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Original Article

Effect of early olfactory training on olfactory recovery after nasal endoscopy in patients with chronic rhinosinusitis and olfactory impairment

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Abstract: Objective: To analyze the effect of early comprehensive olfactory rehabilitation training on olfactory recovery after nasal endoscopy in patients with chronic rhinosinusitis and olfactory impairment. Methods: A retrospective study was conducted on 67 patients with chronic rhinosinusitis combined with olfactory impairment in our hospital from July 2018 to August 2020. Patients were divided into control group and observation group according to the time of implementing comprehensive olfactory rehabilitation training. The control group received non-early comprehensive olfactory rehabilitation training at 2 weeks after nasal endoscopy, and the observation group received early comprehensive olfactory rehabilitation training at 1 week after nasal endoscopy. The minimum detection/recognition threshold, olfactory threshold, olfactory function and quality of life were compared between the two groups. Results: After 3 months of training, T&T olfactory test scores in the observation group were significantly lower than those in the control group (P<0.05). The minimum detection scores in the observation group were lower than those in the control group after 1, 2 and 3 months of training, and the recognition scores in the observation group were higher than those in the control group (P<0.05). The scores of olfactory threshold, odor discrimination, and odor identification of the observation group after 1, 2 and 3 months of training were higher than those of the control group (P<0.05). After 3 months of training, the self-description scores of quality-of-life questionnaires in the observation group were higher than those in the control group, and visual analogue scale (VAS) scores in the observation group were lower than those in the control group (P<0.05). Conclusion: Early comprehensive olfactory training can improve the olfactory threshold and odor discrimination of patients with chronic rhinosinusitis combined with olfactory impairment after nasal endoscopy, improve the quality of life, and have a positive effect on olfactory recovery.

Keywords: Early olfactory training, chronic rhinosinusitis, olfactory impairment, nasal endoscopy, olfactory recovery

Introduction

Olfactory impairment is characterized by varying degrees of olfactory hyposmia or complete loss of smell, and some of them are combined with olfactory hypersensitivity and olfactory hallucination. Chronic rhinosinusitis has a variety of clinical manifestations, and olfactory dysfunction is a common one [1]. Patients with chronic rhinosinusitis combined with olfactory impairment will have clinical symptoms of both chronic rhinosinusitis and olfactory impairment, including purulent nasal discharge, nasal congestion, headache, eye pressure, hyposmia, anosmia, and parosmia. The pathological mechanism of rhinosinusitis combined with olfactory impairment has not been completely elucidated yet. There are two clinical treatments for chronic rhinosinusitis combined with olfactory impairment: drugs and surgery. Drugs can only control the symptoms of the disease for a short time. Many studies suggest that nasal endoscopic surgery could improve patients' olfactory impairment, but most patients still suffer from olfactory hyposmia after surgery.

Therefore, how to promote the recovery of olfactory function after nasal endoscopic surgery has always been the focus of research. Some

studies have found that active olfactory training after nasal endoscopy has positive significance for the improvement of patients' olfactory function. The olfactory sensitivity and olfactory function of patients can be improved through repeated and regular active sniffing of different odors [2, 3]. However, there is no consensus on whether olfactory training is effective for all disease-induced olfactory impairment and how to carry out olfactory training, and different scholars hold different views [4, 5].

In order to explore the effective methods to promote olfactory recovery after nasal endoscopy, 67 patients with chronic rhinosinusitis combined with olfactory impairment were enrolled to compare the effects of comprehensive olfactory rehabilitation training at different time points after surgery, thereby providing evidence to confirm the value of early comprehensive olfactory rehabilitation training.

Materials and methods

Baseline data

A retrospective study was conducted on 67 patients with chronic rhinosinusitis combined with olfactory impairment admitted to our hospital from July 2018 to August 2020. Patients were divided into control group (n=33) and observation group (n=34) according to the time of implementation of comprehensive olfactory rehabilitation training. The control group received non-early comprehensive olfactory rehabilitation training at 2 weeks after nasal endoscopy, and the observation group received early comprehensive olfactory rehabilitation training at 1 week after nasal endoscopy. The study received ethical approval from the Ethics Committee of the Tianjin 4th Central Hospital (No. SZXLL-2018-KY0614).

