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# Subjective distress mediates the association between olfactory dysfunction duration and depression in post COVID 19 patients

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**Olfactory dysfunction (OD) has been reported in individuals who recovered from COVID-19. Those with OD after COVID-19 (COVID-19 group) exhibited more severe psychiatric symptoms than those with OD from other etiologies (non-COVID-19 group). This study investigates differences in psychological symptoms and related clinical factors between these groups. Fifty-two participants (COVID-19 group: 26; non-COVID-19 group: 26) were recruited. Both objective and subjective olfactory function were assessed, and symptoms of depression, anxiety, and perceived stress were measured using self-reported scales. There were no significant differences in objective and subjective olfactory function or psychological symptoms between the groups, except for age and the short version of the Questionnaire of Olfactory Disorders-negative statements (sQOD-NS). The sQOD-NS score was negatively correlated with OD duration only in the COVID-19 group. In both groups, the sQOD-NS was significantly correlated with Patient Health Questionnaire-9 (PHQ-9) scores. Mediation analysis showed that OD duration indirectly affected PHQ-9 scores via the sQOD-NS in the entire sample, particularly in the COVID-19 group. These findings suggest that subjective distress from OD may mediate the relationship between OD duration and depressive symptoms in COVID-19 patients, highlighting the need for targeted psychiatric interventions after recovery from COVID-19.**

**Keywords** Olfaction disorders, COVID-19, Depressive disorder, Anxiety disorders, Psychological distress

Olfactory dysfunction (OD) refers to a range of conditions involving impaired sense of smell, including anosmia (complete loss of smell) and hyposmia (reduced ability to smell)[1]. OD can occur due to a variety of causes, including rhinosinusitis with or without nasal polyps, post viral infections, head trauma, toxic material exposure, and congenital disorders[2,3]. In recent years, the prevalence of OD increased due to the COVID-19 pandemic, with many patients experiencing a decrease in their sense of smell following infection[4,5]. Post COVID-19, the prevalence of OD has been reported to range from approximately 10–55%, depending on race[6]. COVID-19-related OD often appears on the third day following infection and disappears entirely in 4–6 weeks. However, these changes lasted longer than four months in 27% of cases[7] and up to one year in 21.3% of cases[8].

According to Yom-Tov et al., COVID-19 patients with OD had a 30% higher incidence of depression and suicidal ideation than those without OD[9]. An online survey by Coelho et al. involving 322 patients with OD following COVID-19 infection found that depressive symptoms were present in 43% of the participants[10]. Additionally, COVID-19 patients with OD reported higher anxiety levels[11]. These results suggest an association between neuropsychiatric symptoms and OD, and the pivotal role of COVID-19 infection in long-term mental health outcomes.

Previous studies have proposed several mechanisms for the development of neuropsychiatric symptoms in COVID-19-related OD. It has been demonstrated that SARS-CoV-2 can cause damage to the central nervous system[12,13]. Postmortem examination of brain tissues from patients with COVID-19 revealed the presence of

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neuroinflammation, microglia activation, and neuronal death[14,15]. Neuroinflammation can persist long after the acute phase of the disease, sometimes referred to as "long COVID"[16]. According to Stefanou et al., over one-third of patients experienced brain fog, cognitive dysfunction, changes in gustation and smell, and psychiatric manifestations such as mood disorders as long COVID symptoms[13]. This phenomenon was likely caused by persistent systemic inflammation and the existence of viral RNA in the brains of COVID-19 patients after an extended period of time[17].

From a psychosocial perspectives, OD can affect various aspects of life. The inability to smell can lead to a loss of pleasure from enjoyable activities, such as eating and socializing, which can cause significant psychological distress[18,19]. Several lines of evidence demonstrate a significant association between OD and depression, anxiety, and feelings of isolation, which further deteriorate quality of life (QoL)[19–21]. In a study on long COVID, distortion of smell was more prevalent in young people, and negative QoL was more common in people with a post-COVID-19 infection than in other post-infection cases[22]. Thus, OD stemming from COVID-19 can elicit a profound negative impact on psychological well-being, and requires clinical attention.

However, it is not yet clear why the prevalence of psychological symptoms is higher in patients with COVID-19-related OD than in those with OD due to other etiologies such as chronic entorhinal inflammation or trauma. To date, no study has compared stress levels, depression symptoms, and anxiety in OD following COVID-19 infection and OD resulting from other etiologies. Furthermore, the clinical factors that influence mood symptoms in patients with long COVID remain poorly understood.

