

Non-Motor Symptoms in Myasthenia Gravis Patients: Evaluation of Auditory and Olfactory Functions

Özlem AKDOĞAN¹, Alene SAR¹, Tuğrul EREN², Enise AKDEMİR³, Nihal Seden BOYOĞLU², Melih TÜTÜNCÜ⁴
Ufuk Emre TOPRAK¹, Ömer UYSAL⁵

¹Neurology Clinic, Istanbul Training and Research Hospital, University of Health Sciences, Istanbul, Türkiye

²Department of Otorhinolaryngology, Istanbul Training and Research Hospital, University of Health Sciences, Istanbul, Türkiye

³Department of Audiology, Faculty of Health Sciences, Istanbul University–Cerrahpaşa, Istanbul, Türkiye

⁴Department of Neurology, Faculty of Medicine, Istanbul University–Cerrahpaşa, Istanbul, Türkiye

⁵Department of Biostatistics and Medical Informatics, Faculty of Medicine, Istanbul University–Cerrahpaşa, Istanbul, Türkiye

ABSTRACT

Introduction: Myasthenia gravis (MG) is an autoimmune disease characterized by conduction defects at the neuromuscular junction. Recent studies suggest that impairment in acetylcholine neurotransmission occurs not only at the neuromuscular junction but also in the central and peripheral nervous systems. In this context, we aimed to investigate the presence of auditory and olfactory dysfunction, which are non-motor symptoms (NMS), alongside motor symptoms in patients with MG.

Methods: A total of 30 MG patients and 30 healthy controls were enrolled in the study. Demographic characteristics of all participants were recorded. Olfactory functions were assessed using the Connecticut Chemosensory Clinical Research Center (CCCRC) test, while auditory functions were evaluated through pure tone audiometry (PTA) and tympanometric assessment. Additionally, patients were evaluated with MG Foundation of America (MGFA) Clinical Classification, MG-Composite scoring (MGC) and MG-Quality of Life Questionnaire 15-item scale Turkish version (MG-QOL15-T).

Results: No statistically significant difference was found between the MG and control groups for the n-Butanol threshold test score, identification test score, and total test score, which are components of the CCCRC test. There was no significant correlation between the age of disease onset and olfactory scores. A statistically significant moderate negative correlation was found between disease duration and both identification and total olfactory scores ($r=-0.447$, $p=0.013$ and $r=-0.374$, $p=0.042$, respectively). In the PTA test, the hearing threshold at 2000 Hz frequency in the right ear of patients was higher compared to the control group, and this difference was found to be statistically significant. No association was found between the patients' olfactory and auditory functions with the MG-QOL15-T.

Conclusion: This study suggests partial impairment in olfactory and auditory functions, NMS, in MG patients; however, these findings do not seem to effect the patients' quality of life. It should be considered that MG may be accompanied not only by motor symptoms but also by NMS.

Keywords: hearing, myasthenia gravis, neuromuscular junction diseases, olfactory perception

Cite this article as: Akdoğan Ö, Sar A, Eren T, Akdemir E, Seden Boyoğlu N, Tütüncü M et al. Non-Motor Symptoms in Myasthenia Gravis Patients: Evaluation of Auditory and Olfactory Functions. Arch Neuropsychiatry 2026;63:219–225. doi: 10.29399/npa.29067

INTRODUCTION

Myasthenia Gravis (MG) is an autoimmune neuromuscular disorder characterized by impaired transmission at the neuromuscular junction. The primary symptoms manifest as weakness predominantly in skeletal muscles, typically affecting proximal muscles in a symmetric and fluctuating pattern throughout the day. Clinical findings may present as either focal or generalized manifestations. Initial symptoms frequently emerge in the ocular muscles and remain localized in approximately 10–15% of patients. However, in most cases, symptoms gradually spread to other muscle groups within a few years (1). Clinical classification of MG is based on skeletal muscle involvement, clinical distribution (e.g., ocular vs. generalized), age at onset, presence of thymic abnormalities, and serological findings of autoantibodies (2,3).

The primary pathophysiological mechanism of MG involves disruption of the cascade of events leading to muscle contraction at the neuromuscular junction. The impaired cholinergic transmission between nerve terminals and muscle fibers is responsible for the principal clinical symptoms of the disease (3). However, dysfunction in acetylcholine transmission is not limited to skeletal muscles and can also effect other systems (4). This accounts for the presence of non-motor symptoms, which are often overlooked in clinical practice but significantly impact patients' quality of life (5). The primary non-motor symptoms include headache, sensory dysfunctions (hearing, smell, and taste disturbances), autonomic dysfunction, sleep disorders, and cognitive impairments (5–9). Notably, at least one non-motor symptom has been reported in approximately 25% of MG patients associated with thymoma (9,10).

Highlights

- The effects of MG on olfactory and auditory functions were investigated.
- No significant differences were found between groups regarding olfactory functions.
- A significant decrease in olfactory scores was noted as disease duration increased.
- In patients, high-frequency impairment was detected in the PTA test.

