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ORIGINAL STUDY

Peripheric and central smell regions in patients with chronic rhinosinusitis with nasal polyps: An MRI evaluation

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ABSTRACT

OBJECTIVE. We evaluated the effect of olfactory deficiency caused by sinonasal polyposis using a magnetic resonance imaging (MRI) evaluation.

MATERIAL AND METHODS. In this retrospective study, 33 adult patients with bilateral chronic rhinosinusitis with nasal polyps (CRSwNP) (Group 1) and 30 healthy subjects without nasal polyps (Control, Group 2) were included. On coronal T2 weighted SPIR images of the MRI, the olfactory bulb (OB) volume and the olfactory sulcus (OS) depth were measured; the same action was performed on the axial T1 weighted images, for the corpus amygdala and insular gyrus areas.

RESULTS. OB volume, insular gyrus and corpus amygdala areas of the CRSwNP group were significantly lower than those in the control group ($p<0.05$). In the CRSwNP group, there were positive correlations between OB volumes, OS depths, and insular gyrus areas and corpus amygdala areas bilaterally ($p<0.05$). In females, bilateral insular gyrus areas decreased compared to the males ($p<0.05$). When polyp duration got longer, the right corpus amygdala area decreased ($p<0.05$). In older patients with a CRSwNP, the left corpus amygdala area decreased ($p<0.05$).

CONCLUSION. OB volume was found to be smaller in the CRSwNP group. We think that the OB volume has decreased primarily due to decreased transfer of odor particles (sensory input) related to nasal obstruction and inflammation in the presence of nasal polyps. After OB volume shrinkage, the insular gyrus and corpus amygdala areas shrink due to the decreased data transfer to the central odor system. In patients with nasal polyps, olfactory functions may improve after endoscopic sinus surgery.

KEYWORDS: CRSwNP, MRI, olfactory bulb volume, olfactory sulcus depth, insular gyrus area, corpus amygdala area.

INTRODUCTION

Chronic rhinosinusitis with nasal polyposis (CRSwNP) is a chronic inflammatory disease that clears approximately 4% of the population and its pathogenesis is not fully understood[1]. Among the known causes are asthma, allergy, infection, cystic fibrosis and aspirin sensitivity/intolerance. Compared to other causes of chronic rhinosinusitis, male patients, higher body mass index (BMI), smoking and asthma have been observed more in CRSwNP[2]. It is manifested by nasal congestion, anosmia, nasal drip and facial pain[1]. Treatment options are usually medical treatment and surgery.

CRSwNP constitutes 14-30% of conductive olfactory losses[2,3]. In the European Position Paper on Rhinosinusitis and Nasal Polyps 2020, "CRS with or without nasal polyps" in adults is defined as: "presence of two or more symptoms, one of which should be either nasal blockage/obstruction/congestion or nasal discharge (anterior/posterior nasal drip) ± facial pain/pressure ± reduction or loss of smell, for ≥12 weeks; with validation by telephone or interview"[4]. In case of a viral attack, purulent discharge and fever increases[4]. It is also stated that the loss of smell is one of the most severe symptoms in CRSwNP patients, the change in the sense of smell being present in about 60 percent of patients with this pathology[4].

The olfactory bulb (OB) has main role in sense of smell. OB volume is reduced in patients with infections, sinusitis and after trauma[5,6]. OB has such plasticity processes and when olfactory input is decreased, reduction in OB volume was observed. In animal models, it was observed that the volume of OB increases again when the input increases because of the neuroblasts that

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can migrate to the OB[7]. On the other hand, several studies have shown that OB volume changes in case of lack of nasopulmonary airflow[6,8].

Amygdala and insular gyrus are evaluated as cortical centers of smell in brain mapping studies[9-12].

Age and gender are important variables in smell sensitivity. Women are much more sensitive to the olfactory function, and the hormonal effect is discussed although the reason is not clear. Women suffer more from loss of smell due to olfactory sensitivity. With increasing age, olfactory neurons decrease, and olfactory ability decreases accordingly[13].

