ORIGINAL ARTICLE

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Effects of Multiple Sclerosis on the Medial Olivocholear System

Multipl Sklerozun Medial Olivokolear Sistem Üzerine Etkileri

Özlem ERTUĞRUL[1], Gül ÖZBİLEN ACAR[2], Ozan TÜYSÜZ[3], Asuman ORHAN VAROĞLU[4]

[1]İstanbul Medeniyet University Faculty of Health Sciences, Department of Audiology, İstanbul, Türkiye
[2]İstanbul Medeniyet University Faculty of Health Sciences, Department of Otorhinolaryngology, İstanbul, Türkiye
[3]University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital, Clinic of Otorhinolaryngology-Head and Neck Surgery, İstanbul, Türkiye
[4]Göztepe Prof. Dr. Süleyman Yalçın City Hospital, Clinic of Neurology, İstanbul, Türkiye

ABSTRACT

Aim: Multiple sclerosis (MS) is a chronic inflammatory disease characterized by demyelination within the central nervous system. This study aimed to investigate the effects of MS on the medial olivocochlear (MOC) efferent system using transient evoked otoacoustic emissions (TEOAE) and contralateral suppression testing.

Materials and Methods: Peripheral hearing was evaluated using pure-tone audiometry. The function of the MOC system was assessed using TEOAE recordings obtained with and without contralateral broadband noise stimulation. The study included 30 patients with MS and 32 healthy controls. TEOAE measurements were performed bilaterally at 1000, 1500, 2000, 3000, and 4000 Hz. Contralateral suppression was calculated to evaluate MOC reflex activity.

Results: TEOAE amplitudes were significantly reduced in patients with MS compared to controls across all tested frequencies (1000-4000 Hz). In addition, contralateral suppression values at 4000 Hz were significantly lower in the MS group bilaterally ($p<0.05$). Overall, MOC suppression responses were markedly diminished in patients with MS, indicating impaired efferent auditory function.

Conclusion: Given that otoacoustic emissions reflect cochlear Outer hair cell (OHC) function, reduced TEOAE amplitudes in MS patients may indicate early subclinical involvement of OHCs. The observed reduction in contralateral suppression, particularly at 4000 Hz, suggests dysfunction of the MOC efferent system. These findings demonstrate that MS affects the auditory efferent pathways and highlight the importance of evaluating subclinical auditory involvement in this population.

Keywords: Medial olivocochlear reflex, multiple sclerosis, otoacoustic emissions, contralateral suppression, auditory efferent system

ÖZ

Amaç: Multipl skleroz (MS), merkezi sinir sistemi ve omurilikte miyelin hasarı ile karakterize, kronik enflamatuvar bir hastalıktır. Bu çalışmanın amacı, MSin işitsel efferent sistemlerden medioolivokoklear (MOK) sistem üzerindeki etkilerini değerlendirmektir.

Gereç ve Yöntem: Bu çalışmada periferik işitme, saf ses odyometrisi ile değerlendirilmiştir. MOK sistemi ise transient otoakustik emisyon (TEOAE) testi ve kontralateral geniş bant gürültü eşliğinde yapılan supresyon testi ile incelenmiştir. Çalışmaya 30 MS hastası ve 32 sağlıklı kontrol dahil edilmiştir. Tüm katılımcılara sağ ve sol kulakta 1000, 1500, 2000, 3000 ve 4000 Hz frekanslarında TEOAE ölçümleri yapılmış ve MOK refleksini değerlendirmek amacıyla kontralateral supresyon testi uygulanmıştır.

Bulgular: MS hastalarında TEOAE amplitüdlerinin, kontrol grubuna kıyasla tüm frekanslarda (1000-4000 Hz) anlamlı derecede azaldığı saptanmıştır. Ayrıca, bilateral 4000 Hz frekansında kontralateral supresyon değerleri açısından MS ve kontrol grupları arasında anlamlı fark bulunmuştur ($p<0.05$). MS grubunda MOK supresyon yanıtlarının belirgin olarak azaldığı gözlenmiştir.

