

- [1] Chou T. Wake up and smell the coffee –.Caffeine, coffee and the medical consequences. *Western Journal Medicine*. 1992;**157**(5):544-553
- [2] Camargo MCR, Toledo MCF. Teor de cafeína em cafés brasileiros. *Journal of Food Science and Technology*. 1998;**18**(4):421-424. DOI: 10.1590/S0101-20611998000400012

- [3] Lima DR. O Café pode ser bom para a saúde. In: Simpósio de pesquisa dos cafés do Brasil. Brasília: Embrapa; 2002. pp. 195-229. Available at: <http://www.sbicafe.ufv.br/handle/123456789/538>
- [4] Frejo L, Giegling I, Teggi R, Lopez-Escamez JA, Rujescu D. Genetics of vestibular disorders: Pathophysiological insights. *Journal of Neurology*. 2016;**263**(1):45-53. DOI: 10.1007/s00415-015-7988-9
- [5] Claire LS, Stothart G, Mckenna L, Rogers PJ. Caffeine abstinence: An ineffective and potentially distressing tinnitus therapy. *International Journal of Audiology*. 2010;**49**(1):24-29. DOI: 10.3109/14992020903160884
- [6] Trindade A, Robinson T, Phillips JS. The role of caffeine in otorhinolaryngology: Guilty as charged? *European Archives of Oto-Rhino-Laryngology*. 2014;**271**(8):2097-2102. DOI: 10.1007/s00405-013-2648-0
- [7] Mycek MJ, Harvey RA, Champe PC. Estimulantes do SNC. In: Finkel R, editor. *Farmacologia ilustrada*. Porto Alegre: Artmed; 1998. pp. 462-478
- [8] Alves RC, Casal S, Oliveira B. Health benefits of coffee: Myth or reality? *Química Nova*. 2009;**32**(8):2169-2180. DOI: 10.1590/S0100-40422009000800031
- [9] Denaro CP, Brown CR, Jacob P, Benowitz NL. Effects of caffeine with repeated dosing. *European Journal of Clinical Pharmacology*. 1991;**40**(3):273-278
- [10] Fredholm BB, Bättig K, Holmén J, Nehlig A, Zvartau E. Actions of caffeine in the brain with special reference to factors that contribute to its widespread use. *Pharmacological Review*. 1999;**51**(1):83-133
- [11] Bonati M, Latini R, Galletti F, Young JF, Tognoni G, Garattini S. Caffeine disposition after oral doses. *Clinical Pharmacology & Therapeutics*. 1982;**32**(1):98-106
- [12] James JE. *Caffeine & Health*. Londres: Academic Press; 1991. p. 432
- [13] Figueiredo RR, Rates MJA, Azevedo AA, Moreira RKP, Penido NO. Effects of the reduction of caffeine consumption on tinnitus perception. *Brazilian Journal of Otorhinolaryngology*. 2014;**80**(5):416-421
- [14] Siqueira TV. *A cultura do café: 1961-2005*. Rio de Janeiro: BNDES Setorial; 2005
- [15] Silverman K, Evans SM, Strain EC, Griffiths RR. Withdrawal syndrome after the double-blind cessation of caffeine consumption. *The New England Journal of Medicine*. 1992;**327**:1109-1114. DOI: 10.1056/NEJM199210153271601
- [16] Evans SM, Griffiths RR. Caffeine withdrawal: A parametric analysis of caffeine dosing conditions. *The Journal of Pharmacology and Experimental Therapeutics*. 1999;**289**:285-294
- [17] McNerney K, Coad ML, Burkard R. The influence of caffeine on caloric and cervical vestibular evoked myogenic potentials (cVEMPs). *Journal of the American Academy of Audiology*. 2014;**25**:261-267. DOI: 10.3766/jaaa.25.3.5