Olfactory function plays a crucial role in behavior and emotions. Olfactory sensory neuron dendrites reside in the olfactory epithelium, with their axons traversing the cribriform plate to reach the olfactory bulb. Subsequently, signals are transmitted to primary olfactory centers such as the piriform cortex, amygdala, and entorhinal cortex, as well as secondary centers including the hypothalamus, thalamus, and orbitofrontal cortex (11). Similarly, auditory perception is essential for environmental awareness. Sound is a form of energy that propagates through material mediums, causing the movement of particles within the medium. The number of repetitions per second of the resulting repetitive compression and expansion cycles is measured in Hertz (Hz). Humans can generally perceive frequencies ranging from 20 Hz to 20,000 Hz. The cochlea has mechanoreceptors (outer and inner hair cells) embedded in the basilar membrane at the base of the organ of Corti. Hair cell depolarization converts sound energy into electrical energy, transmitting impulses to the auditory nerve (12).

Evidence of neurosensory dysfunction has been reported in MG, a disease characterized by cholinergic system impairment (2). However, the precise physiological mechanisms underlying this phenomenon remain unclear. One hypothesis suggests that cholinergic receptors in the central nervous system may be blocked by autoimmune mechanisms (6,8). Mitral cells in the olfactory bulb enhance sensitivity within odorant receptive fields (ORF), aiding in the differentiation of similar odors (13). Leon-Sarmiento et al. were the first to report olfactory dysfunction in MG patients (2). Studies in mice with reduced α -7 (α 7) expression demonstrated deficits in detecting or distinguishing chemically related odors (14). Tekeli et al. established a clinical correlation between disease severity and olfactory dysfunction in MG patients (6). Medial olivocochlear (MOC) efferent signals regulate cochlear amplification by hyperpolarizing outer hair cells (OHCs) through α 9- α 10 nicotinic acetylcholine receptors (nAChRs) (15–17). Cochlear damage observed in MG patients is thought to be associated with progressive loss of basolateral AChRs in OHCs (18).

In this study, olfactory and auditory functions were clinically evaluated in patients with myasthenia gravis (MG), a disorder characterized by dysfunction of the acetylcholine neurotransmitter, which facilitates communication between nerves and muscles, considering the role of acetylcholine in the olfactory and auditory systems. Additionally, the relationships between the obtained findings and disease duration, status, severity, and quality of life were examined.

METHODS

This prospective case-control study was conducted between December 2022 and December 2023 in the Istanbul Training and Research Hospital Neurology Outpatient Clinic, enrolling 30 MG patients (20 females, 10 males) and 30 age- and sex-matched healthy controls.

As the control group, individuals who did not exhibit neuromuscular disease symptoms and had normal neurological examinations and cranial imaging were selected. To minimize potential confounding factors, individuals similar to the patient group in terms of age and sex were chosen. Participants underwent comprehensive neurological, auditory, and nasal examinations performed by specialists. None of the participants reported olfactory or auditory complaints before the study. Clinical and electrophysiological findings confirmed the MG diagnosis. Additionally, existing records of anti-nicotinic acetylcholine receptor (Anti-AChR) and/or anti-muscle-specific kinase (Anti-MuSK) antibodies were reviewed if available.

Exclusion criteria included individuals with nasal septal deviation, nasal polyposis, congenital olfactory dysfunction, chronic rhinosinusitis, allergic rhinitis, history of nasal or paranasal surgery, hearing disorders, history of head trauma, psychiatric or chronic neurological conditions, chronic diseases, and upper respiratory tract infections on the day of testing.

To evaluate the severity of the disease, the Myasthenia Gravis Foundation of America (MGFA Clinical Classification) was used (19). According to this classification, clinical assessment is divided into 5 main subgroups. 0 indicates asymptomatic; 1 indicates ocular involvement; 2 indicates mild muscle weakness; 3 indicates moderate muscle weakness; 4 indicates severe muscle weakness or intensive care unit admission without intubation; 5 indicates intubation status. MGFA 2, 3, and 4 have subgroups a and b. Axial and extremity muscle involvement is expressed as "a," while bulbar muscle involvement is expressed as "b."

To assess the condition of the disease, the MG-Composite scoring (MGC), which evaluates ocular symptoms with 3 items, bulbar functions with 4 items, and muscle strength with 3 items, was used (20). Each item is scored according to 4 categories, and although the items vary based on the functions being evaluated, higher scores reflect greater disease severity.

The patients' quality of life was assessed using the Myasthenia Gravis-Quality of Life Questionnaire 15-item scale Turkish version (MG-QOL15-T). On the 15-item scale, each item is scored between 0–4. The lowest score is 0, and the highest score is 60. Higher scores indicate poor quality of life. The Turkish validity and reliability study of the scale was conducted by Taşçılar et al. (21).