Address for Correspondence: Prof. Asst. Özlem ERTUĞRUL, İstanbul Medeniyet University Faculty of Health Sciences, Department of Audiology, İstanbul, Türkiye
E-mail: ozlemertugrul70@gmail.com **ORCID ID:** orcid.org/0000-0002-0920-817X
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Sonuç: Elde edilen bulgular, otoakustik emisyonların koklear fonksiyonları yansıttığı göz önüne alındığında, MS hastalarında düşük emisyon yanıtlarının dış tüylü hücrelerin erken subklinik etkilenmesine bağlı olabileceğini düşündürmektedir. Özellikle 4000 Hz'de supresyon değerlerindeki azalma, MOK sistemin etkilendiğini ve MS'in işitsel efferent yollar üzerinde etkisi olduğunu göstermektedir.

Anahtar Kelimeler: Medioolivokoklear refleks, multipl skleroz, otoakustik emisyon, kontralateral supresyon, işitsel efferent sistem

INTRODUCTION

Multiple sclerosis (MS) is a chronic immune-mediated disorder of the central nervous system, characterized by inflammatory demyelination and axonal damage affecting the brain and spinal cord[1,2]. Demyelinating lesions are primarily located in the cerebral white matter but may also involve cortical regions, particularly subpial areas, as well as the spinal cord and optic nerve[2,3]. Clinically, MS presents with a wide spectrum of neurological symptoms, including optic neuritis, diplopia, ataxia, tremor, muscle weakness, and sensory deficits[1].

In addition to these manifestations, demyelinating processes may affect central auditory and vestibular pathways, leading to auditory dysfunction and balance disturbances[4]. Lesions involving the brainstem are of particular importance, as both afferent and efferent components of the auditory system are localized in this region. Previous studies have demonstrated abnormalities in auditory brainstem responses (ABR) in patients with MS, suggesting impaired neural conduction within auditory pathways[5].

Outer hair cells (OHCs), although primarily involved in afferent auditory processing, also play a crucial role in efferent auditory mechanisms. These functions are mediated by the medial olivocochlear (MOC) system, which originates in the medial superior olivary complex and projects predominantly to the contralateral cochlea[6]. A schematic representation of the MOC system is shown in Figure 1. Activation of this pathway modulates cochlear amplification through hyperpolarization of OHCs, thereby improving signal detection in noise and protecting the auditory system from acoustic trauma[7,8].

The functional integrity of the MOC system can be assessed non-invasively using otoacoustic emissions (OAEs) in conjunction with contralateral acoustic stimulation. Specifically, suppression of transient evoked OAEs (TEOAEs) by contralateral noise is considered an indirect indicator of efferent auditory pathway activity[9]. Stronger suppression responses have been associated with improved speech perception in noisy environments, highlighting the clinical relevance of this measure[10].

Despite increasing evidence regarding auditory involvement in MS, the effects of the disease on efferent auditory mechanisms, particularly the MOC system, remain insufficiently understood. Most previous studies have focused on afferent pathways, while limited data are available on MOC reflex function and its potential role in early or subclinical auditory dysfunction in MS.

Therefore, the present study aimed to investigate the integrity of the MOC system in patients with MS using TEOAE-based contralateral suppression measurements. Additionally, TEOAE

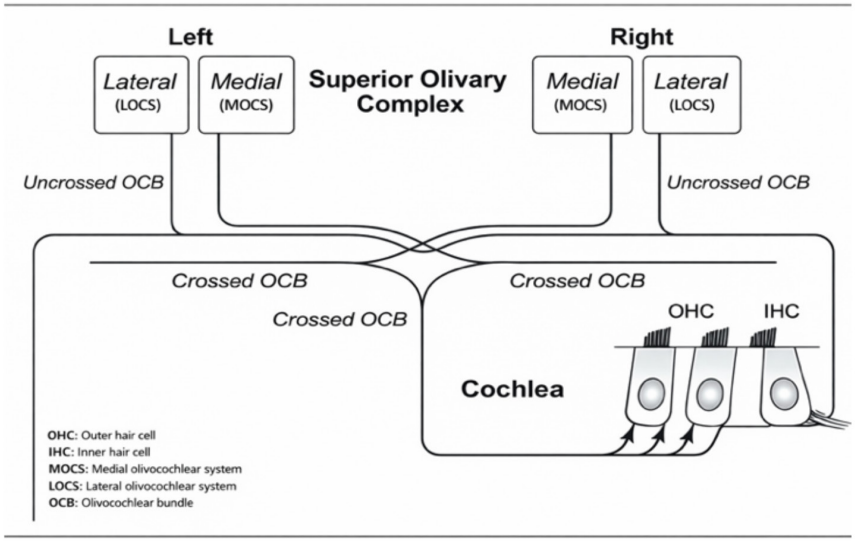

Figure 1. Schematic representation of the medial and lateral olivocochlear pathways and their projections to the cochlea

