CEO Clinical and Experimental Otorhinolaryngology Vol. 19, No. 2: 205-208, May 2026
https://doi.org/10.21053/ceo.2025-00238
pISSN 1976-8710 eISSN 2005-0720

Brief Communication

Subjective and Objective Assessments of Olfactory Function in Patients Taking Anti-obesity Medications

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The global increase in obesity emphasizes the importance of effective treatment strategies, including pharmacological therapy [1]. Anti-obesity medications (AOMs), such as glucagon-like peptide-1 (GLP-1) receptor agonists (liraglutide, semaglutide), support weight reduction by modulating appetite and energy intake [2]. Olfaction, which influences appetite and energy balance, is frequently altered in obesity [3,4]. Although weight loss may affect olfactory function, findings across studies are inconsistent [5,6]. For example, GLP-1 receptor agonist therapy has been reported to improve olfactory test scores, enhance brain activation in response to olfactory stimuli (right parahippocampus), and increase olfactory-evoked neural activation (left hippocampus) [6,7]. Given the complexity of olfactory processing and the absence of standardized testing protocols, comprehensive evaluation using both subjective and validated objective tools is required [8-10]. Accordingly, this study aimed to evaluate olfactory function in patients undergoing AOM therapy and to identify related clinical characteristics.

The study protocol was approved by the Institutional Review Board of Chung-Ang University Hospital (Seoul, Korea; No. 2404-013-598). Participants were recruited from a tertiary hospital outpatient clinic between July 2024 and April 2025. Individuals aged ≥19 years who received a full explanation of the study and provided written informed consent were enrolled. Exclusion criteria were as follows: (1) pregnant or lactating women; (2) individuals with impaired judgment due to cognitive impairment, such as dementia; (3) individuals with systemic health conditions considered unsuitable for medical obesity treatment; (4) individuals with symptoms of rhinitis or sinusitis previously diagnosed as allergic rhinitis or chronic rhinosinusitis; and (5) individuals presenting with nasal symptoms (e.g., nasal obstruction, rhinorrhea) or with abnormal findings on sinus endoscopy.

Anthropometric and laboratory assessments were performed at baseline. Subjective chemosensory symptoms were evaluated using the Questionnaire of Olfactory Disorders (QOD), which included items on general chemosensory discomfort and parosmia. Subjective olfactory discomfort and parosmia were defined as affirmative responses to the corresponding QOD items [11]. Objective olfaction was measured with the Yonsei Olfactory Function Test (YOF) (RHICO Medical Co.), with hyposmia defined as a Threshold-Discrimination-Identification (TDI) score ≤21 [12]. Gustatory function was assessed using a gustatory function test with validated taste solutions developed for the Korean population [13].

Participants received one or more of the currently approved AOMs (phentermine/topiramate, naltrexone/bupropion, liraglutide, semaglutide, and orlistat) for at least 24 weeks. Medications could be prescribed in combination at the physician's discretion based on the patient's baseline condition. Phentermine/topiramate combines a sympathomimetic amine and an anticonvulsant [14], whereas naltrexone/bupropion combines an opioid receptor antagonist and an aminoketone antidepressant, both of which contribute to appetite suppression [15]. Liraglutide and semaglutide are GLP-1 receptor agonists that delay gastric emptying and enhance insulin secretion, thereby producing weight-reducing effects [16]. Orlistat, a gastric and pancreatic lipase inhibitor, facilitates the physical excretion of dietary fat [17]. The distribution of participants according to AOM type was: phentermine/topiramate (n=62), naltrexone/bupropion (n=3), liraglutide (n=3), semaglutide (n=6), and orlistat (n=79). Statistical

• Received July 30, 2025
Revised September 11, 2025
Accepted September 23, 2025

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analyses included the *t*-test, chi-square test, and multivariate linear regression, conducted using R version 4.5.1 (R Foundation). Forest plots were used to visualize the results.

Seventy participants were included in the current analyses (Supplementary Fig. 1). The hyposmia group had a significantly higher body mass index (BMI) (P=0.042) and high-sensitivity C-reactive protein levels (P=0.017) (Table 1). Multiple linear regression analysis demonstrated that younger age (P<0.001), lower BMI (P=0.005), higher body fat percentage (P=0.001), and higher basal metabolic rate (P=0.004) were factors significantly associated with higher TDI scores. In contrast, elevated white blood cell count (P=0.046) and alanine aminotransferase (ALT) (P=0.018) levels were factors significantly associated with lower TDI scores (Fig. 1).

With respect to subjective olfactory dysfunction, 36 participants reported normal function and 34 reported subjective discomfort. Only age significantly differed between the groups, with the abnormal group being older than the normal group (P=0.028) (Supplementary Table 1). Multiple linear regression analysis revealed that higher BMI (P=0.004) and elevated ALT levels (P=0.012) were significantly associated with lower visual analog scale (VAS) scores, indicating less perceived olfactory dysfunction. Conversely, greater waist circumference (P=0.013), higher thyroid-stimulating hormone (P=0.007), and the presence of parosmia (P=0.012) were significantly associated with higher VAS scores (Supplementary Fig. 2).