The Connecticut Chemosensory Clinical Research Center (CCCRC) test is a test that provides both a quantitative and qualitative assessment of olfaction by testing the olfactory threshold and the identification of different odors. The Turkish validity and reliability study of this test was conducted by Veyseller et al. (22). In the olfactory threshold test, participants, with their eyes closed and one nostril blocked by their hands, were asked to smell the contents of two bottles placed directly under the open nostril. One bottle contained water, and the other contained a diluted butanol concentration. Participants were scored for correctly identifying the same butanol concentration consecutively five times. If the concentration was not correctly identified, the test was repeated with a less diluted butanol concentration compared with the water bottle. This method was applied to both nostrils. Finally, the average of the scores for both nostrils was calculated. The strongest butanol concentration (bottle 0) contained 4% butanol in deionized water. Each subsequent dilution (bottles 1–9) was made at a 1:3 ratio with deionized water. Possible scores range from 0 to 9, but all scores of 7 and above are scored as 7 according to the CCCRC test. The odor identification test was performed using seven characteristic odor stimuli (cocoa, coffee, soap, cinnamon, naphthalene, peanut butter, and talcum powder). To evaluate trigeminal nerve function, menthol-containing Vicks were used as a

stimulus, although this was not included in the olfactory function test score. Odor stimuli were placed in bottles, and participants were asked to select the name of the odor they perceived from a provided list. The number of odor stimuli correctly identified by participants was recorded as the odor identification score. The total CCCRC score was calculated by dividing the sum of the threshold and identification scores by two. Participants were classified as anosmic, severely hyposmic, moderately hyposmic, mildly hyposmic, or normosmic based on their total CCCRC test score (23).

To evaluate hearing function, pure-tone audiometry and tympanometric assessment were applied to both ears of each participant. Tympanometric tests were performed using a probe tone of 226 Hz. The mean hearing threshold values were evaluated at frequencies of 250, 500, 1000, 2000, 4000, and 8000 Hz. Air conduction (AC) and bone conduction (BC) hearing thresholds were measured at 500 Hz, 1000 Hz, and 2000 Hz. All tests were performed by the same audiometry specialist using the same devices (Interacoustic AC40, Hybrid, Maico MA-41).

The ethical approval of the study was granted on November 11, 2022, by the Istanbul Training and Research Hospital Clinical Research Ethics Committee with decision number 349. Written informed consent was obtained from all participants.

Statistical Analysis

Statistical analyses were conducted using IBM Statistical Package for Social Sciences (SPSS) program version 26.0. Descriptive statistics summarized demographic data. Normality was assessed using the Shapiro-Wilk test. Continuous variables were analyzed using independent-samples t-tests (for normal distributions) or Mann-Whitney U tests (for non-normal distributions). Categorical variables were analyzed using chi-square tests, while correlations were evaluated using Spearman's rho or Pearson correlation tests. Statistical significance was set at $p < 0.05$.

RESULTS

The study included 30 MG patients (20 females [66.7%], 10 males [33.3%]) and 30 age- and sex-matched healthy controls. The mean age was 45.30 ± 12.45 years in the patient group and 45.27 ± 11.82 years in the control group ($p = 0.992$), with no significant difference between the groups in terms of age and sex. The body mass index (BMI) was 27.19 ± 6.24 in the patient group and 25.55 ± 3.06 in the control group, with no significant difference ($p = 0.202$). The mean age at disease onset was 38.23 ± 15.18 years (range: 2–60 years). The initial symptoms were generalized in 9 (30%) patients, bulbar in 2 (6.7%) patients, ocular in 11 (36.7%) patients, and oculo-bulbar in 8 (26.7%) patients. The mean duration from initial diagnosis to the time of the study was 7.03 ± 8.15 years (range: 1–36 years). The nicotinic acetylcholine receptor antibody (Anti-AChR) was positive in 19 (63.3%) patients, negative in 8 (26.7%) patients, and unknown in 3 (10%) patients. The anti-MuSK serum antibody was negative in 5 (16.6%) patients, while it was unknown in 25 (83.4%) patients. A history of thymectomy was present in 8 (26.7%) patients. Based on the treatments received, 16 (53.3%) patients were treated with cholinesterase inhibitors alone; 5 (16.7%) patients received both cholinesterase inhibitors and glucocorticoids; 4 (13.3%) patients were treated with cholinesterase inhibitors and other immunosuppressants, and 5 (16.7%) patients received cholinesterase inhibitors, glucocorticoids, and other immunosuppressants (Table 1).

According to the MGFA Clinical Classification, 8 (26.7%) patients were classified as Class 1, 20 (66.7%) patients as Class 2, and 2 (6.7%) patients as Class 3. The mean MG Composite (MGC) score was 5.97 ± 5.18 (range: 0–20). The mean score of the Myasthenia Gravis Quality of Life

Questionnaire-15 (MG-QOL15-T) was 19.73 ± 11.72 (range: 0–41). No significant correlation was found between the MGC score and MG-QoL-15 ($p = 0.377$), nor between MGFA classification and MG-QoL-15 ($p = 0.113$).

