Migraine and Cochlear Symptoms*

Xin MA[†], Yu-jie KE[†], Yuan-yuan JING, Tong-xiang DIAO, Li-sheng YU[#]

Department of Otorhinolaryngology, Peking University People's Hospital, Beijing 100044, China

© The Author(s) 2021

[Abstract] Migraine is one of the most common and highest burdens of disease. As a primary cerebral dysfunction illness, migraine might exhibit other system-related symptoms, including vestibular and cochlear symptoms. With the publication of the diagnostic criteria of vestibular migraine, the link between migraine and vestibular symptoms became clear. However, the relationship between migraine and cochlear symptoms is far from straightforward. Therefore, we focus on the correlation between migraine and deafness, sudden sensorineural hearing loss, acute tinnitus, and chronic tinnitus to better understand the relationship between migraine and cochlear symptoms.

Key words: migraine; cochlear symptoms; deafness; tinnitus

The Global Burden of Disease (GBD) 2016 Headache Collaborators indicated that the global age-standardized prevalence of migraine was 14.4% (13.8%–15.0%) overall: 18.9% for women and 9.8% for men, ranking the sixth of all disorders as a GBD cause in 2016^[1]. Notably, with the increasing impact of headache on disability year by year, migraine has become the highest burden of disease and the first cause of disability in individuals under 50 years of age^[2, 3]. Although the ICHD-3 headache classification and diagnostic criteria published in 2018 were more specific, sensitive, and evidence-based than the headache classification system published 30 years ago, the diagnostic criteria of migraine were imperfect and considered “a work in progress”^[4]. As a primary cerebral dysfunction disease, migraine might appear to have other system-related symptoms except for headaches. Some symptoms of the visual, movement, and sensory systems were regarded as aura symptoms of migraine. However, a series of possible related symptoms were significantly undervalued. It is necessary to distinguish these symptoms sufficiently, as doing so could help patients to receive better treatment. Vertigo, tinnitus, and deafness are common neuro-otological symptoms; the relationship between vertigo and migraine has

been described since 1984^[5] and has become clearer since the diagnostic criteria for vestibular migraine were published in 2012^[6]. In addition, migraine was considered closely related to auditory symptoms since the phenomenon of phonophobia has been one of the most important diagnostic criteria for migraine. In 2018, the concept of cochlear migraine was proposed, which provided a definite interpretation of the relationship between recurrent sudden deafness and migraine^[7]. However, the relationship between migraine and cochlear symptoms is far from clear, although there are quite a few studies in regard to migraine and tinnitus, deafness, and especially sudden sensorineural hearing loss (SSNHL). Therefore, we focus on the correlation between migraine and deafness, SSNHL, acute tinnitus, and chronic tinnitus to better understand the relationship between migraine and cochlear symptoms.

1 MIGRAINE AND DEAFNESS

Migraine is closely related to deafness, and the first thing that usually attracts attention is transient and reversible unilateral or bilateral hearing loss during a migraine attack, mentioned in some case reports^[8, 9]. Subsequently, there have been studies about hearing loss during the intermittent period of migraine. The degree of hearing loss was mild in migraineurs, and the incidence in different studies varied greatly: the proportion of abnormal pure tone audiometry was 3.3% to 14%^[10–13]. In another study comparing migraine and normal people, there seemed to be no significant differences in the proportions of pure tone audiometry and speech audiometry abnormalities^[14].

Xin MA, E-mail: 13581709195@163.com; Yu-jie KE, E-mail: kyj1995@163.com

[†]Xin MA and Yu-jie KE are co-first authors and contributed equally to this work.

[#]Corresponding author, E-mail: 13910750400@163.com

*This work was supported by the National Key Research and Development Program of China (No. 2020YFC2005200).

However, during a median follow-up time of 9 years, with the progression of vestibular migraine, cochlear symptoms initially rose from 15% to 49%, hearing loss initially increased from 12% to 26%, and 18% of patients developed mild bilateral sensorineural hearing loss, which mainly involved the low-frequency range^[15]. Although the incidence of hearing impairment gradually increased with the prolongation of the course of the disease, the degree of damage progressed slowly. No patient developed permanent sensorineural deafness after a short-term follow-up of 2 years^[16]. However, the positive rate of auditory brainstem response (ABR) testing was significantly higher; among 20 migraine patients with completely normal hearing, 35% of the ABR was abnormal, manifested by peak latencies and interpeak latencies abnormalities^[17]. In children with migraine, although the medical history was shorter, similar results appeared, and some abnormalities were observed in both peak latencies of wave V and interpeak latencies of I–V, especially during an attack of migraine^[18]. Moreover, another study showed that the ABR of all 50 migraine patients was abnormal at peak latencies and interpeak latencies of different waves, although only 7 of the 50 migraineurs were abnormal in terms of pure tone audiometry^[12]. The abnormal rate of ABR is significantly related to age, the duration of illness, and the frequency of migraine^[19]. This indicated that ABR abnormalities may be the initial manifestation of cochlear damage in migraine patients. The abnormal interpeak latencies further suggested that the central auditory pathway was dysfunctional in migraineurs, which signaled that the mechanism of migraine affects auditory function from top to bottom at the central level. This also explains why, in some studies, the proportion of migraine patients subjectively experiencing hearing loss was significantly higher than that with abnormal audiometric testing^[12].

