The Laryngoscope
Lippincott Williams & Wilkins, Inc.
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Retronasal and Orthonasal Olfactory Function in Relation to Olfactory Bulb Volume in Patients With Posttraumatic Loss of Smell

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Objective: **The aims of this study were to evaluate olfactory function with orthonasal and retronasal testing in patients with posttraumatic olfactory loss and to investigate the relation between residual olfactory function and olfactory bulb (OB) volume.** ***Method:*** **A retrospective study of 25 patients with posttraumatic olfactory loss was performed. Orthonasal olfactory function was assessed with the Sniffin' Sticks test kit; retronasal olfactory function was assessed with intraorally applied odors. Magnetic resonance imaging was used to determine OB volume and cortical damage in the frontal and temporal areas.** ***Results:*** **The main outcomes of the present study were the demonstration of a correlation between olfactory function and OB volume, which was more pronounced for retronasal than for orthonasal olfactory function; retronasal olfactory function was most affected in the patients with the most extensive cerebral damage and was least compromised in patients without such damage; OB volumes were smaller in patients with parosmia compared with those without; and the presence of parosmia was clearly associated with the presence of cerebral damage.** ***Conclusion:*** **The data confirm that OB volume is an indicator of olfactory function but, interestingly, in this study, it is largely determined by retronasal olfactory sensitivity. In addition, these results emphasize the role of higher cortical centers in olfactory function, and especially in parosmia, which may, at least in some cases, be related to lesions in the fronto-orbital and anterior temporal cortices. It would be of interest to investigate OB volume further in relation to the prognosis of the disorder.** ***Key Words:*** **Smell, olfaction, magnetic resonance imaging, posttraumatic olfactory disorder.**

Laryngoscope, **116:901–905, 2006**

INTRODUCTION

Olfactory loss is a frequent sequela of traumatic head injury. Incidence of olfactory disorder after trauma is difficult to estimate because posttraumatic patients often experience other severe complaints and do not become aware of this particular sensorineural deficit until some time after the injury. Current explanations about posttraumatic olfactory disorders include a lesion and/or tearing of the fila olfactoria on their way through the cribriform plate and contusion and/or hemorrhage in the central olfactory pathways such as the olfactory bulb (OB), the olfactory tracts, the orbitofrontal cortex, the frontal lobe (gyrus rectus), or the anteroinferior part of the temporal lobe.[1] Olfactory loss is related to the severity of the trauma. Minor trauma, however, can lead to severe olfactory loss. Patients usually report anosmia rather than hyposmia. Like in postinfectious olfactory loss, patients may develop parosmia and/or phantosmia.[2]

Recovery from smell disorders is observed in approximately 20% to 30% of patients, with some patients experiencing partial recovery of their olfactory abilities even after several years have elapsed.[1,3] Primary mechanisms leading to this recovery are related to the regeneration of olfactory receptor neurons.[3] In addition, the OB maintains continuing synaptogenesis throughout life, which contributes to the plasticity of the sense of smell.[4–6]

The aim of this study was to investigate whether OB volume may be related to the residual olfactory function assessed with orthonasal and retronasal olfactory testing in patients with posttraumatic olfactory loss.

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Editor's Note: This Manuscript was accepted for publication January 31, 2006.

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DOI: 10.1097/01.mlg.0000217533.60311.e7

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MATERIALS AND METHODS

Subjects

This study was conducted at the Department of Otorhinolaryngology of the Saint Luc University Hospital in Brussels between January 2004 and July 2005. Patients with posttraumatic olfactory loss had an otorhinolaryngologic investigation, including nasal endoscopy, had a detailed interview with an experienced otorhinolaryngologist, went through psychophysical tests of olfactory function assessed both for the orthonasal (olfactory perception during sniffing) and retronasal routes (olfactory perception during eating, drinking), and had magnetic resonance imaging of the brain. The diagnostic criteria for posttraumatic olfactory loss included 1) a history of olfactory disorder after head injury, 2) patency of the olfactory cleft at endoscopic examination, 3) evidence of olfactory dysfunction, and 4) exclusion of others causes of olfactory disorders such as sinonasal disease.[1] The duration between head injury and clinical evaluation was recorded. Specific questions about the presence of parosmia or phantosmia were also asked. Parosmia was defined as the perception of distorted odors in the presence of an odor source.[7]

