Lateralized Differences in Olfactory Function and Olfactory Bulb Volume Relate to Nasal Septum Deviation

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Abstract: One of the most common reasons for partial nasal obstruction is nasal septal deviation (NSD). The effect of a partial lateralized nasal obstruction on olfactory bulb (OB) volume remains unclear. Thus, the aim of this study was to investigate the side differences in olfactory function and OB in patients with serious NSD. Sixty-five volunteers were included: 22 patients with serious right NSD and 43 patients with left NSD. The patients' mean age was 22 years. All participants received volumetric magnetic resonance imaging scans of the entire brain and detailed lateralized olfactory tests. The majority of the patients exhibited an overall decreased olfactory function (as judged for the better nostril: functional anosmia in 3%, hyposmia in 72%, normosmia in 25%), which seems to be mostly due to the overall severe changes in nasal anatomy. As expected, olfactory function was significantly lower at the narrower side as indicated for odor thresholds, odor discrimination, and odor identification ($P \leq 0.005$). When correlating relative scores and volumes (wider minus narrower side), a significantly positive correlation between the relative measures emerged for OB volume and odor identification, odor discrimination, and odor thresholds. Our study clearly highlights that septal deviation results in decreased olfactory function at the narrower side.

Key Words: Olfactory bulb, nasal septal deviation, olfaction, magnetic resonance imaging, psychophysiology

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It is well known that the olfactory bulb (OB) plays a central role in the processing of olfactory information. Odorants enter the nose and stimulate neuroepithelial receptor cells located in the upper third of the nasal cavity. The axons of these olfactory receptor cells coalesce into bundles that pass through the cribriform plate to synapse with glomeruli of the OB. The connections from the OB to central locations into the brain are numerous and widely distributed: they include the piriform cortex, the entorhinal cortex, the orbitofrontal cortex, the anterior olfactory nucleus, the periamygdaloid-hippocampal region, and the hypothalamus. There are numerous other tertiary connections to the limbic and autonomic systems in the brain. Olfactory bulbs are paired and of round/oval shape that occupy the most anterior portion of the skull base.[1] Experimental animal studies show that one of the most pronounced effects of bilateral olfactory deprivation is the reduction of OB size.[2,3]

The OB volume measured by planimetric manual contouring on magnetic resonance imaging (MRI) was recently demonstrated to be a reliable measure of olfactory function.[4,5] Actually, several studies have shown that OB volume is reduced in patients with postinfectious and posttraumatic olfactory loss.[6–9] Furthermore, OB volume reduction has been reported in postlaryngectomy patients, possibly because of lack of nasal airflow.[10,11] Moreover, OB volume changes have been demonstrated in different neurological diseases.[12,13] The effect of a partial lateralized olfactory block on OB volume remains, however, unclear. One of the most common reasons for partial obstruction is nasal septal deviation (NSD). The aim of this study was to investigate the side differences in olfactory function and OB in patients with serious NSD.

MATERIALS AND METHODS

Volunteers and Study Design

We conducted a cross-sectional study, including 65 male volunteers with serious NSD at the Otorhinolaryngology Department, Gülhane Military Medical Academy (GATA) Haydarpaşa Training Hospital and Istanbul Surgery Hospital. All investigations were performed in accordance with the Declaration of Helsinki on biomedical studies involving human subjects. The study was approved by the local institutional review board (10.05.13-83045809/11280). Informed consent was obtained from all study subjects who were recruited at the outpatient clinic after explanation of the research purpose. The severity of deviation was determined after full shrinkage of nasal cavity with 0.25% phenylephrine spray. Deviation touching the lateral nasal wall after the phenylephrine application was accepted as serious NSD. Twenty-two of 65 volunteers had serious NSD to the right, and 43 had serious NSD to the left. All participants had received volumetric MRI scans of the entire brain and detailed lateralized olfactory tests, and the lateralized olfactory tests and OB volume measurements were grouped according to the width of the nasal passages. Narrow nasal passage measurements were compared with the measurements of the wide side.