Inclusion criteria: patients aged 18-80 years; patients with primary treatment of sinusitis and olfactory dysfunction in accordance with Chinese guidelines for diagnosis and treatment of chronic rhinosinusitis [6] with the disease duration >6 months; patients with preoperative olfactory impairment (75% alcohol was used as odorant, which was not recognized by the patient); patients with a olfactory impairment grade (quantified by CT scan of the sinuses, using Lund-Mackay scale) of 1-5 (grade 1 was mild, grades 2-4 were moderate, and grade 5 was severe); patients who underwent elective nasal endoscopic treatment, conforming to the indications of nasal endoscopy: (1) to find the site of epistaxis and stop the bleeding under endoscopic vision, (2) to find the source of purulent secretion, (3) to localize early nasal and nasopharyngeal tumors and have biopsy under direct vision, (4) to localize fistula for cerebrospinal fluid rhinorrhea; patients with clear consciousness, good compliance, and signed the study consent form.

Exclusion criteria: patients who received previous treatment of nasal-sinus surgery or cranial surgery; patients combined with other diseases such as Alzheimer's disease that could cause olfactory impairment; patients with previous treatment before enrollment; patients who had contraindications to surgery or anesthesia; patients with postoperative olfactory impairment; patients with serious complications such as bleeding or cerebrospinal fluid leakage after nasal endoscopy; patients with poor compliance with rehabilitation training; patients who failed to follow-up.

Methods

Comprehensive olfactory rehabilitation training method. Four types of odorants (30 mL per brown glass bottle, prepared from lilac flowers, lemon slices, rose flowers and peppermint leaves) were placed in a well-ventilated and odorless room. Patients were instructed to sniff each type of odorant for 10 sec each time, and then another 20 sec later. The four odorants were sniffed for 5 min each time, and the patients were trained every morning and evening for 3 months.

At the beginning of the training, the patients were given odorants and written materials regarding the training procedures. The nursing staff provided detailed instructions to the patients during their hospitalization to ensure that they had mastered the method, and after discharge, they were trained with the same method. During the out-of-hospital training, the nursing staff followed up the patients by telephone once a week to understand the training progress and give guidance when patients encountered difficulties.

In the observation group, the training was started 1 week after the removal of nasal stuffing, while in the control group, the training was started 2 weeks after the operation. The two groups received the same training methods, training frequency, and duration.

Outcome measurement

Baseline data: The age, gender, body mass index (BMI), duration of chronic rhinosinusitis, nasal endoscopic approach, and degree of olfactory impairment were compared between the two groups.

Olfactory function: The T&T olfactometer produced by Daiichi Pharmaceutical Industry Co., Ltd. (Tokyo, Japan) was applied to measure the olfactory function [7]. There were 5 types of odorants used in the meter, and the concentration of each type of odorant was divided into 8 levels from -2 to 5, with -2 indicating the lowest concentration and 5 indicating the highest concentration, and the higher concentration indicates the poorer olfactory function of the patient. During the test, the odorless filter paper was dipped into the odorant and placed 1-2 cm under the nostril to be sniffed 2-3 times. A 20-second interval was set between two odorant tests. The evaluation was performed before and 3 months after training, respectively.

Minimum detection threshold and minimum recognition threshold were evaluated by CC-CRC test [8]. The detection threshold was tested with n-butanol, the maximum concentration of n-butanol in ionized water was 4%. The dilution concentration used in the test ranged from 4% to 2.3×10^{-5} %, and 12 levels were recorded as 0 to 11, corresponding to 0-11 points. The higher score indicated the better olfactory detection threshold. Eight daily items were selected as odorant for olfactory recognition thresholds test. The odorant was placed in a plastic bucket covered with gauze and tested on both sides of the nostrils. Patient smelled and gave the name of odorant. One correct answer was recorded as 1 point, and the total score was 8 points. The higher score indicated the better olfactory recognition threshold. The evaluation was performed before and 1, 2 and 3 months after training, respectively.

