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Classical and Speech Therapy Olfactory Training in the Treatment of COVID-19–Related Olfactory Disorders

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Background: Loss of smell can impair quality of life. Olfactory disorders are often caused by viral infections, including SARS-CoV-2. The aim of the study was to evaluate the effectiveness of a structured, multidisciplinary rehabilitation program, including pharmacological treatment and speech therapy–guided olfactory training, in patients with post-COVID olfactory disorders.

Material/Methods: A total of 75 patients (15 men, 60 women) were allocated to a study group (n = 50) or control group (n = 25) using a systematic assignment method. Both groups received the same pharmacological treatment (intranasal corticosteroids and topical vitamin A), saline nasal irrigation, and elements of speech therapy–guided olfactory training. In addition, the study group performed classical olfactory training using 4 odorants twice daily. Olfactory function was assessed using the Sniffin' Sticks Test (SST).

Results: For the total SST score, the mean change before and after intervention in the study group was 7.9 points ($P < 0.001$). In the control group, the mean change was 2.8 points ($P = 0.006$).

Conclusions: Classical olfactory training was associated with greater improvement in post-COVID olfactory disorders compared with pharmacological treatment supplemented with speech therapy–guided olfactory training alone. The observed effects may be related to the combined use of intranasal corticosteroids, topical vitamin A, and saline nasal irrigation; however, the individual contribution of these interventions cannot be determined. The potential contribution of a multidisciplinary approach involving a physician, speech therapist, and psychologist remains to be established.

Keywords: COVID-19 • Olfactory Disorders • Olfactory Training • Otolaryngology • Speech Therapy

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Introduction

Loss of smell can impair quality of life [1]. It can lead to anxiety in social situations ("I won't know if I'm sweating"); anxiety surrounding an inability to identify danger, such as a fire or gas leak; discomfort in preparing and eating shared meals; and the ruling out of certain professions, such as being a cook. All of these situations can cause anxiety and lack of self-confidence. Olfactory disorders (ODs) are often caused by viral infections [2]. The increasing prevalence of post-infectious olfactory dysfunction, particularly following SARS-CoV-2 infection, has created a growing need for effective rehabilitation strategies. Persistent post-COVID ODs represent an ongoing clinical problem despite the resolution of acute infection in many patients, and current therapeutic options remain limited.

The incidence of OD in COVID-19 is estimated at 41% to 67%, depending on the method of investigation (self-assessment or smell test) and the population studied [3-5]. The incidence of OD also depends on the strain of the SARS-CoV-2 virus predominating at any given time; for instance, the Alpha and Delta variants cause OD much more frequently than did the Omicron variety [6,7]. In most cases, olfactory function eventually improves spontaneously, but in approximately 7% to 20% of patients, OD persists after other COVID-19 symptoms have resolved [5,8,9].

COVID-19–associated OD (post-COVID OD) is mainly associated with damage to the olfactory epithelium. When SARS-CoV-2 penetrates the supporting cells of the olfactory epithelium, it can trigger a massive inflammatory response. Damage to these cells leads to dysfunction and subsequent atrophy of olfactory neurons within the olfactory epithelium, resulting in conductive OD [10]. In addition, penetration of SARS-CoV-2 into the central nervous system causes sensory-nervous OD [11,12]. The results of olfactory tests indicate that post-COVID OD is more peripheral than central [13-15]. It is likely that the greater the epithelial damage, the longer the duration of the olfactory impairment. Post-COVID OD can be both quantitative (hyposmia or anosmia) and qualitative (parosmia or phantosmia) [16].

Currently, there is no known effective pharmacological treatment for post-COVID OD. Guidelines in the European position paper on olfactory dysfunction primarily recommend the use of olfactory training (OT) for a minimum of 12 weeks [17]. Various adjunctive pharmacological and supportive interventions have been proposed, but evidence regarding their additive clinical benefit is inconsistent. Previously published studies have examined, among other things, the effect of OT and intranasal corticosteroids (INCS) on improving olfactory function in patients with postinfectious (including post-COVID) OD. The results suggest that INCS may enhance the effect of OT [17]. Asseri et al presented the results of a meta-analysis that showed the addition of a chelating agent (EDTA) or ultramicronized palmityloethanolamide (PEA) and lutein improves the efficacy of OT, whereas adding corticosteroids to OT showed fewer benefits, and no benefits were observed from the use of alpha-lipoic acid [18].