- [18] Strain EC, Griffiths RR. Caffeine dependence: Fact or fiction? *Journal of the Royal Society of Medicine*. 1995;**88**(8):437-440
- [19] Kitahara T, Okamoto H, Fukushima M, Sakagami M, Ito T, Yamashita A, Ota I, Yamanaka T. A two-year randomized trial of interventions to decrease stress hormone vasopressin production in patients with Meniere's disease – A pilot study. *PLoS ONE*. 2016;**11**(6):e0158309. DOI: 10.1371/journal.pone.0158309
- [20] Rauch SD. Clinical hints and precipitating factors in patients suffering from Meniere's disease. *Otolaryngologic Clinics of North America*. 2010;**43**(5):1011-1017. DOI: <http://dx.doi.org/10.1016/j.otc.2010.05.003>
- [21] Knox GW, McPherson A. Ménière's disease: Differential diagnosis and treatment. *American Family Physician*. 1997;**55**(4):1185-1190
- [22] Luxford E, Berliner KI, Lee J, Luxford WM. Dietary modification as adjunct treatment in Ménière's disease: Patient willingness and ability to comply. *Otology and Neurotology*. 2013;**34**(8):1438-1443. DOI: <http://dx.doi.org/10.1097/MAO.0b013e3182942261>
- [23] Grandjean AC, Reimers KJ, Bannick KE, Haven MC. The effect of caffeinated, non-caffeinated, caloric and non-caloric beverages on hydration. *The Journal of the American College of Nutrition*. 2000;**19**:591-600
- [24] Tyrrell JS, Whinney DJD, Ukoumunne OC, Fleming LE, Osborne NJ. Prevalence, associated factors, and comorbid conditions for Ménière's disease. *Ear and Hearing*. 2014;**35**(4):e162-e169. DOI: 10.1097/AUD.0000000000000041
- [25] Mikulec AA, Faraji FF, Kinsella LJ. Evaluation of the efficacy of caffeine cessation, nortriptyline, and topiramate therapy in vestibular migraine and complex dizziness of unknown etiology. *American Journal of Otolaryngology*. 2012;**33**(1):121-127. DOI: <http://dx.doi.org/10.1016/j.amjoto.2011.04.010>
- [26] Shepard NT, Telian SA. Avaliação do funcionamento do sistema vestibular. In: Katz J, editor. *Tratado de Audiologia Clínica*. 4th ed. São Paulo: Manole; 1999. pp. 421-443
- [27] Flores MR, Franco ES. Computerized vectoelectronystamography: Pós nystagmus testing by caloric air stimulation in individuals without complaints. *International Archives of Otorhinolaryngology*. 2003;**7**(4):252-256
- [28] Paulino CA, Prezotto AO, Calixto RF. Association between stress, depression and dizziness: A brief review. *Revista Equilíbrio Corporal e Saúde (RECES)*. 2009;**1**(1):33-45. DOI: 10.17921/2176-9524.2009v1n1p%25p
- [29] Cal R, Bahmad Jr, F. Migraine associated with auditory-vestibular dysfunction. *Brazilian Journal of Otorhinolaryngology*. 2008;**74**(4):606-612. DOI: 10.1590/S0034-72992008000400020
- [30] Bittar RSM, Bottino MA, Simoceli L, Venosa AR. Vestibular impairment secondary to glucose metabolic disorders: Reality or myth? *Brazilian Journal of Otorhinolaryngology*. 2004;**70**(6):800-805. DOI: 10.1590/S0034-72992004000600016

