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Review

Research Progress in the Treatment of Olfactory Dysfunction

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Abstract: Olfaction is one of the primitive sensory functions in humans, and olfactory dysfunction often leads to a decline in patients' quality of life. However, clinical research on the treatment of olfactory dysfunction still faces certain challenges. This article reviews the global research progress in the treatment of olfactory dysfunction in recent years. The main approaches include pharmacotherapy, such as corticosteroids and biologics; olfactory training; surgical treatment; and several novel therapies, including intranasal platelet-rich plasma injection, electrical stimulation of the olfactory system, and olfactory mucosa transplantation. Among the various administration routes, oral, ultrasonic nebulized inhalation, and nasal irrigation therapies have demonstrated superior efficacy compared to intranasal corticosteroids. The researchers compared the efficacy and safety of eight monoclonal antibodies in the treatment of chronic rhinosinusitis with nasal polyps. In terms of improving the olfactory function: Dupilumab ranks first. Olfactory training is applicable for the treatment of post-infectious, post-traumatic, neurodegenerative, and idiopathic olfactory disorders. Compared with traditional training, the novel nasal plug-based olfactory training is more convenient, discreet, and diversified in scent selection, effectively reducing olfactory fatigue and significantly improving patient compliance and therapeutic outcomes. Although its short-term advantages have been demonstrated, further studies are required to validate its long-term efficacy and generalizability. Surgery is a double-edged sword: it can enhance olfactory function, but it may also lead to iatrogenic olfactory impairment. Currently, its main application is still in conductive olfactory disorders, especially for olfactory improvement in individuals with chronic rhinosinusitis accompanied by nasal polyps.

Keywords: Olfactory Function; Olfaction; Olfactory Dysfunction; Biological Drug; Sinus Surgery

1. Introduction

Olfaction has functions such as identification, early warning, enhancing appetite and influencing emotions [1]. For ordinary people, olfactory dysfunction can lead to difficulties in cooking and a reduced appetite, potentially affecting nutritional structure and weight management over the long term. Olfaction serves as a natural alarm system. Individuals with olfactory dysfunction may fail to detect hazardous odors such as gas leaks and smoke, are unable to promptly identify the smell of spoiled or decaying food, and cannot recognize pungent odors from disinfectants or harmful chemical agents. These impairments pose significant threats to health. Affected individuals are more prone to consuming spoiled food, which may cause gastrointestinal discomfort, and are less capable of responding to emergencies such as fires or gas leaks in a timely manner, thereby substantially reducing their daily safety. Additionally, they miss out on pleasant scents in life—such as floral aromas or the smell of cooked meals—which not only diminishes their sense of well-being but also adds considerable inconvenience to daily living. Moreover, patients may be unaware of their own body odor, adversely impacting personal hygiene, physical health, and social

interactions. Beyond these issues, olfactory dysfunction can also affect emotional well-being. Research indicates that the prevalence of depressive symptoms among patients with olfactory [2]. For certain professionals, such as chefs, wine taster, perfumers, odor judges, and firefighters, a keen sense of smell is particularly essential. The COVID-19 pandemic has led to a sharp increase in the prevalence of olfactory dysfunction in recent years [3,4]. The pandemic also emphasized the lack of therapeutic options for olfactory dysfunction. Consequently, a growing number of studies have been devoted to olfactory dysfunction, and various attempts and novel therapeutic approaches have been gradually introduced into clinical practice. This article aims to summarize and review recent advances in the treatment of olfactory dysfunction.

2. Pharmacotherapy

2.1. Corticosteroids

To date, corticosteroids remain one of the primary medications for the treatment of olfactory dysfunction. It is known that in the treatment of neurosensory olfactory dysfunction, the response rate to corticosteroids can reach 25%–50% [5,6]. Corticosteroids are also effective for conductive olfactory dysfunction. Intranasal corticosteroids (INCS) can reduce polyp size and improve symptoms such as nasal blockage and olfactory dysfunction [7]. After endoscopic nasal surgery, INCS can effectively inhibit the growth of vesicles, granulation tissue, and small polyps, promote mucosal regeneration and epithelialization of the surgical cavity, and prevent adhesions; oral corticosteroids can significantly reduce nasal exudation and alleviate mucosal reactive edema. Seiden found that among patients with conductive olfactory dysfunction, intranasal corticosteroids treatment led to olfactory improvement in 25% of patients, while oral corticosteroids treatment was effective in 83% of patients [8]. A double-blind, randomized, vehicle-controlled trial conducted by Blomqvist et al. also confirmed that patients with olfactory dysfunction due to local inflammation could experience improvement in olfaction after 10 days of combined intranasal and oral corticosteroids therapy [9]. However, continued use of intranasal corticosteroids did not lead to further olfactory improvement. Based on the available evidence, oral administration remains the preferred route for corticosteroids therapy. The side effects of corticosteroids exhibit clear dose-dependency and time accumulation. Short-term, low-dose use carries lower risks, whereas long-term, high-dose systemic administration (oral) may induce multi-system adverse reactions. The main side effects include: metabolic disorders, osteoporosis, femoral head necrosis, significantly increased infection risk, and induction or exacerbation of peptic ulcers.

