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Effects of classical olfactory training in patients with COVID-19-related persistent loss of smell

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Abstract

Purpose The management of post-COVID-19 persistent olfactory dysfunction (OD) is uncertain. Currently, olfactory training is the only evidence-based therapy for post-viral OD. In this study, we evaluated the effectiveness of classical olfactory training (COT) in the treatment of post-COVID-19 persistent OD.

Materials and methods Patients with persistent OD after COVID-19 were assessed using the Sniffin' Sticks test. Fifty-one patients were then divided into two groups based on personal preference: the COT group ($n=31$) included subjects who performed COT over 12 weeks, and the control group ($n=20$) included subjects who did not receive any treatment. After the exclusion of eight patients, the olfactory performances of 43 patients were re-evaluated and compared to the baseline values.

Results A significantly higher proportion of patients in the COT group improved their olfactory scores above the clinically important difference compared to the control group (40% versus 6%) ($p=0.014$). The subjective smell improvement by COT was independent of age, gender, OD duration, presence of parosmia, or the initial olfactory score (all $p>0.05$).

Conclusion Twelve weeks of COT appears to increase the olfactory sensitivity in patients with persistent OD following COVID-19.

Keywords Olfactory training · Olfactory dysfunction · Loss of smell · COVID-19 · Anosmia · Hyposmia

Introduction

Loss of the sense of smell is a well-recognized symptom of coronavirus disease-2019 (COVID-19) with an estimated prevalence of 40 to 75% [1]. Loss of smell resolves completely in the vast majority of cases within two to four weeks of disease resolution [2–4], but it persists in 15–20% of cases [5]. Hence, persistent olfactory dysfunction (OD) is the most frequent long-term morbidity in COVID-19.

Loss of smell can severely impair quality of life due to its negative effects on food enjoyment, nutritional balance, social communication, cognitive skills, and mental functioning. Furthermore, it exposes patients and their families to hazardous situations [6, 7]. Considering the prevalence of COVID-19 in the general community, it is likely that a large number of people will seek treatment for this disabling symptom. To date, various therapies have been investigated for the treatment of post-viral olfactory dysfunction (PVOD), and olfactory training (OT) has emerged as a promising treatment option [8–11]. OT involves daily smelling of a set of odorants over a period of several months to improve olfactory function based on the neuronal plasticity of the human olfactory system [12]. Hummel et al. [12] first described a structured method for OT using suprathreshold concentrations of four odors (rose, eucalyptus, lemon, and cloves), which is now called 'classical olfactory training' (COT). They reported the benefit of COT over 12 weeks in the treatment of olfactory disorders of various etiologies. Since its introduction, OT has been an attractive therapeutic approach because of its ease of administration, low cost, and negligible adverse effects [13].

The exact pathophysiological mechanism underlying the OD associated with COVID-19 remains incompletely understood, but it is thought to be different from that of other respiratory viruses [14, 15]. This raises the question of whether

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the efficacy of OT on COVID-19-related OD differs from that of other respiratory viruses. In this context, our aim was to conduct a prospective, controlled study to investigate the effect of COT on post-COVID-19 persistent OD.

Materials and methods

Patients

Consecutive patients who complained of loss of smell following COVID-19 were assessed in the Rhinology Clinic of the Department of Otorhinolaryngology of Kocaeli University, Kocaeli, Turkey. Patients were either self-referred to our department or referred from the Post-COVID-19 Follow-up Clinic held in the Infectious Disease Department. All patients were subjected to the Sniffin' Sticks test in order to identify those with dysosmia. Patients also underwent a thorough medical history, and a complete otorhinolaryngologic examination, which included a nasal endoscopy for assessing the patency of the olfactory cleft and identifying other sinonasal pathologies. The inclusion criteria were as follows: (1) adults 18 years of age or older; (2) confirmed history of COVID-19 (positive real-time polymerase chain reaction test for severe acute respiratory syndrome coronavirus 2); (3) anosmia/hyposmia diagnosed using the Sniffin' Sticks test; and (4) loss of smell for more than four weeks. The exclusion criteria were as follows: pregnancy; active cigarette smoking; previous OD; diagnosis of sinonasal disease; any respiratory allergy; any neurodegenerative diseases; and prior nasal/paranasal sinus surgery.