Classical OT is typically performed under the guidance of otorhinolaryngology specialists, whereas speech therapy–guided olfactory training (SOT) [19] has been proposed as a complementary rehabilitation approach aimed at enhancing odor awareness and sensory-verbal integration using everyday olfactory stimuli. However, empirical data evaluating the clinical effectiveness of SOT, particularly in combination with classical OT, are currently insufficient. Therefore, this study aimed to evaluate the effectiveness of combined olfactory rehabilitation incorporating classical OT and SOT in patients with post-COVID OD.

Material and Methods

This paper presents the results of a prospective, single-center study. The study protocol, the consent forms for participation in the study and processing of personal data, and patient leaflet were approved by the Bioethics Committee of the Institute of Physiology and Pathology of Hearing (No. KB.IFPS 7/2021) and were in accordance with the World Medical Association's Declaration of Helsinki. Participation in the study was voluntary and free of charge. All patients interested in participating in the study signed an informed consent form at the outset. An outline of the study is shown in **Figure 1**. This was an open-label study, with no blinding procedures applied.

Participants

The study included 75 patients (15 men and 60 women) aged 18 to 73 years (mean 42.3 years, SD = 14.1). Patients were allocated to the study and control groups using a systematic assignment method, whereby a third of eligible patients were assigned to the control group. Because a systematic assignment method was used, allocation concealment was not implemented. The study group included 50 patients (40 women and 10 men) aged 18 to 73 years (mean 42.9 years, SD = 13.7), and the control group included 25 patients (20 women and 5 men) aged 18 to 68 years (mean 40.9 years, SD = 15.0). Most patients in both groups had higher education. Regarding place of residence, the patients in the study group more frequently lived in large cities (> 500 000 inhabitants), whereas the distribution in the control group was more even across categories. Detailed data are presented in **Table 1**. All of the participants were referred to the Institute of Physiology and Pathology of Hearing due to subjective OD associated with COVID-19.

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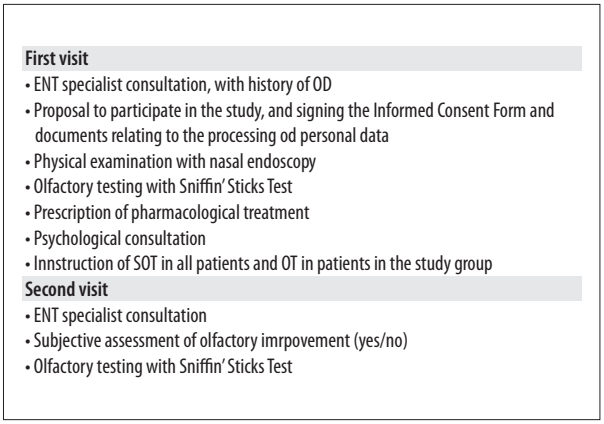

Figure 1. Outline of the present study. Each patient visited the clinic twice at an interval of about 12 weeks. Abbreviations: ENT, ear, nose, and throat; OD, olfactory disorder; OT, olfactory training; SOT, speech therapy–guided olfactory training.

Inclusion and Exclusion Criteria

The main inclusion criterion for the study was experiencing an OD that occurred during COVID-19 and lasted at least 1 month after the acute symptoms had resolved. Only patients with a positive SARS-CoV-2 virus test during acute infection were included. Patients who did not have a COVID-19 test performed at the time of OD or who had a negative test result were excluded. Patients in whom subjective OD existed before COVID-19 were also excluded. Further exclusion criteria were conditions or diseases that may affect normal olfactory function, based on medical history and physical examination, and pregnancy. Following the olfactory test, patients with results within normal limits and patients who were unable to complete the test reliably (eg, non-compliance, inability to follow instructions) were excluded.

Study Group and Control Group

The patients were randomly divided into a study group and a control group. All patients underwent the same olfactory test, ear, nose, and throat (ENT) specialist consultation, and psychological consultation, after which they received identical recommendations for pharmacological treatment and instructions for SOT using odors present in everyday life. Patients in the study group additionally received a set of therapeutic applicators for OT containing 4 specific odors and strict instructions for their use.

Olfactory Testing

After reviewing the literature of available olfactory tests, the researchers selected the Sniffin' Sticks Test (SST) because it allows assessment of an olfactory threshold, has the ability to discriminate and identify odors, is low cost, and can be used repeatedly. The SST was developed in 1997, and a Polish adaptation was published in 2014 [20-22]. The SST is made of markers soaked in fragrances dissolved in a solution of propylene glycol. During the test, the tip of the stick is held approximately 2 cm from the nostrils for 3 seconds. The test is divided into 3 parts: a threshold test, a discrimination test, and an

Table 1. Demographic characteristics of the participants.