Magnetic resonance imaging (MRI) is one of the best imaging options to evaluate the brain functions; also, ideal to evaluate olfactory bulb volume and area of the corpus amygdala and insular gyrus[14,15].

We investigated CRSwNP related olfactory changes as measuring OB volume, olfactory sulcus (OS) depth, corpus amygdala and insular gyrus areas by cranial MRI.

MATERIAL AND METHODS

This is a retrospective study performed under the Declaration of Helsinki principles, using cranial MRI data of the Radiology Department, Medical Faculty, Kırıkkale University. The approval of the Kırıkkale University Non-Invasive Research Ethics Committee (Date: 20.03.2019, Number: 2019.02.16) was taken. There was no need to take an informed consent from patients because data evaluation was performed retrospectively.

Subjects

Cranial MRI images of 33 adult patients with bilateral CRSwNP (Group 1) were selected from our Hospital's PACS system as going to the past. There were 19 males and 14 females. All patients had stage 2 or 3 nasal polyps according to Lawson's classification[16], obstructing the nasal cavity roof. The mean ages of the Group 1 were 49.45 ± 10.73 years (age range from 30 to 84 years).

Group 2 (control group) consisted of 30 healthy subjects without nasal polyps (16 males, 14 females). Their cranial MRIs, taken for vertigo or headache, were all normal. Their mean ages were 48.90± 8.46 years (ranging from 36 to 65 years).

Exclusion criteria were as follows: patients with trauma history, tumors of the sinonasal or cranial region, marked facial deformities, prominent septal deformity, chronic cranial degenerative diseases such as multiple sclerosis, Parkinson, etc.

Previous viral infection history was not present for our patients, which is the limitation of our study.

Cranial MRI measurements

1.5 Tesla MRI (Philips MRI Systems, Achieva Release 3.2 Level 2013-10-21, Philips Medical Systems Nederland B.V.) with the cranial coil was used. For the axial plane, T1-weighted images were obtained (TR msn/TE msn; 596/15, FOV 230 x 183 mm and matrix 256x205 mm), while for the coronal plane, T2-weighted images were used (TR msn/TE msn; 6557/100, FOV 220×175 mm and matrix 224×165 mm). Slice thickness was 5 mm, intersection gap was 1 mm. Coronal sections of 25-30 were obtained. All measurements were evaluated by a single radiologist (M.I.).

Peripheral regions of smell

The OB volume (mm^3) was measured at SPIR sequence of coronal T2-weighted images[17-19] (Figure 1).

For the OS depth (mm) the measurement was performed in the SPIR sequence of coronal T2-weighted images (Figure 2). For the measurement, a virtual tangent line was drawn from the inferior orbital gyrus to the gyrus recti in the posterior plane of the orbit. A new perpendicular line was then drawn from this tangent line to the deepest point of the OS. The depth of this line denoted

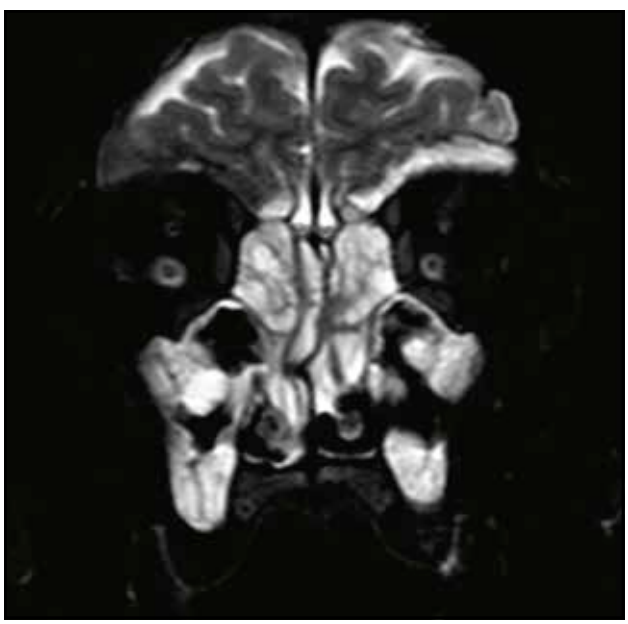


Figure 1. Cranial MRI, coronal T2-weighted image, CRSwNP group: olfactory bulb areas measured at the maximum section.