Olfactory performance: It was evaluated by Sniffin' Sticks method [9], which comprises 3 subtests. (1) Odor threshold test consisted 48 pen-like sticks, with 3 pens as 1 set, for a total of 16 sets. Each set included 2 blanks and 1 n-butanol pen. The highest score was 16 (the lowest concentration could be identified), and the lowest score was 0 (the highest concentration could not be identified), with higher scores indicating better olfactory sensation. (2) Odor discrimination test consisted 48 pen-like sticks, with 3 pens as 1 set, for a total of 16 sets. Each set contained two identical odorant pens and a third with a different odorant. All sets that were correctly discriminated scored 16, with higher scores indicating better odor discrimination. (3) Odor identification consisted 16 pen-like sticks. Patients were asked to identify the correct odor from a list of four alternatives after sniffing each pen, with 16 scores for all correct identifications, and with higher scores indicating better odor identification. At the end of the 3 subtests, the threshold score (T), discrimination score (D), and identification score (I) were summed up to obtain the TDI score, which was used to assess olfactory performance. TDI score of 48-31 indicated normosmia, 30-16 indicated hyposmia, and ≤ 15 indicated functional anosmia. The evaluation was performed before and 1, 2 and 3 months after training, respectively.

Quality of life was evaluated by Questionnaire of Olfactory Disorders (QOD) [10], which is divided into description section and VAS section. The former includes 29 questions on olfactory impairment, quality of survival, and honesty entries. Each question was scored 0-3, and the total score was 0-87, with the higher score indicating the higher quality of life. The VAS was used to evaluate the degree of annoyance, the frequency of perceived impairment, the impact of dysfunction on work, recreation, and private life, ranging 0-10. The higher score indicated the lower quality of life. The evaluation was performed before and after 3 months of training, respectively.

Statistical methods

SPSS 23.0 was used to analyze all data. The count data was presented as [n (%)], which was examined by X^2 test. The measurement

Table 1. Comparison of baseline data ($\bar{x}$±sd)/[n (%)]

Data		Observation group (n=34)	Control group (n=33)	t/X^2	*P*
Gender	Male	18 (52.94)	19 (57.58)	0.146	0.703
	Female	16 (47.06)	14 (42.42)		
Age (years)		46.35±22.16	48.81±23.64	0.440	0.662
BMI (kg/m^2)		23.16±2.18	23.13±2.34	0.054	0.957
Duration of chronic rhinosinusitis (months)		12.76±4.95	13.05±5.12	0.236	0.814
Nasal endoscopic approach	Unilateral approach	20 (58.82)	21 (63.64)	0.163	0.686
	Bilateral entry	14 (41.18)	12 (36.36)		
Degree of olfactory impairment	Mild	10 (29.41)	11 (33.33)	0.132	0.936
	Moderate	16 (47.06)	15 (45.45)		
	Severe	8 (23.53)	7 (21.21)		