Psychophysical Testing of Olfactory Performance

Orthonasal Testing. Psychophysical testing of olfactory function was performed with the validated Sniffin' Sticks test.[8] Odors are presented to the patients in felt tip pens. For birhinal stimulation, the tip of the pens is placed approximately 2 cm in front of both nostrils. This test encompasses three different approaches. First, odor thresholds are assessed for n-butanol with stepwise dilutions in a series of 16 dilutions. Thresholds are determined using the single staircase technique based on a three-alternative forced-choice task. Second, patients are asked to discriminate between different odors. For each discrimination task, three pens are presented, two containing the same odor and the third containing the target odorant which, again, comprises a three-alternative forced-choice task. The target odors should be recognized in a series of 16 trials. Third, a series of 16 odors was presented to the patients together with a list of four verbal descriptors for identification. Subjects were asked to identify the odors using this multiple forced-choice approach. For healthy subjects, the threshold/discrimination/identification (TDI) score at the 10th percentile is 28.8 for people aged 36 to 55 years and 27.5 for people aged >55 years. Functional anosmia (further termed "anosmia") is diagnosed if the TDI score is less than 16. With a TDI score between 16 and 28, patients are considered hyposmic.

Retronasal Testing. We performed retronasal olfactory testing by using odorized powders as described and previously standardized presented to the oral cavity[9] so that orthonasal and gustatory stimuli were avoided. Twenty odors were chosen for the retronasal testing: coffee, vanilla, cinnamon, cacao, raspberry, orange, garlic, strawberry, cloves, nutmeg, onion, cheese, curry, milk, banana, mushroom, coconut, lemon, paprika, and celery. Odorous powders were applied to the midline of the tongue on a fenestrated plastic stick for 3 seconds. Like with orthonasal testing, participants were asked to identify the odor from a list of four items. After administration of each powder, participants rinsed their mouth with tap water. For healthy subjects, retronasal testing yielded a median score of 18 for those aged 36 to 55 years and 16 for those aged >55 years.

Magnetic Resonance Imaging Protocol and Measurements

Patients were examined on a 1.5-Tesla magnetic resonance imaging system (Signa Echospeed; GEMS, Milwaukee, WI, USA) using a standardized protocol for OB analysis. The protocol included: 1) 5-mm-thick standard T2-weighted fast spin-echo images covering the whole brain without interslice gap to rule out any organic brain disorder; 2) 5-mm-thick T2-weighted gradient-echo images using the echoplanar imaging technique (EPI-GRE-T2*) covering the whole brain to rule out the presence of any parenchymal or meningeal posttraumatic hemosiderin deposit; and 3) 2-mm-thick T1- and T2-weighted fast spin-echo images without interslice gap in the coronal plane covering the anterior and middle segments of the base of the skull. Two observers performed the analysis following a standardized method.[10] In summary, OB volumes were calculated by planimetric manual contouring (surface in square millimeters) and all surfaces were added and multiplied by two because of the 2-mm slice thickness to obtain a volume in cubic millimeters. Brain volume loss, fibrotic brain sequelae, and/or residual hemorrhagic blood products were recorded in the frontal lobes and in the anteroinferior temporal lobes.

Statistical Analysis

All statistics were performed using SPSS software version 12.0 (SPSS Inc., Chicago, IL, USA). Results were submitted to analyses of variance (ANOVA) with "presence of cerebral damage" (see subsequently) as the between-subject factor. Correlations (Pearson) were computed between volumetric measurements of the OB and functional measurements. The level of significance was set at 0.05.