All patients were informed about the natural course of PVOD and the COT procedure was explained. Fifty-one patients who met the study criteria were then asked to choose between following the COT scheme or waiting for spontaneous recovery. According to their preference, participants were stratified into two groups: (1) patients who opted to perform classical olfactory training (COT group); and (2) patients who decided to wait for spontaneous recovery (control group). Demographic information about the participants was collected, including age, gender, and duration of loss of smell. The presence or absence of parosmia and/or phantosmia was also noted. All participants were warned of the dangers of loss of smell, and recommendations were made regarding the use of smoke and gas detectors and monitoring expiration dates on foods.

The study was performed in accordance with the Declaration of Helsinki on Biomedical Studies Involving Human Subjects. The study design was approved by the ethics committee of the Medical Faculty of Kocaeli University, Kocaeli, Turkey (KAEK 2021/01.06.). All participants provided signed informed consent.

Olfactory performance assessment

The Sniffin' Sticks test (Burghart GmbH, Wedel, Germany) was used for the psychophysical assessment of olfactory function [16]. This test has been validated in a Turkish population [17]. The Sniffin' Sticks test contains three separate felt-tip pen-like odor dispenser sets for odor threshold, discrimination, and identification. The odor threshold (*T*) is assessed by a single-staircase, three-alternative forced-choice procedure. Subjects had to detect the odorized stick among three samples with the other two blank control sticks. Odor discrimination (*D*) is determined by distinguishing the target odor in a triplet from two other identical odors. Odor identification (*I*) is carried out using 16 common odors, which have to be identified as a multiple-choice task from four possibilities presented as terms. The sum of the three tests (*T*, *D*, and *I*) scores gives the threshold–discrimination–identification (TDI) score with a maximum of 48 points. According to the most recent update of TDI normative values by Oleszkiewicz et al. [18], normosmia, hyposmia and anosmia were respectively defined by $TDI \geq 30.75$, $30.5 \geq TDI \geq 16.25$ and $TDI \leq 16$. The Sniffin' Sticks test was performed twice, at the baseline and at the follow-up visit 12 weeks later.

Olfactory training

In the present study, OT was performed in accordance with the protocol of Hummel et al. [12]. Patients in the training group were provided with four odorants (lemon, rose, cloves, and eucalyptus) in amber-colored glass jars and a written document describing the training procedure. Patients were instructed to expose themselves to each odor twice a day for 12 weeks. Patients were advised to sniff each jar for 20 s, with a 20-s break between each scent. Each session lasted about three to five minutes. Participants were asked to keep diaries throughout the training period to enable the monitoring of their adherence to the training scheme. Patients who did not complete at least 90% of their training sessions were excluded from the study. Patients in the OT group were also all contacted via telephone by the experimenter during the first and second months of the treatment period to give guidance when patients encountered difficulties and also to encourage adherence to the protocol. Patients in the control group did not receive any treatment.

Outcome measures

The primary outcome was the comparison of the clinical improvement in olfactory sensitivity at 12 weeks between the COT group and the control group. As previously

described, a TDI score increase of 5.5 points or more was considered a minimal clinically important difference for subjective improvement in olfactory function [19]. Other outcome measures were the comparison of mean TDI and subunit (*T*, *D*, and *I*) scores between the groups. Additionally, the variables that might have been associated with clinical improvement in olfactory function, including age, gender, duration of OD, presence of parosmia, and baseline TDI score, were evaluated. Furthermore, the adherence rate of the patients to the training scheme was assessed. Any side effects related to COT were noted.

Statistical analysis

All statistical analyses were performed using IBM SPSS for Windows, version 20.0 (SPSS, Chicago, IL, USA). The Shapiro–Wilk test was used to assess the assumption of normality. Descriptive statistics of qualitative data are presented in the form of numbers and percentages, whereas for quantitative data mean ± standard deviation (SD) is used when the data fitted the normal distribution, and median and interquartile range (IQR) if they did not. Categorical variables are summarized as counts (percentages). Comparisons of continuous variables between groups were performed using an independent samples *t* test or Mann–Whitney *U* test, as appropriate. Comparisons of dependent samples were carried out by the paired *t* test or the Wilcoxon signed rank test. A chi-square test was used to determine relationships between categorical variables. Associations between continuous variables were assessed by Pearson or Spearman's correlation analyses. The significance level was $p < 0.05$.