		Study group (n = 50)	Control group (n = 25)	Test result
Age	Range	18-73	18-68	U = 582.0; $P = 0.629$
	Mean (SD)	42.9 (13.7)	40.9 (15.0)	
Sex	Male	10 (20%)	5 (20.0)	$\chi^2 = 0.00$; $p > 0.999$
	Female	40 (80%)	20 (80.0)	
Education level	Primary/vocational	2 (4%)	1 (4%)	$\chi^2 = 0.98$; $P = 0.806$
	Secondary	10 (20%)	5 (20%)	
	Higher	31 (62%)	12 (48%)	
	NA	7 (14%)	7 (28%)	
Place of residence	Rural	9 (18%)	7 (28%)	$\chi^2 = 6.02$; $P = 0.198$
	City ≤ 100 k	8 (16%)	5 (20%)	
	City 100-500 k	4 (8%)	3 (12%)	
	City > 500 k	22 (44%)	4 (16%)	
	NA	7 (14%)	6 (24%)	

Abbreviations: NA, not available; k, thousand inhabitants.

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Table 2. Compounding nasal ointment formula.

Formula	Dosage
Liquid vitamin A 1.0 g Lanoline 3.0 g Liquid paraffin 3.0 g Vaseline 3.0 g Mixed into an ointment	2 times a day into both nasal cavities

identification test. The threshold test is based on 16 sets of sticks. Each set contains 2 odorless sticks and 1 stick impregnated with a solution of n-butanol or 2-phenylethanol (PEA). The initial concentration of the solutions is 4%, and the solution in subsequent tests is twice as weak. During the test, 3 odors are presented, starting with the set with the weakest concentration of n-butanol or PEA (in our study, we used sticks with n-butanol). The patient indicates the stick that has an odor. A correct indication is called the first break. Next, sticks with decreasing scent concentrations are presented until an incorrect answer is given (second break). From this point on, sticks with increasing scent concentrations are presented again. The procedure should be repeated until 7 breaks are obtained. The average of the last 4 breaks is the test result. The patient needs to indicate which stick carries the odor. The discrimination test consists of 16 sets of sticks: 2 with the same odor and 1 with a different odor. The patient indicates the stick with the different odor. The identification test consists of 16 sticks and the patient names the odor using 4 prompts. A maximum of 16 points can be obtained in each part of the test, and a total of 48 points can be obtained in the whole test. A score above 30 indicates normosmia, between 15 and 30 indicates hyposmia, and below 16 indicates anosmia [23].

ENT Consultation

During the ENT consultation, a medical history was taken, primarily concerning the OD: its onset, temporal relationship to COVID-19 history (confirmed by a test), subjective nature of the disorder (weakness/complete loss), and the patient's other symptoms and diseases. Each patient then underwent a thorough physical examination, including nasal endoscopy. The ENT specialist recommended to all patients the use of mometasone furoate (an INCS taken as 2 doses of 50 µg into each nostril once per day for a total dose of 200 µg per day, the standard INCS dosing), a nasal ointment containing vitamin A (1 g per 10 g of ointment [24] (**Table 2**). It was recommended that saline irrigation was used before the application of nasal medication.

Psychological Consultation

The aim of the psychological consultations was to diagnose the patient's psychological state, assess the impact of OD on

Table 3. Description of olfactory exercises as part of speech therapy olfactory training.

Type of exercises	Description of exercises
Odor detection	• The patient smells the odors and answers the question: 'Can you smell it?' • If the patient can smell the odor, less of the odorous product is used in the next test to reduce the intensity of the smell
Odor discrimination	• The patient smells 2 samples with different concentrations and answers the question: 'Which of the 2 smells is stronger?' • The patient smells 2 samples and answers the question: 'Are these 2 smells the same or different?' • The patient smells 3 samples and answers the question: 'Find the same scent among the 3 samples'
Odor identification	• The patient smells the sample and is asked to name the odor they detect
Multisensory integration	• The patient smells the selected product while looking at it, tastes it (for food products) and touches it, focusing on its consistency and texture
Olfactory memory	• The patient smells odors and remembers their order • Finding a specific odor among several samples (a "smell memory" game) • Comparing whether the scent detected is similar to the one the patient remembers from before the onset of the olfactory disorder • Recalling situations in which the scent was detected (eg, "The smell of apple pie reminds me of visiting my grandmother")
Semantic training	• The patient describes the nature of the odor (eg, sour, pungent, spicy, artificial) • The patient describes what the smell reminds them of (eg, "used in Chinese cuisine", "my favorite cosmetics smell like this", "this smell can be detected in the forest")

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Figure 2. Set of olfactory training applicators used by the patient. Odors used (from left): rose, eucalyptus, lemon, and clove.

the patient's functioning, and establish an intervention plan, including a course of OT and SOT. During the consultation, an interview was also conducted about the patient's previous olfactory conditions, ability to recognize odors, and taste and smell preferences. Information was gathered about the patient's methods of coping with OD: what resources they used for support and what obstacles they faced. Patients were asked to carry out OT and SOT in conditions of relative calm and tranquility, with no time pressure. Advice on stress reduction and sleep hygiene was also provided.