RESULTS

A total of 25 patients were included in this study (12 men, 13 women; mean age, 43.9 years; age range, 20–70 years). The mean duration of symptoms from head injury to clinical evaluation was 14.9 months (range, 3–60 months). Parosmia was present in seven patients. Orthonasal testing showed that 20 of the patients had anosmia and five were hyposmic. Descriptive statistics of TDI scores, retronasal olfaction scores, and OB volumes are shown in Table I.

The mean retronasal olfaction score was 9.5 (range, 4–15) or 47.5% (range, 20–75%) expressed as the percentage of the maximal score of 20. Mean orthonasal function for odor identification was 4.5 (range, 1–14) or 29% (range, 6–88%) expressed as the percentage of a maximum score of 16. These scores differed significantly ($t_{24} = 6.36$; $P < .001$), indicating that retronasal function was less affected than orthonasal function (Fig. 1).

Correlations among orthonasal scores, retronasal olfactory function, and OB volume revealed that retronasal odor identification correlated significantly with OB volume ($r_{25} = 0.53$; $P = .007$), whereas this was not the case for orthonasal odor identification ($r_{25} = 0.37$; $P = .07$). These analyses suggested that, at least in this study, OB volume is of greater significance in retronasal function than in orthonasal function.

Apart from this, a significant correlation was found between odor thresholds and OB volume ($r_{25} = 0.46$; $P = .021$) but not between odor discrimination and OB volume ($r_{25} = 0.26$; $P = .21$).

Patients with anosmia had significantly smaller OB volumes than those with hyposmia ($t_{23} = 2.69$; $P = .013$). Patients with parosmia had significantly smaller OB volumes than those without ($t_{19.2} = 2.81$; $P = .011$; OB

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TABLE I.
Descriptive Statistics of the Results From Olfactory Testing (orthonasal and retronasal) and Measurements of Olfactory Bulb Volume (n = 25).

	Minimum	Maximum	Mean	Standard deviation
Odor threshold score Orthonasal	1	7	2.52	1.5
Odor discrimination score Orthonasal	1	10	4.96	2.3
Odor identification score Orthonasal	1	14	4.64	2.9
Threshold/discrimination/identification score Orthonasal	3	29	12	5.8
Odor identification score Retronasal	4	16	9.6	3.1
Olfactory bulb volume (mm^3), right	3.2	35.3	19.2	9.1
Olfactory bulb volume (mm^3), left	3.2	37.8	17.6	9.7
Olfactory bulb volume (mm^3), left + right	6.4	79.8	36.9	18.3

volumes: patients with parosmia, 23.5 mm^3 ± 11.9; patients without parosmia, 42.2 mm^3 ± 20.9).

Damage to the frontal lobes was noted in 15 patients (60%); seven of these patients exhibited additional damage of the anteroinferior temporal lobe. When comparing functional and structural measurements for patients without cortical lesions (WITHOUT group) with those with frontal lobe damage (FRONTAL group) and those with damage to the frontal and anteroinferior temporal lobes (FRONTOTEMPORAL group), retronasal olfactory function differed significantly ($F_{2,22} = 5.52$, $P = .011$) as did OB volumes ($F_{2,22} = 11.7$, $P < .001$), but not orthonasal measurements of olfactory function ($P > .25$). Retronasal olfactory function was most compromised in the FRONTOTEMPORAL group (35.0 ± 8.2) and was least affected in the WITHOUT group (57.5 ± 13.2). Measurements for the FRONTAL group lay between the other groups (47.5 ± 17.2; Fig. 2). Similarly, OB volumes were largest in the WITHOUT group (51.3 mm^3 ± 17.2), smallest in the FRONTOTEMPORAL group (15.8 ± 7.5), and were of medium size in the FRONTAL group (37.6 ± 16.3; Fig. 2).

Parosmia was associated with damage to the frontal or temporal lobes with the frequency of parosmia being 0% in the WITHOUT group, four of eight (50%) in the FRONTAL group, and three of seven (43%) in the FRONTOTEMPORAL group. Examples of magnetic resonance imaging in patients with posttraumatic olfactory loss are shown in Figures 3, 4, 5, and 6.