Therefore, this study aimed to compare olfactory function and emotional state in two groups of participants: those who experienced OD due to COVID-19 and those who experienced long-term olfactory loss due to chronic entorhinal disease. Furthermore, we investigated the potential associations between OD duration, subjective distress, and mood symptoms, such as depression and anxiety, using mediation analyses.

## Results

Table 1 details the patient demographics, illustrating a mean participant age of the approximately 44 years; the COVID-19 group was significantly younger than the non-COVID-19 group ($p$=.048). Among 52 participants with subjective olfactory loss, approximately 71% were confirmed to have OD according to psychophysical test results. The subjective and objective olfactory parameters did not differ significantly between the COVID-19 and non-COVID-19 groups, except for the total QOD-NS score (11.08 ± 5.05 vs. 7.81 ± 5.47, $p$=.030). Based on the cutoff for each psychological measure, 38.5% of the participants had depressive symptoms (20/52), and 21.2% had moderate-to-severe anxiety (11/52). Furthermore, 78.8% of the participants had moderate-to-severe perceived stress (41/52).

In 38 participants with OD, OD duration did not differ significantly between the COVID-19 and non-COVID-19 groups (3.83 ± 3.22 vs. 3.34 ± 2.97 months, respectively, $p$=.625). According to the correlation analysis of various olfactory functions and psychological parameters, the sQOD-NS was negatively correlated with OD duration with marginal significance (Table 2). The correlation analysis between OD duration and the PHQ-9, GAD-7, and PSS-10 scores did not show significant results. In contrast, the sQOD-NS was significantly correlated with the PHQ-9 and GAD-7. The QOD-VAS also exhibited a moderate-to-high correlation with the PHQ-9 and GAD-7, and a low correlation with the PSS-10. However, the total YOF score showed either a negligible or no correlation with psychological parameters. In the COVID-19 group, a significant negative correlation was observed between OD duration and the sQOD-NS (Fig. 1A). In contrast, no such correlation was observed in the non-COVID-19 group. The sQOD-NS and PHQ-9 scores were significantly correlated in both groups (Fig. 1B), whereas the correlation between the sQOD-NS and GAD-7 scores was not significant (Fig. 1C).

A mediation model with the sQOD-NS as the mediator showed a significant indirect effect (Fig. 2A; effect size, 0.47; 95% Bootstrap CI [0.10, 1.04]) of OD duration on the PHQ-9 scores of all participants. In the COVID-19 group ($n$=20), mediation effects were observed between the OD duration and PHQ-9 scores mediated by the sQOD-NS (Fig. 2B; effect size, 0.30; 95% Bootstrap CI [0.00, 0.92]). However, there was no significant indirect

| | Total ($n$=52) | COVID-19 ($n$=26) | Non-COVID-19 ($n$=26) | $p$ value |
|---|---|---|---|---|
| **Age (year-old)** | **44.21 ± 18.24** | **39.23 ± 16.12** | **49.19 ± 19.16** | **0.048** |
| Sex (male) | 27 | 14 | 13 | 0.781 |
| **sQOD-NS total score** | **9.44 ± 5.47** | **11.08 ± 5.05** | **7.81 ± 5.47** | **0.030** |
| QOD-VAS total score | 32.31 ± 11.33 | 31.85 ± 9.64 | 32.77 ± 12.97 | 0.772 |
| YOF total score | 15.91 ± 7.47 | 16.99 ± 7.00 | 14.84 ± 7.90 | 0.303 |
| Patients with objective OD (n) | 37 | 19 | 18 | 0.760 |
| PHQ-9 score | 8.23 ± 6.77 | 7.27 ± 6.10 | 9.19 ± 7.37 | 0.310 |
| GAD-7 score | 5.24 ± 5.61 | 3.79 ± 5.13 | 6.64 ± 5.80 | 0.076 |
| PSS-10 | 18.04 ± 6.48 | 17.58 ± 7.53 | 18.46 ± 5.44 | 0.637 |