Results

Patients' characteristics

Of 51 patients, 31 (61%) chose the COT option and 20 (39%) chose not to undergo COT and were thus included in the control group. However, eight were excluded from the study due to missed follow-up ($n = 4$, two in the control group and two in the COT group) or insufficient commitment to the training scheme ($n = 4$). Thus, 43 of 51 cases were included in the analysis of therapeutic effect, of whom 24 (56%) were female. The median age was 38 years (IQR 26–46; range 18–67). The median duration of OD was 5 months (IQR 2–8; range 1–11). Parosmia was present in 54% of the subjects, while phantosmia was present in 7%.

The COT group consisted of 25 patients (15 female and 10 male, mean age 38 ± 14 years, range: 18–67 years) and the control group of 18 patients (9 female and 9 male, mean age 37 ± 10 years, range 22–58 years). The mean duration of OD in the COT group was 5.8 ± 3.4 months (range 1–11 months) and 4.7 ± 3.3 months (range 1–11 months) in the control group. In the COT group, 64% of patients had parosmia and 4% had phantosmia; in the control group, these values were 39% and 11%, respectively. At baseline assessment, there were no statistically significant differences between the two groups in terms of age, sex distribution, duration of OD, and presence of parosmia (all $p > 0.05$) (Table 1).

Baseline olfactory evaluation

The initial mean TDI score in the COT group was 22.99 ± 5.24 ($T = 5.39 \pm 2.54$, $D = 9.12 \pm 1.48$, and $I = 8.48 \pm 2.43$) and in the control group was 22.61 ± 6.36 ($T = 4.67 \pm 1.87$, $D = 9.56 \pm 2.81$, and $I = 8.56 \pm 2.53$). The TDI scores were dominated by the deterioration of threshold ability. At baseline, there was no significant difference between the groups in respect of measured olfactory function ($p = 0.312$ for *T*, $p = 0.513$ for *D*, $p = 0.922$ for *I*, and $p = 0.832$ for TDI). Concerning the degree of OD, there were 4 anosmic (16%) and 21 hyposmic (84%) patients in the COT group, and 3 anosmic (17%) and 15 hyposmic (83%) patients in the control group.

Follow-up olfactory evaluation

After 12 weeks, the mean TDI score in the COT group was 28.67 ± 5.94 ($T = 6.91 \pm 2.60$, $D = 11.36 \pm 2.14$, and $I = 10.40 \pm 2.52$) and in the control group, this was 24.07 ± 6.64 ($T = 5.07 \pm 1.81$, $D = 9.72 \pm 2.93$, and $I = 9.28 \pm 2.70$) (Table 2, Fig. 1). The mean TDI score changed by 5.68 ± 2.78 in the COT group and 1.46 ± 3.19 in the control group (Fig. 2). A statistically significant change in the mean TDI score was observed in the COT group ($p < 0.001$) but not in the control group ($p = 0.077$). Patients in the COT group exhibited significantly higher mean scores in all subsets (*T*, *D*, and *I*) of the Sniffin' Sticks test (all $p < 0.001$), whereas only the *I* score showed a statistically

Table 1 Baseline characteristics of the training and control groups

	COT group ($n = 25$)	Control group ($n = 18$)	*p* value
Age, years	38 ± 14	37 ± 10	0.789
Sex distribution	15F, 10M	9F, 9M	0.948
Duration of olfactory dysfunction, months	5.8 ± 3.4	4.7 ± 3.3	0.308
Patients with parosmia, *n* (%, within group)	16 (64%)	7 (39%)	0.236

Data are presented as mean ± standard deviation for continuous variables

COT classical olfactory training, *F* female, *M* male, *n* number

Table 2 Baseline and twelfth week olfactory test results

	Baseline	Twelfth week	*p* value
T score			
COT group ($n=25$)	5.39 ± 2.54	6.91 ± 2.60	**< 0.001**
Control group ($n=18$)	4.67 ± 1.87	5.07 ± 1.81	0.261
D score			
COT group ($n=25$)	9.12 ± 1.48	11.36 ± 2.14	**< 0.001**
Control group ($n=18$)	9.56 ± 2.81	9.72 ± 2.93	0.740
I score			
COT group ($n=25$)	8.48 ± 2.43	10.40 ± 2.52	**< 0.001**
Control group ($n=18$)	8.56 ± 2.53	9.28 ± 2.70	**0.022**
TDI score			
COT group ($n=25$)	22.99 ± 5.24	28.67 ± 5.94	**< 0.001**
Control group ($n=18$)	22.61 ± 6.36	24.07 ± 6.64	0.077