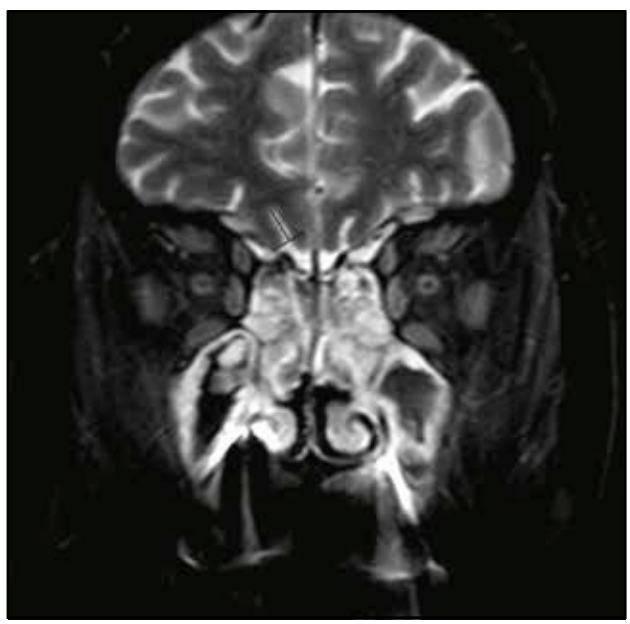


Figure 2. Cranial MRI, coronal T2-weighted image, CRSwNP group: olfactory sulcus depth measured at the maximum section.

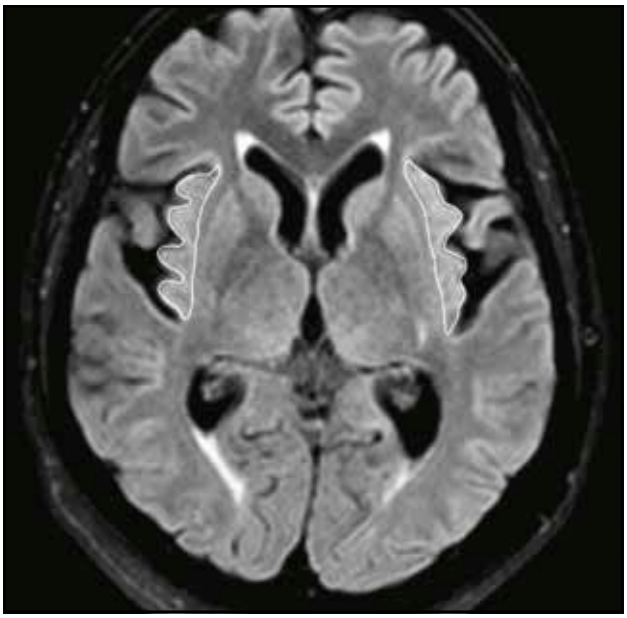


Figure 3. Cranial MRI, axial T2-FLAIR sequence, CRSwNP group: bilateral insular gyrus area measured in the sections in which the head of the caudate nucleus and the putamen are seen; the insular gyrus is observed as maximum.