In addition, other routes of administration have been explored by some researchers. Reychler et al.'s experiment demonstrated that the therapeutic efficacy of ultrasonically nebulized corticosteroids inhalation for olfactory dysfunction was equivalent to that of oral corticosteroids, and both were superior to intranasal corticosteroid sprays [10]. Following treatment, the total Sniffin' Sticks test scores increased by 5.5 and 5.8 points for the nebulized inhalation and oral administration groups, respectively, whereas the score for the intranasal spray group decreased by 1.1 points. Reychler's measurements indicated that ultrasonic nebulization resulted in greater deposition of corticosteroids in the distal nasal cavity compared to nasal sprays, facilitating better access to the olfactory region. This may explain the ineffectiveness of intranasal corticosteroids sprays. While high-volume (>50 mL), low-pressure nasal irrigation is established as the most effective technique for pan-sinonasal coverage, the subsequent popularity of high-volume steroid nasal rinses (HSNR) for inflammation control exists in a regulatory gray area [11]. Despite their widespread use, HSNR applications are considered off-label and have not received formal FDA approval. A systematic review has confirmed the therapeutic efficacy of corticosteroid nasal irrigation in improving clinical symptoms, including olfactory dysfunction, among CRS patients [12]. HSNR demonstrated a trend toward superior outcomes compared with nasal spray administration in terms of symptom relief and quality of life improvement, without significant systemic adverse effects such as adrenal suppression being observed [13]. A randomized controlled trial (RCT) further indicated that the combination of budesonide nasal irrigation with olfactory training resulted in significantly greater improvement in olfactory function scores compared with olfactory training alone [14]. The aforementioned study suggests that the method of corticosteroids administration influences the treatment outcomes of olfactory dysfunction, although the underlying mechanisms remain unclear.

2.2. Biologicals

Currently, biologicals can be classified into the following categories based on the different targets they act upon. Biological therapies have emerged as a pivotal component in the management of chronic rhinosinusitis with nasal polyps (CRSwNP), particularly in severe or refractory cases. These treatments target specific cytokines and immune pathways associated with the type 2 inflammatory response characteristic of CRSwNP, thereby offering innovative strategies for effective disease management.

2.2.1. Anti-IgE Biologics

IgE levels in nasal polyp tissues are associated with local eosinophil infiltration and disease severity. Omalizumab exerts its therapeutic effects by binding to free IgE. Studies have demonstrated that Omalizumab can improve olfactory function in patients with chronic rhinosinusitis with nasal polyps(CRSwNP) [15]. The labeled indications of Omalizumab are allergic asthma and chronic spontaneous urticaria.

2.2.2. Anti-IL-5 Biologics

IL-5 is a key cytokine for the survival, maturation, and activation of eosinophils at inflammatory sites. Studies have demonstrated that in patients with CRSwNP, a statistically significant difference in the olfactory Visual Analog Scale (VAS) score was observed between the mepolizumab group and the control group starting from week 9, and this difference increased with prolonged treatment duration [16]. The labeled indications of Mepolizumab are eosinophilic granulomatosis with polyangiitis (EGPA) and severe eosinophilic asthma.

