Is tinnitus in normal-hearing patients accompanied by hemifacial spasm also a type of hyperactive neurovascular compression syndrome? A magnetoencephalography study

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Abstract

Background

Traditionally, tinnitus accompanied by hemifacial spasm is considered a type of hyperactive neurovascular compression syndrome similar to hemifacial spasm alone because of the anatomically close relationship between the facial nerve and cochlear nerve, and the hyperactive clinical nature.

Methods

We used magnetoencephalography to investigate 29 patients with hemifacial spasm, with or without tinnitus on the ipsilateral side, to estimate the activity of the cochlear nerve. We compared the difference in the latency and the ratio of equivalent current dipole (ECD) strength between the ipsilateral and contralateral sides of the spasm and tinnitus.

Results

Cochlear nerve activity with tinnitus was increased with a shorter latency \( (p = 0.016) \) and stronger ECD strength \( (p = 0.028) \).

Conclusion

Normal-hearing tinnitus accompanied by hemifacial spasm originates from the central nervous system. Sensory input from the facial spasm may contribute to normal-hearing tinnitus accompanied by hemifacial spasm.

Keywords: hemifacial spasm, magnetoencephalography, pathophysiology, tinnitus
Background

Contralateral tinnitus associated with hemifacial spasm (HFS) is not uncommon, and is seen in approximately 7% of patients with HFS.[1] If tinnitus is accompanied by HFS, surgical outcome following microvascular decompression is generally acceptable, especially in cases in which the cochlear nerve is affected.[2] Therefore, some types of tinnitus, but not all, have similar pathophysiology as HFS.

The pathophysiologic process in HFS has been relatively well studied.[3] However, the pathophysiology of tinnitus is still controversial, especially if tinnitus is accompanied by HFS. To investigate the pathophysiology of tinnitus accompanied by HFS, we used magnetoencephalography (MEG) to study patients and analyzed the relationship between the presence of tinnitus and the MEG results.
Methods

Participants

Inclusion criteria were as follows: 1) patients with unilateral HFS, 2) patients with tinnitus on the same side as HFS if the patient had tinnitus, 2) patients with a hearing level better than 20 dB at 1000 Hz, and better than 25 dB at each frequency examined (250 Hz to 3000 Hz with pure tone audiometry as measured by an otorhinolaryngologist), 3) patients without otologic disorders, 4) patients with differences between left and right in hearing levels of 5 dB or less, and 5) patients who could undergo MEG and magnetic resonance imaging (MRI). The diagnosis of HFS was made according to clinical symptoms and MRI findings of vascular conflict of the facial nerve. From January 2011 to December 2011, 29 patients met these criteria and underwent MEG.

This study was approved by the Korean Food and Drug Administration. All participants provided written informed consent, and the study was approved by the Institutional Review Board of Severance Hospital, Seoul, Korea (IRB no. 1-2011-0088).

Stimulation and MEG measurement

Tone bursts of 100-ms duration (10-ms slope) were employed for the acoustic stimulation protocol. Pure tones of 1000 Hz were applied to the patient’s left and right ear. The acoustic stimulation consisted of 100 epochs of a random inter-stimulus interval between 900 and 1000 ms. Individual hearing thresholds were determined before the stimulation. Tones were delivered at a comfortable 40-dB level above threshold through two 2.5-m-long silicon tubes (ER-30, Etymotic Research, Inc., USA). Sound stimuli were generated with a STIM2 system (Compumedics Neuroscan, USA).

MEG data for all patients were recorded with a whole-head MEG system (KRISS, Daejeon, Korea) with 152 axial first-order gradiometers. Sound triggered epochs (including a 100-ms prestimulus baseline) were filtered online with a bandpass of 0.1-100 Hz and recorded at a sampling rate of 1000 Hz.

The measured auditory evoked field (AEF) waveforms were filtered offline with 3-40 Hz band-
pass filtering, and the neuromagnetic responses to the auditory stimuli were averaged to improve the signal-to-noise ratio. The baseline for the waveforms was defined as a mean amplitude between −100 and 0 ms relative to tone onset.

We selected neuromagnetic data in the hemisphere contralateral to the stimulus to calculate equivalent current dipoles (ECDs).[4] Dipolar moment at N100m response was used to detect peak latency of the N100m and to explain magnetic field patterns during the N100m (70-140 ms). The goodness-of-fit (%) of the N100m dipole was calculated and merged with the patient’s MRI to verify the anatomical location of the N100m dipole. To compare the effect of each clinical factor on N100m latency and ECD strength, the latency difference of N100m (the latency of N100m on the tinnitus side − the latency of N100m on the normal side) and the ratio of the ECD strength of N100m (the ECD strength of N100m on the tinnitus side / the ECD strength of N100m on the normal side) were calculated.

Clinical data and MEG data were analyzed together. To compare ECD strength and N100m latency, the latency difference of N100m and the ratio of ECD strength of N100m were analyzed with the paired t-test and the non-parametric Mann-Whitney test. Statistical tests were performed using SPSS v.18.0 (NCSS statistical software, Kaysville, UT, USA). All statistical tests were two-tailed. The threshold for statistical significance was set at $p < 0.05$. 
Results and discussion

The patients were six males and 23 females with a mean age of 48.9 years (range, 33-69 years). The most frequent offending vessels were the anterior inferior cerebellar artery, followed by posterior inferior cerebellar artery. Eight patients had ipsilateral tinnitus.