Data are presented as mean ± standard deviation for continuous variables

Bold values denote statistical significance at the $p < 0.05$ level

COT classical olfactory training, *T* odor threshold, *D* odor discrimination, *I* odor identification, *TDI* threshold–discrimination–identification score

significant change in the control group ($p=0.261$ for *T*, $p=0.740$ for *D*, and $p=0.022$ for *I*). When evaluated individually, TDI scores improved in all 25 patients (100%) in the COT group, whereas this was observed in 14 of 18 patients in the control group (78%). Deterioration in TDI score was observed in 4 of the 18 (22%) subjects in the control group.

Finally, the change in measured olfactory function according to clinical significance was evaluated (≥ 5.5 point increase in TDI score). Ten of 25 (40%) subjects in the COT group exhibited a clinical improvement, whereas it was observed in only 1 of 18 (6%) subjects in the control group. The comparison of clinical improvement rates between the groups was significant ($p=0.014$). Age ($p=0.567$), gender ($p=0.678$), duration of OD ($p=0.818$), presence of parosmia ($p=0.803$), and initial TDI score ($p=0.800$) had no effect on clinical improvement after COT.

When investigating the patients in terms of the degree of olfaction, in the training group, 3 of the 4 anosmic patients became hyposmic and 1 remained anosmic; 10 of 21 hyposmic patients became normosmic and 11 continued to be hyposmic. In the control group, 2 of 3 anosmic patients became hyposmic and 1 remained anosmic; 3 of 15 hyposmic patients became normosmic and 12 continued to be hyposmic.

In terms of adherence, the average commitment rate to the training sessions was 87%. Four out of 29 patients did not reach our specified compliance rate; subsequently, they were excluded from the study. None of the patients reported any side effects related to olfactory training.

Discussion

The current study showed that COT for 12 weeks was effective in improving persistent OD associated with COVID-19. Specifically, the COT group had a higher rate of olfactory score above the minimal clinically relevant difference for subjective improvement of smell than those in the control group who did not receive any therapy (40% versus 6%). All patients who performed COT exhibited an increase in their TDI scores. The TDI scores of almost three-quarters of patients in the control group also improved, albeit they showed less increase in their olfactory test scores compared

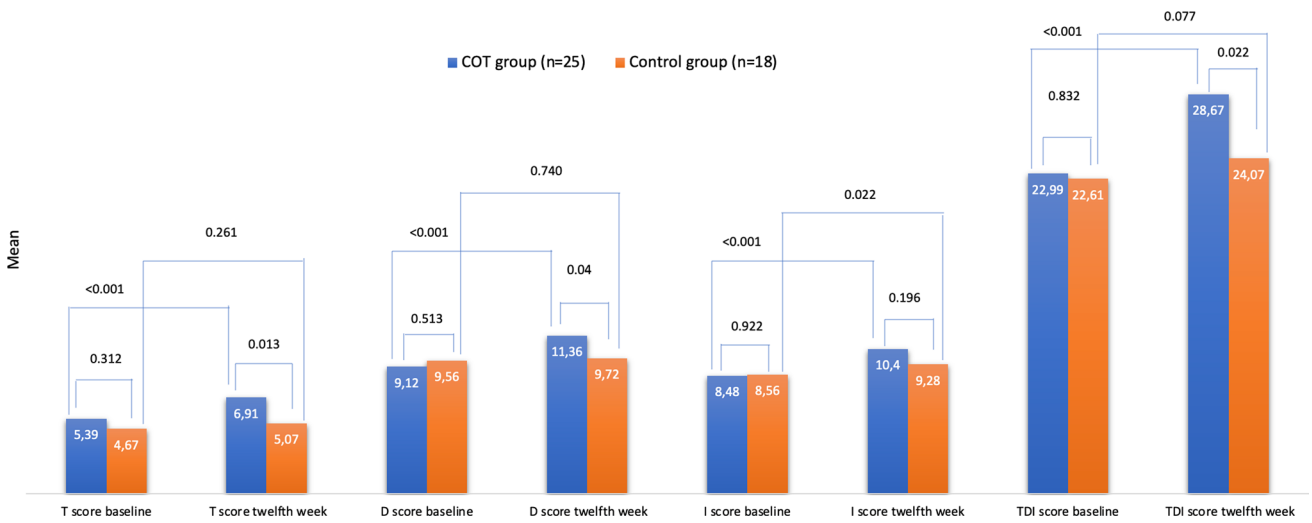

Fig. 1 Mean threshold (*T*), discrimination (*D*), identification (*I*), and composite TDI scores at the beginning and twelfth weeks for the control group (no training) and the COT (classical olfactory training) group