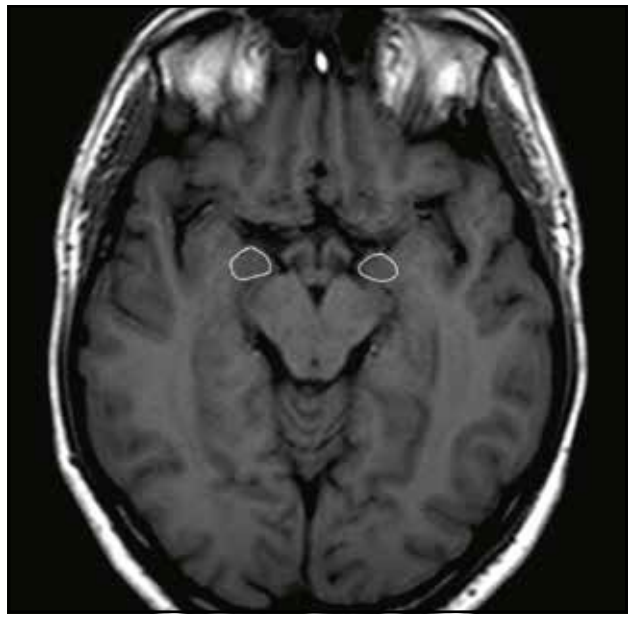


Figure 4. Cranial MRI, axial T1-weighted, CRSwNP group: bilateral corpus amygdala areas measured in images in which they were maximum observed.

Table 1. Measurement results for the evaluated parameters (olfactory bulb volume, olfactory sulcus depth, corpus amygdala area, insular gyrus area).

		Group 1 (CRSwNP group) (n=33)			Group 2 (Control group) (n=30)			P*
		Mean	Median	Std.Dev.	-0.015	-0.028	-0.010	
Age		49.45	50.00	10.73	0.836	0.708	0.889	0.822
Measurements results								
Olfactory bulb (OB) volume (mm^3)	**R**	12.83	10.50	8.73	23.20	21.75	9.55	0.000
	L	13.04	10.50	9.68	24.65	25.00	10.11	0.000
	P**		0.803			0.321		
Olfactory sulcus (OS) depth (mm)	**R**	7.51	7.50	0.75	7.81	7.80	0.74	0.120
	L	7.13	7.00	0.77	7.24	7.40	0.96	0.598
	P**		0.004			0.001		
Insular gyrus area (mm^2)	**R**	246.21	240.00	37.63	272.80	274.00	35.87	0.006
	L	240.06	236.00	38.15	269.73	270.50	39.03	0.003
	P**		0.191			0.191		
Corpus amygdala area (mm^2)	**R**	93.54	97.00	20.37	117.00	118.50	20.94	0.000
	L	88.45	88.00	20.31	110.36	114.00	19.04	0.000
	P**		0.005			0.026		

*p -value shows the Independent samples t-test; **p-value shows the results of Paired samples t-test

the OS depth, which was recorded in millimeters[17-19].

Central regions of the smell

At axial T1-weighted images, the insular gyrus area (mm^2) was measured in the sections in which it was observed as maximum (Figure 3). We performed the measurements on the images where the putamen and caudate nucleus head were seen[20,21].

At axial T1-weighted images, the corpus amygdala area (mm^2) was measured in the sections in which it was observed as maximum[20,21] (Figure 4).

Statistical Analysis

The statistical analysis was performed using the SPSS for Windows 16.0 (SPSS, INC, an IBM Company, Chicago, Illinois). Paired samples t-test, Chi-square test, independent samples t-test, Spearman's correlation rho efficient test and Pearson correlation test were used.

A p-value < 0.05 was considered as statistically significant.

RESULTS

There were 19 males (57.6%) and 14 females (42.4%) in Group 1, 16 males (53.3%) and 14 females in Group 2 (46.7%) (p=0.735, $\chi 2$=0.115). No difference was found between two group's ages (p=0.822) (Table 1).

Polyp duration

In the CRSwNP group (Group 1), the nasal polyp duration was 7.2±3.1 years (ranged from 2.0 to 13.0 years).

Olfactory bulb volume

OB volume of the Group 1 (CRSwNP group) was significantly lower than those in the control group bilaterally (p<0.05) (Table 1).