Speech therapy–guided olfactory training

SOT involved working with smells that are present in patients' everyday lives. The exercises included attempting to identify spices, fruits, vegetables, and cosmetics without the use of sight, followed by continued smelling with the involvement of other senses (appearance, taste, and texture of food products, color and consistency of cosmetics, and sound associated with spraying perfume or deodorant). The exercises also involved the patients' memories associated with a given smell, including an assessment of whether the smell was perceived as pleasant or unpleasant before the deterioration of the sense of smell. The exercises covered various areas: odor detection, discrimination and identification, as well as multisensory training and olfactory memory exercises. Detailed information is provided in **Table 3**. No restrictions were imposed on the number and duration of these exercises, only that daily performance was recommended.

Olfactory Training

Applicators soaked in the following fragrances were used to perform OT: lemon, clove, eucalyptus, and rose (**Figure 2**). The applicators were placed close to 1 nostril and sniffed for about 15 seconds, and then repeated for the other nostril. During a single session, all the sticks (1 for each odor) needed to be applied, and this process was performed twice per day. The applicators were manufactured on behalf of the Institute of Hearing Physiology and Pathology and had medical device status.

Statistical Analysis

The demographic and clinical characteristics of the study and control groups were examined using descriptive statistics and percentages. A Kolmogorov-Smirnov test was used to check the assumption of normality of variables. Differences across groups were assessed through a χ^2 test and Mann-Whitney U test. The relationship between improvement in olfactory sensitivity and age and between improvement in olfactory sensitivity and delay in presentation to ENT specialist was evaluated with a rho-Spearman correlation coefficient. A mixed-design ANOVA was used to evaluate the change in olfactory sensitivity before and after intervention in the study and control groups. Assumptions for the mixed-design ANOVA, including normality, homogeneity of variances, and sphericity, were checked. Statistical significance was specified as a *P* value less than 0.05. Data analysis was conducted using IBM SPSS Statistics v. 24.

Adverse Events

Participants were provided with the researchers' telephone number and email address and were instructed to report any adverse events related to the therapy, including those associated with the medications or olfactory applicators used in the study. Additionally, the occurrence of adverse events was assessed during the second study visit. No adverse events were reported during the study period.

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Table 4. Descriptive statistics for Sniffin' Sticks test scores obtained by the study and control groups before and after intervention.

	Study group (n = 50)				Control group (n = 25)				Intervention effect	Group effect	Interaction effect
	Pre		Post		Pre		Post				
	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
Thresholds	1.87	2.34	5.11	3.98	1.41	1.55	3.04	3.03	F = 48.6 *P* < 0.001	F = 3.8 *P* = 0.056	F = 5.3 *P* = 0.024
Discrimination	9.28	3.14	11.30	2.55	9.52	2.80	10.28	3.05	F = 18.4 *P* < 0.001	F = 0.4 *P* = 0.536	F = 3.8 *P* = 0.056
Identification	8.74	2.94	11.54	3.35	9.12	3.29	9.40	3.33	F = 21.5 *P* < 0.001	F = 1.5 *P* = 0.220	F = 14.4 *P* < 0.001
Total score	19.91	6.57	27.85	8.22	20.05	5.97	22.80	6.84	F = 80.3 *P* < 0.001	F = 2.2 *P* = 0.139	F = 18.9 *P* < 0.001

Abbreviations: SD, standard deviation.

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Results

The results of this study demonstrate that combined olfactory rehabilitation, incorporating OT and SOT, was associated with improvement in olfactory function, thereby addressing the primary objective of evaluating the effectiveness of this therapeutic approach in patients with post-COVID OD.

Characteristics of Patients

Patients presented to the ENT specialist at different times after the onset of post-COVID OD. In the study group, the time between the onset of OD and presentation to the doctor ranged from 2 to 20 months (mean = 8.7; SD = 5.1); in the control group, it was between 4 and 20 months (mean = 8.1; SD = 3.8). There were 5 smokers and 45 non-smokers in the study group and 2 smokers and 23 non-smokers in the control group. Additional information regarding age, sex, educational level, and place of residence is presented in **Table 1**. No statistically significant differences were observed between the groups with respect to these variables, indicating that the groups were comparable in terms of sociodemographic characteristics.