**Table 1**. Participant demographics. QOD, Questionnaire of Olfactory Disorders; VAS, visual analog scale; sQOD-NS, short version of QOD-negative statements; YOF, YSK olfactory function; PHQ-9, Patient Health Questionnaire-9; GAD-7, Generalized Anxiety Disorder 7-item scale; PSS-10, Perceived Stress Scale.

| | Variables | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Age | 1 | | | | | | | |
| 2 | OD Duration | 0.011 | 1 | | | | | | |
| 3 | sQOD-NS | −0.107 | −0.318† | 1 | | | | | |
| 4 | QOD-VAS | 0.064 | 0.123 | −0.567** | 1 | | | | |
| 5 | YOF, total | −0.205 | −0.242 | −0.149 | 0.242 | 1 | | | |
| 6 | PHQ-9 | 0.032 | −0.107 | −0.539** | 0.715** | 0.179 | 1 | | |
| 7 | GAD-7 | 0.035 | −0.242 | −0.471** | 0.644** | 0.136 | 0.838** | 1 | |
| 8 | PSS-10 | 0.093 | −0.131 | −0.160 | 0.461** | 0.260 | 0.372* | 0.488** | 1 |

**Table 2**. Spearman's correlation matrix of olfactory function and psychological variables ($n = 38$). † $p = .051$; *$p < .05$; **$p < .01$. OD, olfactory dysfunction; QOD, Questionnaire of Olfactory Disorders; VAS, visual analog scale; sQOD-NS, short version of QOD-negative statements; YOF, YSK olfactory function; PHQ-9, Patient Health Questionnaire-9; GAD-7, Generalized Anxiety Disorder 7-item scale; PSS-10, Perceived Stress Scale.

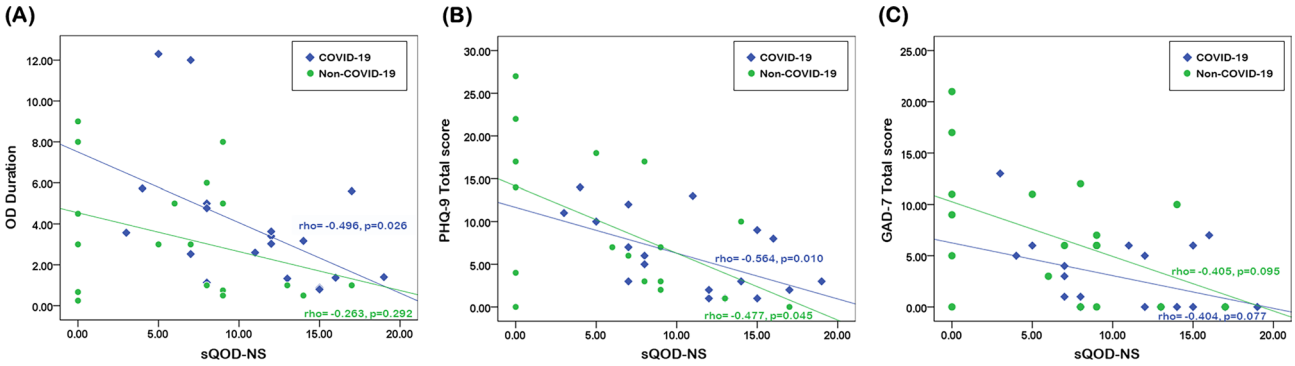


**Fig. 1**. Association between sQOD-NS scores and clinical and psychological variables in participants with olfactory dysfunction (OD). Scatter plots showing the relationship between (**A**) sQOD-NS and OD duration, (**B**) sQOD-NS and PHQ-9 total scores, and (**C**) sQOD-NS and GAD-7 total scores.