Regarding parosmia symptoms, 50 of the 70 participants (71.4%) reported experiencing parosmia. Participants with parosmia showed significantly lower olfactory threshold scores than those without parosmia (P=0.016), suggesting reduced olfactory sensitivity (Supplementary Table 2). Additionally, low-density lipoprotein (LDL) cholesterol levels were significantly lower in the parosmia group (P=0.036). Multiple linear regression analysis showed that higher BMI (P=0.012), basal metabolic rate (P=0.031), and sum VAS score (P=0.020) were factors significantly associated with higher parosmia scores, indicating more severe parosmia. In contrast, higher body weight (P=0.019), skeletal muscle mass (P=0.045), and uric acid levels (P=0.036) were associated with lower parosmia scores (Supplementary Fig. 3).

In this study, 7% of participants were diagnosed with hyposmia based on the YOF, whereas 48.6% reported subjective olfactory disturbances and 71.4% reported experiencing parosmia. These findings highlight the importance of the assessment method used to evaluate olfactory function. Because different methodologies can produce divergent results, they should be carefully considered when interpreting olfactory function in both clinical and research contexts.

The YOF results indicated that BMI was the only factor consistently associated with both hyposmia diagnosis and TDI score. Interestingly, higher body fat mass was significantly associated with better olfactory function, as reflected by higher TDI scores. Few previous studies have directly compared BMI and body fat mass with objectively measured olfactory function or hyposmia. As demonstrated in this study, BMI and body fat may exert different health effects [18]. Further research is therefore needed to clarify their distinct roles in olfactory function and dysfunction.

The factors associated with YOF outcomes and those associat-

Table 1. Characteristics of participants in the hyposmia and normosmia groups based on the YOF test

Variable	Hyposmia (n=5)	Normosmia (n=65)	*P*-value
Age (yr)	46.60±15.82	41.25±10.50	0.293
Sex			0.290
Male	2 (40)	13 (20)	
Female	3 (60)	52 (80)	
Non-smoker	5 (100)	61 (93.85)	1.000
Anthropometry			
Height (cm)	158.76±10.53	163.30±7.77	0.223
Weight (kg)	89.64±19.24	80.29±19.99	0.316
Body mass index (kg/m^2)	35.36±5.47	29.89±5.70	0.042
Skeletal muscle (kg)	29.54±9.17	27.05±6.30	0.412
Body fat percent (%)	41.58±6.17	38.10±6.28	0.236
Basal metabolic rate (kcal)	1,506.00±310.92	1,430.58±225.81	0.485
Waist circumference (cm)	107.68±11.61	97.09±14.63	0.120
YOF test			
Threshold	2.80±0.91	4.02±1.01	0.011
Discrimination	6.80±1.30	9.14±1.27	<0.001
Identification	10.80±1.30	11.72±0.52	0.001
TDI	20.40±0.82	24.88±1.58	<0.001
QOD test			
Discomfort (yes:no)	4:1	32:33	0.358
Parosmia score	20.00±19.18	20.51±19.88	0.956
Chemical taste test			
Taste threshold	5.20±0.45	5.54±0.56	0.193
Taste identification	16.00±2.55	18.20±3.27	0.147
Laboratory test			
WBC (×10^9/L)	7.46±2.31	6.72±1.91	0.408
hs-CRP (mg/L)	7.22±10.12	2.68±3.26	0.017
Fasting glucose (mg/dL)	100.20±10.71	105.95±27.61	0.647
Uric acid (mg/dL)	6.48±2.10	5.15±1.46	0.062
AST (IU/L)	33.20±26.75	29.03±28.16	0.750
ALT (IU/L)	53.40±58.13	32.26±26.87	0.129
Insulin (mU/L)	42.42±62.24	14.51±34.57	0.107
Total cholesterol (mg/dL)	190.40±48.64	208.72±37.01	0.300
Triglyceride (mg/dL)	155.80±113.19	120.12±69.01	0.292
HDL cholesterol (mg/dL)	48.20±12.46	56.32±14.26	0.221
LDL cholesterol (mg/dL)	101.20±32.56	121.06±35.12	0.225
Cortisol (μg/dL)	6.44±4.69	9.14±2.97	0.064
Free T4 (ng/dL)	1.40±0.24	1.28±0.17	0.120
TSH (μIU/mL)	2.41±1.26	2.49±1.51	0.913

Values are presented as mean±standard deviation or number (%).
YOF, Yonsei Olfactory Function Test; TDI, threshold discrimination identification; QOD, Questionnaire of Olfactory Disorders; WBC, white blood cell; hs-CRP, high-sensitivity C-reactive protein; AST, aspartate aminotransferase; ALT, alanine aminotransferase; HDL, high-density lipoprotein; LDL, low-density lipoprotein; Free T4, free thyroxine; TSH, thyroid-stimulating hormone.