amplitudes and suppression values across multiple frequency bands were compared between MS patients and healthy controls to evaluate potential alterations in efferent auditory function.

MATERIALS AND METHODS

A total of 30 MS patients, between the ages of 26-63, diagnosed by the Department of Neurology at the at a tertiary care university hospital were included as the study group, and 32 healthy individuals from the same age group who presented to the Department of Otorhinolaryngology at the same hospital were included in the study, which was conducted in the same hospital Department of Audiology. Ethical approval for this study was obtained from the İstanbul Medeniyet University Göztepe Training and Research Hospital Clinical Research Ethics Committee (approval no: 2017/0332, date: 07.11.2017). Since participation in the study was voluntary, an informed consent form was signed by all volunteers in the study after being informed by the evaluator. Otoscopic examination, hearing test to evaluate peripheral hearing, and TEOAE test was performed, and the MOC reflex was evaluated by applying the contralateral suppression test. First of all, an otoscopic examination was performed by an otorhinolaryngologist and the plug in the outer ear canal was cleaned when necessary. After this examination, individuals with a scar on the tympanic membrane, acute or chronic otitis, any pathology in the external ear canal and hearing loss were excluded from the study. The following audiological evaluations were performed on the participants who were examined.

Audiometric Tests

Audiological examinations were performed using the Interacoustics AC40 (Denmark) device.

Measurements were made at 250, 500, 1000, 2000, 4000, 6000, 8000 Hz in a sound-treated room meeting industrial acoustics company standards.

Transient Evoked Otoacoustic Emission: TEOAE tests were performed with Otometrics Madsen Capella (Denmark) in a quiet room. Non-linear click stimuli were used at an intensity of 80±3 dB sound pressure level (SPL). Recordings were obtained across frequency bands of 1, 1.5, 2, 3, and 4 kHz. Only responses with reproducibility exceeding 65% and stimulus stability above 70% were accepted. A total of 260 transient averages were collected within a 20 ms analysis window. A signal-to-noise ratio (SNR) of ≥3 dB SPL was considered indicative of a valid response.

Contralateral Suppression Test with TEOAE: TEOAE measurements were performed in a quiet room. For suppression evaluation, white noise at 70 dB SPL was presented to the contralateral ear. Recordings were obtained in two stages: without noise and with contralateral noise. Suppression was calculated as the difference between baseline OAE amplitudes and those measured during noise stimulation across all frequency bands. A decrease in emission amplitude in the noise condition was interpreted as the presence of the suppression reflex. If there was no reduction in emission values of more than 3dB between the thresholds with and without a mask, the reflex was considered absent

Statistical Analysis

Statistical analysis was performed using SPSS (Statistical Package for Social Sciences) for Windows version 21.0. Data distribution was assessed for normality, and for normally distributed variables, the independent samples t-test was applied, while non-normally distributed variables were analyzed using the Mann-Whitney U test. The chi-square test was used for categorical variables, and Pearson correlation analysis was performed to assess relationships between quantitative variables. A p-value of <0.05 was considered statistically significant.

RESULTS

Thirty MS patients constituted the study group, while 32 healthy individuals served as the control group. The mean age of the MS patients is 40.8±7.4, and the mean age of the control group is 37.4±7.6 (Table 1).

As a result of the audiometric examination, hearing was obtained within normal limits in both MS patients and the control group. The average hearing values of the MS patient group and the control group for right and left ears are shown in Table 2, and no statistically significant difference was found between the two groups ($p>0.05$).