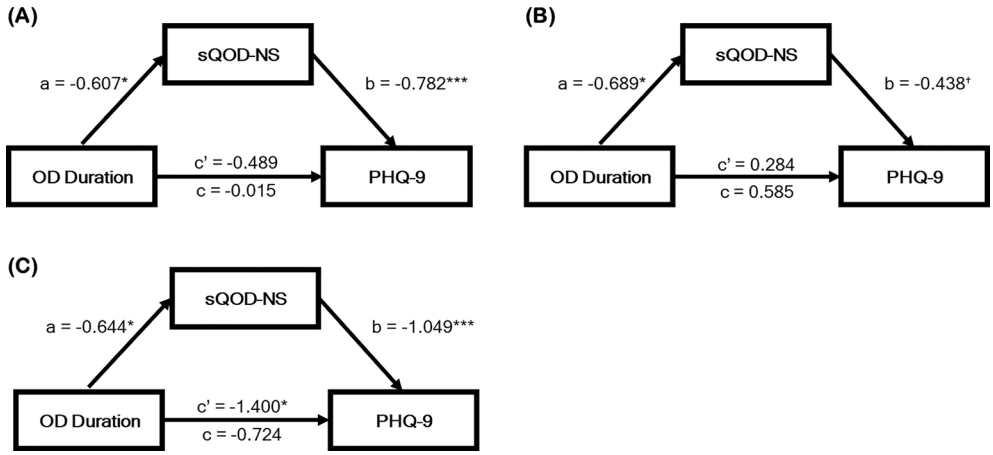


**Fig. 2**. Standardized regression coefficients for the sQOD-NS-mediated association between the duration of olfactory dysfunction and PHQ-9 total score. (**A**) Entire sample ($n = 38$), (**B**) COVID-19 group ($n = 20$), (**C**) Non-COVID-19 group ($n = 18$). Note: *$p < .05$, **$p < .01$, ***$p < .001$, †$p = .054$. All presented effects are unstandardized; Path a is the effect of OD duration on the mediators; Path b is the effect of mediators on the PHQ-9; Path c' is the direct effect of OD duration on PHQ-9; Path c is the total effect of OD duration on PHQ-9.

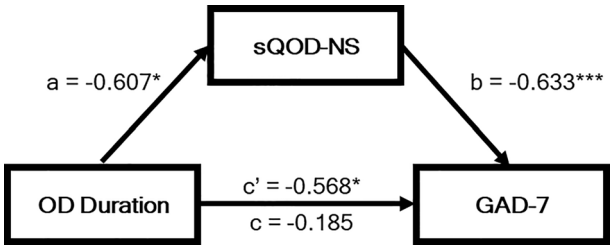


**Fig. 3**. Standardized regression coefficients for the sQOD-NS-mediated association between the duration of olfactory dysfunction and GAD-7 total score in the entire sample ($n = 38$). Note: $^{*}p < .05$, $^{**}p < .01$. All presented effects are unstandardized; Path a is the effect of OD duration on mediators; Path b is the effect of mediators on GAD-7; Path c' is the direct effect of OD duration on GAD-7; and Path c is the total effect of OD duration on GAD-7.

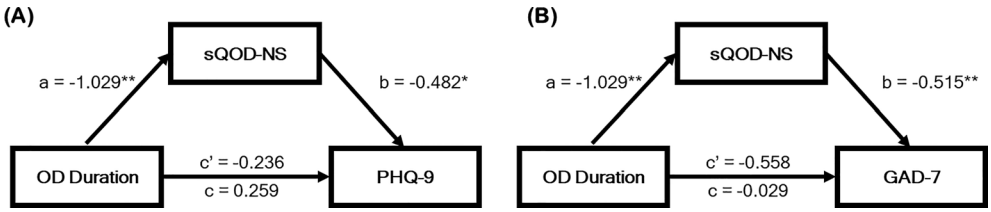


**Fig. 4**. Standardized regression coefficients for the sQOD-NS-mediated association between the duration of olfactory dysfunction and mood symptom in the subjects with objective OD ($n = 26$). (**A**) A mediation model for PHQ-9, (**B**) A mediation model for GAD-7. Note: $^{*}p < .05$, $^{**}p < .01$. All presented effects are unstandardized; Path a is the effect of OD duration on mediators; Path b is the effect of mediators on mood symptoms; Path c' is the direct effect of OD duration on mood symptoms; and Path c is the total effect of OD duration on mood symptoms.

effect of OD duration on the PHQ-9 mediated by the sQOD-NS (Fig. 2C; effect size, 0.68; 95% Bootstrap CI [−0.24, 1.68]) in the non-COVID-19 group.

For all participants, an indirect effect of the sQOD-NS was also significant in the mediation model with the GAD-7 as the dependent variable (Fig. 3; effect size, 0.38; 95% Bootstrap CI [0.09, 0.88]). However, the sQOD-NS was not significant as a mediator in the subgroup analyses of the COVID-19 (effect size, 0.23; 95% Bootstrap CI [−0.14, 0.83]) and non-COVID-19 groups (effect size, 0.47; 95% Bootstrap CI [−0.15, 1.24]).