Change in the SST Before and After Intervention

In the first measurement, the SST total score ranged from 3 to 31 points in the study group, with a mean score of 19.91 (SD = 6.57). In the control group, the range was 9 to 29 points, with a mean score of 20.05 (SD = 5.97). **Table 4** shows SST results obtained in the clinic from the patients from the study group and the control group in both measurements. The study group showed larger improvements in thresholds, identification, and total SST score compared with the control group, whereas changes in discrimination were similar between groups.

The intervention effect was statistically significant for all analyzed variables: for thresholds ($F = 48.6$, $P < 0.001$, $\eta^2 = 0.40$); for discrimination ($F = 18.4$, $P < 0.001$, $\eta^2 = 0.20$); for identification ($F = 21.5$, $P < 0.001$, $\eta^2 = 0.23$); and for total score ($F = 80.3$, $P < 0.001$, $\eta^2 = 0.52$). The group effect showed no significance for each variable.

The interaction effect (group × intervention) was statistically significant for 3 variables: thresholds ($F = 5.3$, $P = 0.024$, $\eta^2 = 0.07$); identification ($F = 14.4$, $P < 0.001$, $\eta^2 = 0.17$); and total score ($F = 18.9$, $P < 0.001$, $\eta^2 = 0.21$); whereas it was not significant for discrimination ($F = 3.8$, $P = 0.056$, $\eta^2 = 0.05$). The interaction effect is illustrated in **Figure 3**.

For odor thresholds, the mean change before and after intervention in the study group was 3.2 points and was statistically significant ($P < 0.001$); the effect size was $\eta^2 = 0.47$. In the control group, the mean change was 1.6 points and was also statistically significant ($P = 0.006$), but the effect size was smaller, at $\eta^2 = 0.10$. For odor discrimination, the mean change before and after intervention in the study group was 2 points and was statistically significant ($P < 0.001$); the effect size was $\eta^2 = 0.29$. In the control group, the mean change was 0.8 points and showed no significant difference ($P = 0.155$). For odor identification, the mean change before and after intervention in the study group was 2.8 points and was statistically significant ($P < 0.001$); the effect size was $\eta^2 = 0.42$. In the control group, the mean change was 0.3 points and showed no significant difference ($P = 0.607$). For total SST score, the mean change before and after intervention in the study group was 7.9 points and was statistically significant ($P < 0.001$); the effect size was $\eta^2 = 0.65$. In the control group, the mean change was 2.8 points and was also statistically significant ($P = 0.006$); the effect size was $\eta^2 = 0.10$. These changes indicate a clinically meaningful improvement in olfactory function in the study group compared with the control group, particularly in thresholds, identification, and total score.