- [31] Tiensoli LO, Couto ER, Mitre EI. Vertigo or dizziness associated factors in individuals with normal vestibular function test. *Revista CEFAC*. 2004;**6**(1):94-100
- [32] Klagenberg KF, Zeigelboim BS, Jurkiewicz AL, Martins-Basseto J. Vestibulocochlear manifestations in patients with type I diabetes mellitus. *Brazilian Journal of Otorhinolaryngology*. 2007;**73**(3):353-358
- [33] Mor R, Fragoso M, Taguchi CK, Figueiredo JFFR. *Vestibulometria na prática Fonoaudiológica*. São Paulo: Pulso; 2012
- [34] Mariotto LDF, Alvarenga KF, Filho OAC. Avaliação vestibular na perda auditiva sensorioneural unilateral: Estudo vesto-eletronistagmográfico. *Distúrbios da Comunicação*. 2006;**18**(1):27-38
- [35] Fukunaga JY, Ganança CF, Perrella ACM, Makibara RR, Quitschal RM, et al. Ice air caloric test in normal subjects. *Acta Otolaryngol*. 2009;**27**(1):27-31
- [36] Koga KA, Resende BD, Mor R. Study of giddiness/vertigo related to head position changes and vestibular disorders associated to computerized vectoelectronystagmography. *Revista. CEFAC*. 2004;**6**(2):197-202
- [37] Ruwer SL, Rossi AG, Simon LF (2005) Balance in the elderly. *Brazilian Journal of Otorhinolaryngology*. 2005;**71**(3):298-303. DOI: 10.1016/S1808-8694(15)31326-4
- [38] Felipe L, Simões LC, Gonçalves DU, Mancini PC. Evaluation of the caffeine effect in the vestibular test. *Brazilian Journal of Otorhinolaryngology*. 2005;**71**(6):758-762
- [39] Sousa AMA, Suzuki FA. Effect of caffeine on cervical vestibular-evoked myogenic potential in healthy individuals. *Brazilian Journal of Otorhinolaryngology*. 2014;**80**(3):26-30. <http://dx.doi.org/10.1016/j.bjorl.2014.02.004>
- [40] McNerney K, Coad ML, Burkard R. The influence of caffeine on the sensory organization test. *Journal of the American Academy of Audiology*. 2014;**25**:521-528. DOI: 10.3766/jaaa.25.6.2
- [41] Jastreboff PJ, Hazell JW. A neurophysiological approach to tinnitus: Clinical implications. *British Journal of Audiology*. 1993;**27**:7-17. DOI: 10.3109/03005369309077884
- [42] Alsalman OA, Tucker D, Vanneste S. Salivary Stress-Related responses in tinnitus: A preliminary study in young male subjects with tinnitus. *Frontiers in Neuroscience*. 2016;**20**(10):338. DOI: 10.3389/fnins.2016.00338.
- [43] Valente JPP, Pinheiro LAM, Carvalho GM, Guimarães AC, Mezzalira R, Stoler G, Paschoal JR, et al. Evaluation of factors related to the tinnitus disturbance. *International Tinnitus Journal*. 2012;**17**(1):21-25
- [44] Glicksman JT, Curhan SG, Curhan GC. A prospective study of caffeine intake and risk of incident tinnitus. *American Journal of Medicine*. 2014;**127**(8):739-743. DOI: 10.1016/j.amjmed.2014.02.033.
- [45] Dixit A, Vaney N, Tandon OP. Effect of caffeine on central auditory pathways: An evoked potential study. *Hearing Research*. 2006;**220**(1-2):61-66. DOI:10.1016/j.heares.2006.06.017

- [46] Gürkov R, Pyykö I, Zou J, Kentala E. What is Menière's disease? A contemporary re-evaluation of endolymphatic hydrops. *Journal of Neurology*. 2016;**263**(Suppl 1):71-81. DOI: 10.1007/s00415-015-7930-1
- [47] Slepecky S, Ulfendahl M, Flock A. Effects of caffeine and tetracaine on outer hair cells shortening suggest intracellular calcium involvement. *Hearing Research*. 1988;**32**:11-22
- [48] Yamamoto T, Kakehata S, Yamada T, Saito T, Saito H, Akaike N. Caffeine rapidly decreases potassium conductance of dissociated outer hair cells of guinea pig cochlea. *Brain Research*. 1995;**677**:89-96
- [49] Skellett RA, Crist JR, Fallon M, Bobbin RP. Caffeine-induced shortening of isolated outer hair cells: an osmotic mechanism of action. *Hearing Research*. 1995;**87**:41-48