In this study, OAEs values in the right and left ears showed a significant difference between MS patients and the control group ($p<0.05$). OAE values in both ears were lower in the MS group than in the control group. These results show that the functions of OHCs in both ears are affected in MS patients (Figure 2).

Table 1. Age and sex distribution of the study and control group

	MS group (n=30)	Control group (n=32)
Age (years)		
Mean ± SD	40.8±7.4	39.4±7.6
Min-max	26-63	24-61
Sex, n (%)		
Male	26 (86.6%)	13 (40.6%)
Female	4 (13.4%)	19 (59.4%)

SD: Standard deviation, MS: Multiple sclerosis

Table 2. Right and left ear multiple sclerosis and control group hearing thresholds and statistical comparison						
Frequency (Hz)	Left ear MS (dB)	Left ear control (dB)	p-value	Right ear MS (dB)	Right ear control (dB)	p-value
500	11.6	9.6	>0.05	11.3	10.3	>0.05
1000	9.5	8.3	>0.05	10.3	9.5	>0.05
2000	9.8	8.8	>0.05	10.6	9.6	>0.05
4000	9.8	12.5	>0.05	10.6	12.0	>0.05
8000	11.5	13.0	>0.05	12.1	13.6	>0.05
MS: Multiple sclerosis. No statistically significant differences were observed (p>0.05)						

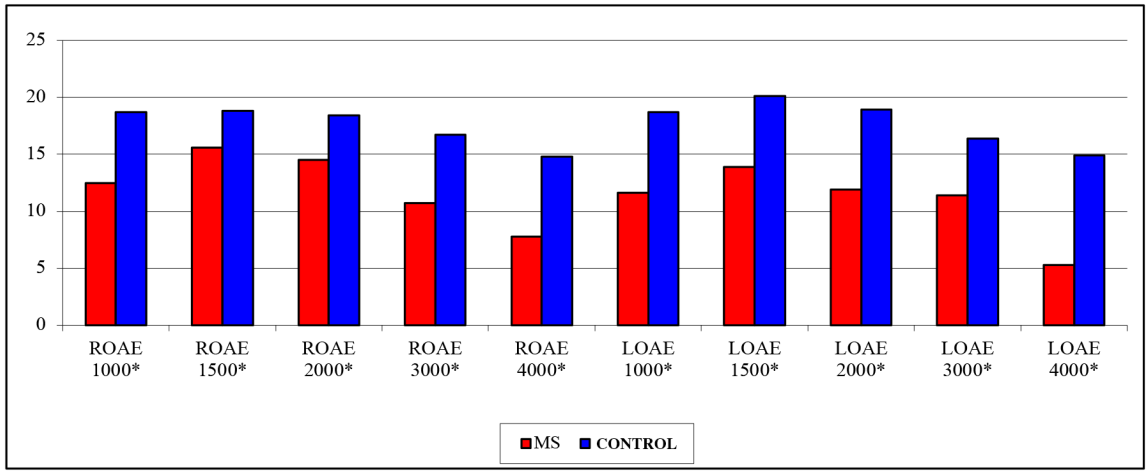

Figure 2. Comparison of TEOAE measurement differences between MS and control

*MS: Multiple sclerosis, TEOAE: Transient evoked otoacoustic emissions, ROAE: Right otoacoustic emission, LOAE: Left otoacoustic emission, MS: Multiple sclerosis, *p<0.05 was considered statistically significant*

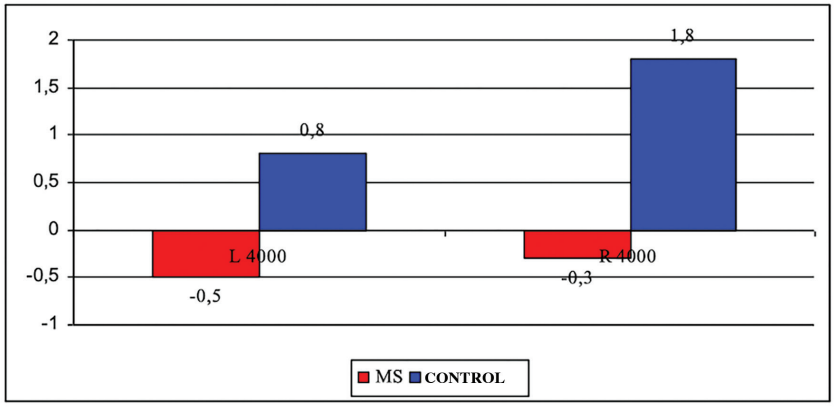

Figure 3. Comparison of differences in measurement results of TEOAE and TEOAE with contralateral noise between MS and control group in right and left ear