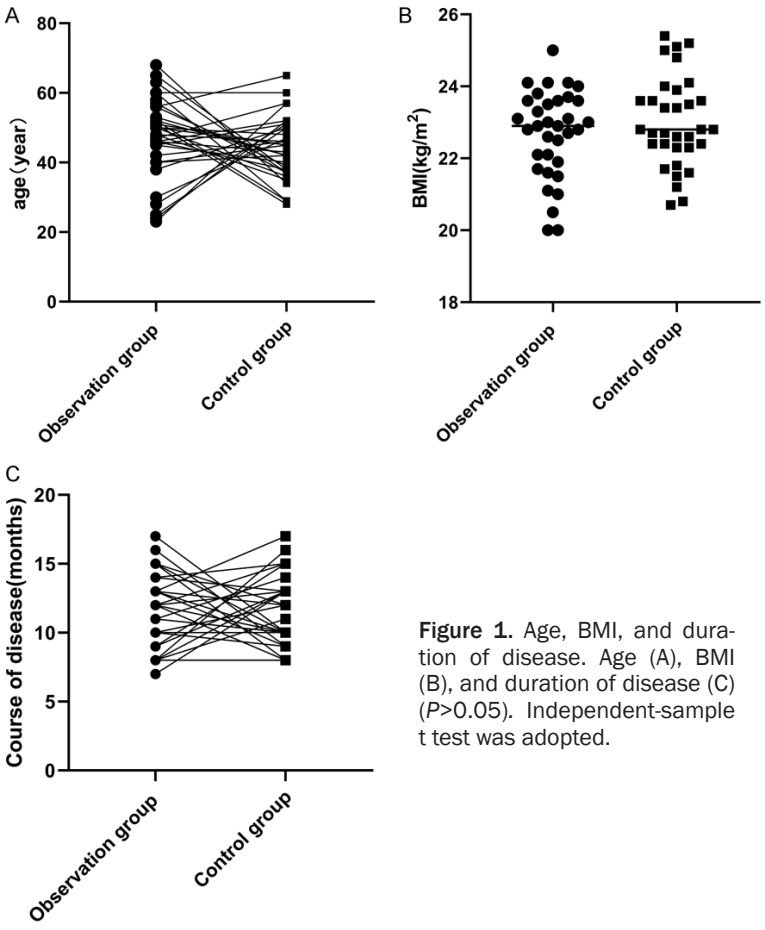

Figure 1. Age, BMI, and duration of disease. Age (A), BMI (B), and duration of disease (C) (*P*>0.05). Independent-sample t test was adopted.

Results

Baseline data

There was no statistical difference in gender, mean age, mean BMI, mean duration of chronic rhinosinusitis, nasal endoscopic approach, and degree of olfactory impairment between the two groups (*P*>0.05) (**Table 1**; **Figure 1**).

Olfactory function

There was no significant difference in T&T olfactory test scores between the two groups before training (*P*>0.05). T&T olfactory test scores of both groups after 3 months of training were lower than those before training (*P*<0.05). T&T olfactory test scores of the observation group were significantly lower than those of the control group after 3 months of training (*P*<0.05) (**Table 2**; **Figure 2**).

data were expressed as ($\bar{x}$±sd) and examined with independent sample t-test for comparison between groups, and paired t-test for intra-group comparison. ANVOA followed by LSD post hoc test was performed for comparisons among multiple groups. Graphs were produced by Graphpad Prism 8. *P*<0.05 was considered statistically significant.

Minimum detection threshold and minimum recognition threshold

The differences in olfactory minimum detection threshold and minimum recognition threshold scores were not statistically significant between the two groups before training (*P*>0.05). After 1, 2 and 3 months of training, the minimum

Table 2. Comparison of olfactory function ($\bar{x}$±sd, points)

Subgroup	Number of cases	Before training	After 3 months of training
Observation group	34	3.64±0.29	-0.86±0.26*
Control group	33	3.59±0.32	1.72±0.34*
t		0.671	34.955
P		0.505	<0.001

Compared with before training, *P<0.05.

