

# Olfactory Dysfunction After Oral and Maxillofacial Surgery

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## Case Study

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# Abstract

**Background:** Although anesthesia can contribute to olfactory dysfunction, it is a rare complication after oral and maxillofacial surgery by general anesthesia.

**Cases presentation:** In this study, we introduced 3 cases of patient suffering from anosmia (complete loss of smell), after oral and maxillofacial surgery by general anesthesia. We also investigated possible etiologies of anosmia.

**Conclusions:** There are some evidences that anosmia is caused by nasotracheal intubation, which may cause OM injury and/or swing of the nasal septum in patients with nasal septum deviation. Olfactory dysfunction via general anesthetic drugs, however, may have a different etiology.

## Background

Olfaction is one of our major “chemical” senses, essential for daily life and danger detection. As a result, a decreased or loss of olfaction will not only reduce patients’ quality of life, but also diminish their perception of a dangerous environment. It is reported that anosmia (complete loss of smell) represents 4.7% of the general population, hyposmia (diminished sense of smell) represents 16%, while, parosmia (distorted sense of smell, in the presence of an odor) and phantosmia (distorted sense of smell, in the absence of an odor) represents 2.1% and 0.8% respectively[1]. The etiologies of olfactory dysfunction include upper respiratory tract infection, nasal and sinonasal disease, head trauma, and endoscopic sinus surgery. Multiple drugs, namely, anti-infectives, antihypertensives, and antilipidemics have also been implicated in olfactory disorders[2]. BT et al. reported approximately 3.5% of patients suffer from smell and/or taste disorder, after general anesthesia[3]. However, there are no reports, thus far, of a loss of smell after general anesthesia in oral surgery. We introduce, in this paper, 3 cases of anosmia after oral and maxillofacial surgery by general anesthesia.

## Cases Presentation

### Case 1

A 30-year-old female, non-smoker, received a bilateral sagittal split ramus osteotomy (BSSRO) + anterior mandibular subapical osteotomy, due to mandibular excess. She had no special medical history related to olfactory dysfunction, such as nasal or sinonasal disease or head trauma. Midazolam, sufentanil, and etomidate were used for the induction of anesthesia, and the anesthetic effect was maintained using propofol, sevoflurane, and sufentanil. Endotracheal intubation was performed through the right nostril. After recovery from general anesthesia, there was no initial abnormality. However, one week later, the patient lost the ability to smell without any other causes. A month later, she partially regained her sense of smell, without any treatment, and 3-month later, she made a complete recovery. Please refer to Table 1 for details. The preoperative and postoperative posteroanterior cephalometry are illustrated in Fig. 1.

Table 1

Clinical data of 3 cases of anosmia in patients undergoing oral and maxillofacial surgery by general anesthesia

Cases	Case1	Case2	Case3
<b>Diagnosis</b>	Mandibular Excess	Dentigerous Cyst of Left Maxillary	Mandibular Excess
<b>Procedures of Surgeries</b>	BSSRO + Anterior Mandibular Subapical Osteotomy	Dentigerous Cyst Curettage	BSSRO
<b>Anesthesia</b>	General Anesthesia	General Anesthesia	General Anesthesia
<b>Endotracheal Intubation Type</b>	Nasotracheal Intubation though Right Nasal	Nasotracheal Intubation though Right Nasal	Nasotracheal Intubation though Right Nasal
<b>Anesthetic Drug</b>	Midazolam Sufentanil Etomidate Propofol Sevoflurane	Midazolam Propofol Etomidate Sevoflurane Sufentanil	Midazolam Sufentanil Propofol Etomidate Isoflurane
<b>Clinical Symptoms</b>	Anosmia	Anosmia	Anosmia
<b>Treatment</b>	None	Citicoline Sodium VitaminB1 and B12 Mecobalamin	None
<b>Prognosis</b>	Complete Recovered in 3month	No Recovery	Complete Recovered 1month Later

## Case 2

A 42-year-old male, non-smoker, was diagnosed with dentigerous cyst of the left maxillary, and was scheduled for a dentigerous cyst curettage. He denied having any medical history of olfactory dysfunction. Midazolam, sufentanil, and etomidate were used for the induction of anesthesia, and the anesthetic effect was maintained by propofol, sevoflurane, and sufentanil. Endotracheal intubation was performed through the right nostril. The patient reported loss of smell immediately after recovery from operation. He was provided with medical treatment, including Citicoline sodium, vitamin B1, vitamin B12, and mecobalamin. Unfortunately, the treatment was unsuccessful (Table 1). The preoperative and postoperative cone beam CT (CBCT) are presented in Figs. 2 and 3.