The mean n-Butanol threshold test score was 6.00 ± 1.43 in the MG group and 6.07 ± 1.43 in the control group. The mean identification test score was 2.87 ± 1.65 in the MG group and 3.60 ± 1.63 in the control group. The mean total CCCRC test score was 4.43 ± 1.30 in the MG group and 4.83 ± 1.28 in the control group. No statistically significant differences were found between the MG and control groups for any of the three test scores ($p > 0.05$) (Table 2). Based on CCCRC test scores, 2 patients and 1 control were classified as anosmic, 2 patients and 3 controls as severely hyposmic, 13 patients and 8 controls as moderately hyposmic, 10 patients and 11 controls as mildly hyposmic, and 3 patients and 7 controls as normosmic (Figure 1). When CCCRC test score was considered as a categorical variable, no statistically significant difference was observed between the patient and control groups (Fisher's Exact Test, $p = 0.504$). Olfactory scores did not significantly differ by sex in either group (Table 3). The identification test score and total CCCRC test score showed a significant negative correlation with both age and BMI in the MG group,

Table 1. Demographic and clinical characteristics of myasthenia gravis patients

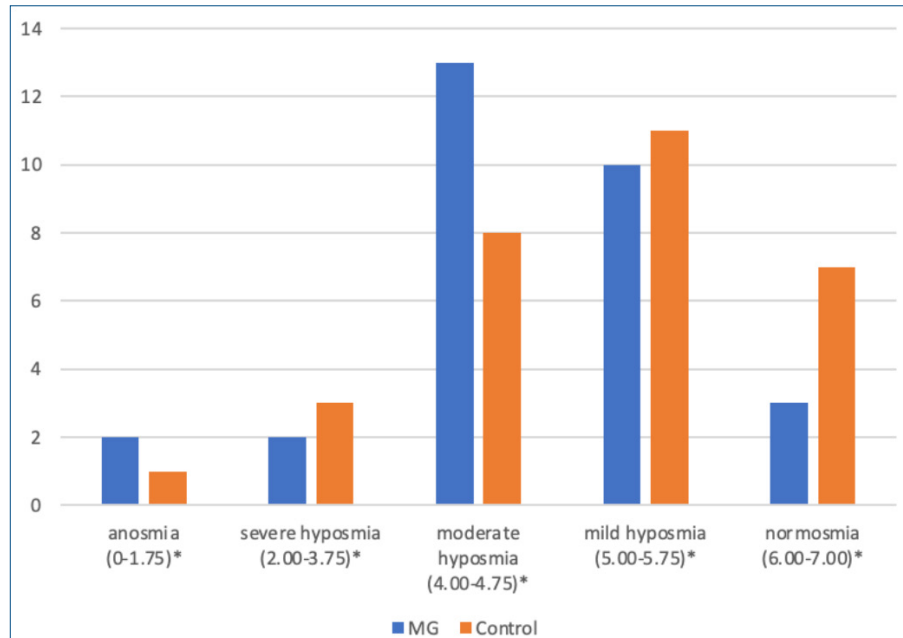
Variable	n (%) / (Mean ± SD)
MG patients	30
Male (n)	10
Female (n)	20
BMI (Mean ± SD)	27.19±6.24
Age, years (Mean ± SD)	45.30±12.45
Age at disease onset, years (Ort ± SD)	38.23±15.18
Disease duration, years (Ort ± SD)	7.03±8.15
Initial symptoms, n (%)	
Generalized	9 (30)
Bulbar	2 (6.7)
Ocular	11 (36.7)
Oculo-bulbar	8 (26.7)
Antibodies, n (%)	
Anti-AChR (positive, negative, unknown)	19 (63.3), 8 (26.7), 3 (10)
Anti-MuSK (positive, negative, unknown)	0 (0), 5 (16.6), 25 (83.4)
Thymectomy, n (%)	
Yes	8 (26.7)
No	22 (73.3)
Treatment, n (%)	
ChEIs (only)	16 (53.3)
ChEIs + corticosteroids	5 (16.7)
ChEIs + other	4 (13.3)
ChEIs + corticosteroids + other	5 (16.7)
MGC score (Mean ± SD)	5.97±5.18
MGFA Classification (n, %)	
Class 1	8 (26.7)
Class 2	20 (66.7)
Class 3	2 (6.7)
MG-QOL15-T (Mean ± SS)	19.73±11.72

Anti-AChR: anti-acetylcholine receptor; Anti-MuSK: anti-muscle-specific kinase; BMI: body mass index (BMI); ChEIs: cholinesterase inhibitors; MG: myasthenia gravis; MGC: MG composite; MGFA: Myasthenia Gravis Foundation of America; MG-QOL15-T: MG quality of life questionnaire 15 - Turkish version; other: azathioprine, intravenous immunoglobulin, plasma exchange; SD: standard deviation.

Table 2. Comparison of CCCRC test scores between control and MG groups

	MG (Mean ± SD) median (Min-Max)	Control (Mean ± SD) median (Min-Max)	p
n-Butanol threshold test score	6.00±1.43 6(1-7)	6.07±1.43 7(2-7)	0.648
Identification test score	2.87±1.65 3(0-6)	3.60±1.63 3.5(0-7)	0.115
Total CCCRC test score	4.43±1.30 4.5(0.5-6.5)	4.83±1.28 5(1-7)	0.173

CCCRC: Connecticut Chemosensory Clinical Research Center; MG: myasthenia gravis; Mann-Whitney U test was applied for analysis.