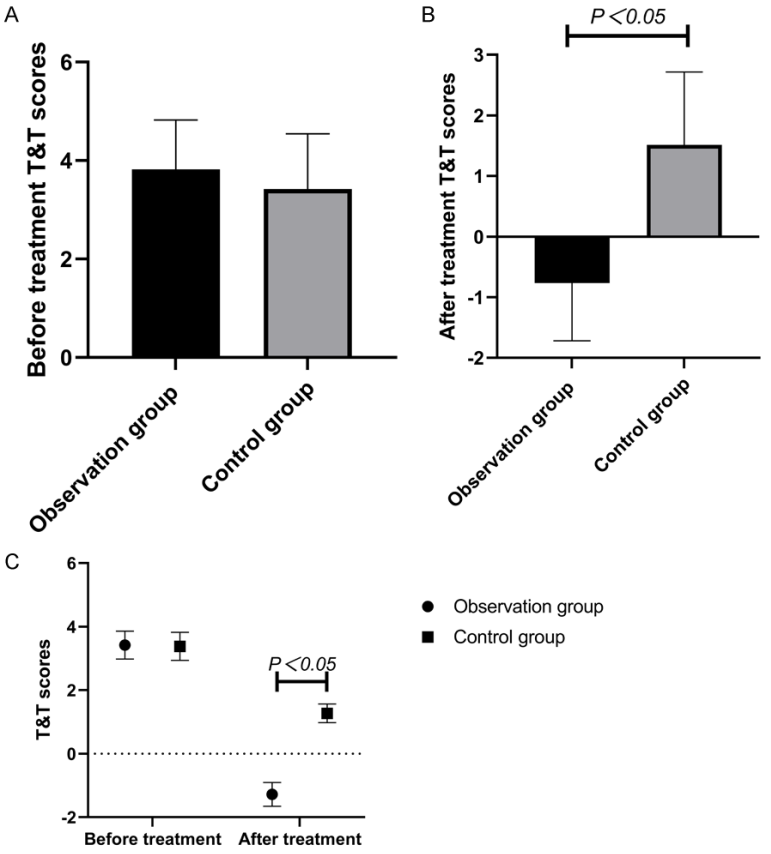

Figure 2. Olfactory function. T&T test scores (A, C) of olfactory function before training (P>0.05); T&T test scores (B, C) after 3 months of training (P<0.05). Compared with control group, P<0.05. Independent-sample t test and paired t test were adopted.

detection threshold scores and minimum recognition threshold scores in both groups were higher than those before training (P<0.05). The minimum detection threshold scores and minimum recognition threshold scores in the observation group were higher than those in the control group after 1, 2 and 3 months of training (P<0.05) (**Table 3**; **Figure 3**).

Olfactory performance

The differences in olfactory threshold, odor discrimination and odor identification scores were not statistically significant between the two groups before training (P>0.05). After 1, 2 and 3 months of training, the scores of olfactory threshold, odor discrimination, and odor identification in both groups were higher than those before training (P<0.05). The scores of olfactory threshold, odor discrimination, and odor identification of the observation group after 1, 2 and 3 months of training were higher than those of the control group (P<0.05) (**Table 4**; **Figure 4**).

Quality of life

There was no statistically significant difference in quality of life between the two groups before training (P>0.05). After 3 months of training, the description scores of both groups were higher than those before training, and the VAS scores were lower than those before training (P< 0.05). The description scores of the observation group were higher, whereas the VAS scores of the observation group were lower than those of the control group after 3 months of training (P<0.05) (**Table 5**; **Figure 5**).

Discussion

Some patients with chronic rhinosinusitis combined with olfactory impairment still have olfactory impairment after nasal endoscopy, and it was found that some patients could not recover normal olfactory function at 6 months after nasal endoscopy [11]. The persistence of olfactory impairment may reduce odor discrimination, which may lead to life-threatening risks in some hazardous events, such as the inability to recognize harmful odors such as gases [12]. Moreover, persistent postoperative olfactory impairment can gradually affect the sense of taste of patients, leading to loss of appetite and weight loss, affecting the quality of postoperative recovery. Studies have shown

Table 3. Comparison of olfactory minimum detection and recognition thresholds ($\bar{x}\pm$sd, points)

Subgroup	Indicator	Before training	After 1 month of training	After 2 months of training	After 3 months of training
Observation group (n=34)	Minimum detection threshold	3.02±0.43	5.16±0.28*	8.71±0.62*	9.52±0.41*
	Minimum recognition threshold	1.13±0.32	3.05±0.50*	5.06±0.37*	6.72±0.19*
Control group (n=33)	Minimum detection threshold	3.05±0.41	4.06±0.33*	5.19±0.42*	7.09±0.44*
	Minimum recognition threshold	1.10±0.33	1.75±0.36*	3.54±0.19*	4.95±0.26*
t/P Minimum detection threshold of olfaction between groups		0.292/0.771	14.728/0.000	27.125/0.000	23.396/0.000
t/P Minimum recognition threshold between groups		0.378/0.707	12.181/<0.001	21.055/<0.001	31.884/<0.001

Compared with before training, *P<0.05.