In the sensitivity analysis, the effect of the sQOD-NS between the OD duration and PHQ-9 remained significant (Fig. 4A; effect size, 0.50; 95% bootstrap CI [0.05, 1.49]) among participants with objective OD ($n = 26$). Mediation effects were observed between the OD duration and GAD-7 mediated by the sQOD-NS (Fig. 4B; effect size, 0.53; 95% bootstrap CI [0.13, 1.35]).

## Discussion

This study aimed to determine the differences in psychological symptoms between people with post-COVID-19 OD and OD not related to COVID-19. Comparisons of the two groups demonstrated no significant differences in clinical characteristics and symptoms of depression, anxiety, and perceived stress, except for age and sQOD-NS scores. In the COVID-19 group, the sQOD-NS score was significantly negatively correlated with the OD duration, whereas in the non-COVID-19 group, it was not. However, significant correlations between the sQOD-NS and PHQ-9 scores were found in both groups. Mediation analysis demonstrated a significant indirect effect of the OD duration on PHQ-9 scores via the sQOD-NS in all participants and in the COVID-19 group.

Existing literature has identified significant associations between OD and mood symptoms[9–11,23]. The causes of OD are diverse, encompassing a range of conditions, including SARS-CoV-2 infection, entorhinal diseases, and trauma. However, it is not yet known whether the mechanisms of psychological symptoms differed between people who experienced OD following COVID-19 and those who did not. To the best of our knowledge, this is the first study to demonstrate that the relevant clinical factors associated with psychological symptoms after OD onset may vary according to OD etiology.

In this study, approximately 70% of the patients who reported subjective OD were diagnosed with actual olfactory impairment through psychophysical tests. Inconsistencies between subjective and objective olfactory test results have been reported in a previous study[24]. Compared to the non-COVID-19 group, the COVID-19 group was younger in age and reported less subjective distress (sQOD-NS). However, there were no significant differences between the groups in terms of depression, anxiety, stress, and OD duration. The present findings differ from those of Stankevice et al.[22], who found that people with SARS-CoV-2 infection had a greater complaint rate for distorted sensations but a lower prevalence of olfactory abnormalities. This discrepancy in outcomes can be attributed to age differences between the study populations. Specifically, the younger population

in the COVID-19 group may have had more access to healthcare resources, which influenced their outcomes, compared to the non-COVD-19 group that included older patients who may have had additional comorbidities.

In contrast, the correlation results for the sQOD-NS scores demonstrated disparate patterns between the groups. In the COVID-19 group, sQOD-NS scores were significantly correlated with PHQ-9 scores and OD duration; however, these associations were not found in the non-COVID-19 group. These findings demonstrate that despite having less subjective distress, the COVID-19 group displayed a clear pattern of correlation in response to the OD duration and a moderate impact on depression severity. This finding aligns with previous studies suggesting that the subjectivity of sensory perception might be a crucial factor, potentially even surpassing the significance of the perceptual problem in groups with post-COVID-19 OD[25]. However, we did not find a significant correlation between OD duration and depressive symptoms. This finding is in line with prior research showing that depressive symptoms were significantly correlated only with COVID-19-related OD[26]. Furthermore, Liu et al. reported that the QOD-NS score was a strong predictor of depressive symptoms in patients with OD, while the OD duration was not[26], this is consistent with our findings.

The mediation analyses revealed a significant indirect mediation effect between OD duration and PHQ-9 scores in the entire sample and in the COVID-19 group. In contrast, the direct effect of OD duration on PHQ-9 was not significant and had the opposite effect on the indirect pathway. This pattern of coefficients may indicate a suppressive effect of sQOD-NS. This particular mediation path suggests that participants with high sQOD-NS scores did not have a long-term reduction in depressive symptoms. Patients with COVID-19 may have expected that once they had recovered from the infection, they would also recover from the resulting loss of smell. However, in some patients, recovery was markedly delayed, with OD persisting for several months or even longer after onset[27]. This discrepancy may influence subjective distress, resulting in the emergence of additional psychological symptoms. In contrast, this mediating effect was not evident in the non-COVID-19 group, because OD may have been a chronic and predictable course of the underlying diseases in this group. Additionally, the results of the sensitivity analysis demonstrated that the sQOD-NS indirectly mediated the effect of OD duration on the PHQ-9 and GAD-7, even when the analysis was restricted to objective OD. These results imply that even in cases of overt OD, subjective distress from OD is an important factor mediating the relationship between OD duration and mood symptoms. Therefore, assessment of mental health problems would be important in individuals with subjective OD after COVID-19 infection.