Olfactory sulcus depth

No difference was found between two group's OS depths (p>0.05) (Table 1). In each of the Groups 1 and 2, right OS depth was significantly higher than the one on the left side (p<0.05), as can be seen in Table 1.

Insular gyrus area

Group 1's (CRSwNP group) insular gyrus area was significantly lower than those in Group 2 (the control group) bilaterally (p<0.05) (Table 1).

Corpus amygdala area

Analysing the corpus amygdala area, one can observe that those of Group 1 (CRSwNP group) were significantly lower than those in Group 2 (the control group) bilaterally (p<0.05) (Table 1). In each of the Groups 1 and 2 separately, the right corpus amygdala area was significantly higher than the one on the left side (p<0.05) (Table 1).

Correlation test results in Group 1

Positive correlations were detected between all measurements (bilateral OS depths, OB volumes, insular gyrus areas and corpus amygdala areas) (p<0.05) (Table 2). The same observation was made between the left corpus amygdala area and the right insular gyrus area (p<0.05), as one can see in Table 2.

As the patients age, in older patients with a CRSwNP, the left corpus amygdala area got lower (p<0.05) (Table 2). There was also a difference between genders. In females, bilateral insular gyrus areas decreased compared to males (p<0.05) (Table 2).

As CRSwNP duration got longer, the right corpus amygdala area decreased (p<0.05) (Table 2).

DISCUSSIONS

Nasal polyps originate from the mucosa of the nasal cavity or from the mucosa of the paranasal sinuses. They have an uncertain etiology and their recurrence characteristic makes nasal polyposis a difficult to cure disease. The follow-up after diagnosis and treatment is a long process for the otolaryngologists. Also, it is an important disease for the respiratory system, its effects on chronic obstructive pulmonary diseases and asthma being well known.

Litvack et al. reported that in 61-83% of patients with chronic rhinosinusitis, odor dysfunction was reported, while the highest odor dysfunction occurred in patients with nasal polyposis[22]. Our results showed that OB volume, insular gyrus and corpus amygdala areas of the CRSwNP group were significantly lower compared to those in the control group, whereas no significant differences between OS depth values in both groups were noted.

Veyseller and his colleagues have reported decreased OB volume in total laryngectomy patients. This study shows that the lack of nasal airflow and the lack of afferent conduction affected OB volume[6].

Our study used MRI imaging to show a reduction in OB volume and central smell regions in patients with CRSwNP as compared with healthy controls. Previous studies with rodents showed that smell deficiency caused OB volume reduction. At the same time, the lack of nasal airflow and the lack of afferent conduction reaching OB has been shown to cause cell loss in OB[23,24]. In Herzallah and his colleagues' MRI study[25], there is a significant difference between the nasal polyp group and control group on OB volume. In our study, we found similar results in OB volume measurement in CRSwNP patients.

Previous neuroanatomy studies show that the amygdala is relevant for olfactory memory and smell definition. Bunchanan et al. reported that odor–name matching and odor recognition memory were impaired severely related to damage of the amygdala bilaterally[11].

In our CRSwNP group, positive correlations were detected between all measurements (bilateral OS depths, OB volumes, insular gyrus areas and corpus amygdala areas). In females, bilateral insular gyrus areas decreased compared to the males. Previous studies showed that olfactory dysfunction affected women more severely. In women, decreased of olfactory function caused more complaints than men. We think that these views support our result[13,26].

Age is a significant factor of effective olfactory capacity and OB volume, so control and study groups were standardized in our study. In Group 1, nasal polyp duration was 7.2±3.1 years (ranged from 2.0 to 13.0 years). In the present study, when polyp duration got longer, the right corpus amygdala area decreased. In older patients with a CRSwNP, left corpus amygdala area decreased. Our results showed that older age and longer polyp duration affected central smell region of the corpus amygdala.

Table 2. Correlation test results in Group 1 (CRSwNP group).