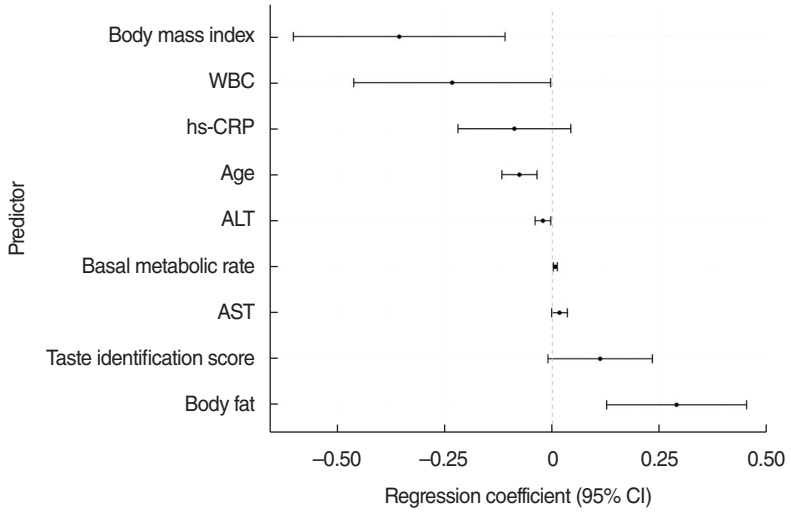


Fig. 1. Forest plot illustrating the associations between clinical variables and Threshold-Discrimination-Identification scores. WBC, white blood cell; hs-CRP, high-sensitivity C-reactive protein; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

ed with the sum of VAS scores did not fully overlap. Notably, higher BMI was associated with hyposmia diagnosis and lower TDI scores, yet it showed an inverse correlation with sum VAS scores. This suggests that BMI influences subjective olfactory discomfort and objective TDI scores in opposite directions. Such divergence underscores the importance of incorporating culturally validated subjective olfactory assessment tools, such as the QOD, when evaluating olfactory function in patients with obesity. Previous studies have reported associations between BMI and both objective and subjective measures of olfactory function. For example, BMI has been negatively correlated with TDI scores in patients with obesity compared to normal-weight controls [13], and a meta-analysis demonstrated that increasing BMI was linked to reduced olfactory threshold sensitivity [5]. However, studies in adolescents have shown that higher BMI may be associated with greater olfactory sensitivity, suggesting possible differences related to age or developmental stage [19]. In addition, one study reported that patients with subjective olfactory dysfunction had higher BMI values [20]. These findings indicate that future prospective studies with larger cohorts are needed to clarify the complex relationships between BMI, age, and olfactory function.

We also found that LDL cholesterol was the only clinical factor significantly associated with parosmia. Cardiovascular disease history is known to be linked with a higher prevalence of olfactory disorders [21,22], and LDL cholesterol plays a central role in the development and progression of atherosclerosis. The observed association between LDL cholesterol and parosmia may partially explain the relationship between cardiovascular disease and impaired olfactory function. Furthermore, a pharmacovigilance study reported olfactory adverse events, including parosmia, among neurological side effects related to GLP-1 receptor agonist use [23]. Since no objective olfactory function test currently exists for specifically assessing parosmia, its reported prevalence may be overestimated. Nonetheless, incorporating parosmia assessment, at least through subjective scoring, may be essential when evaluating olfactory function in patients with obesity.

This study has some limitations. First, the sample size was relatively small, and only a few participants were diagnosed with hyposmia. Larger, prospective studies with comprehensive olfactory evaluation are needed to confirm these findings. Second, this cohort included only patients receiving AOMs and lacked a comparable control group. Consequently, the mechanisms underlying the discrepancy between subjective and objective assessments could not be determined. Finally, although we attempted to exclude other conditions that may influence olfaction, such as chronic rhinosinusitis and allergic rhinitis, based on symptoms and medical history, it is not possible to rule out all confounding factors completely.

Despite these limitations, we identified clinical factors associated with different olfactory parameters and showed that these factors may differ or even exert opposite associations depending on the outcome measure. This novel finding underscores the complexity of olfactory evaluation in this patient population.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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AUTHOR CONTRIBUTIONS

Conceptualization: HJL, HJM. Data collection: HJL, HJM. Formal analysis: IYK. Writing–original draft: HJL, HJM. Writing–review & editing: HJL, HJM. All authors read and agreed to the published version of the manuscript.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found online at https://doi.org/10.21053/ceo.2025-00238.

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