## Case 3

A 22-year-old female, non-smoker, was diagnosed with mandibular excess, and received a BSSRO. Midazolam and etomidate were used for the induction of anesthesia, while sufentanil, propofol, and isoflurane were used to maintain it. Endotracheal intubation was performed through the right nostril. After recovery from general anesthesia, she complained of loss of smell. A month later, she regained her sense of smell without any specific therapy (Table 1). The preoperative and postoperative posteroanterior cephalometry are presented in Fig. 4.

## Discussion

The formation of the sense of smell is extremely complex. It involves olfactory mucosa (OM), located in the upper regions of the nasal cavity [4], which is composed of a pseudo-stratified columnar epithelial layer [5], averaging 1 cm<sup>2</sup> of surface area in each nostril [6]. Also, involved in this process, are olfactory nerve, trigeminal nerve, glossopharyngeal nerve, and vagus nerve [6]. Interestingly, a person's sense of smell is also influenced by personal hobbies, age, culture, and experience [7]. Among the olfactory epithelium that makes up the OM, there are 4 categories of cells, namely olfactory receptor cells, sustentacular cells, microvillar cells, and basal cells [5]. Sustentacular cells generally surround olfactory receptor neurons and may contribute to the regulation and maintenance of the internal environment, making it conducive for olfactory transduction [6]. Microvillar cells, first introduced in 1982, may serve as a chemoreceptor within the OM. From what is known about their function, they express elements of the bitter taste transduction cascade and regulate the olfactory epithelium by releasing acetylcholine, like the solitary chemosensory cells [8]. Basal cells, otherwise known as the olfactory epithelial stem cells, remain on the basement membrane, and, under stimuli, differentiate into new olfactory receptor and other cells [9]. The olfactory receptor cells are replaced every 30–60 days [10] and act as bipolar neurons with its dendrite reaching the OM surface and axons approaching the olfactory bulb. Generally, the dendritic terminal expands to form an olfactory vesicle and sends out several cilia to capture odorant molecules in the air. The axons join together and pass through the cribriform plate to synapse within the olfactory bulb. The olfactory bulb, located in the anterior cranial fossa, is composed of six layers: the olfactory nerve layer, the glomerular layer, the external plexiform layer, the mitral cell layer, the internal plexiform layer, and the granule cell layer. Changcheng Sun [11] reported that the leptin-mediated reduction in odor discrimination may be correlated with reduced neural activity in mitral cells, prompted by alterations in potassium channels. The olfactory bulb axons project to the cerebral cortex, where different odors can be recognized, however the transmission mechanism in olfactory cortex remain unclear. Emerging studies have demonstrated that odor memories are stored in the anterior olfactory nucleus, and their activities are crucial and necessary for the animal's odor cognitive and behavioral demands [12]. Interestingly, a study of perceptual asymmetry in olfactory discrimination once demonstrated a right-nostril advantage, but the nature and origin of this advantage remains unclear [13].

When odorants bind to olfactory receptor cells, they depolarize neurons and send signals along axons. These axons project to the mitral and tufted cell layer of the olfactory bulb through the cribriform plate. The axon terminals of neural receptors synapse within the same glomeruli. The corresponding glomeruli

of the olfactory bulb become activated and generate a unique excitation pattern for each odor in the olfactory bulb[6]. The axons of all the glomeruli cells project to different cerebral structures, including the anterior olfactory nucleus, thalamus, and numerous cortical regions that together form the primary olfactory cortex, the piriform, and periamygdaloid cortices, rostral entorhinal cortex, amygdala, and olfactory tubercle[14].

Factors affecting this pathway may lead to olfactory dysfunction, such as upper respiratory tract infection, nasal and sinonasal disease, head trauma, endoscopic sinus surgery, congenital anosmia, and other causes like intoxication and brain surgery, even COVID-19 can cause olfactory dysfunction. The leading etiology of adult olfactory disorder is upper respiratory tract infection[15]. Unlike adult patients, about 2/3 of the olfactory dysfunction in children are congenital [16]. In addition, olfactory dysfunction occurs in patients who suffer from neurological diseases such as Alzheimer's [17]and Parkinson's disease[18].

None of the patients, reported in this paper, underwent nasal surgery. In one case, a patient underwent cyst curettage, due to a maxillary dentigerous cyst close to the maxillary sinus, the operation itself did not involve the maxillary sinus. The CBCT exhibited left maxillary sinusitis after the operation. The oral and maxillofacial surgery, received by the patients in this paper, did not involve the olfactory system, so surgical damage to the olfactory pathway can be ruled out.