2.2.3. Anti-IL-4/IL-13 Biologics

IL-4 and IL-13, acting through the shared receptor IL-4Rα, are involved in processes such as IgE synthesis, eosinophil activation, mucus secretion, and airway remodeling. They play a pivotal role in type 2 inflammatory responses. A meta-analysis conducted by Oykhman et al. indicated that Dupilumab demonstrates the most favorable efficacy for olfactory dysfunction [17]. In animal studies, Dupilumab has also been shown not only to exert "anti-inflammatory and anti-edema" effects, thereby improving conductive olfactory loss, but also to directly protect olfactory sensory neurons and suppress neuroinflammation in the olfactory bulb, leading to rapid improvement in neurosensory olfactory dysfunction [18]. Dupilumab showed significant improvements versus Omalizumab in UPSIT(University of Pennsylvania Smell Identification Test) and VAS(Visual Analog Scale). An improvement in the VAS olfactory score was still observable up to 12 months after treatment with dupilumab [19]. The labeled indications of Dupilumab include moderate-to-severe atopic dermatitis, asthma, and nodular prurigo. The labeled indications for Stapokibart include moderate-to-severe atopic dermatitis, CRSwNP, and seasonal allergic rhinitis.

2.2.4. Anti-TSLP Biologics

Tezepelumab is the first and currently only approved monoclonal antibody targeting thymic stromal lymphopoietin (TSLP) worldwide. TSLP is a key driver of type 2 inflammation. As a first-in-class human monoclonal antibody, it inhibits TSLP, a critical epithelial cytokine positioned at the apex of the inflammatory cascade, thereby blocking multiple inflammatory pathways upstream. This mechanism provides a novel therapeutic option for patients with severe asthma and CRSwNP.

Compared with the vehicle, a statistically significant improvement in olfactory scores was observed in Network of Patient Safety Databases (NPSD) as early as Day 7. After 52 weeks of treatment, the tezepelumab group demonstrated a mean improvement of approximately 9.5 points in the University of Pennsylvania Smell Identification Test (UPSIT) score over the vehicle group, indicating a substantial enhancement in objective olfactory function. At Week 52, the prevalence of anosmia in the tezepelumab group was only 31.5%, whereas it remained as high as 75.8% in the vehicle group [20,21].

Wang compared the efficacy and safety of eight monoclonal antibodies in the treatment of CRSwNP [22]. The eight monoclonal antibodies are as follows: Dupilumab (anti-IL-4Rα), Stapokibart (a China-originated anti-IL-4Rα monoclonal antibody), Omalizumab (anti-IgE), Mepolizumab (anti-IL-5), Benralizumab (anti-IL-5Rα), Depemokimab (anti-IL-5), Tezepelumab (anti-TSLP), and GR1802(anti-IL-4Rα). All biologics significantly reduced Nasal Polyp Score, Stapokibart ranked first. Both Dupilumab and Stapokibart improved the UPSIT score, indicating a recovery

of olfactory function. In terms of improving the olfactory function: Dupilumab ranks first, and Stapokibart ranks second. Monoclonal antibodies are currently primarily utilized for the treatment of type 2 inflammation associated with chronic rhinosinusitis. To date, there have been no reports on the use of monoclonal antibodies for the treatment of patients with isolated olfactory dysfunction.

3. Other Medications

In addition to corticosteroids, other pharmacological agents have been explored in clinical practice. Aiba administered oral zinc supplementation at a dose of 300 mg daily for one week to 872 patients with olfactory dysfunction [23]. The results demonstrated significant improvement in olfactory function, which may be attributed to the role of zinc in promoting the regeneration of olfactory receptor cells. However, further high-quality randomized controlled trials are required to validate these findings. A retrospective study involving 170 patients with olfactory dysfunction indicated that intranasal administration of 10,000 IU of vitamin A daily for two months significantly improved the patients' TDI (Threshold, Discrimination, Identification) scores [24]. The evaluation criteria for the Sniffin' Sticks olfactory test primarily consist of four aspects: threshold testing (T), discrimination testing (D), identification testing (I), and the assessment of the TDI total score. Regarding the method of vitamin A supplementation, the researchers found that daily oral administration of vitamin A in conjunction with olfactory training did not yield additional improvements in the therapeutic outcomes for olfactory dysfunction [25].

Insulin exhibits anti-inflammatory, antithrombotic, vasodilatory, and anti-apoptotic effects. Insulin receptors are distributed in the olfactory mucosa and intracranial regions such as the olfactory bulb. The olfactory bulb is the organ with the highest insulin uptake in the central nervous system. Insulin can increase the production of growth factors. Hummel suggested that intranasal insulin administration may represent a potential therapeutic approach to influence the regenerative capacity of the olfactory mucosa [26]. Subsequently, this method has been applied by researchers to address olfactory dysfunction induced by COVID-19. A gelatin sponge soaked with 40 units of insulin was placed at the top of the nasal cavity for 15 min per session, once a week, over a period of four weeks. The TDI score improved in 93% of the patients, and no significant difference in blood glucose levels was observed before and after the intervention [27].