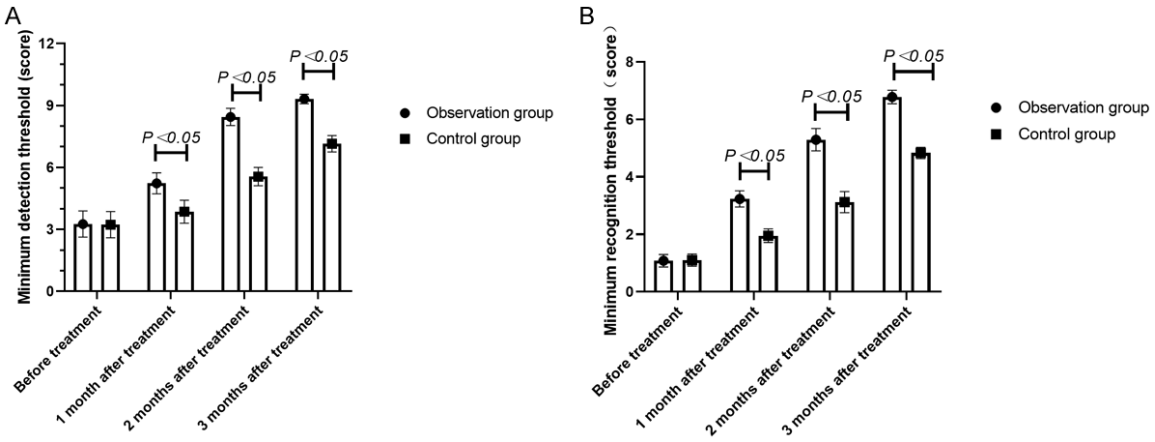

Figure 3. Olfactory minimum detection threshold and minimum recognition threshold. Olfactory minimum detection threshold (A) and minimum recognition threshold (B) after 1, 2 and 3 months of training (P<0.05). Compared with control group, P<0.05. Independent-sample t test was adopted.

Table 4. Ability of olfactory performance ($\bar{x}\pm$s, points)

Subgroup	Indicator	Before training	After 1 month of training	After 2 months of training	After 3 months of training
Observation group (n=34)	Olfactory threshold score	4.13±1.39	6.95±1.58*	9.01±1.64*	12.76±1.13*
	Odor discrimination score	5.86±1.33	7.54±1.39*	10.19±1.22*	12.84±1.16*
	Odor identification score	4.03±1.31	7.01±1.29*	10.39±1.22*	12.76±1.26*
Control group (n=33)	Olfactory threshold score	4.83±1.47	5.86±1.52*	7.86±1.61*	10.62±1.15*
	Odor discrimination score	5.61±1.32	6.19±1.38*	8.51±1.26*	10.81±1.19*
	Odor identification score	4.02±1.27	5.29±1.31*	8.02±1.23*	10.72±1.22*
t/P intergroup threshold		0.503/0.617	14.178/0.000	12.105/0.000	25.621/0.000
t/P intergroup discrimination		0.700/0.487	6.907/0.000	5.444/0.000	9.440/0.000
t/P intergroup identification		0.679/0.500	9.821/0.000	6.730/0.000	18.422/0.000

Compared with before training, *P<0.05.

that long-term olfactory abnormalities may affect memory, impair the ability to control emotions, and adversely affect patients' social life, which can significantly affect the quality of life [13].

In order to promote the recovery of olfactory function after nasal endoscopy, a variety of methods have been tried clinically, such as pharmacological treatment with antibacterial drugs and glucocorticoids, and nasal irrigation to regulate the nasal environment and improve mucosal edema, although the effectiveness and safety has not been widely proven. In this study, comprehensive olfactory rehabilitation training was adopted early in pa-