All patients received inhalational anesthesia, combined with intravenous anesthesia. The endotracheal intubation, often performed during oral surgeries, is completely different from the intubations conducted during other forms of surgery. The nasotracheal intubation is the best form of oral general anesthesia while, in other cases, the orotracheal intubation is preferred. As described previously, OM is distributed throughout the upper regions of the nasal cavity[4]. Additionally, emerging evidence revealed that OM contains sensory neurons, but their functional significance remains unknown[19]. The top of the nasal septum is adjacent to the cribriform plate, and the olfactory receptor axon pass through the cribriform plate to synapse with the olfactory bulb. The incidence rate of the nasal septum deviation is high. In this study, the nasal septum deviation was found in all three cases via X-ray (posteroanterior cephalometry and CBCT presented in in Figs. 1, 3, and 4), and all 3 cases underwent nasotracheal intubation. Olfactory dysfunction may be related to intubation because of the deviation of nasal septum. The olfactory pathway is likely injured during intubation. Intubation may cause swing of the deviated septum and affect the conduction of the axon. When the swing amplitude is too large, it can fracture the axon and cause olfactory dysfunction.

Olfactory dysfunction, after general anesthesia, is reported in prior literature, with special criticism given to the general anesthetic drugs for causing the olfactory disorders. In one such study, Konstantinidis et al. reported the case of a 60- year-old female who experienced general anesthetics-induced olfactory dysfunction for 3 months post urological surgery[20]. Baker et al. disclosed that a 69-year-old male lost his ability to smell and taste, due to receiving general anesthesia, namely, remifentanil and propofol, for a laparoscopic inguinal hernia repair [21]. Similarly, in another report, a 57-year-old female who underwent

laparoscopic cholecystectomy, under general anesthesia, namely midazolam, fentanyl, propofol, and sevoflurane, also experienced a loss of smell and taste, likely due to adverse reaction to the anesthesia [22]. Lastly, a 32-year-old woman, who underwent a uterine curettage surgery, experienced anesthesia-induced anosmia and hypogeusia after recovering from anesthesia, induced by propofol[23].

The neurotoxicity of anesthetic drugs is mostly reported in animal studies. Deng et al. reported that isoflurane induced the neuronal cell death in newborn mice forebrain, and the dentate gyrus and olfactory bulb nerve were also damaged in juvenile and young adult mice [24]. Moreover, it has been shown that the basal ganglia and primary olfactory system are vulnerable to neurodegeneration after prolonged sevoflurane exposure in perinatal rats [25]. It was also found that ketamine or midazolam resulted in a dose-dependent, statistically significant increase in nerve cell apoptosis, and that the combination of the two drugs produced a higher rate of nerve cell apoptosis than either drug alone[26]. Moreover, induction of neuroapoptosis in young mice requires only propofol at 1/4 anesthetic dose[27]. Clinical trials revealed that although sevoflurane does not alter olfactory activity, it is detrimental to olfactory memory[28]. Sevoflurane also produced a short-term olfactory identification impairment, and simultaneously suppressed melatonin levels[29]. This may be related to its influence on the binding of GABAA receptor ligand[30]. However, some studies have shown that general anesthesia, using desflurane (6%), has no marked impact on short-term olfactory memory[31]. In another study, it was demonstrated that general anesthesia can induce reversible short-term memory loss, which corrects itself once the anesthetic drug is removed from the body[32].

In summary, 3 patients suffered from olfactory dysfunction after general anesthesia during oral and maxillofacial surgery. This was likely caused by nasotracheal intubation, which may produce OM injury and/or swing of the nasal septum in patients with nasal septum deviation. Olfactory dysfunction via general anesthetic drugs, however, may have a different etiology. The conclusions from this study would aid the perioperative team in increasing their understanding of postoperative complications of the oral and maxillofacial surgery by general anesthesia, and, therefore, provide basis for strengthening the management of perioperative patients, such as the choice of intubation mode of oral general anesthesia, need for X-ray examination to clarify the nasal septum, strategies to avoid injury to the nasal septum during operation, and the choice of narcotic drugs.

## Abbreviations

GABA: Gamma amino butyric acid; CBCT: cone beam CT; BSSRO: bilateral sagittal split ramus osteotomy; OM: olfactory mucosal.

## Declarations

### Ethics approval and consent to participate

This study was approved by the local ethics review board (approval number 2021008) and was conducted in accordance with the recommendations of the institutional ethics committee of the Guangxi Medical University, College of Stomatology, China.