Over the years, various other medications have been attempted for the treatment of olfactory dysfunction, including alpha-lipoic acid, sodium citrate, theophylline, ginkgo biloba, antihistamines, and sodium valproate. Although some poorly controlled case reports have suggested potential benefits, none of these agents has demonstrated definitive efficacy. Further investigation is required for all of these treatments.

4. Olfactory Training

Olfactory training is a therapeutic approach developed in Europe in recent years, which has demonstrated efficacy in the clinical management of certain olfactory disorders. Based on the principles of cortical plasticity and the inherent regenerative capacity of the olfactory epithelium, it has become one of the effective treatments for olfactory dysfunction resulting from various etiologies [28]. In mammals, both the olfactory epithelium and the olfactory bulb retain regenerative capacity throughout life [29]. Studies have shown that repeated olfactory stimulation can enhance the electrophysiological responses of the olfactory epithelium in subjects, suggesting that olfactory training may contribute to olfactory epithelial remodeling by increasing the number of human olfactory neurons [30]. In addition to directly participating in the remodeling of the olfactory epithelium, olfactory training has also been shown to significantly increase the volume of the olfactory bulb. Olfactory training is applicable for the treatment of post-infectious, post-traumatic, neurodegenerative, and idiopathic olfactory disorders.

Initially, olfactory training required the use of at least four basic odors [31]. Patients were instructed to inhale each odor for approximately 10 s, with 10-s intervals between different odors. Each session lasted 5 min and was performed twice daily, with a total treatment duration generally ranging from 2 to 6 months. During the recent COVID-19 pandemic, many patients continued to experience olfactory dysfunction 16 weeks after infection, significantly impairing their quality of life. A systematic review and meta-analysis confirmed that olfactory training sustained for more than 8 weeks significantly improved long-term smell disorders associated with COVID-19 [32]. In practice, restrictions regarding odor concentration or brand are unnecessary, which helps reduce treatment costs and simplify the procedure [27]. Although not all patients showed improvement, the success rate was indeed

higher compared to spontaneous recovery alone [33,34]. A recent study comparing training with 4 versus 7 odors demonstrated that 4 odors were sufficient to improve patients' Sniffin' Sticks TDI scores [35].

For most patients, particularly those who are employed during the daytime, adherence to olfactory training is challenging. A novel olfactory training method using a "nasal plug-style fragrance training stick" [36] has been shown not only to yield superior outcomes compared to conventional olfactory training but also to significantly enhance patient compliance and completion rates. This innovation offers the following advantages: First, patients can engage in training while cooking, working, or walking, without being confined to using perfume bottles. Second, the training is more discreet and natural; the nasal plug resembles a breathing strip, making its use socially unobtrusive. Third, it provides a greater variety of scents; users can switch between different fragrance types daily (e.g., lemon, cherry, mint), thereby reducing olfactory fatigue. Fourth, it imposes minimal psychological burden; rather than feeling like a medical treatment, it is perceived as "living with fragrance." Preliminary evidence suggests that this method offers advantages over traditional approaches in terms of compliance and effectiveness, though its long-term efficacy and generalizability require further validation.

5. Surgical Treatment

The primary objectives of surgical treatment are to relieve sinus obstruction, enlarge the sinus ostium, resect irreversibly diseased tissue, and create a patent conduit and adequate space for topical medical therapy, all while maximizing the preservation of normal mucosa and physiological function. In conductive olfactory dysfunction such as CRS, endoscopic sinus surgery can restore the patency of the olfactory cleft, allowing odor molecules to reach and stimulate the sensory neurons within the olfactory epithelium, thereby creating favorable conditions for the resolution of sinonasal inflammation and the restoration of physiological function. During endoscopic sinus surgery, the mucosa on the medial aspect of the middle turbinate, the superior turbinate, and the corresponding nasal septum should be preserved to the greatest extent to prevent postoperative adhesions, which may otherwise affect the patient's postoperative olfactory function. Studies have demonstrated that the overall improvement rate of olfactory function following endoscopic sinus surgery in patients with CRS is approximately 50% [37]. A meta-analysis by Kohli et al. revealed that Endoscopic Endonasal Surgery(ESS) can enhance both subjective and objective olfactory function in CRS patients, with a greater degree of postoperative olfactory improvement observed in CRSwNP patients [38]. Similarly, Hernandez et al. reported that CRSwNP patients exhibited more significant olfactory function improvement after ESS [39]. In patients undergoing endoscopic sinus surgery, placing a nasopore nasal packing soaked with triamcinolone acetonide injection in the olfactory cleft can effectively improve olfactory function [40]. In terms of surgical techniques and approaches, researchers have identified that the use of a nasal septal mucosal flap for skull base reconstruction during endoscopic sinus surgery may lead to significant olfactory impairment. Conversely, the application of fascia lata from the thigh for skull base repair can minimize damage to olfactory function [41].