**Figure 1.** Evaluation of olfactory function according to CCCRC scores

CCCRC: Connecticut Chemosensory Clinical Research Center; MG: Myasthenia Gravis; *=CCCRC test score

Table 3. Comparison of CCCRC Test Scores by Gender Between Control and MG Groups

		Female		Male		p
		Mean ± SD	Median (Min-Max)	Mean ± SD	Median (Min-Max)	
Control	n-Butanol threshold test score	6.05±1.39	6.5(2-7)	6.10±1.59	7(2-7)	0.717
	Identification test score	3.65±1.53	3.5(1-7)	3.50±1.90	3.5(0-6)	0.946
	Total CCCRC test score	4.85±1.18	5.0(2-7)	4.80±1.54	5(1-6.5)	0.824
MG	n-Butanol threshold test score	5.90±1.37	6(1-7)	6.20±1.61	7(2-7)	0.178
	Identification test score	3.05±1.60	3(0-6)	2.50±1.78	2.5(0-5)	0.409
	Total CCCRC test score	4.47±1.26	4.5(0.5-6.5)	4.35±1.45	4.5(1.5-6)	0.911

CCCRC: Connecticut Chemosensory Clinical Research Center; MG: myasthenia gravis. Mann-Whitney U test was applied for analysis.

whereas in the control group, a significant negative correlation was found only with age. No significant correlation was observed between the age at disease onset and olfactory scores. However, a statistically significant moderate negative correlation was found between disease duration and both identification score and total olfactory score (Spearman's Rho test, $r=-0.447$, $p=0.013$; $r=-0.374$, $p=0.042$, respectively).

Our measurements revealed Type A tympanograms in all subjects. A statistically significant difference was found between the patient and control groups in terms of the average hearing threshold at 2000 Hz in the right ear. However, no statistically significant differences were observed between the two groups for the average hearing threshold values at the

other frequencies (single frequencies) (Table 4). No statistically significant difference was found between the patient and control groups for both air conduction (AC) and bone conduction (BC) in either ear (AC-right $p=0.279$, BC-right $p=0.242$, AC-left $p=0.876$, BC-left $p=0.374$) (Table 5). Bilateral acoustic reflexes were tested between 500–2000 Hz in both groups, and no significant difference was detected between the groups (Table 6).

No statistically significant association was found between having undergone thymectomy and olfactory test scores ($p > 0.05$). Additionally, no significant association was observed between a history of thymectomy and pure-tone audiometry results for either ear at 250, 500, 1000, 2000, 4000, or 8000 Hz ($p > 0.05$).

Table 4. Comparison of pure-tone audiometry test results between groups

Frequency (Hz)	Right (dB HL)		p	Left (dB HL)		p
	MG median (IQR)	Control median (IQR)		MG median (IQR)	Control median (IQR)	
250	10.00[5.00–15.00]	10.00[10.00–15.00]	0.503	10.00[5.00–10.00]	10.00[5.00–15.00]	0.858
500	5.00[5.00–11.25]	10.00[5.00–15.00]	0.520	10.00[5.00–11.25]	10.00[5.00–15.00]	0.746
1000	10.00[5.00–16.25]	10.00[5.00–10.00]	0.560	10.00[5.00–16.25]	10.00[5.00–11.25]	0.723
2000	10.00[5.00–26.25]	10.00[5.00–10.00]	0.041	10.00[5.00–16.25]	10.00[5.00–10.00]	0.563
4000	15.00[8.75–30.00]	10.00[5.00–21.25]	0.138	15.00[5.00–25.00]	12.50[10.00–21.25]	0.994
8000	20.00[8.75–40.00]	10.00[5.00–15.00]	0.108	17.50[5.00–31.25]	15.00[5.00–21.25]	0.546

MG: myasthenia gravis; IQR: interquartile range; Mann-Whitney U test was applied for analysis.

Table 5. Comparison of air and bone conduction characteristics between groups

	MG (n=30) median (IQR)	Control (n=30) median (IQR)	p
AC-right	10.00 [8.00–20.25]	9.00 [6.00–13.00]	0.279
BC-right	3.00 [0.00–13.25]	1.00 [0.00–4.00]	0.242
AC-left	10.50 [5.75–14.25]	9.00 [8.00–14.00]	0.876
BC-left	3.00 [0.00–8.25]	1.00 [0.00–4.25]	0.374

AC: air conduction; BC: bone conduction; MG: myasthenia gravis; IQR: interquartile range; Mann-Whitney U test was applied for analysis.

Table 6. Comparison of acoustic reflex characteristics between patient and control groups

	MG median (IQR)	Control median (IQR)	p
Right			
500 Hz	105.00 [100.00–105.00]	102.50 [95.00–105.00]	0.345
1000 Hz	100.00 [95.00–110.00]	100.00 [95.00–105.00]	0.243
2000 Hz	100.00 [95.00–105.00]	100.00 [95.00–105.00]	0.741
Left			
500 Hz	100.00 [95.00–105.00]	95.00 [95.00–105.00]	0.586
1000 Hz	100.00 [95.00–110.00]	100.00[95.00–107.50]	0.339
2000 Hz	105.00 [95.00–105.00]	95.00 [95.00–105.00]	0.166

IQR: interquartile range; Mann-Whitney U test was applied for analysis.