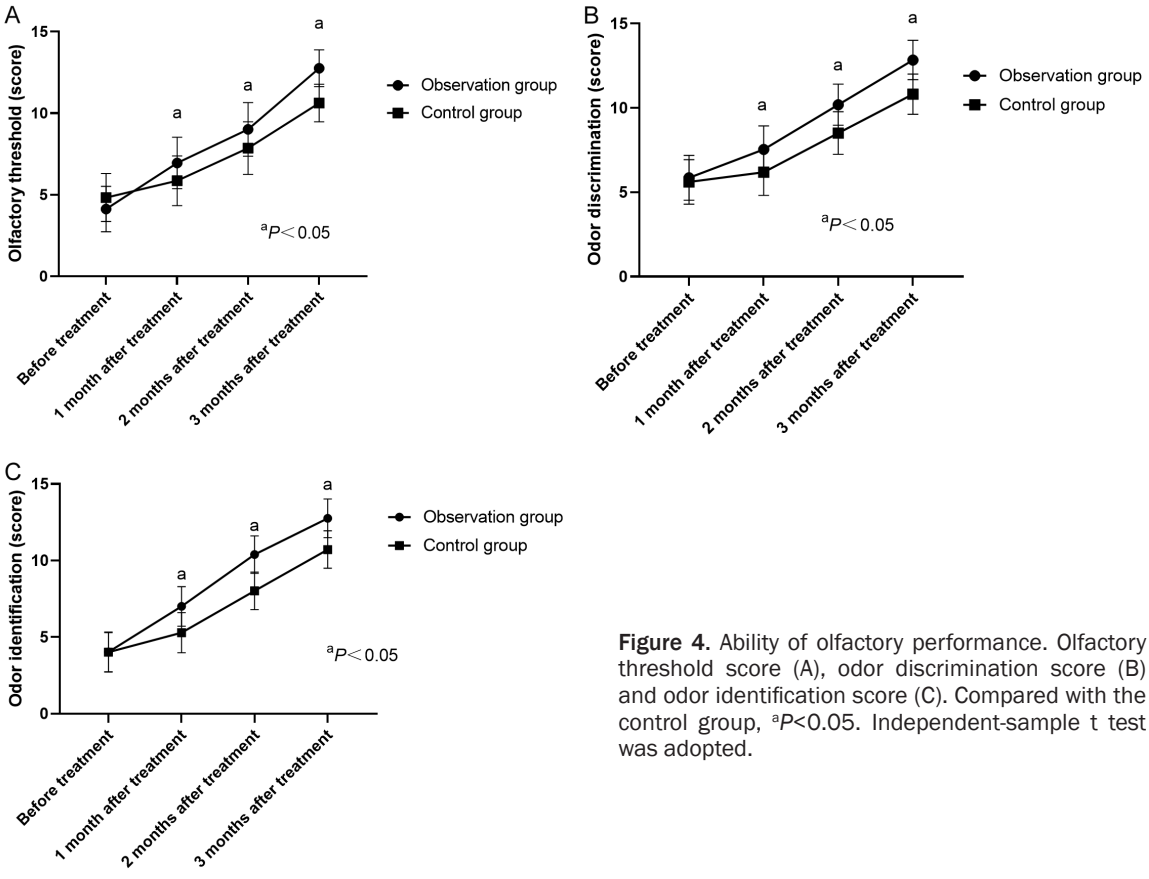

Figure 4. Ability of olfactory performance. Olfactory threshold score (A), odor discrimination score (B) and odor identification score (C). Compared with the control group, $^{a}P<0.05$. Independent-sample t test was adopted.

Table 5. Comparison of quality of life ($\bar{x}\pm$sd, points)

Subgroup	Description		VAS	
	Before training	After 3 months of training	Before training	After 3 months of training
Observation group (n=34)	29.76±2.19	60.18±3.61*	8.11±1.06	2.86±0.62*
Control group (n=33)	28.97±2.23	45.19±2.87*	8.03±1.04	5.26±0.58*
t	1.463	18.778	0.312	16.351
P	0.148	<0.001	0.756	<0.001

Compared with before training, $^{*}P<0.05$.

tients after nasal endoscopy, enabling patients to smell different odors several times in a short period of time to help accelerating the regeneration of olfactory neurons or achieve the reconstruction of synaptic pathways leading to the olfactory cortex, thus improving the olfactory sensitivity [14, 15]. Studies have confirmed that olfactory training plays a significant role in promoting the recovery of olfactory function [16]. The results of this study indicated that the early postoperative comprehensive olfactory rehabilitation training could significantly improve the olfactory function, increase the minimum olfactory detection and recognition thresholds, enhance the ability of olfactory performance of patients, and improve the quality of life of patients compared with the patients who received the comprehensive olfactory training later. Evidence has shown significant improvement in identification threshold but poor improvement in recognition threshold after olfactory training in patients with olfactory impairment [17, 18], and the difference may be related to different study subjects, study regimens and timing of intervention. Other studies have shown that repeated exposure to odor leads to increased sensitivity of olfactory epithelium, thus helping patients bet-