Olfactory Testing

Psychophysical testing of olfactory function was performed with the validated "Sniffin' Sticks" test. Odorants were presented in commercially available felt-tip pens (Burghart GmbH, Wedel, Germany).[14,15] Olfactory testing comprised 3 tests, namely, tests for odor threshold (testing by means of a single-staircase procedure), odor discrimination (3-alternative forced choice), and odor identification (4-alternative forced choice). For odor presentation, the pen's cap was removed by the experimenter for approximately 3 seconds, and the tip of the pen was placed approximately 1 to 2 cm in front of 1 nostril, whereas the other nostril was closed by a tape. Instead of liquid dye, the tampon of the pens for threshold testing was filled with phenyl ethyl alcohol (a rose-like odor) diluted in propylene glycol (dilution ratio 1:2, starting from 4%). Odors were presented in a total of 16 triplets of pens, 1 containing diluted phenyl ethyl alcohol and 2 containing only propylene glycol serving as blanks. The interval between presentations of individual pens of a triplet was approximately 3 seconds, and presentation of the triplets to a subject occurred every 20 seconds. Using a 3-alternative, temporal forced-choice paradigm, the subjects had to identify the pen that contained the odorant. Subjects were blindfolded to prevent visual identification of the odor-containing pens. Thresholds were determined using a single-staircase technique. In the present 3-alternative, temporal forced-choice paradigm, 2 successive correct identifications of the pen containing the odor or 1 incorrect identification triggered a reversal of the staircase to the next higher or the next lower dilution step, respectively. Seven reversals had to be obtained. The odor thresholds were determined as the mean of the last 4 staircase reversals. Assessment of odor threshold was followed by a test of odor discrimination.[14] For odor discrimination, 16 triplets of pens were presented, with 2 containing the same odorant and 1 containing the target odorant. The subjects' task was to identify the sample that had a different smell. To prevent visual detection of the target pen, subjects were blindfolded with a sleeping mask. Subjects were only once allowed to sample the odor. Presentation of triplets was separated by at least 30 seconds. The test result was a sum score of correctly identified pens. In a final step, a test of odor identification was performed to completely assess the subject's objective function.[14] Odor identification was assessed by means of 16 common odors. Using a multiple forced-choice paradigm, identification of individual odors was performed from a list of 4 verbal descriptors each. Each odorant was presented by the experimenter, and there was an interval of at least 30 seconds to prevent olfactory desensitization.[14] Subjects were free to sample the odors as often as necessary to make a decision. The test result was a sum score of the correctly identified odors. Results from olfactory testing can be analyzed separately from each other. Overall olfactory function is expressed as the sum of the scores from the 3 individual tests.[16]

Magnetic Resonance Imaging

All examinations were performed at a 1.5-T MRI system (Avanto; Siemens, Erlangen, Germany) using a 12-channel head coil. Sections were angulated perpendicular to the anterior base of the skull or cribriform plate. We used three-dimensional T2 STIR (short-term inversion recovery) SPACE covering the anterior and middle segments of the base of the skull. Parameters of the three-dimensional T2 STIR SPACE sequence were as follows: echo time: 224 milliseconds, repetition time: 1440 milliseconds, bandwidth: 350 Hz/pixel, field of view: 190 × 190, matrix: 520 × 512, slice thickness: 1 mm, interslice gap: 0. Syngo MMWP software (Siemens, Berlin, Germany) was used to determine the volume of the right and left OBs. The volumetric measurement has previously been described in great detail.[17] In the current study, we used the same anatomical landmarks. Volume measurements were performed by an experienced radiologist blinded to the clinical diagnosis. Before volumetric measurement, a midsagittal image of the OB was chosen, and the length of both OBs was measured. Then, measurements of the right and left OB volumes were performed by the manual segmentation of the coronal slices by planimetric manual contouring (surface in pixels), then all pixels were added and multiplied by x, y, and z axis ($0.36 \times 0.37 \times 1$ number of pixels) to obtain a volume in mm^3 (Fig. 1).

Statistical Analysis

Data were analyzed by means of SPSS 21.0 (SPSS Inc, Chicago, IL). Mann-Whitney U test, Wilcoxon signed rank test, and t tests were used wherever appropriate. The level of significance was set at 0.05.

RESULTS

This study was carried out in 65 male volunteers, between the ages of 21 and 23 years. The mean age of the patients was 21.9 ± 0.9 years. The majority of the patients exhibited an overall decreased olfactory function, as judged for the thresholds for odor discrimination and identification score obtained in the wider nostril: functional anosmia in 3%, hyposmia in 72%, and normosmia in 25%, which appeared to be mostly due to the severe overall changes in nasal anatomy. Descriptive statistics of the results from olfactory testing and measurement of OB volume are shown in Table 1.

Olfactory function was significantly lower at the narrower side as indicated for odor thresholds, odor discrimination, and odor identification ($P \leq 0.005$). Furthermore, OB volumes were found to be larger on the wider side than of the narrower side ($P < 0.01$). When correlating relative scores and volumes (wider minus narrower side), a significantly positive correlation between the relative measures