2 MIGRAINE AND SSNHL

SSNHL is a common disease in the otolaryngology department that mostly manifests as unexplained hearing loss of more than 30 dB for three consecutive frequencies within 72 h^[20]. The incidence of SSNHL is 5 to 400 per 100 000^[20–22] and is increasing year by year with the development of economics and increasing social pressure. Therefore, SSNHL has been one of the most challenging hotspots in the field of otology. The earliest literature on SSNHL and migraine was reported by Virre and Baloh in 1996 for 13 patients who met the diagnosis of migraine and had SSNHL^[23], and the following articles are all case reports^[24, 25]. Several recent big data studies have shown a close relationship between SSNHL and migraine, indicating that the incidence of SSNHL in the migraine group was

1.8 times, 1.22 times, and 1.34 times that of the control group, respectively^[26–28]. The cause of SSNHL has been the subject of debate for many years; suggested theories include viral infection, vasospasm or embolism of the inner ear, endolymphatic hydrops, and immune-mediated reactions^[22]. Vascular factors are currently recognized as the most likely influencing factors, but SSNHL occurs most frequently at the age of 40 to 50^[22], which is not the age with high incidence of vascular disease. Patients hospitalized for SSNHL were 1.6 times more likely to have a stroke in the following 5 years than those without a history of SSNHL^[29]. However, among the high-risk factors for stroke, the role of migraine cannot be ignored^[30]. It seems that SSNHL and the associated increased risk of stroke may be the result of a juxtaposition of some unknown mechanisms, rather than an association between SSNHL and stroke. Previous studies suggested that migraine causes inner ear vasospasm through vascular mechanisms, which leads to SSNHL^[23, 24]. Recently, it was believed that migraine is a kind of cerebral dysfunction mainly involving the trigeminovascular system, although vascular mechanisms may still be involved in the pathogenesis of migraine. The trigeminal nerve supplies the labyrinthine artery of the inner ear through the ophthalmic nerve. In patients with migraine, abnormally activated trigeminal nerve axons release neurotransmitters, including calcitonin gene-related peptide (CGRP) and substance P (SP), which cause vascular dilation in the inner ear, trigger a series of aseptic inflammatory manifestations, subsequently affect inner ear function, and result in SSNHL^[31]. As it is a functional change in the inner ear, SSNHL patients with migraine have a better prognosis than those without migraine.

3 MIGRAINE AND ACUTE TINNITUS

Tinnitus is the perception of sound without an external source. The tinnitus guidelines of different countries divided the course of primary tinnitus according to the time of onset, taking 3 months (Japan) and 6 months (China, the U.S., and Europe) as the dividing points of acute and chronic tinnitus, respectively^[32–35]. The proportion of tinnitus was 7.5% to 50% in different studies about cochlear symptoms of migraine^[12, 13, 15–17]. During a median follow-up time of 9 years, with the progression of migraine, auditory symptoms initially increased from 15% to 49%, and tinnitus initially rose from 10% to 33%^[15]. A study on tinnitus showed that 27% of tinnitus patients had concurrent headache, and the side of the headache was significantly related to the side of the tinnitus. A total of 54.9% of the patients had headaches before tinnitus, 34.7% had tinnitus before a headache, and 10.4% experienced both ailments simultaneously^[36].

Epidemiology has indicated that migraine is a risk factor for tinnitus^[37]. Big data from Taiwan revealed that the incidence of tinnitus in migraine patients was 3.3 times that of the control group^[27]. To clarify the possible correlation between migraine and tinnitus, we first need to understand the mechanism of tinnitus.