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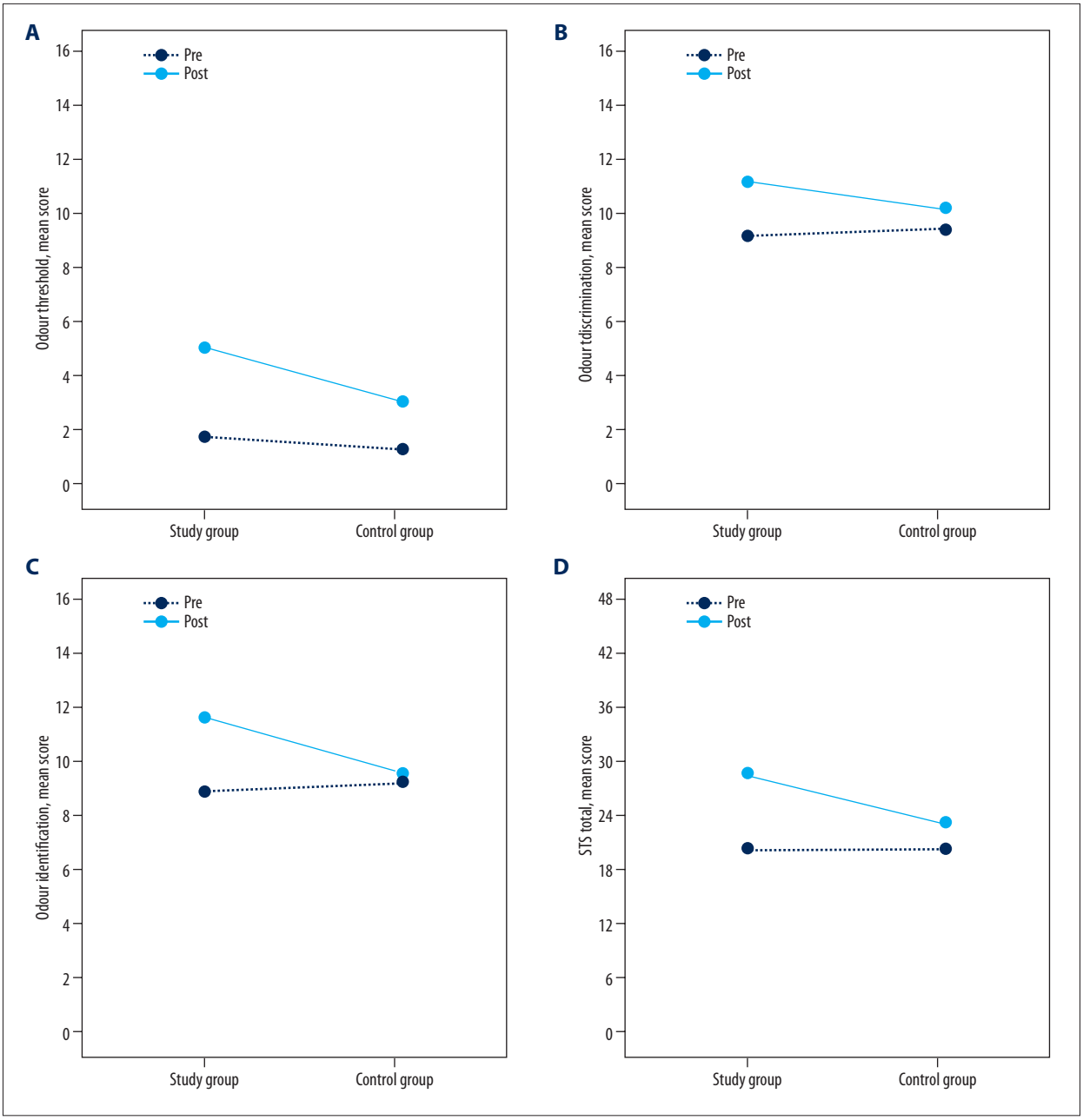

Figure 3. Mean levels of odor thresholds (**A**), discrimination (**B**), identification (**C**), and total Sniffin' Sticks Test score (**D**) before (dashed lines) and after (solid lines) intervention for the study and control groups.

Subjective Improvement and Clinically Significant Improvement in Olfactory Sensitivity

In the study group, there were 37 patients (74%) who said they had improved, while 13 patients reported no improvement. In the control group, improvement was reported by 12 patients (48%), and lack of improvement was reported by 13 patients. The difference between the groups was statistically significant ($\chi^2 = 4.97$; $P = 0.026$).

According to Gudziol et al [25], a clinically significant improvement in SST is an improvement of at least 5.5 points. In our study, there were 33 patients (66%) in the study group and 6 patients (24%) in the control group whose SST improved by more than 5.5 points. The difference between the groups was statistically significant ($\chi^2 = 11.78$; $P = 0.001$).

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Improvement in Olfactory Sensitivity in Terms of Age, Smoking, and Delay in Presentation

The change in the total SST score before and after intervention was taken as an indicator of improvement in olfactory sensitivity. A negative correlation between age and improvement was found (rho = -0.25, $P = 0.029$). The older the patients were, the less they improved; however, the strength of the correlation was weak. There was a statistically significant difference between men and women (U = 298.5, $P = 0.044$). The mean improvement in men (8.9; SD = 1.4) was slightly higher than in women (5.4; SD = 5.0). The correlation between delay in presenting to an ENT specialist and change in the SST score showed no significance (rho = 0.11, $P = 0.336$). The difference between smokers and non-smokers showed no significant difference (U = 207.0; $P = 0.571$). A correlation analysis between baseline olfactory function (SST total score at the first measurement) and the improvement in olfactory performance revealed no significant relationship (Spearman's rho = -0.14, $P = 0.239$), indicating that the degree of improvement was not dependent on the initial level of olfactory function.

The results indicate that the combination of OT and SOT was associated with greater improvement in objective olfactory outcomes compared with pharmacological therapy supplemented only with SOT. Although both groups demonstrated some degree of improvement, clinically meaningful changes were observed more frequently and with larger effect sizes in the group performing additional OT, particularly for threshold, identification, and total SST scores. Overall, the findings suggest that structured multidisciplinary rehabilitation was associated with clinically and statistically significant improvement in olfactory function, supporting the potential benefit of the combined intervention in post-COVID OD.