			OB volume (mm3)		OS depth (mm)		Insular gyrus area (mm2)		Corpus amygdala area (mm2)	
			R	L	R	L	R	L	R	L**
OB volume (mm^3)	R	r		0.866	0.120	0.233	0.047	0.143	0.185	0.153
		P*		0.000	0.505	0.192	0.796	0.428	0.302	0.394
	L	r	0.866		0.243	0.307	0.138	0.206	0.162	0.141
		P*	0.000		0.173	0.083	0.444	0.251	0.367	0.433
OS Depth (mm)	R	r	0.120	0.243		0.577	0.082	-0.071	-0.094	-0.121
		P*	0.505	0.173		0.000	0.652	0.694	0.604	0.501
	L	r	0.233	0.307	0.577		0.088	0.254	0.177	0.125
		P*	0.192	0.083	0.000		0.627	0.155	0.323	0.489
Insular gyrus area (mm^2)	R	r	0.047	0.138	0.082	0.088		0.756	0.258	0.357
		P*	0.796	0.444	0.652	0.627		0.000	0.147	0.041
	L	r	0.143	0.206	-0.071	0.254	0.756		0.294	0.335
		P*	0.428	0.251	0.694	0.155	0.000		0.096	0.057
Corpus amygdala area (mm^2)	R	r	0.185	0.162	-0.094	0.177	0.258	0.294		0.885
		P*	0.302	0.367	0.604	0.323	0.147	0.096		0.000
	L	r	0.153	0.141	-0.121	0.125	0.357	0.335	0.885	
		P*	0.394	0.433	0.501	0.489	0.041	0.057	0.000	
Age		r	-0.145	-0.207	-0.134	0.044	-0.097	-0.010	-0.326	-0.377
		P*	0.419	0.247	0.458	0.810	0.592	0.957	0.064	0.030
Gender (Code 1: Male, Code 2: Female)		r	-0.265	-0.225	-0.123	-0.329	-0.473	-0.589	-0.309	-0.193
		P**	0.137	0.207	0.496	0.061	0.005	0.000	0.080	0.281
Polyp duration		r	-0.335	-0.282	-0.065	-0.233	-0.016	-0.304	-0.353	-0.217
		P*	0.057	0.112	0.720	0.192	0.930	0.086	0.044	0.224

*P-value shows the results of the Pearson correlation test; **P-value shows the results of Spearman's correlation rho efficient test; OB: Olfactory bulb, OS: Olfactory sulcus.

The main cause of odor disorders in patients is "nasal polyps and airway obstruction", that block the airway that comes into contact with "odor-sensitive receptors". Another less likely cause is the injury of the olfactory system due to microbial toxins. Therefore, the removal of polyps and emptying of the sinuses and controlling infections usually increase the sense of smell[27,28]. Schriver et al.[29] reported that the olfactory function improved significantly 3.5 months after rhino-sinusal surgery and that the olfactory recovery was not noticed within 12 months. However, after 3.5 and 12 months, olfactory recovery was reported in "19% and 17% of patients, respectively"[29].

OB forms the main center between the peripheral and central olfactory tracts. Data from peripheral neurons are transmitted to the central nervous system via OB. The most known centers in the central nervous system are insular gyrus and amygdala[10,11].

CONCLUSIONS

Rombaux et al.[30] found that sinonasal diseases and inflammation causes decreased sensory input and OB volume decreased consequently. In our study, OB volume was found to be smaller in the CRSwNP group. We think that the OB volume has decreased primarily due to decreased transfer of odor particles (sensory input) related to nasal obstruction and inflammation in the presence of nasal polyps. In patients with CRS with nasal polyposis, toxicity of mediators related to inflammatory process and the localization of polyp tissue near the olfactory cleft may also increase olfactory disorders. After OB volume shrinkage, the insular gyrus and corpus amygdala areas shrink due to the decreased data transfer to the central odor system.

In patients with nasal polyps, olfactory functions may improve

after endoscopic sinus surgery.