Conversely, some studies have reported postoperative anosmia or diminished olfactory function following ESS [42]. Surgical intervention may directly damage the olfactory neural structures beneath the olfactory mucosa, thereby inducing "neurogenic" olfactory dysfunction. This finding is corroborated by Lee, who performed biopsies of the olfactory mucosa in patients who developed olfactory impairment following EES [43]. The results demonstrated a significant reduction in the number of olfactory neurons compared to normal individuals, accompanied by extensive respiratory epithelial metaplasia. Currently, surgery remains primarily indicated for conductive olfactory dysfunction and has limited efficacy in cases of neurosensory olfactory impairment.

6. Other Treatment Methods

6.1. Intranasal Injection of "RPR"

Patel attempted a novel therapeutic approach involving the injection of autologous platelet-rich plasma (PRP), derived from the patient's own blood, to treat persistent olfactory dysfunction associated with COVID-19 [44]. PRP is a concentrated form of plasma obtained by centrifugation of autologous whole blood, yielding a platelet-rich concentrate. It contains a variety of growth factors and proteins, among which growth factors are particularly noteworthy as compounds that facilitate tissue regeneration. Clinically, PRP injections have been utilized in the management of mild arthritis when administered into joints, for wrinkle reduction following facial injection, and even

to promote hair regeneration when injected into the scalp. A small-scale randomized controlled trial conducted by Patel demonstrated that, compared with the vehicle group, PRP treatment resulted in greater improvement in odor discrimination. However, no significant differences were observed in odor identification or threshold measures. Researchers administered two injections of PRP into the olfactory cleft of patients with long-term olfactory dysfunction [45]. TDI significantly increased after both first and second injections across all olfactory dysfunction subgroups. A study evaluated the efficacy of PRP injection in 33 patients with post-traumatic olfactory dysfunction. Following PRP administration, 66.7% of the patients reported subjective improvement in symptoms. The patients' scores for TDI were significantly elevated. Furthermore, the post-traumatic injection group demonstrated significantly higher TDI scores at the three-month follow-up compared to the olfactory training group [46]. A systematic review and meta-analysis involving seven studies (four RCTs, three non-RCTs) with a total of 789 patients demonstrated that, compared with vehicle, platelet-rich plasma therapy resulted in significantly better olfactory recovery at both one month and twelve months post-treatment [47]. This effect was particularly pronounced in young adult. Larger-scale studies are warranted to further evaluate its therapeutic efficacy.

6.2. Electrical Stimulation of the Olfactory System

Previous animal experiments have been conducted on frogs and rats. Electrical stimulation studies have also been performed on the olfactory mucosa, olfactory bulb, and various brain regions—such as the subdural space, cortex, and thalamus—in patients with central nervous system disorders such as epilepsy. The studies suggest that electrical stimulation can lead to different and specific odor sensations depending on stimulation parameters and location of the stimulus [48].

Olfactory implants are a novel form of neuroprosthesis, modelled on existing implants for other sensory deficits such as hearing loss. Specialists across the discipline have collaborated to summarize the latest advances and innovative techniques concerning olfactory implantation [49]. Furthermore, they have developed consensus-based expert guidelines covering core clinical and theoretical considerations for this procedure. These standardized recommendations address key components, such as candidate screening criteria, optimal surgical placement, possible adverse events, and essential aftercare protocols following implant surgery. The system comprises the following components: a sensor (electronic nose) responsible for detecting odorant molecules in the air; a processor that converts chemical signals into electrical impulses; and a stimulator, which uses microelectrodes to "awaken" the central olfactory pathway. The microelectrodes may be placed at the olfactory epithelium, olfactory bulb, or higher olfactory centers. The indications for olfactory implantation include: (1) complete or near-complete anosmia that has been stable for ≥2–3 years; (2) a well-established etiology, such as post-traumatic causes, congenital absence, or severe chronic rhinosinusitis; (3) failure to respond to standardized olfactory training (≥3 months) combined with pharmacological or surgical interventions; (4) age and cognitive status sufficient to tolerate general anesthesia; (5) identifiable olfactory bulb volume on magnetic resonance imaging (MRI); and (6) patient expectations aligned with those of the medical team, along with adequate socioeconomic support to complete postoperative rehabilitation.