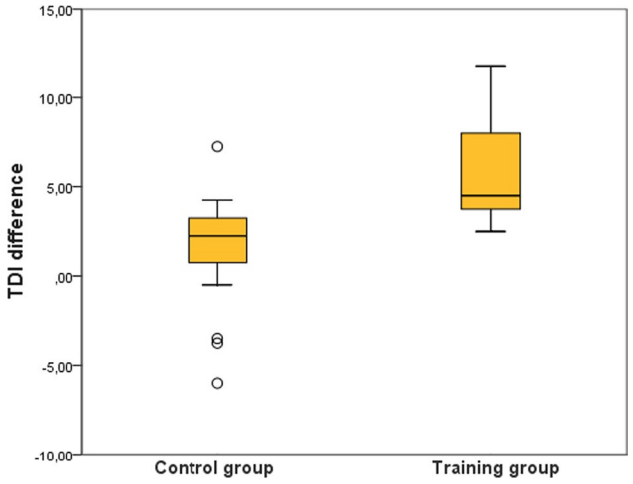

Fig. 2 Boxplot indicates the difference in the mean threshold–discrimination–identification (*TDI*) score between the end of the twelfth week and the start of the study for the control (no training) and COT (classical olfactory training) groups

to the training patients. Significant improvements in the means of odor discrimination, odor identification, and odor threshold were accompanied by an improvement in the mean TDI score in the COT group.

Since the initial description of OT by Hummel et al. [12], several meta-analyses [10, 11, 20] have demonstrated the beneficial effects of this method and its modifications in the treatment of PVOD. In a recent meta-analysis, Kattar and colleagues [20] pooled only the results from the COT regimens with different follow-up intervals and revealed that COT is associated with a higher rate of clinical improvement in PVOD compared to controls. They also pointed out that longer OT duration is associated with greater improvements in olfactory function. However, all five included studies that included 12 weeks of COT had clinically significant improvements in olfactory function at rates of 21% [21], 23% [22], 27% [7], 28% [12], and 53.3% [23]. In the present study, 12 weeks of COT was also effective in post-COVID-19 persistent OD, with a clinical improvement rate of 40%.

To date, there are only a few studies investigating the efficacy of olfactory training in the treatment of post-COVID-19 persistent OD. A recent study by Vandersteen and colleagues [24] reported a significant clinical recovery after OT in patients with COVID-19-related persistent OD. Their cohort was comprised of forty-three patients with a mean OD duration of 5.8 ± 3.2 months. All participants underwent OT based on the protocol of Hummel et al. [12], with an average period of 14 weeks. They observed a significant increase of 6.2 points in the average TDI score (from 24.7 ± 8.9 to 30.9 ± 9.8) following OT. The patients and symptom characteristics in this study were similar, and the results were consistent with our study. However, as the study of Vandersteen et al. did not include a control group, we could not compare the spontaneous recovery rates. In another study, Altundag et al. [25] reported that modified olfactory training (MOT) is effective in the treatment of post-COVID-19 parosmia. Among the findings of this study, statistically significant increases in the mean TDI scores of the MOT group in the third, sixth, and ninth months were observed. In keeping with our findings, at the end of the first trimester of the MOT, the mean TDI score significantly increased by 4.4 points. Another prospective study by Le Bon et al. [26] reported that the combination of a short course of oral corticosteroids (OCS) plus OT was safe and may be beneficial in the treatment of patients with long-lasting dysosmia due to COVID-19. Patients in the OCS + OT group improved their olfactory scores by 7.7 points on average after 10 weeks, compared to a 2.1 point increase in the OT-only group. In contrast to our findings, they did not find a significant improvement in OD by OT alone. This result may be due to a lower adherence rate of 31% to the training scheme and possibly a slightly shorter training period compared to that used in our study.