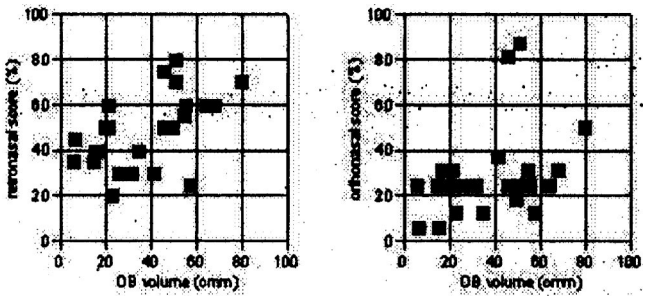

Fig. 1. Results from (A) retronasal odor identification and (B) orthonasal odor identification plotted against olfactory bulb volume.

DISCUSSION

The main results of the present study were: 1) the demonstration of a correlation between olfactory function and OB volume; 2) the correlation between olfactory function and OB volume was more pronounced for retronasal olfactory function than for orthonasal olfactory function;

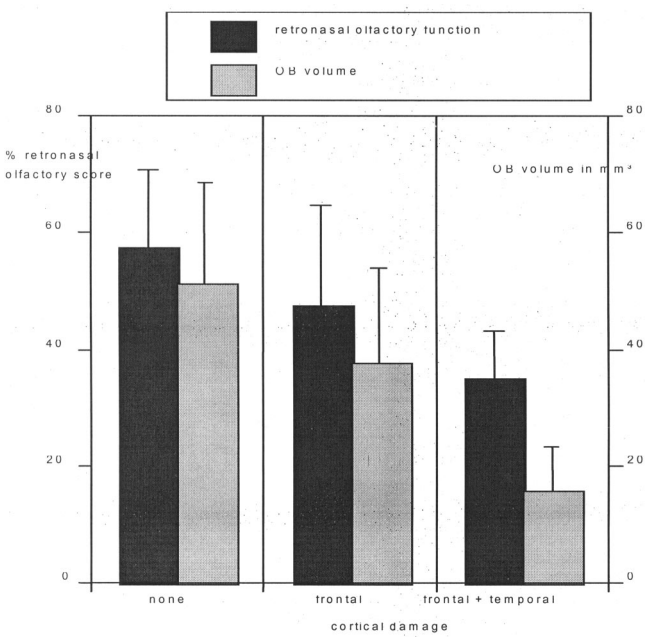

Fig. 2. Mean values and standard deviations of scores for retronasal olfactory testing (in percent; black filled bars) and olfactory bulb volumes (in cubic millimeters; gray filled bars) in patients with no cortical damage, frontal damage, and frontal and temporal damage.

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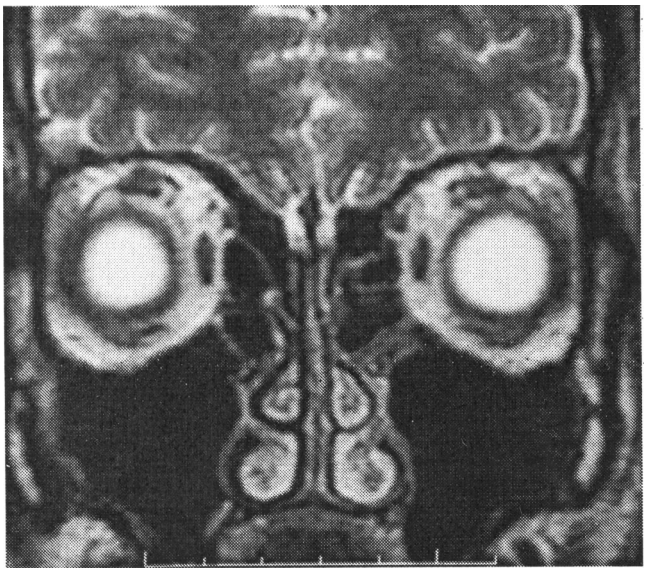

Fig. 3. T2-weighted coronal image with decreased olfactory bulb volume and absence of damage in the frontal lobe area.