Discussion

To the best of our knowledge, there are currently no published studies evaluating in detail multidisciplinary rehabilitation protocols combining OT and SOT in patients with post-COVID ODs. Therefore, the present study provides preliminary clinical data on this therapeutic approach. The results of our study suggest that classical OT combined with SOT and standard pharmacological therapy was associated with greater improvement in post-COVID OD compared with pharmacological treatment supplemented with elements of speech therapy training alone. Based on the SST results, 66% of patients in the study group achieved significant improvement in olfactory function, while in the control group, this percentage was only 24%. The changes were statistically significant for all SST parameters in the study group, while in the control group, they were insignificant for the discrimination and identification tests. Importantly, even patients with low baseline scores could benefit from repeated exposure to odors, as OT is known to enhance residual receptor activity and central olfactory system plasticity. The inclusion of patients with varying degrees of smell loss therefore reflects real clinical conditions and is consistent with the observed improvement, particularly in the study group. This may partly reflect the fact that patients in the study group were provided with exercise applicators, which may have increased engagement and adherence to the training protocol. The small size of applicators meant they could be used at any place and time. However, differences between groups may also partly reflect unmeasured variation in adherence to home-based OT. It has been shown that increased concentration and attention on sniffed odors increases the effectiveness of OT [26]. The OT used in our study was modeled on the training developed by Hummel et al [27]. Repeated short-term exposure to odorants has been hypothesized to improve olfactory function by increasing the responsiveness of residual olfactory receptor neurons and by promoting neuroplastic changes within the olfactory system, including the olfactory bulb and central olfactory pathways [27]. The therapeutic effects of OT are therefore considered to be related to activity-dependent sensory stimulation and neural plasticity; however, based on the present study design, no definitive conclusions regarding the underlying mechanisms can be drawn.

Multisensory stimulation may further enhance olfactory rehabilitation outcomes. A study by Li et al suggested that the effect of OT may be enhanced when other sensory modalities, such as vision and hearing, are simultaneously engaged [26]. Multisensory stimulation has previously been applied in speech therapy and may be relevant not only in ODs associated with sinonasal disease, but also in rehabilitation of patients after laryngectomy, as well as in cognitive and neurodegenerative conditions. During SOT, additional sensory modalities (taste, vision, and touch) are activated, which may facilitate retrieval of memory traces [28]. Stimulation of this multisensory semantic network may be associated with improved olfactory function if the additional stimuli reaching the senses during the training session are congruent with the odorant used [26]. Although the involvement of speech therapists in OD therapy may be beneficial to patients, it is not widely implemented, possibly due to limited awareness of SOT [29]. The present results suggest that SOT alone, without structured control of training frequency, may provide limited benefit in improving olfactory function. However, these findings should be interpreted cautiously due to the lack of objective adherence monitoring.

Patients in the control group demonstrated improvement mainly in the threshold component of the SST, although this may be related to pharmacological treatment and/or spontaneous recovery and measurement variability. Overall, the mechanisms underlying the observed improvements cannot be definitively

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established based on the present study design. OT is generally considered to promote recovery through repeated sensory stimulation, potentially enhancing residual receptor activity and supporting neural plasticity in peripheral and central olfactory pathways. The multisensory components of SOT may additionally increase attention to olfactory stimuli and potentially enhance odor perception through cognitive-sensory integration. However, based on present study design, no definitive conclusions can be drawn regarding the mechanisms of action.

At the time of planning this study, no guidelines for the pharmacological treatment of post-COVID OD were known; therefore, we decided to use the treatment of INCS and vitamin A ointment described previously in studies of non-COVID post-infectious OD. Enhancement of OT by the addition of INCS may improve olfactory function in patients with post-infectious OD, especially in discrimination and odor identification [30,31]. In their studies, Abdelalim et al showed that the use of INCS alone has no benefit in the treatment of post-COVID OD, while Kasiri et al showed that post-COVID OD therapy with OT in combination with INCS (mometasone furoate was used in the study) can accelerate the return of normal olfactory function compared with OT alone [32,33]. When INCS is included in therapy, it is more beneficial to administer the drug as a rinse instead of a spray due to the possibility of more drug reaching the olfactory cleft [17]. In our study, patients used INCS in spray form due to the unavailability of the rinse form in Poland. Although the inclusion of INCS in OD therapy may be of benefit, further research is needed to establish exact treatment regimens, namely INCS dosage and duration of treatment [34,35].