It is widely accepted that tinnitus is initiated by hearing loss that subsequently causes abnormal hyperexcitability and neural synchronization in the central auditory system, including the primary auditory cortex, which leads to a spatial arrangement disorder of frequency in the primary auditory cortex and enhances the electrical activity of neurons around the damaged frequency. Therefore, it is generally believed that although hearing loss may be the initial source of tinnitus, a subsequent cascade of neural changes in the central cortex is responsible for the existence of chronic tinnitus. This process is called the remodeling process of the auditory center; hence, tinnitus is considered to belong to the “Central Remodeling Disease” category^[38]. Studies have confirmed that the most active auditory compensation after hearing loss occurs at the level of the thalamus, and these compensatory signals can be perceived as tinnitus only when they are transmitted to the senior auditory cortex. In this process, tinnitus signals will be evaluated by a tinnitus removal system based on the nucleus accumbens, which acts as a “gatekeeper” to deal with meaningless information^[39–41]. This could explain the phenomena of hearing loss without tinnitus and the tendency of self-healing in acute and chronic tinnitus. During a migraine attack, not only may the auditory system be damaged and acute tinnitus may be initiated, but the central sensitization in the context of migraine will produce excessively high and distorted auditory signals in the central compensation^[42, 43], which is more likely to be perceived. Therefore, migraine-related acute tinnitus is prevalent and cannot be ignored.

There are many reasons for the occurrence of acute tinnitus, and it is a huge challenge to classify tinnitus. Whether it is accompanied by headache may be one of the criteria for classification^[43]. The role of migraine mechanisms should be fully considered in managing acute tinnitus. With the recovery of migraine dysfunction, inner ear function and fluctuations in the emotional system gradually recovered. After a certain period of time, the tinnitus gradually became alleviated. It is recommended to provide positive consultation to patients regarding the reversibility of migraine, and corresponding anti-migraine treatment can be given to stabilize peripheral and central lesions as soon as possible, which is of great help in the recovery of acute tinnitus. This is consistent with the recommendations in the U.S. guidelines for young tinnitus patients with a relatively short history, who are more likely to heal on their own^[32].

4 MIGRAINE AND CHRONIC TINNITUS

In the Chinese and American tinnitus guidelines, chronic tinnitus was divided into compensated tinnitus and decompensated tinnitus^[32, 35]. In these two types superscript of chronic tinnitus, the involvement of the non-auditory system, especially the emotional system, is completely different. By comparing clinical tinnitus patients (decompensated tinnitus) and tinnitus population (compensated tinnitus), the incidence of mental illness was 50% *versus* 20%, respectively. Compensated chronic tinnitus is more related to physiological factors, including the presence of unstable lesions in the cochlea and the decreased function of the tinnitus clearance system^[44]. Migraine repeatedly affects the inner ear and central function and repeats the process of acute tinnitus, which is one of the important reasons for the chronicity of tinnitus.

Overinvolvement of the emotional system is the most important cause of decompensated chronic tinnitus, which was elaborated by Jastreoff’s neuropsychological model of tinnitus^[45]. Studies have verified that excessive anxiety and depression at the onset of tinnitus are important risk factors for severe tinnitus suffering (STS)^[46]. Meanwhile, anxiety and depression were two to ten times more prevalent in patients with migraine than in the general population^[47]. One study found that the gray and white matter volumes of brain were smaller in migraine patients with depression than in patients with depression alone, migraine alone, or neither condition^[48]. There is a bidirectional association between depression and migraine, and they share a common pathophysiological mechanism in the control of serotonin and other neurotransmitters^[49]. Therefore, emotional system involvement may be the most important risk factor for chronic decompensated tinnitus. Migraine anxiety-related tinnitus (MART) is the most critical component of chronic tinnitus and the main connotation of cochlear migraine. Consequently, more attention should be given to the mechanism of migraine in the management of chronic tinnitus.

Currently, there is a growing interest in the concept of vestibular migraine, while the concept of cochlear migraine has just been proposed. Due to its cochlear symptoms, most of these patients were treated in the otolaryngology department. Moreover, migraine is a cerebral dysfunction disease that can involve multiple systems, and requires multiple disciplines to focus on the different manifestations of the same pathogenesis from different professional perspectives^[50]. In sum, it is essential that the diagnosis and treatment of migraine-related cochlear symptoms have the active participation of the otolaryngology department, which is an important piece of the mysterious migraine puzzle.

Open Access

This article is licensed under a Creative Commons Attribution 4.0 International License <https://creativecommons.org/licenses/by/4.0/>, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>.

Conflict of Interest Statement

The authors have no conflict of interest.