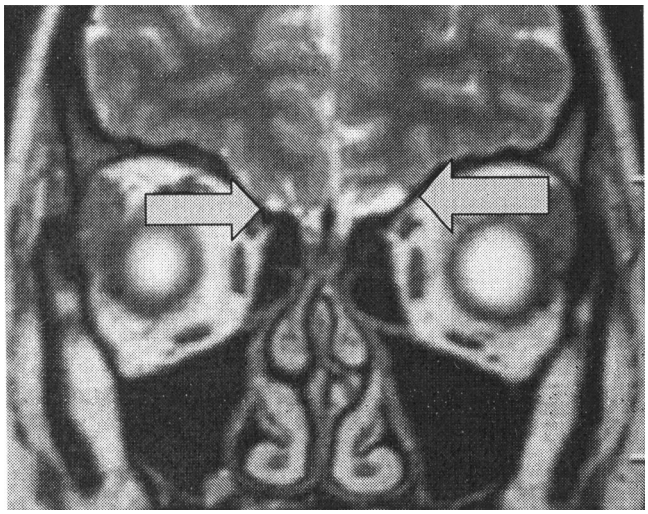

Fig. 5. T2-weighted coronal image with decreased olfactory bulb volume and moderate damage in the frontal lobe area (arrows).

3) retronasal olfactory function was most affected in those patients with the most extensive cerebral damage and was least compromised in those patients without such damage; 4) OB volumes were smaller in patients with parosmia compared with those without; and 5) the presence of parosmia was clearly associated with the presence of cerebral damage.

Magnetic resonance imaging volumetric measurements of the OB have been studied in postinfectious and posttraumatic olfactory loss.[10–14] These studies have already demonstrated that OB volume is a gauge of residual olfactory function supporting previous observations in which a loss of sensory input resulted in reduced OB volume. Our study confirms these results and in addition demonstrates the relationship between retronasal olfactory function in particular and OB volume. To our knowledge, there is no data on how long it takes the OB volume to decrease after trauma.

Orthonasal and retronasal olfactory testing are validated techniques that allow the evaluation of olfactory identification abilities both in healthy subjects and in patients.[9,15] The present results indicate that retronasal test scores correlate significantly with OB volume, which was not the case for the results from the orthonasal odor identification test. In other words, retronasal function predicts the size of anatomic structures in patients with posttraumatic olfactory loss. Moreover, these data also suggest that orthonasal odor identification decreases more than retronasal odor identification (expressed as a percentage of the maximum score). Considering that ortho-

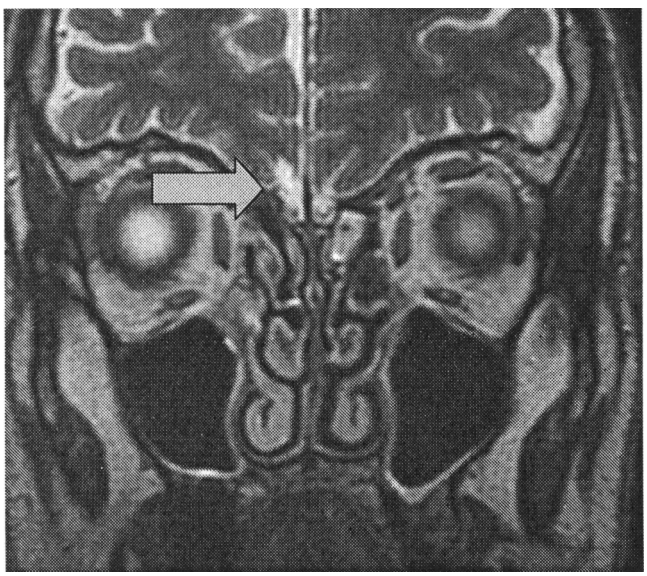

Fig. 4. T2-weighted coronal image with decreased olfactory bulb volume and slight damage in the frontal lobe area (arrow).