No significant relationships were found between MGC, MGFA, and MG-QoL-15 scores and either olfactory test scores (threshold, identification, and total) or pure-tone audiometry results ($p > 0.05$).

DISCUSSION

The results of this study indicate that olfactory and auditory functions, which are non-motor symptoms in patients with Myasthenia Gravis (MG), show minor differences compared to the normal population but are not significantly impaired. We observed a tendency for olfactory perception to decline with the progression of the disease. Additionally, our findings suggest that notable differences in hearing may arise only at higher frequencies.

Acetylcholine is an important neurotransmitter involved in the regulation of both olfactory and auditory functions. The reduction in olfactory function in MG patients is thought to stem from cholinergic system dysfunction. Case reports have indicated that olfactory dysfunction may appear years before the onset of motor symptoms (8,24). However, whether the cholinergic dysfunction affecting the sense of smell is peripheral or central remains unclear (1,25). Findings have shown that $\alpha 7$

nAChRs play a significant role in odor recognition and the interpretation of perceived smells (26). In our study, no statistically significant difference was found between the olfactory test scores of the MG and control groups. However, when olfactory function was assessed qualitatively, it was observed that the number of normosmic individuals in the patient group was lower than in the control group. This finding supports the notion that olfactory function in MG patients may be partially affected, even if not to a statistically significant extent. No significant correlation was found between age at disease onset and olfactory scores in our study. This finding may suggest that the age of onset does not directly impact olfactory function. However, the presence of a significant negative correlation between disease duration and olfactory function suggests that the sense of smell may decline as the disease progresses. Our findings indicate that disease duration may be an important factor affecting olfactory function in MG patients.

It has been reported that otoacoustic emissions, which indicate the healthy functioning of outer hair cells (OHCs), have lower amplitudes in MG patients (17). These findings suggest that functional loss in nAChRs on OHCs may begin before clinical symptoms emerge (14). In our study, when comparing hearing thresholds between groups, a

statistically significant difference was found only at 2000 Hz in the right ear, which may suggest that the effects of the disease are localized and limited to higher frequencies. It is believed that cochlear outer hair cell function is particularly affected at high frequencies in MG (27). This effect on cochlear function has been associated with irreversible damage that occurs as the disease progresses (18). Our findings may indicate that in later stages of clinical symptoms, hearing function could also be affected at lower frequencies. Subclinical dysfunction in the cholinergic neurotransmission of cochlear outer hair cells has been reported in MG patients via otoacoustic emission (OAE) measurements. The correlation between these findings and Anti-AChR antibody titers and electrophysiological data supports the potential use of OAEs as a biomarker in MG patients (27). In our study, no differences were observed between groups regarding acoustic reflexes and air and bone conduction in either ear.

A population-based study found that 51% of MG patients initially presented with isolated ocular involvement, and 55% of these eventually progressed to generalized MG (28). When evaluating our patients based on disease onset type, ocular involvement was most common, followed by generalized involvement, in agreement with the literature. Bulbar involvement without prominent ocular symptoms may be seen as an initial symptom in approximately 15% of cases, especially in older patients (29). The 6.7% rate of bulbar involvement in our patients may be explained by the average age of onset being in the fourth decade. The fact that the majority of our patients had mild muscle weakness corresponding to MGFA Class 2 may be attributed to their relatively young age. Additionally, the average MGC score used to assess disease severity was found to be consistent with the clinical characteristics of the patient group. No significant relationship was found between quality of life and either disease severity or clinical classification. Factors influencing this outcome may include the small sample size and the fact that the patients enrolled did not have advanced symptoms.

While AChR antibodies are the most frequently detected in MG patients (approximately 70%), MuSK antibodies are observed in 1–10% of cases. In line with the literature, we detected AChR antibodies in 63.3% of our patients (30). Myasthenia gravis associated with thymoma is generally reported beginning at a younger age, with a more severe clinical course and worse prognosis. These patients are also reported presenting with more severe clinical forms at onset based on MGFA classification (31). In our study, no association was found between a history of thymectomy and olfactory or auditory functions. This may be related to the exclusion of older patients or those with more severe clinical profiles from the study.

Myasthenia gravis patients have been observed to experience a decline in quality of life due to both physical and cognitive impairments (32). In our study, no relationship was found between olfactory function and quality of life. Additionally, we found no differences in olfactory function based on disease severity or clinical classification. Furthermore, no association was observed between auditory function and quality of life. The MG-QoL-15 does not include assessments of olfactory or auditory functions, and the fact that the primary clinical features of MG are neuromuscular symptoms may lead patients to overlook potential sensory impairments. Moreover, possible subclinical changes in olfactory and auditory functions may prevent patients from recognizing sensory deficits. In MG, non-motor symptoms are often unnoticed since the disease is classically characterized by motor symptoms, yet they may significantly impact patients' quality of life (5). Alopecia areata and taste disturbances have been observed more frequently in MG patients with thymoma than in the general population (33). In recent years, cognitive impairment has also been increasingly reported in MG patients (34).