REFERENCES

- Collaborators GH. Global, regional, and national burden of migraine and tension-type headache, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol*, 2018,17(11):954-976
- Collaborators GDaIaP. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*, 2018, 392(10159):1789-1858
- Steiner TJ, Stovner LJ, Vos T, *et al*. Migraine is first cause of disability in under 50s: will health politicians now take notice? *J Headache Pain*, 2018,19(1):17
- Tinsley A, Rothrock JF. What Are We Missing in the Diagnostic Criteria for Migraine? *Curr Pain Headache Rep*, 2018,22(12):84
- Kayan A, Hood JD. Neuro-otological manifestations of migraine. *Brain*, 1984,107(Pt 4):1123-1142
- Lempert T, Olesen J, Furman J, *et al*. Vestibular migraine: diagnostic criteria. *J Vestib Res*, 2012,22(4):167-172
- Lai JT, Liu TC. Proposal for a New Diagnosis for Cochlear Migraine. *JAMA Otolaryngol Head Neck Surg*, 2018,144(3):185-186
- Lipkin AF, Jenkins HA, Coker NJ. Migraine and sudden sensorineural hearing loss. *Arch Otolaryngol Head Neck Surg*, 1987,113(3):325-326
- Lee H, Whitman GT, Lim JG, *et al*. Hearing symptoms in migrainous infarction. *Arch Neurol*, 2003,60(1):113-116
- Harno H, Hirvonen T, Kaunisto MA, *et al*. Subclinical vestibulocerebellar dysfunction in migraine with and without aura. *Neurology*, 2003,61(12):1748-1752
- Battista RA. Audiometric findings of patients with migraine-associated dizziness. *Otol Neurotol*, 2004, 25(6):987-992
- Dash AK, Panda N, Khandelwal G, *et al*. Migraine and audiovestibular dysfunction: is there a correlation? *Am J Otolaryngol*, 2008,29(5):295-299
- Dieterich M, Brandt T. Episodic vertigo related to migraine (90 cases): vestibular migraine? *J Neurol*, 1999, 246(10):883-892
- Bolay H, Bayazit YA, Gündüz B, *et al*. Subclinical dysfunction of cochlea and cochlear efferents in migraine: an otoacoustic emission study. *Cephalalgia*, 2008,28(4):309-317
- Radtke A, von Brevern M, Neuhauser H, *et al*. Vestibular migraine: long-term follow-up of clinical symptoms and vestibulo-cochlear findings. *Neurology*, 2012,79(15):1607-1614
- Kırkırm G, Mutlu B, Olgun Y, *et al*. Comparison of Audiological Findings in Patients with Vestibular Migraine and Migraine. *Turk Arch Otorhinolaryngol*, 2017,55(4):158-161
- Bayazit Y, Yılmaz M, Mumbru S, *et al*. Assessment of migraine-related cochleovestibular symptoms. *Rev Laryngol Otol Rhinol (Bord)*, 2001,122(2): 85-88
- Firat Y, Ozturan O, Bıçak U, *et al*. Auditory brainstem response in pediatric migraine: during the attack and asymptomatic period. *Int J Pediatr Otorhinolaryngol*, 2006,70(8):1431-1438
- Hamed SA, Youssef AH, Elattar AM. Assessment of cochlear and auditory pathways in patients with migraine. *Am J Otolaryngol*, 2012,33(4):385-394
- Chandrasekhar SS, Tsai Do BS, Schwartz SR, *et al*. Clinical Practice Guideline: Sudden Hearing Loss (Update). *Otolaryngol Head Neck Surg*, 2019,161(1_ suppl):S1-S45
- Michel O. The revised version of the german guidelines "sudden idiopathic sensorineural hearing loss". *Laryngorhinootologie (German)*, 2011,90(5):290-293
- Editorial Board of Chinese Journal of Otorhinolaryngology Head and Neck Surgery; Society of Otorhinolaryngology Head and Neck Surgery CMA. [Guideline of diagnosis and treatment of sudden deafness (2015)]. *Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi (Chinese)*, 2015,50(6):443-447
- Vierre ES, Baloh RW. Migraine as a cause of sudden hearing loss. *Headache*, 1996,36(1):24-28
- Lee H, Lopez I, Ishiyama A, *et al*. Can migraine damage the inner ear? *Arch Neurol*, 2000,57(11):1631-1634
- Piovesan EJ, Kowacs PA, Werneck LC, *et al*. Oscilloculus and sudden deafness in a migraine patient. *Arq Neuropsiquiatr*, 2003,61(3b):848-850
- Chu CH, Liu CJ, Fuh JL, *et al*. Migraine is a risk factor for sudden sensorineural hearing loss: a nationwide population-based study. *Cephalalgia*, 2013,33(2):80-86
- Hwang JH, Tsai SJ, Liu TC, *et al*. Association of Tinnitus and Other Cochlear Disorders With a History of Migraines. *JAMA Otolaryngol Head Neck Surg*, 2018,144(8):712-717
- Kim SY, Kim MK, Lim JS, *et al*. Migraine increases the proportion of sudden sensorineural hearing loss: A longitudinal follow-up study. *Auris Nasus Larynx*, 2019,46(3):353-359
- Lin HC, Chao PZ, Lee HC. Sudden sensorineural hearing loss increases the risk of stroke: a 5-year follow-up study. *Stroke*, 2008,39(10):2744-2748
- Schürks M, Rist PM, Bigal ME, *et al*. Migraine and cardiovascular disease: systematic review and meta-analysis. *Bmj*, 2009,339:b3914
- Lai RC, Liu QL. Inner ear migraine: vestibular migraine and cochlear migraine. *Lin Chung Er Bi Yan Hou Tou*