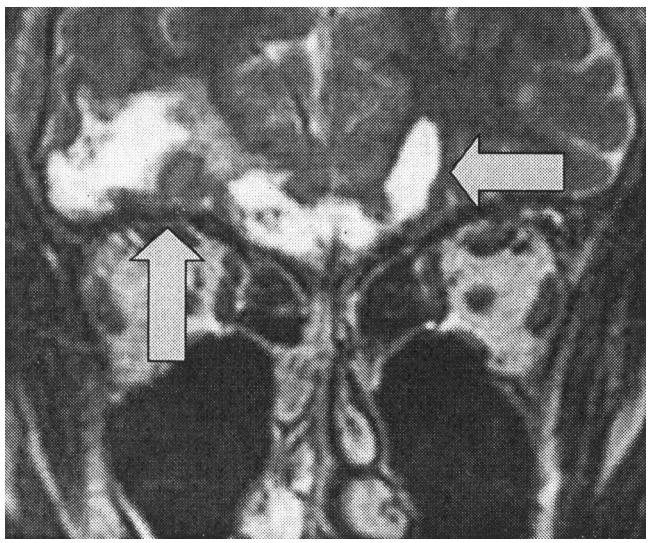

Fig. 6. T2-weighted coronal image with decreased olfactory bulb volume and significant damage in the frontal lobe area and in the temporal area (arrows). Note that this section is more posterior than Figures 3, 4, and 5.

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nasal olfactory function may involve olfactory fibers passing through the anterior portion of the cribriform plate, whereas retronasal olfactory function may be transmitted through more posterior fibers, it could be hypothesized that head trauma would have a stronger effect on orthonasal than on retronasal olfactory function because it might affect anterior olfactory fibers to a greater degree than retronasal ones.

The present study also showed that if retronasal odor identification was strongly affected, damage to the frontal and anterior temporal lobes was more pronounced. This clearly suggests that posttraumatic olfactory loss seen as a sequela of trauma is not only the result of the tearing of the fila olfactoria, but that it also results from lesions of cerebral areas related to the processing of olfactory information such as the orbitofrontal cortex or the anterior temporal lobe. It would be interesting to see in cross-sectional studies whether patients without additional brain lesions have a higher chance of recovery compared with patients exhibiting such defects.

Patients with parosmia exhibit a smaller OB volume. It has been suggested that a decrease in the number of OB interneurons is associated with the generation of parosmia. It could be that a decreased number of OB interneurons results in a decrease of lateral inhibition.[5] In turn, this may allow olfactory activation to produce an irregular pattern, which may result in a "parosmic odor." The present study supports this hypothesis in that parosmias were present only in subjects with small OB volumes and additional cerebral lesions. This may be interpreted as either the combination of decreased OB volume plus cerebral deficits is relevant in the generation of parosmias or that the decreased OB volume is a consequence of decreased top-down activation from higher brain centers involved in the processing of the odor information and that parosmias are the result of the distorted cortical processing of odors. Based, therefore, on the present results, posttraumatic olfactory parosmia may be explained by at least two different mechanisms: 1) severing of olfactory fibers with the subsequent decrease of OB size and decreased number of OB interneurons, and 2) cortical damage in the orbitofrontal and anteroinferior temporal area.

To summarize, the present data confirm that OB volume is an indicator of olfactory function in patients with posttraumatic olfactory loss. Interestingly, it is largely a function of retronasal olfactory sensitivity, at least in the present study. In addition, our results emphasize the role of higher cortical centers in terms of olfactory function, especially with regard to parosmia, which may, at least in some cases, be related to lesions in the frontoorbital and anterior temporal cortices. It would be of interest to investigate OB volume further in relation to the prognosis of the disorder, especially because there is no established treatment to restore olfactory function in posttraumatic olfactory loss.

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