*R: Right, L: Left, MS: Multiple sclerosis, TEOAE: Transient evoked otoacoustic emissions, *p<0.05 was considered statistically significant*

Evaluation of the MOC reflex using the contralateral suppression test demonstrated a significant difference at 4000 Hz in both ears when comparing the MS group with the control group ($p<0.05$) (Figure 3).

A significant inverse correlation was found between the Expanded Disability Status scale (EDSS) values indicating the severity of MS disease and the MOC reflex being affected at 4000 Hz in the left ear. Accordingly, as the EDSS value increased, the difference between TEOAE and contralateral suppression measurements at a frequency of 4000 in the left ear decreased (no suppression was observed) ($p=0.033$) (Table 3). According to these results, it was found that the MOC reflex decreased as the severity of the disease increased. In addition, a significant inverse correlation was found between the duration of the disease in the right ear and the involvement of the MOC reflex in the right ear at 1000 Hz and 4000 Hz. These results showed that as the duration of the disease increases, the MOC reflex is negatively affected at 1000 Hz and 4000 Hz in the right ear ($p=0.038$, $p=0.010$) (Table 3).

DISCUSSION

In the present study, we observed that patients with MS showed reduced TEOAE amplitudes together with weaker contralateral suppression responses, particularly at 4000 Hz. These findings point to a possible involvement of both cochlear and efferent auditory pathways, even in patients with clinically normal hearing thresholds.

Previous research has suggested that auditory dysfunction in MS may remain subclinical for a long period. For instance, Di Mauro et al.[12] reported reduced OAEs amplitudes in newly diagnosed patients without detectable brainstem involvement, indicating that cochlear changes may occur early in the disease process. In line with these findings, the decreased TEOAE amplitudes in our study may reflect early OHC dysfunction.

Beyond cochlear involvement, our results also suggest an alteration in efferent auditory function. We found that suppression responses, especially at higher frequencies, were reduced in MS patients. Since the MOC system originates from the superior olivary complex in the brainstem, this finding may indicate that demyelinating processes affect efferent pathways at the brainstem level. This is not unexpected, as the brainstem is known to be particularly vulnerable in MS[4]

Another important observation in our study was the relationship between disease severity and MOC function. As EDSS scores increased, suppression responses tended to decrease. A similar pattern was also seen with longer disease duration. Taken together, these findings suggest that efferent auditory dysfunction may progress over time and may be related to the overall disease burden. This highlights the potential of efferent auditory measures as early biomarkers of neural involvement in MS.

From a functional perspective, impairment of the MOC system may have consequences beyond cochlear mechanics. The efferent auditory system plays a role in improving speech perception in noisy environments by enhancing the SNR[10,11]. Therefore, even in the absence of measurable hearing loss, patients with MS may experience difficulties in speech understanding in daily listening situations.

Di Mauro et al.[12] evaluated newly diagnosed relapsing MS patients in remission with clinically normal hearing using a comprehensive audiological battery. Although pure tone audiometry and ABR findings were within normal limits, both transient-evoked and distortion product OAE amplitudes were significantly reduced at mid frequencies (1000-3000 Hz) compared to controls. These findings suggest subclinical cochlear involvement in early-stage MS, even in the absence of detectable brainstem pathology. In line with these results, the reduced OAE amplitudes observed in our study further support the presence of early peripheral auditory dysfunction and may reflect early dysfunction of OHC electromotility and impaired MOC efferent regulation. Accordingly, OAE measurements appear to be a sensitive tool for detecting early auditory involvement in MS patients[12].