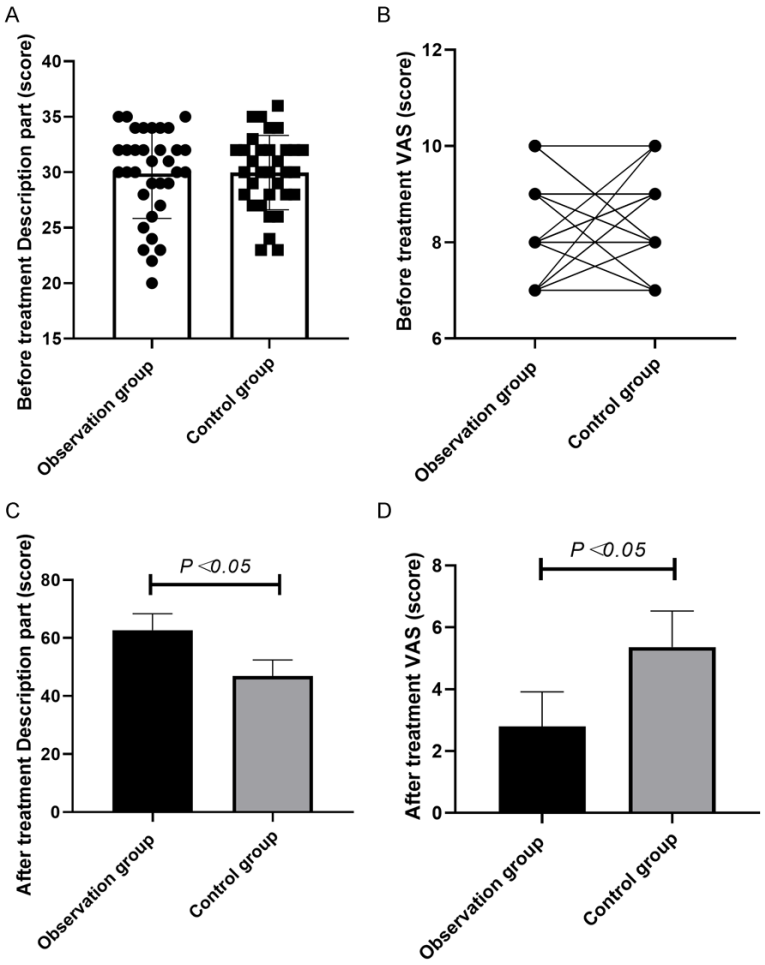

Figure 5. Quality of life. Description part (A) and VAS (B) before the intervention (P>0.05); Description part (C) and VAS (D) after 3 months of intervention (P<0.05). Compared with control group, P<0.05. Independent-sample t test was adopted.

ter recognize odors [19, 20]. Through continuous olfactory training, horizontal basal cells in the olfactory epithelium can be activated and induced to differentiate into spherical basal cells, thus promoting the slow repair of the olfactory mucosa and improving olfactory function [21, 22]. In a similar study that compared the recovery of olfactory function with or without olfactory training, it was found that the recovery was significantly faster in the training group. The reason is that repeated olfactory training can induce changes in the function of neural regional connections to form the functional network of olfactory nerves, which also confirms that olfactory nerves have plasticity [23]. Olfactory training can change the size of the olfactory bulb, which is a relay station for olfactory impulses to the nervous system and regulate the afferent olfactory information. This mechanism is closely related to the recovery of olfactory function, so it is believed that olfactory training can promote the recovery of olfactory function [24, 25].

In conclusion, early comprehensive olfactory rehabilitation training can improve the olfactory identification and recognition thresholds and enhance the quality of life in patients with chronic rhinosinusitis combined with olfactory impairment after nasal endoscopy. However, this study was a single-center retrospective study with too few subjects included. It is necessary to conduct a multicenter, large-scale prospective study to fully elucidate the mechanism of olfactory training on olfactory function in the future.

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Disclosure of conflict of interest

None.

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