### **Consent for publication**

All the patients provided consent for publication of the article.

### **Availability of data and materials**

Not applicable.

### **Competing interests**

The authors declare that they have no competing interests.

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### **Authors' contributions**

Yaxi Wang, Hua Li: Contributed to conception, design, data acquisition and interpretation, performed all statistical analyses, drafted the manuscript. Nuo Zhou and Xuanping Huang: contributed to critically revised the manuscript. Yaxi Wang, and Hua Li have contributed equally to this work and should be considered as co-first authors. All the authors wrote and approved the manuscript.

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### **Competing interests**

The authors declare that they have no competing interests.

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## Figures



Figure 1

Preoperative and postoperative posteroanterior cephalometry of case 1



Figure 2

Preoperative CBCT of case 2

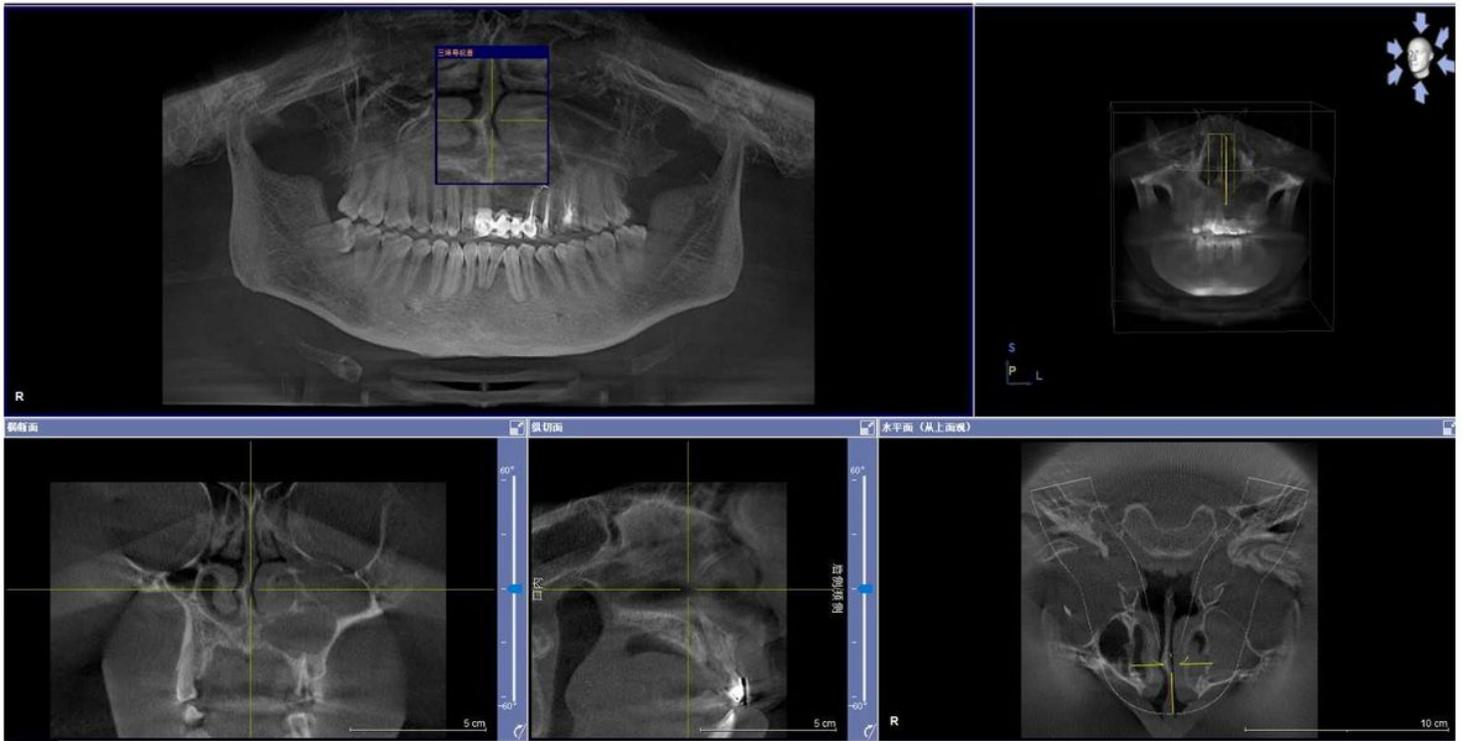


Figure 3

Postoperative CBCT of case 2



Figure 4

Preoperative and postoperative posteroanterior cephalometry of case 3