- Jing Wai Ke Za Zhi (Chinese), 2019,33(3):200-203
- 32 Tunkel DE, Bauer CA, Sun GH, *et al.* Clinical practice guideline: tinnitus. *Otolaryngol Head Neck Surg*, 2014, 151(2 Suppl):S1-S40
 - 33 Cima RFF, Mazurek B, Haider H, *et al.* A multidisciplinary European guideline for tinnitus: diagnostics, assessment, and treatment. *Hno*, 2019,67(Suppl 1):10-42
 - 34 Ogawa K, Sato H, Takahashi M, *et al.* Clinical practice guidelines for diagnosis and treatment of chronic tinnitus in Japan. *Auris Nasus Larynx*, 2020,47(1):1-6
 - 35 Surgery EBoCJoOHaN. Interpretation of Chinese 2012 tinnitus experts consensus. *Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi (Chinese)*, 2012,47(9):709-712
 - 36 Langguth B, Hund V, Busch V, *et al.* Tinnitus and Headache. *Biomed Res Int*, 2015,2015:797416
 - 37 Sindhusake D, Golding M, Newall P, *et al.* Risk factors for tinnitus in a population of older adults: the blue mountains hearing study. *Ear Hear*, 2003,24(6):501-507
 - 38 Lai JT, Ma X. Renaissance of Tinnitus management. *Chin J Otol (Chinese)*, 2016,14(02):140-144
 - 39 Rauschecker JP, Leaver AM, Mühlau M. Tuning out the noise: limbic-auditory interactions in tinnitus. *Neuron*, 2010,66(6):819-826
 - 40 Rauschecker JP, May ES, Maudoux A, *et al.* Frontostriatal Gating of Tinnitus and Chronic Pain. *Trends Cogn Sci*, 2015,19(10):567-578
 - 41 Lai RZ, Ma X. [Hearing loss and the switch of tinnitus-NAc]. *Lin Chuang Er Bi Yan Hou Tou Jing Wai Ke Za Zhi (Chinese)*, 2017,31(7):493-495
 - 42 Volcy M, Sheftell FD, Tepper SJ, *et al.* Tinnitus in migraine: an allodynic symptom secondary to abnormal cortical functioning? *Headache*, 2005,45(8):1083-1087
 - 43 Langguth B, Hund V, Landgrebe M, *et al.* Tinnitus Patients with Comorbid Headaches: The Influence of Headache Type and Laterality on Tinnitus Characteristics. *Front Neurol*, 2017,8:440
 - 44 Yu LS, Ma X. Compensation and decompensation of tinnitus. *Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi (Chinese)*, 2017,52(8):630-633
 - 45 Jastreboff PJ. Phantom auditory perception (tinnitus): mechanisms of generation and perception. *Neurosci Res*, 1990,8(4):221-254
 - 46 Holgers KM, Zöger S, Svedlund K. Predictive factors for development of severe tinnitus suffering-further characterisation. *Int J Audiol*, 2005,44(10):584-592
 - 47 Minen MT, Begasse De Dhaem O, Kroon Van Diest A, *et al.* Migraine and its psychiatric comorbidities. *J Neurol Neurosurg Psychiatry*, 2016,87(7):741-749
 - 48 Gudmundsson LS, Scher AI, Sigurdsson S, *et al.* Migraine, depression, and brain volume: the AGES-Reykjavik Study. *Neurology*, 2013,80(23):2138-2144
 - 49 Zhang Q, Shao A, Jiang Z, *et al.* The exploration of mechanisms of comorbidity between migraine and depression. *J Cell Mol Med*, 2019,23(7):4505-4513
 - 50 Luzeiro I, Luís L, Gonçalves F, *et al.* Vestibular Migraine: Clinical Challenges and Opportunities for Multidisciplinarity. *Behav Neurol*, 2016,2016:6179805

(Received May 11, 2021; accepted July 11, 2021)