Conflict of interest: The author Ziya SENCAN declares that he has no conflict of interest. The author Nuray BAYAR MULUK declares that she has no conflict of interest. The author Mikail INAL declares that he has no conflict of interest. The author Selmin Perihan KOMURCU ERKMEN declares that she has no conflict of interest. The author Ela COMERT declares that she has no conflict of interest.

Ethics committee approval: This study is retrospective. Ethics committee approval was obtained from Kırıkkale University Non-invasive Research Ethics Committee (Date: 20.03.2019, Number: 2019.02.16).

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REFERENCES

1. Newton JR, Ah-See KW. A review of nasal polyposis. Ther Clin Risk Manag. 2008;4(2):507-12. DOI: 10.2147/tcrm.s2379.
2. Raviv JR, Kern RC. Chronic sinusitis and olfactory dysfunction. Otolaryngol Clin North Am. 2004;37(6):1143-57, v-vi. DOI: 10.1016/j.otc.2004.06.003.
3. Seiden AM, Duncan HJ. The diagnosis of a conductive olfactory loss. Laryngoscope. 2001;111(1):9-14. DOI: 10.1097/00005537-200101000-00002.
4. Fokkens WJ, Lund VJ, Hopkins C, Hellings PW, Kern R, Reitsma S, et al. European Position Paper on Rhinosinusitis and Nasal Polyps 2020. Rhinology. 2020;58(Suppl S29):1-464.
5. Mueller A, Rodewald A, Reden J, Gerber J, von Kummer R, Hummel T. Reduced olfactory bulb volume in post-traumatic and post-infectious olfactory dysfunction. Neuroreport. 2005;16(5):475-8. DOI: 10.1097/00001756-200504040-00011.
6. Veyseller B, Aksoy F, Yildirim YS, Bayraktar FGI, Gurbuz D, Savas Y, et al. Reduced olfactory bulb volume in total laryngectomy patients: a magnetic resonance imaging study. Rhinology. 2011;49(1):112-6. DOI: 10.4193/Rhino10.001.
7. Boesveldt S, Postma EM, Boak D, Welge-Luessen A, Schopf V, Mainland JD, et al. Anosmia-A clinical review. Chem Senses. 2017;42(7):513-23. DOI: 10.1093.chemse/bjx025.
8. Veyseller B, Ozucer B, Aksoy F, Yildirim YS, Gurbuz D, Balikci HH, et al. Reduced olfactory bulb volume and diminished olfactory function in total laryngectomy patients: a prospective longitudinal study. Am J Rhinol Allergy. 2012;26(3):191-3. DOI: 10.2500/ajra.2012.26.3768.
9. Huart C, Rombaux P, Hummel T. Plasticity of the human olfactory system: the olfactory bulb. Molecules. 2013;18(9):11586-600. DOI: 10.3390/molecules180911586.
10. Stephani C, Fernandez-Baca Vaca G, Maciunas R, Koubeissi M, Lüders HO. Functional neuroanatomy of the insular lobe. Brain Struct Funct. 2011;216(2):137-49. DOI: 10.1007/s00429-010-0296-3.
11. Buchanan TW, Tranel D, Adolphs R. A specific role for the human amygdala in olfactory memory. Learn Mem. 2003;10(5):319-25. DOI: 10.1101/lm.62303.
12. Yao L, Yi X, Pinto JM, Yuan X, Guo Y, Liu Y, et al. Olfactory cortex and Olfactory bulb volume alterations in patients with post-infectious Olfactory loss. Brain Imaging Behav. 2018;12(5):1355-62. DOI: 10.1007/s11682-017-9807-7.
13. Hummel T, Landis BN, Huttenbrink KB. Smell and taste disorders. GMS Curr Top Otorhinolaryngol Head Neck Surg 2011;10:Doc04. DOI: 10.3205/cto000077.