The mean N100m latencies on the normal and HFS sides were 99.1 ± 10.0 ms and 101.3 ± 14.3 ms, respectively (Paired t-test, \( p = 0.198 \)). The mean ECD strengths of the normal and HFS sides were 24.8 ± 11.6 nAm and 27.5 ± 9.4 nAm, respectively (paired t-test, \( p = 0.265 \)). The latency difference of N100m in patients with tinnitus was shorter than that in patients without tinnitus (−4.1 ± 6.5 with tinnitus vs. 4.6 ± 8.6 without tinnitus, Mann-Whitney test, \( p = 0.016 \)). The ratio of ECD strength in patients with tinnitus was greater than that in patients without tinnitus (1.7 ± 0.6 with tinnitus vs. 1.1 ± 0.4 without tinnitus, Mann-Whitney test, \( p = 0.028 \)) (Figure 1, 2). However, the latency difference of N100m and the ratio of ECD strength of N100m were not significantly different according to gender, age, and offending vessel. (Table 1).

The concept of a hyperactive neurovascular compression syndrome such as HFS and trigeminal neuralgia has been accepted since Dandy’s first report, and microvascular decompression for these syndromes has acceptable surgical outcomes.[5-8] Because of the anatomically close relationship between the cochlear nerve and facial nerve, some attempts have been made to perform microvascular decompression to treat tinnitus, based on the assumption that tinnitus is a type of hyperactive neurovascular compression syndrome. However, the response rate of microvascular decompression for tinnitus varies from 40 to 77%, and the tinnitus-free rate is lower than the response rate.[9-12] In contrast, an interesting report about tinnitus accompanied by HFS has been published. Ryu et al. investigated the result of microvascular decompression for tinnitus accompanied by HFS. Tinnitus in seven of ten (70%) patients was completely resolved after surgery, which is comparable to the surgical result for HFS and trigeminal neuralgia.[1] Thus, we postulate that the pathophysiologic mechanism of tinnitus accompanied by HFS is different than that of tinnitus alone.
MEG results of AEF for patients in our series with tinnitus accompanied by HFS showed simultaneously increased auditory cortical activity and decreased N100m latency compared with patients with HFS without tinnitus (Table 1). This result suggests that tinnitus accompanied by HFS is likely not a type of hyperactive neurovascular compression syndrome, which typically shows simultaneously decreased nerve conduction velocity and cranial nerve function due to demyelination of the cranial nerve.[3]

Recently, a study was published about normal hearing patients with tinnitus. The authors observed shortening of I-V latency and enlarged Na and Pa amplitudes in an electrophysiologic study, and concluded that the cause of tinnitus in these patients seemed to have originated in the central nervous system.[13] Although the patients of that study did not have HFS, the other conditions regarding tinnitus were similar to the patients in our series, and this study suggested that the tinnitus in the patients in our series may have originated in the central nervous system, rather than the cranial nerve or the root entry zone.

Although the pathophysiology of tinnitus is still controversial, the dorsal cochlear nucleus in the pons that is modulated by multi-sensory input is a strong candidate for the origin of tinnitus.[14-16] According to this theory, multi-sensory input affects dorsal cochlear nucleus granule cells, leading to changes in dorsal cochlear nucleus principal cells.[17] Thus, sensory stimuli can modulate cochlear function and may be the cause of tinnitus. Another clue about the relationship between sensory stimuli and tinnitus is found in patients with tinnitus who are treated with botulimum toxin. Abnormal movement in the head and neck area can be associated with tinnitus, and this type of tinnitus is successfully cured with botulinum toxin injection into the affected muscle.[18,19]

Normal-hearing tinnitus accompanied by HFS may originate not from demyelination by neurovascular compression but from facial sensory stimuli caused by HFS. Furthermore, control of HFS, regardless of treatment with microvascular decompression or botulimum toxin injection, is expected to be sufficient for relieving tinnitus in normal-hearing patients with HFS.
Conclusions

The pathophysiologic mechanism of normal-hearing tinnitus accompanied by HFS is unclear. Following MEG analysis of patients, we conclude that the origin of tinnitus in these patients is not the cranial nerve or root entry zone but the central nervous system, and control of HFS may be sufficient to relieve tinnitus. Further investigation and clinical correlation are required to obtain more information.
List of abbreviations

Auditory evoked field, AEF; equivalent current dipole, ECD; Hemifacial spasm, HFS; magnetoencephalography, MEG; magnetic resonance imaging, MRI.

Competing interests

None

Authors' contributions

Won Seok Chang organized the research project and wrote the first draft; Bong Soo Kim performed the research project and reviewed the manuscript; Hyun Ho Jung organized the research project and reviewed the manuscript; Ki-Woong Kim, Hyuk Chan Kwon, and Yong Ho Lee conceived and organized the research project; Jin Woo Chang conceived the research project and reviewed and criticized the manuscript.

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Figure legend

Figure 1. The comparison of the difference of N100m latency and the ratio of equivalent current dipole strength (ECDs) of N100m

Figure 2. The example of average dipoles after auditory stimulation (A and B). The ECDs of N100m, and N100m latency of the patient with tinnitus accompanied by left side hemifacial spasm are greater and faster after auditory stimulation at symptom side (A). However, these findings were not observed in the patients without tinnitus (B).
Figure 1

Lt. side symptom and Lt. side stimulation:
- 83 ms (N100m latency)
- 37.7 nAm (ECDs of N100m)

Lt. side symptom and Rt. side stimulation:
- 100 ms (N100m latency)
- 22.1 nAm (ECDs of N100m)
Figure 2

Lt. side symptom and Lt. side stimulation:
- 92 ms (N100m latency)
- 27.9 nAm (ECDs of N100m)

Lt. side symptom and Rt. side stimulation:
- 88 ms (N100m latency)
- 20.1 nAm (ECDs of N100m)