Regarding the effectiveness of OT across three different olfactory abilities—smell identification, discrimination, and threshold—several meta-analyses [10, 11, 20] reported a great variance in the improvement of these subscores. In patients with post-COVID-19 persistent OD who performed OT, Vandersteen and colleagues [24] observed a significant *T* and *I* improvement, followed by a non-significant *D* improvement. Our study, however, produced a significant increase in the mean values of all subsets of the Sniffin' Sticks test after the COT. This result suggests that the therapeutic effect of COT may occur in both the peripheral and central olfactory systems.

In terms of characteristics that predict the success of OT in PVOD, some studies commented that a shorter duration of OD prior to OT initiation was associated with greater improvement in olfactory function [21, 27]. Liu et al. revealed that higher residual olfactory function and older age were inversely associated with relevant improvement in olfactory function after OT, while gender had no impact [28]. Furthermore, in another study by Liu et al. [29], it was found that patients who had parosmia accompanying PVOD had better outcomes after OT in terms of odor identification and discrimination compared with those who did not have parosmia. The current study did not yield any significant effect of age, gender, duration of OD, presence of parosmia, or initial olfactory score on the clinical improvement of olfaction after 12 weeks of COT. Thus, clear conclusions regarding whether these factors have any impact on the success of OT in COVID-19-related OD could not be made. A larger sample size

would be required to provide a definitive assessment of such variables.

The adherence rate to the 12-week training plan in the present study was high at 87%. Fornazieri et al. [30] reported an 88% adherence rate after three months of OT, and a moderate decline after that. Some studies [30, 31] suggested that adequate adherence to the training scheme was significantly correlated with the improvement in olfactory test scores derived from OT. Our high adherence rate can be attributed to factors such as the short training period, a high rate of smell improvement during the training period, the keeping of a diary, and regular interactive feedback via direct contact with the experimenter. None of the patients in our study reported any adverse effects during the training period.

The strengths of our study were: (1) the participants had a homogenous etiology for their OD; (2) the inclusion of a control group to exclude the confounding effect of spontaneous recovery; (3) similar baseline patient characteristics in both the COT and control groups; (4) the inclusion of only those patients with an adherence rate of more than 90% to training sessions; and (5) using a well-validated tool to assess olfactory function.

This study has limitations, which must be considered when interpreting the data. First, our study was not a placebo-controlled study. Subsequently, due to the lack of intervention in the control group, the second olfactory test results might have been affected by the loss of motivation. However, odorless training jars could be detected by subjects or relatives. Second, the COT and control groups were formed according to the patient's preference rather than through random allocation. However, a random assignment may not be ethical. Third, this was a single-center study with a limited number of patients. Therefore, the statistical power was low. A final limitation was that the adherence rate to the training scheme was evaluated entirely by gathering data from patients' records in their diaries. This might have resulted in unreliable data to assess the adherence rate of the training scheme. Despite these limitations, this is the first study to investigate the effect of COT in patients with persistent OD after COVID-19, involving a control group to eliminate the effect of spontaneous recovery. Larger cohort studies are needed to confirm our findings and develop alternate methods to enhance the efficacy of OT.

Conclusion

In patients with persistent olfactory dysfunction after COVID-19, classical olfactory training produced significantly better improvement in olfactory sensitivity than that of the natural course of the disease in this cohort. A twelve-week period of classical olfactory training is a useful, practical, and well-tolerated procedure with a high level of compliance.

Author contributions AY conceptualized and designed the study, conducted the data collection, conducted the analyses, drafted the initial manuscript, coordinated the study, and revised the manuscript. EA drafted the initial manuscript, performed statistical analysis and revised the manuscript. DRA and AÖ conducted the data collection and participated in the literature collection. AK conceptualized the study and critically reviewed the manuscript. All authors have read and approved the final version of the manuscript, and agree with the order of presentation of the authors.

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Declarations

Conflict of interest The authors have no conflict of interest to declare.

Ethics approval The study was performed in accordance with the Declaration of Helsinki on Biomedical Studies Involving Human Subjects. The study protocol was approved by the ethics committee of the Medical Faculty of Kocaeli University, Kocaeli, Turkey (KAEK 2021/01.06.)

Consent to participate Informed written consent was obtained from all participants to participate in the study.