In addition, previous studies have emphasized that sudden sensorineural hearing loss (SNHL) can occasionally be an early manifestation of MS. Di Stadio et al.[13] conducted a systematic review evaluating hearing loss characteristics in MS patients using studies that included both audiological assessments and magnetic resonance imaging findings. Their results demonstrated that SNHL is more frequently observed

Table 3. Correlation of MOC reflex with disease duration and EDSS values

Parameter	p-value	Correlation coefficient (r)
EDSS-left ear (4000 Hz)	**0.033***	−0.455
Disease duration-right ear (1000 Hz)	**0.010***	0.447
Disease duration-right ear (4000 Hz)	**0.038***	−0.394

r: Correlation coefficient, EDSS: Expanded Disability Status scale, MOC: Medial olivocochlear, *p<0.05 was considered statistically significant

in the early stages of MS, whereas progressive SNHL tends to occur in later stages. Lesions were often identified in the brain or internal auditory canal in patients presenting with sudden hearing loss, suggesting early involvement of auditory pathways[13]. These findings support the notion that auditory dysfunction may emerge before overt neurological progression. In line with this, the reduced TEOAE amplitudes and altered suppression responses observed in our study further indicate that both cochlear and efferent auditory mechanisms may be affected at early stages of the disease, even in the absence of clinically evident hearing loss.

The reduced OAE amplitudes and the absence of contralateral suppression at 4000 Hz observed in our study suggest impairment of the MOC reflex pathways in MS. Demyelination, a key pathological feature of MS, is known to disrupt neural conduction and synaptic transmission, particularly within central auditory structures such as the thalamocortical network. This disruption may affect neuronal firing patterns and auditory signal processing, contributing to subclinical auditory dysfunction[14]. In our study, the association between reduced suppression responses and higher EDSS scores further supports the notion that efferent auditory pathway involvement increases with disease severity. Moreover, previous studies have shown that focal brainstem lesions, particularly those involving the superior olivary complex, can impair binaural auditory processing and sound localization abilities[15]. Taken together, these findings indicate that both cochlear and central auditory pathways, including efferent mechanisms, may be progressively affected in MS, even in the absence of overt hearing loss.

Overall, our results suggest that MS is not limited to afferent auditory dysfunction but also involves efferent regulatory mechanisms, particularly the MOC system. Evaluating both TEOAE amplitudes and contralateral suppression responses may therefore provide useful information for detecting subtle auditory changes in MS patients.

Study Limitations

This study has some limitations. The relatively small sample size and the cross-sectional design restrict the generalizability of the findings. In addition, longitudinal data were not available, making it difficult to assess the progression of auditory dysfunction over time. Future studies including larger cohorts and follow-up assessments would help to clarify these issues.

CONCLUSION

In conclusion, our findings indicate that MS may affect both cochlear function and efferent auditory pathways. Reduced TEOAE amplitudes together with decreased suppression responses suggest early involvement of the MOC system. These changes may occur even in patients with normal hearing thresholds and may be associated with disease severity and duration. These findings highlight the importance of incorporating efferent auditory system assessment into the clinical evaluation of MS patients, even in the absence of overt hearing loss.

From a clinical perspective, the combined use of OAEs and contralateral suppression testing may provide a practical and non-invasive approach for identifying early auditory involvement in MS. Further studies are needed to confirm these findings and to better understand their potential role in clinical follow-up.

Ethics

Ethics Committee Approval: Ethical approval for this study was obtained from the İstanbul Medeniyet University Göztepe Training and Research Hospital Clinical Research Ethics Committee (approval no: 2017/0332, date: 07.11.2017).

Presentation: This study was presented as an oral presentation at the 4th International Congress of the Mirko Tos Hearing Research Center, "Preclinic, Clinic and Innovative Approaches in Inner Ear Diseases: A Multidisciplinary Symposium," held on October 23–25, 2025, in Ankara, Türkiye.

Informed Consent: Since participation in the study was voluntary, an informed consent form was signed by all volunteers in the study after being informed by the evaluator.

Footnotes

Authorship Contributions

Concept: Ö.E., G.Ö.A., Design: Ö.E., O.T., Data Collection or Processing: Ö.E., A.O.V., Analysis or Interpretation: G.Ö.A., O.T., A.O., A.O.V., Literature Search: Ö.E., G.Ö.A., O.T., A.O., A.O.V., Writing: Ö.E., O.T.

Conflict of Interest: No conflict of interest was declared by the authors.

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