14. Hummel T, Smitka M, Puschmann S, Gerber JC, Schaal B, Buschhuter D. Correlation between olfactory bulb volume and olfactory function in children and adolescents. Exp Brain Res. 2011;214(2):285-91. DOI: 10.1007/s00221-011-2832-7.
15. Haehner A, Rodewald A, Gerber JC, Hummel T. Correlation of olfactory function with changes in the volume of the human olfactory bulb. Arch Otolaryngol Head Neck Surg. 2008;134(6):621-4. DOI: 10.1001/archotol.134.6.621.
16. Lawson W. The ıntranasal ethmoidectomy: an experience with 1,077 procedures. Laryngoscope. 1991;101(4 Pt 1):367-71. DOI: 10.1002/lary.1991.101.4.367.
17. Kandemir S, Muluk NB, Melikoglu B, Dag E, Inal M, Sarin O. Smell functions in patients with multiple sclerosis: a prospective case-control study. B-ENT. 2016;12(4):323-31.
18. Duprez TP, Rombaux P. Imaging the olfactory tract (cranial nerve #1). Eur J Radiol. 2010;74(2):288-98. DOI: 10.1016/j.ejrad.2009.05.065.
19. Buschhüter D, Smitka M, Puschmann S, Gerber JC, Witt M, Abolmaali ND, et al. Correlation between olfactory bulb volume and olfactory function. Neuroimage. 2008;42(2):498-502. DOI: 10.1016/j.neuroimage.2008.05.004.
20. Hastings RS, Parsey RV, Oquendo MA, Arango V, Mann JJ. Volumetric analysis of the prefrontal cortex, amygdala, and hippocampus in major depression. Neuropsychopharmacology. 2004;29(5):952-9. DOI: 10.1038/sj.npp.1300371.
21. Rombaux P, Duprez T, Hummel T. Olfactory bulb volume in the clinical assessment of olfactory dysfunction. Rhinology. 2009;47(1):3-9.
22. Litvack JR, Mace JC, Smith TL. Olfactory function and disease severity in chronic rhinosinusitis. Am J Rhinol Allergy. 2009;23(2):139-44. DOI: 10.2500/ajra.2009.23.3286.
23. Cummings DM, Knab BR, Brunjes PC. Effects of unilateral olfactory deprivation in the developing opossum, Monodelphis domestica. J Neurobiol. 1997;33(4):429-38.
24. Mandairon N, Sacquet J, Jourdan F, Didier A. Long-term fate and distribution of newborn cells in the adult mouse olfactory bulb: influences of olfactory deprivation. Neuroscience. 2006;141(1):443-51. DOI: 10.1016/j.neuroscience.2006.03.066.
25. Herzallah IR, Askar SM, Amer HS, Ahmed AF, El-Anwar MW, Eesa MH. Olfactory bulb volume changes in patients with sinonasal polyposis: a magnetic resonance imaging study. Otolaryngol Head Neck Surg. 2013;148(4):689-93. DOI: 10.1177/0194599813477606.
26. Frasnelli J, Hummel T. Olfactory dysfunction and daily life. Eur Arch Otorhinolaryngol. 2005;262(3):231-5. DOI: 10.1007/s00405-004-0796-y.
27. Stevens MH. Steroid-dependent anosmia. Laryngoscope. 2001;111(2):200-3. DOI: 10.1097/00005537-200102000-00002.
28. Kern RC. Candidate's Thesis: chronic sinusitis and anosmia: pathologic changes in the olfactory mucosa. Laryngoscope. 2000;110(7):1071-77. DOI: 10.1097/00005537-200007000-00001.
29. Schriever V, Gupta N, Pade J, Szewczynska M, Hummel T. Olfactory function following nasal surgery: a 1-year follow-up. Eur Arch Otorhinolaryngology. 2013;270(1):107-11. DOI: 10.1007/s00405-012-1972-0.
30. Rombaux P, Potier H, Bertrand B, Duprez T, Hummel T. Olfactory bulb volume in patients with sinonasal disease. Am J Rhinol. 2008;22(6):598-601. DOI: 10.2500/ajr.2008.22.3237.

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