This study had several limitations. First, we employed self-report scales to assess depression, anxiety, and stress. However, expert interviews were not conducted for checking current and past mental illnesses. This raises the possibility that some participants had preexisting mental health issues prior to the OD onset. Second, this study only focused on patients who visited the hospital with subjective symptoms of OD and did not include an analysis of the population without OD. This may have resulted in a sampling bias. Third, this study was conducted in a limited area, and the sample size was relatively small. Additionally, the participants had the same ethnic and cultural backgrounds. Therefore, the current findings cannot be generalized to larger populations in diverse regions. Fourth, we could not measure OD symptoms at the same stage of the disease or at the same interval after disease onset because the time of awareness and reasons for OD varied among participants. Finally, the mediation analysis only included patients who clearly recalled the OD duration. Participants who were unable to recall the exact time point of their OD were excluded. Therefore, future studies should include a larger number of participants from diverse regional, racial, and cultural groups and collect comprehensive data using structured psychiatric interview, including the OD duration and various factors that may influence mental health outcomes.

## Conclusion

We found a substantial indirect influence of OD duration on PHQ-9 scores via sQOD-NS scores in the COVID-19 group, although there were no discernible differences between the levels of anxiety, depression, and perceived stress compared with the non-COVID-19 group. The results indicated that high subjective distress from OD, even after recovery from COVID-19, may have a negative impact on mental health outcomes. Accordingly, it is imperative that we proactively identify and address subjective distress in patients with OD following COVID-19 infection, and adopt an assertive approach to treatment with the objective of fostering long-term mental health outcomes.

## Methods

### Study population

This retrospective cohort study included 52 patients who presented with subjective olfactory dysfunction and visited our tertiary hospital between January 2022 and August 2023. All the participants were Korean and had the same ethnic and cultural backgrounds. Patients who had already been diagnosed with psychiatric or other underlying neurological diseases were excluded. The COVID-19 diagnosis was confirmed by SARS-CoV-2 real-time reverse transcription polymerase chain reaction (RT-PCR) using respiratory samples. COVID-19-related OD was determined based on patients' statements. If patients reported having no smell-related issues previously and stated that OD onset occurred after their COVID-19 diagnosis, it was regarded as COVID-19-associated OD (COVID-19 group). All participants in the COVID-19 group were recruited during the post-acute COVID-19 period—four weeks or more after the onset of COVID-19 infection. In patients with OD that was not associated with COVID-19 (non-COVID-19 group), the causes of OD included head trauma ($n=5$), brain hemorrhage ($n=1$), post-SARS-CoV-2 mRNA vaccination ($n=2$), post-upper respiratory infection ($n=2$), chronic rhinosinusitis ($n=2$), iatrogenic causes ($n=1$; anterior skull base surgery for olfactory groove meningioma), and unknown etiologies ($n=13$). All participants completed subjective and objective evaluations of olfaction. Psychological assessments were conducted using various questionnaires.

This study was conducted in accordance with the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board of our tertiary hospital (approval number: 2023AS0087). Written informed consent was obtained from all participants.

## Olfactory function assessment

We evaluated subjective olfactory function using the Korean version of the Questionnaire of Olfactory Disorders (QOD)[28]. Among the subdomains of the QOD, we used the QOD-Visual Analog Scale (QOD-VAS) and the short version of QOD-Negative Statements (sQOD-NS). The Korean version of the QOD-VAS comprises five questions on an 11-point scale (0–10), with a higher score indicating poorer subjective olfactory function. In contrast, the Korean version of the sQOD-NS consists of seven questions rated on a 4-point scale (0–3), with a higher score indicating better subjective olfactory function. Objective olfactory function was evaluated using the psychophysiological YSK olfactory function (YOF) test[29]. The YOF test consisted of three subtests for threshold (T), discrimination (D), and identification (I), using familiar odorants in the Korean context. The YOF subtests scores ranged from 1 to 12 for the threshold test, 0–12 for the discrimination and identification tests, and 1–36 for the total TDI score. The diagnostic cutoff for the YOF test was established as ≤14.5 for anosmia and ≤21.0 for hyposmia[29].