The olfactory system has the ability to regenerate neurons [36], a process in which vitamin A is thought to play an important role. Retinoic acid, a metabolite of vitamin A, regulates transcription and thus affects tissue development during embryogenesis and the regeneration of adult neurons [37,38]. Disorders of neuronal regeneration of the olfactory system manifest clinically as OD. In a study by Reiden et al, no beneficial effect of oral vitamin A in the treatment of OD was observed [39], whereas Hummel et al suggested that intranasal vitamin A may be helpful in the treatment of post-infectious OD [40]. In the present study, patients receiving OT combined with intranasal vitamin A achieved better olfactory outcomes than those receiving OT alone; however, the study design does not allow determination of the independent effect of intranasal vitamin A. Vitamin A nasal ointment also moisturizes the nasal mucosa, potentially protecting it against adverse effects of intranasal corticosteroids, such as dryness, crusting, and epistaxis. A complementary pharmacological intervention, nasal saline irrigation, was recommended due to its beneficial effects on the nasal mucosa, including mucus thinning, reduction of edema, and removal of retained secretions [41]. To avoid rinsing out previously administered medications, saline irrigation was advised prior to their application.

Patients received guidance on reducing stress in daily life, which is important because of the negative impact of stress on the treatment of ODs, due to the inhibition of the process of neurogenesis [42]. Participants were also asked to perform mindfulness exercises, which consist of learning to focus on the stimuli perceived by the different senses. Meditation may have beneficial effects on health, including reducing anxiety and emotional stress, lowering blood pressure, and increasing recognition and working memory; it also improves perceptual awareness and allows for increased attention [43]. Oleszkiewicz et al asked a group of people to count the odors they perceived during the day; the test group included people with ODs, the study group included healthy people. In both groups, they observed that the perception of odors can be improved by consciously focusing on them, and, in this way, olfactory sensitivity can be increased [44].

Study Limitations

This study has limitations. The main limitation of this study is the inability to objectively verify patients' compliance with the OT protocol. Since olfactory rehabilitation was conducted at home, variability in the frequency and accuracy of training may have influenced the magnitude of the observed effects. The creation of a tool, perhaps a mobile application, to remind patients and assist them with OT would help improve patient compliance and monitor progress. Patients reported to the research center only after the onset of olfactory impairment, and, therefore, the baseline condition of their sense of smell is unknown. In case of an observed improvement, we cannot be sure whether it occurred as a result of OT or whether it occurred spontaneously. Therefore, the therapeutic effect of the intervention should be interpreted cautiously. On the other hand, in the case of patients in whom no improvement was seen, we could rely only on information from the patients themselves, as we could not verify whether OT had been applied correctly or consistently. Studies by Haas et al show that some patients will drop out of the recommended OT as soon as they feel an improvement in their sense of smell or when rapid improvement is lacking [45]. An additional limitation is that the study group received supplementary OT materials and more structured home-training support (OT applicators), which may have increased participant engagement and adherence compared with the control group, potentially influencing the observed outcomes. An additional limitation is the lack of knowledge of the SARS-CoV-2 variant with which the participants were infected; only information on which variant was prevalent at the time of the illness is known. The systematic allocation method used in this study may also introduce potential selection bias and should be considered when

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interpreting the results. Future studies should consider randomized controlled designs, objective monitoring of training adherence, and stratification according to viral variants and baseline olfactory severity.

In summary, the results of this study suggest that multidisciplinary rehabilitation combining OT with SOT may be associated with clinically significant improvement in olfactory function in patients with OD after COVID. The observed benefits were particularly evident in the threshold, identification, and total SST scores, with a higher percentage of patients achieving clinically significant improvement in the combined rehabilitation group. Although the study design does not allow for determining the relative contribution of individual therapeutic components or ruling out spontaneous improvement, the results suggest the potential value of supervised, team-based olfactory rehabilitation in real-world clinical practice. Further randomized studies are needed to confirm these observations, including objective monitoring of adherence to training recommendations and stratification of virus variants.

Conclusions

Classical OT combined with SOT and standard pharmacological therapy was associated with greater improvement in post-COVID OD compared with pharmacological treatment supplemented with elements of speech therapy training. Although the use of intranasal corticosteroids, intranasal vitamin A, and saline irrigations may have contributed to the observed improvement, the individual effects of these components cannot be determined because all participants received the same therapeutic regimen, and treatment adherence was not objectively monitored. The study supports the potential value of olfactory rehabilitation using a multidisciplinary approach, while the specific contributions of individual therapeutic components remain to be established.

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Institution Where Work Was Done

This work was conducted in the Otorhinolaryngosurgery Clinic, World Hearing Center, Institute of Physiology and Pathology of Hearing, Warsaw/Kajetany, Poland.

Informed Consent

Informed consent was obtained from all participants involved in the study.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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