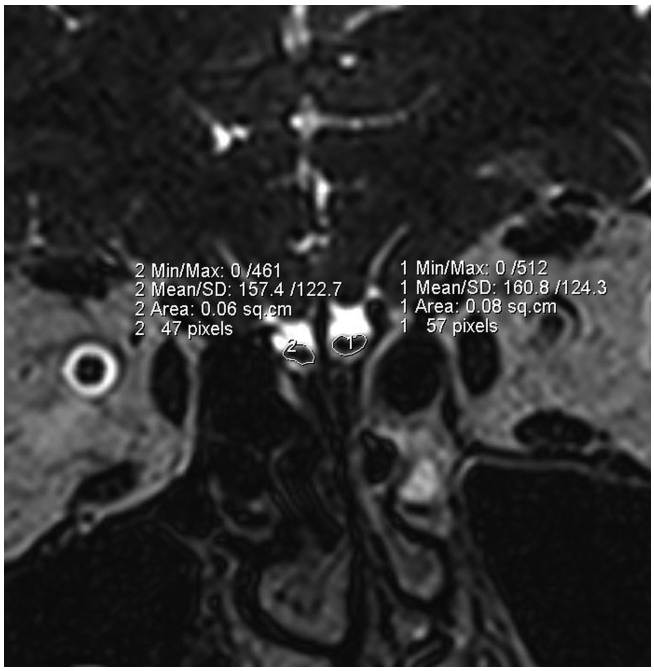

FIGURE 1. Measurement of the OB volume by planimetric manual contouring in a patient on coronal three-dimensional T2 STIR (short tau inversion recovery) SPACE (sampling perfection with application optimized contrasts using different flip angle evolution) image.

TABLE 1. Descriptive Statistics of Results From Olfactory Testing and Measurements of OB Volume (n = 65)

Variable		Mean	SD	*P*
Odor threshold score	Narrow side	6.07	3.5	<0.001
	Wide side	7.75	1.7	
Odor discrimination score	Narrow side	10.7	2.01	<0.001
	Wide side	11.9	1.5	
Odor identification score	Narrow side	6.42	3.51	<0.001
	Wide side	8.75	2.43	
TDI score	Narrow side	23.2	6.61	<0.001
	Wide side	27.1	4.74	
OB volume, mm^3	Narrow side	36.9	10.9	0.01
	Wide side	43.6	10.8	

TDI: composite score of "Sniffin' Sticks" olfactory subtests, namely threshold, discrimination, identification

emerged for OB volume and odor identification, odor discrimination, and odor thresholds ($P < 0.05$).

DISCUSSION

The current investigation produced 2 major findings: (1) as expected, olfactory function was decreased at the narrower side of the nose compared with the wider side[18]; and (2) there were significantly positive correlations between the relative measures for OB volume and odor identification, odor discrimination, and odor thresholds, indicating that OB volumes were larger for the wider side.

Olfactory bulb size has been studied in patients with post-traumatic and postinfectious olfactory deficits, congenital anosmia, and neurodegenerative diseases and in subjects with a normal sense of smell.[6–8,19–23] These cross-sectional studies indicate that (1) OB volume seems to change in parallel to smell function, (2) OB volume decreases with duration of olfactory loss, and (3) patients with parosmia present with smaller OBs compared with those without.

The change of the OB volume may depend on numerous factors, for example, (1) continuous neuronal supply from the subventricular zone (SVZ), where neuroblasts migrate along the rostral migratory stream and replace interneurons (periglomerular cells and granular cells) in the OB[24]; (2) continuous synaptogenesis that occurs mainly between incoming axonal projections of olfactory receptor neurons and dendrites of mitral/tufted cells at the glomerular level.[25] By maintaining a continuous neurogenesis sensitive to environmental influences, this "neuronal recruitment" may lead to a change of the OB volume and to an improvement in sensory abilities.[26] In a recent study including human brain specimens, ranging in age from birth to 84 years, about SVZ and its potential of containing immature neurons, it was shown that the region of SVZ around the anterior lateral ventricules was highly active, producing many tangentially migrating immature neurons. Based on the presence of a rostral migratory stream containing chains of immature neurons, they concluded that at least some of these progenies were destined for the OB, but were largely limited to early childhood.[27] However, whether there is neurogenesis in the human OB is currently a matter of debate.[28]

The average OB volume (40.2 mm^3) in our study group was found lower than that previously reported (69.5 mm^3 for males) in a larger study group conducted on 125 healthy individuals.[9] Also the majority of the patients were hyposmic according to the Sniffin' Sticks olfactory testing. This might be explained by the severe nasal changes in nasal anatomy. One of the reasons for serious NSD was head and face trauma, and this was also an important reason for decreased olfactory functions.

In the current study, a significantly positive correlation between the relative measures emerged for the OB volume and odor identification, odor discrimination, and odor thresholds. These present findings appear to be similar to what has been shown before in humans. In a recent study, it has been shown that side differences in olfactory function in normosmic subjects are reflected in lateralized differences in OB volume.[29] Here, it seemed to be the rule that OB volume is positively related to olfactory function.[2,29,30]

On the other hand, the effect of septoplasty operation on the OB volume and olfactory functions remains to be answered. Thus, more research is needed to further investigate the currently observed differences of OB volumes in relation to septal deviation and its surgical treatment.

CONCLUSIONS

Our study confirms that septal deviation results in decreased olfactory function at the narrower side. Also, OB volumes were the larger for the wider side, and there were positive correlations between OB volumes and olfactory functions.

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