## Psychological distress assessment

Various psychological assessments were performed, using the Korean version of the Patient Health Questionnaire-9 (PHQ-9) to evaluate depressive mood, Generalized Anxiety Disorder 7-item scale (GAD-7) to evaluate anxiety, and Perceived Stress Scale (PSS-10) to evaluate stress level.

The PHQ-9 is a self-reported questionnaire that was designed for use in primary care settings to efficiently establish psychiatric diagnoses based on the DSM-IV criteria[30]. It is composed of nine items, and respondents are asked to select the degree of their symptoms on a scale of 0 to 3 for each item. The scores are summed for a maximum total score of 27, with the cutoff point of 10 indicating the presence of depressive symptoms.

The GAD-7 is a self-rated assessment developed by Spitzer et al. to screen for generalized anxiety disorder in primary care populations[31]. It comprises seven items, and respondents are asked to select the degree of their symptoms on a scale of 0 to 3 for each item, with the cut-off point of 9 used to screen for anxiety[31].

The PSS-10 is a self-rated assessment developed by Cohen et al. to assess an individual's overall perception and interpretation of stress experienced during the past month, rather than specific stressful events[32]. It is composed of 10 items. Respondents are asked to select the degree of their symptoms using a 5-point Likert scale (0–4). The PSS-10 is not intended for diagnostic purposes; thus, there is no universally accepted cutoff score for interpreting the score for each item. However, Swaminathan et al. proposed the criteria for classifying the degree of perceived stress as follows: low perceived stress (0–13), moderate perceived stress (14–26), and high perceived stress (27–40). In this study, we classified stress levels according to these criteria.

## Statistics

Statistical analyses were conducted using the Statistical Package for Social Sciences version 21 (IBM Corporation, Armonk, NY, USA). The $\chi^2$ test was used to compare categorical variables, and the independent t-test was used to compare continuous variables between patient groups based on their experience of olfactory impairment. Spearman's correlation coefficient was used to assess the relationships between OD and psychological parameters. The magnitude of the correlation coefficient (Spearman's rho) was interpreted using Hinkle's suggestion (very high: 0.9 to 1.00; high: 0.7 to 0.9; moderate: 0.5 to 0.7; low: 0.3 to 0.5; and negligible: 0 to 0.3).

Furthermore, we examined the relationships between OD duration, the sQOD-NS, and mood symptoms (depression and anxiety), which showed significant correlations. Individuals who were unable to recall the OD duration were excluded from further analysis, resulting in 38 participants (20 in the COVID-19 group and 18 in the non-COVID-19 group) being included in the mediation analysis.

We postulated that a longer OD duration may increase the severity of mood symptoms (direct effect) and that the sQOD-NS may serve as a mediating factor between OD duration and mood symptoms (indirect effect). Mediation analyses were performed using the SPSS PROCESS macro[33] with Model 4 (single mediator model). The PROCESS macro can be used to perform mediation analyses in small samples, as it supports nonparametric testing using bootstrapping. The validity of the mediation model was examined in three groups: the entire study sample, the COVID-19 group, and the non-COVID-19 group. Using bootstrapping, 95% bias-corrected bootstrap confidence intervals (CI) for indirect effects based on 5,000 bootstrap resamples were calculated.

In the sensitivity analysis, we determined that the group with only subjective OD was likely to show a psychological effect. Therefore, we conducted additional mediation analyses with only those participants who had an objective OD, as determined by a total TDI score of ≤21 on the YOF test. The mediating effect of the sQOD-NS on OD duration and mood symptoms was examined in 26 participants with objective hyposmia and anosmia. Per-group analysis was not performed to account for the number of participants with objective OD.

## Data availability

The datasets generated and/or analyzed during the current study are not publicly available due to information that could compromise the privacy of research participants but are available from the corresponding author on reasonable request.

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## Author contributions

JHY and MYS analyzed the data and wrote the manuscript. TSK and SHL designed the study and prepared the manuscript. JHY and MYS collected the data. JSK, TSK, and MYS reviewed and revised the manuscript.

## Declarations

### Competing interests
The authors declare no competing interests.

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