References

1. Ohla K, Veldhuizen MG, Green T et al (2022) A follow-up on quantitative and qualitative olfactory dysfunction and other symptoms in patients recovering from COVID-19 smell loss. Rhinology. https://doi.org/10.4193/Rhin21.415.10.4193/Rhin21.415
2. Lechien JR, Chiesa-Estomba CM, De Siati D et al (2020) Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study. Eur Arch Oto-rhino-laryngol 277(8):2251–2261. https://doi.org/10.1007/s00405-020-05965-1
3. Boscolo-Rizzo P, Menegaldo A, Fabbris C et al (2021) Six-month psychophysical evaluation of olfactory dysfunction in patients with COVID-19. Chem Senses 46:bjab006. https://doi.org/10.1093/chemse/bjab006
4. Niklassen AS, Draf J, Huart C, Hintschich C, Bocksberger S, Trecca E, Klimek L, Le Bon SD, Altundag A, Hummel T (2021) COVID-19: recovery from chemosensory dysfunction. A multicentre study on smell and taste. Laryngoscope 131(5):1095–1100. https://doi.org/10.1002/lary.29383
5. Klein H, Asseo K, Karni N, Benjamini Y, Nir-Paz R, Muszkat M, Israel S, Niv MY (2021) Onset, duration and unresolved symptoms, including smell and taste changes, in mild COVID-19 infection: a cohort study in Israeli patients. Clin Microbiol Infect 27(5):769–774. https://doi.org/10.1016/j.cmi.2021.02.008
6. Saniasiaya J, Prepageran N (2021) Impact of olfactory dysfunction on quality of life in coronavirus disease 2019 patients: a systematic review. J Laryngol Otol 135(11):947–952. https://doi.org/10.1017/S0022215121002279
7. Qiao XF, Wang GP, Li X, Bai YH, Zheng W (2019) Analysis of the clinical effect of olfactory training on olfactory