Our study demonstrated limited changes in olfactory and auditory functions in MG patients. Nonetheless, it should be considered that impairments in both smell and hearing functions in MG patients may begin before clinical symptoms manifest.

This study has several limitations. Although no quantitative differences in olfactory function were found between groups, a qualitative difference was observed, which may be related to the small sample size. Additionally, the relatively young age of the patients and the absence of advanced disease may have limited the statistical significance of the findings regarding olfactory and auditory function.

In recent years, the recognition of non-motor symptoms in MG patients has highlighted the systemic nature of the disease. Partial impairment of smell and hearing, which are senses that protect us from external dangers, suggests that MG is not solely a disease affecting muscles. We believe that a multidisciplinary approach is essential in both the diagnosis and treatment process of this disease.

Ethics Committee Approval: The ethical approval of the study was granted on November 11, 2022, by the Istanbul Training and Research Hospital Clinical Research Ethics Committee with decision number 349.

Informed Consent: Written informed consent was obtained from all participants.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept- ÖA, UET; Design- ÖA; Supervision- ÖA, UET; Resource- ÖA, AS; Materials- ÖA; Data Collection and/or Processing- AS, TE, EA, ÖU; Analysis and/or Interpretation- ÖA, UE, ÖU; Literature Search- ÖA, NSB, UET, MT; Writing- ÖA, NSB; Critical Reviews- UET, NSB, MT.

Conflict of Interest: The authors declared that there is no conflict of interest.

Financial Disclosure: This study received no financial support from any institution.

REFERENCES

- Jayam Trough A, Dabi A, Solieman N, Kurukumbi M, Kalyanam J. Myasthenia gravis: a review. *Autoimmune Dis.* 2012;1–10. [\[Crossref\]](#)
- Leon-Sarmiento FE, Bayona EA, Bayona-Prieto J, Osman A, Doty RL. Profound olfactory dysfunction in myasthenia gravis. *PLoS One.* 2012;7:e45544. [\[Crossref\]](#)
- Dresser L, Wlodarski R, Rezanian K, Soliven B. Myasthenia gravis: epidemiology, pathophysiology and clinical manifestations. *J Clin Med.* 2021;10(11):2235. [\[Crossref\]](#)
- Gotti C, Clementi F, Zoli M. Special issue: the multifaceted activities of nervous and non-nervous neuronal nicotinic acetylcholine receptors in physiology and pathology. *Pharmacol Res.* 2024;205:107239. [\[Crossref\]](#)
- Jones SM, Gwathmey KG, Burns TM. Quality of life measures for myasthenia gravis and evaluation of non-motor symptoms. *Clin Exp Neuroimmunol.* 2015;6:32–39. [\[Crossref\]](#)
- Tekeli H, Senol MG, Altundag A, Yalcinkaya E, Kendirli MT, Yaşar H, et al. Olfactory and gustatory dysfunction in myasthenia gravis: a study in Turkish patients. *J Neurol Sci.* 2015;356:188–192. [\[Crossref\]](#)
- Tong O, Delfiner L, Herskovitz S. Pain, headache, and other non-motor symptoms in myasthenia gravis. *Curr Pain Headache Rep.* 2018;22:1–8. [\[Crossref\]](#)
- Leon-Sarmiento FE, Leon-Ariza DS, Doty RL. Dysfunctional chemosensation in myasthenia gravis: a systematic review. *J Clin Neuromuscul Dis.* 2013;15:1–6. [\[Crossref\]](#)
- Tajima Y, Yaguchi H, Mito Y. Non-motor comorbidity of myasthenia gravis: myasthenia gravis as a systemic immunological disorder involving non-motor systems. *Intern Med.* 2019;58:1341–1347. [\[Crossref\]](#)
- Suzuki S, Utsugisawa K, Suzuki N. Overlooked non-motor symptoms in myasthenia gravis. *J Neurol Neurosurg Psychiatry.* 2013;84(9):989–994. [\[Crossref\]](#)
- Patel RM, Pinto JM. Olfaction: anatomy, physiology, and disease. *Clin Anat.* 2014;27:54–60. [\[Crossref\]](#)
- Peterson DC, Reddy V, Launico MV, Hamel RN. *Neuroanatomy, auditory pathway.* StatPearls Publishing, Treasure Island (FL); 2023. p.1–12.