However, there remains a lack of clinical studies on electrical stimulation specifically in patients with isolated olfactory dysfunction.

6.3. Stem Cell or Olfactory Mucosa Transplantation

The bone marrow contains heterogeneous cell populations, including multipotent stem cells, progenitor cells, and differentiated cells. The high plasticity of bone marrow cells enables them to home to various tissues and differentiate into distinct cell lineages. This potential makes bone marrow cells promising candidates for cell therapy [50]. Studies have shown that in animal experiments, the growth rates of locally injected and intravenously injected cell transplants are comparable [51]. Kurtenbach et al. found that in mice receiving local injections of stem cells, electro-olfactogram measurements and behavioral tests demonstrated better outcomes in the experimental group compared to the control group. The transplanted cells not only appeared to engraft and differentiate within the olfactory mucosa but also contributed to improved olfactory function [52]. Although the potential of stem cell therapy for olfactory dysfunction appears promising, a major challenge remains the safety of this therapeutic approach, particularly concerning uncontrolled cell development, cell migration, and the associated risk of degeneration.

Both olfactory mucosa transplantation into the olfactory cortex and into the olfactory bulb were performed.

The survival rate of grafts at both sites was 83%. The multilayered structure of the olfactory mucosa was preserved, and ciliated cells were observed on the epithelial surface; however, no functional synapses with the olfactory bulb were formed [53].

7. Conclusion

In summary, for most patients with olfactory dysfunction, oral corticosteroids remain the first-line pharmacological treatment, while ultrasonic nebulized corticosteroid inhalation may serve as an alternative. The efficacy of intranasal corticosteroids still requires further validation. However, the side effects of OCS are generally higher than those of INCS, and INCS do not exhibit significant hypothalamic–pituitary–adrenal (HPA) axis suppression [54]. Injectable corticosteroids (ICS) provide prolonged symptom relief and may carry a reduced risk of adrenal suppression compared to OCS; however, supporting data remain limited [55]. Biologics are primarily used to treat type 2 inflammation associated with chronic rhinosinusitis and have demonstrated benefits in improving olfactory function. Whether their indications can be expanded to include other types of olfactory dysfunction in the future still requires further rigorous clinical trials. Intranasal vitamin A and intranasal insulin have demonstrated efficacy in certain small-scale trials; however, further clinical validation is required. Olfactory training has become more convenient and feasible, allowing for earlier initiation and better adherence. Clinicians still require more widely available and accessible odorants to assist patients in conducting olfactory training. Endoscopic endonasal surgery is a double-edged sword: while it can improve olfactory function in select patients, intraoperative care must be taken to protect the mucosa innervated by olfactory nerve fibers.

The treatment of anosmia should still involve a careful weighing of benefits and risks, as the sense of smell is often considered less critical than hearing or vision. In the field of hearing, cochlear implant technology, which utilizes electrical stimulation, has provided hearing improvement for a large number of patients with severe hearing loss. Similarly, retinal implants have been developed for the treatment of degenerative retinal diseases. The first such implant was approved in the United States in 2013 [56]. Literature suggests that direct electrical stimulation of the olfactory bulb may represent a therapeutic option for treating anosmia. However, it remains unclear how to precisely control the stimulation parameters to elicit specific odor perceptions, as well as when to initiate such stimulation following the onset of olfactory dysfunction. To date, electrical stimulation in humans has often required surgical intervention, including in some cases craniotomy, which carries inherent invasiveness and associated risks. From a trauma perspective, the use of stem cells would be preferable, as it can be administered relatively easily via intranasal injection. Nevertheless, the application of stem cells for olfactory disorders remains largely confined to animal models, and the potential oncogenic risk of such therapies must be carefully considered. Furthermore, the source of grafts for olfactory mucosal transplantation in humans remains a subject of debate. In summary, both electrical stimulation and stem cell transplantation represent promising approaches for treating olfactory dysfunction; however, we believe further research is needed in these areas to enhance their safety for future human applications.

Current conventional treatment strategies for olfactory dysfunction continue to undergo refinement and advancement. Concurrently, emerging therapeutic approaches demonstrate promising potential and are expected to yield novel breakthroughs in the clinical management of this condition.

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