dysfunction after upper respiratory tract infection. Acta Otolaryngol 139(7):643–646. https://doi.org/10.1080/00016489.2019.1614224
8. Hura N, Xie DX, Choby GW, Schlosser RJ, Orlov CP, Seal SM, Rowan NR (2020) Treatment of post-viral olfactory dysfunction: an evidence-based review with recommendations. Int Forum Allergy Rhinol 10(9):1065–1086. https://doi.org/10.1002/alr.22624
9. Miwa T, Ikeda K, Ishibashi T, Kobayashi M, Kondo K, Matsuwaki Y, Ogawa T, Shiga H, Suzuki M, Tsuzuki K, Furuta A, Motoo Y, Fujieda S, Kurono Y (2019) Clinical practice guidelines for the management of olfactory dysfunction—secondary publication. Auris Nasus Larynx 46(5):653–662. https://doi.org/10.1016/j.anl.2019.04.002
10. Pekala K, Chandra RK, Turner JH (2016) Efficacy of olfactory training in patients with olfactory loss: a systematic review and meta-analysis. Int Forum Allergy Rhinol 6(3):299–307. https://doi.org/10.1002/alr.21669
11. Sorokowska A, Drechsler E, Karwowski M, Hummel T (2017) Effects of olfactory training: a meta-analysis. Rhinology 55(1):17–26. https://doi.org/10.4193/Rhino16.195
12. Hummel T, Rissom K, Reden J, Hähner A, Weidenbecher M, Hüttenbrink KB (2009) Effects of olfactory training in patients with olfactory loss. Laryngoscope 119(3):496–499. https://doi.org/10.1002/lary.20101
13. Patel ZM, Wise SK, DelGaudio JM (2017) Randomized controlled trial demonstrating cost-effective method of olfactory training in clinical practice: essential oils at uncontrolled concentration. Laryngosc Investig Otolaryngol 2(2):53–56. https://doi.org/10.1002/lio2.62
14. Ojha P, Dixit A (2022) Olfactory training for olfactory dysfunction in COVID-19: a promising mitigation amidst looming neurocognitive sequelae of the pandemic. Clin Exp Pharmacol Physiol 49(4):462–473. https://doi.org/10.1111/1440-1681.13626
15. Huart C, Philpott C, Konstantinidis I, Altundag A, Whitcroft KL, Trecca E, Cassano M, Rombaux P, Hummel T (2020) Comparison of COVID-19 and common cold chemosensory dysfunction. Rhinology 58(6):623–625. https://doi.org/10.4193/Rhin20.251
16. Hummel T, Sekinger B, Wolf SR, Pauli E, Kobal G (1997) "Sniffin" sticks': olfactory performance assessed by the combined testing of odor identification, odor discrimination and olfactory threshold. Chem Senses 22(1):39–52. https://doi.org/10.1093/chemse/22.1.39
17. Tekeli H, Altundağ A, Salihoğlu M, Cayönü M, Kendirli MT (2013) The applicability of the "Sniffin' Sticks" olfactory test in a Turkish population. Med Sci Monitor 19:1221–1226. https://doi.org/10.12659/MSM.889838
18. Oleszkiewicz A, Schriever VA, Croy I, Hähner A, Hummel T (2019) Updated Sniffin' Sticks normative data based on an extended sample of 9139 subjects. Eur Arch Oto-rhino-laryngol 276(3):719–728. https://doi.org/10.1007/s00405-018-5248-1
19. Gudziol V, Lötsch J, Hähner A, Zahnert T, Hummel T (2006) Clinical significance of results from olfactory testing. Laryngoscope 116(10):1858–1863. https://doi.org/10.1097/01.mlg.0000234915.51189.cb
20. Kattar N, Do TM, Unis GD, Migneron MR, Thomas AJ, McCoul ED (2021) Olfactory training for postviral olfactory dysfunction: systematic review and meta-analysis. Otolaryngol Head Neck Surg 164(2):244–254. https://doi.org/10.1177/0194599820943550
21. Altundag A, Cayonu M, Kayabasoglu G, Salihoglu M, Tekeli H, Saglam O, Hummel T (2015) Modified olfactory training in patients with postinfectious olfactory loss. Laryngoscope 125(8):1763–1766. https://doi.org/10.1002/lary.25245
22. Hummel T, Whitcroft KL, Rueter G, Haehner A (2017) Intranasal vitamin A is beneficial in post-infectious olfactory loss. Eur Arch Oto-rhino-laryngol 274(7):2819–2825. https://doi.org/10.1007/s00405-017-4576-x
23. Gellrich J, Han P, Manesse C, Betz A, Junghanns A, Raue C, Schriever VA, Hummel T (2018) Brain volume changes in hyposmic patients before and after olfactory training. Laryngoscope 128(7):1531–1536. https://doi.org/10.1002/lary.27045
24. Vandersteen C, Payne M, Dumas L-É et al (2022) Olfactory training in post-COVID-19 persistent olfactory disorders: value normalization for threshold but not identification. J Clin Med 11(12):3275. https://doi.org/10.3390/jcm11123275
25. Altundag A, Yilmaz E, Kesimli MC (2022) Modified olfactory training is an effective treatment method for COVID-19 induced parosmia. Laryngoscope 132(7):1433–1438. https://doi.org/10.1002/lary.30101
26. Le Bon SD, Konopnicki D, Pisarski N, Prunier L, Lechien JR, Horoi M (2021) Efficacy and safety of oral corticosteroids and olfactory training in the management of COVID-19-related loss of smell. Eur Arch Oto-rhino-laryngol 278(8):3113–3117. https://doi.org/10.1007/s00405-020-06520-8
27. Konstantinidis I, Tsakiropoulou E, Constantinidis J (2016) Long term effects of olfactory training in patients with post-infectious olfactory loss. Rhinology 54(2):170–175. https://doi.org/10.4193/Rhino15.264
28. Liu DT, Pellegrino R, Sabha M, Aytug A, Aytug A, Damm M, Poletti SC, Croy I, Hohner A, Oleszkiewicz A, Mandy C, Hummel T (2021) Factors associated with relevant olfactory recovery after olfactory training: a retrospective study including 601 participants. Rhinology 59(1):91–97. https://doi.org/10.4193/Rhin20-262
29. Liu DT, Sabha M, Damm M, Philpott C, Oleszkiewicz A, Hähner A, Hummel T (2021) Parosmia is associated with relevant olfactory recovery after olfactory training. Laryngoscope 131(3):618–623. https://doi.org/10.1002/lary.29277
30. Fornazieri MA, Garcia E, Lopes N, Miyazawa I, Silva G, Monteiro R, Pinna FR, Voegels RL, Doty RL (2020) Adherence and efficacy of olfactory training as a treatment for persistent olfactory loss. Am J Rhinol Allergy 34(2):238–248. https://doi.org/10.1177/1945892419887895
31. Saatci O, Altundag A, Duz OA, Hummel T (2020) Olfactory training ball improves adherence and olfactory outcomes in post-infectious olfactory dysfunction. Eur Arch Oto-rhino-laryngol 277(7):2125–2132. https://doi.org/10.1007/s00405-020-05939-3