13. Chaudhury D, Escanilla O, Linster C. Bulbar acetylcholine enhances neural and perceptual odor discrimination. *J Neurosci*. 2009;29:52–60. [\[Crossref\]](#)
14. Hellier JL, Arevalo NL, Blatner MJ, Dang AK, Clevenger AC, Adams CE, et al. Olfactory discrimination varies in mice with different levels of $\alpha 7$ -nicotinic acetylcholine receptor expression. *Brain Res*. 2010;1358:140–150. [\[Crossref\]](#)
15. Elgoyhen AB, Johnson DS, Boulter J, Vetter DE, Heinemann S. $\alpha 9$: an acetylcholine receptor with novel pharmacological properties expressed in rat cochlear hair cells. *Cell*. 1994;79:705–715. [\[Crossref\]](#)
16. Elgoyhen AB, Vetter DE, Katz E, Rothlin CV, Heinemann SF, Boulter J. $\alpha 10$: a determinant of nicotinic cholinergic receptor function in mammalian vestibular and cochlear mechanosensory hair cells. *Proc Natl Acad Sci U S A*. 2001;98:3501–3506. [\[Crossref\]](#)
17. Guinan Jr JJ. Physiology of olivocochlear efferents. In: Dallos P, Popper AN, Fay RR, editors. *Springer Handbook of Auditory Research*, vol 8. The Cochlea. New York, NY: Springer; 1996. p. 435–502. [\[Crossref\]](#)
18. Hamed S, Elattar A, Hamed E. Irreversible cochlear damage in myasthenia gravis-otoacoustic emission analysis. *Acta Neurol Scand*. 2006;113:46–54. [\[Crossref\]](#)
19. Jaretzki A, Barohn RJ, Ernstoff RM, Kaminski HJ, Keesey JC, Penn AS, et al. Myasthenia gravis: recommendations for clinical research standards. *Ann Thorac Surg*. 2000;70:327–334. [\[Crossref\]](#)
20. Burns TM, Conaway M, Sanders DB. The MG Composite: a valid and reliable outcome measure for myasthenia gravis. *Neurology*. 2010;74:1434–1440. [\[Crossref\]](#)
21. Taşçılar NF, Saraçlı Ö, Kurçer MA, Ankaralı H, Emre U. Reliability and validity of the Turkish version of myastheniagravis-quality of life questionnaire-15 item. *Turk J Med Sci*. 2016;46:1107–1113. [\[Crossref\]](#)
22. Veyseller B, Ozucer B, Karaaltın AB, Yildirim Y, Degirmenci N, Aksoy F, et al. Connecticut (CCCRC) olfactory test: normative values in 426 healthy volunteers. *Indian J Otolaryngol Head Neck Surg*. 2014;66:31–34. [\[Crossref\]](#)
23. Cain WS, Gent J, Catalanotto FA, Goodspeed RB. Clinical evaluation of olfaction. *Am J Otolaryngol*. 1983;4:252–256. [\[Crossref\]](#)
24. Ying C, Li W, Li Z, Ying G. Ocular myasthenia gravis accompanied by anosmia. *J Tradit Chin Med*. 2016;36:125–130. [\[Crossref\]](#)
25. Jaretzki 3rd A, Barohn RJ, Ernstoff RM, Kaminski HJ, Keesey JC, Penn AS, et al. Myasthenia gravis: recommendations for clinical research standards. Task Force of the Medical Scientific Advisory Board of the Myasthenia Gravis Foundation of America. *Neurology*. 2000;55:16–23. [\[Crossref\]](#)
26. Hellier JL, Arevalo NL, Smith L, Xiong K-N, Restrepo D. $\alpha 7$ -Nicotinic acetylcholine receptor: role in early odor learning preference in mice. *PLoS One*. 2012;7:e35251. [\[Crossref\]](#)
27. Choi J, Kim N-H, Park S-H, Cho CG, Lee H-J, Kim SU, et al. Abnormalities of otoacoustic emissions in myasthenia gravis: association with serological and electrophysiological features. *Front Neurol*. 2018;9:1124. [\[Crossref\]](#)
28. Hendricks TM, Bhatti MT, Hodge DO, Chen JJ. Incidence, epidemiology, and transformation of ocular myasthenia gravis: a population-based study. *Am J Ophthalmol*. 2019;205:99–105. [\[Crossref\]](#)
29. Estephan EdP, Baima JPS, Zambon AA. Myasthenia gravis in clinical practice. *Arq Neuropsiquiatr*. 2022;80:257–265. [\[Crossref\]](#)
30. Gilhus NE, Skeie GO, Romi F, Lazaridis K, Zisimopoulou P, Tzartos S. Myasthenia gravis-autoantibody characteristics and their implications for therapy. *Nat Rev Neurol*. 2016;12:259–268. [\[Crossref\]](#)
31. Álvarez-Velasco R, Gutiérrez-Gutiérrez G, Trujillo JC, Martínez E, Segovia S, Arribas-Velasco M, et al. Clinical characteristics and outcomes of thymoma-associated myasthenia gravis. *Eur J Neurol*. 2021;28:2083–2091. [\[Crossref\]](#)
32. Basta IZ, Pekmezović TD, Perić SZ, Kisić-Tepavčević DB, Rakočević-Stojanović VM, Stević ZD, et al. Assessment of health-related quality of life in patients with myasthenia gravis in Belgrade (Serbia). *Neurol Sci*. 2012;33:1375–1381. [\[Crossref\]](#)
33. Uzawa A, Suzuki S, Kuwabara S, Akamine H, Onishi Y, Yasuda M, et al. Taste disorders and alopecia in myasthenia gravis. *BMC Neurol*. 2024;24:139. [\[Crossref\]](#)
34. Zhou X, Cao S, Hou J, Gui T, Zhu F, Xue Q. Association between myasthenia gravis and cognitive disorders: a PRISMA-compliant meta-analysis. *Int J Neurosci*. 2023;133:987–998. [\[Crossref\]](#)