Correlation of Olfactory Function With Changes in the Volume of the Human Olfactory Bulb

Antje Haehner, MD; Antje Rodewald, MD; Johannes C. Gerber, MD; Thomas Hummel, MD

Objective: To investigate changes of olfactory bulb (OB) volume over time in relation to olfactory function.

Design: Prospective, before-after trial.

Setting: Outpatient clinic of a university clinic for otorhinolaryngology.

Patients: A total of 20 patients with olfactory loss participated in the study. The duration of olfactory deficits ranged from 3 months to 6 years.

Main Outcome Measures: Olfactory function was assessed for phenyl ethyl alcohol odor threshold, odor discrimination, and odor identification. Olfactory bulb volume was determined using magnetic resonance imaging.

Results: In initially hyposmic patients (n=13), changes in OB volume were found to correlate with odor threshold changes (r=0.82; P=.001); no such correlation was found for odor discrimination or odor identification.

Conclusion: As demonstrated in a longitudinal study for the first time to our knowledge, the human OB is a highly plastic structure that responds to individual changes in olfactory status.


MAGNETIC RESONANCE imaging (MRI) offers an ideal means to reliably evaluate the volume of the olfactory bulb (OB), which appears to be of interest in olfactory loss. Olfactory bulb size has been studied in patients with posttraumatic1-4 and postinfectious olfactory deficits,3,5 congenital anosmia,1,6 and neurodegenerative diseases7,8 and in subjects with a normal sense of smell.7 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.3,5

Experimental animal studies show that the OB remains highly plastic throughout adult life. Bulbar neurogenesis relates to the activity level of sensory input from the olfactory epithelium,9 leading to a reduction in OB size or to an improvement of sensory abilities.10 In addition, contributing to the plasticity of this structure in humans, neuroblasts migrate to the OB via a lateral ventricular extension OB volume.11

The question arises whether changes of OB volume may reflect changes in olfactory function. This would support the idea of OB volumetry as a prognostic tool in assessing the course of postinfectious and posttraumatic olfactory loss. For the first time to our knowledge, the present study aimed to longitudinally investigate possible differences of OB volume over a period in patients with peripheral olfactory deficits (ie, postinfectious and posttraumatic olfactory dysfunction) in relation to changes in olfactory function. It was hypothesized that OB volume should increase in patients exhibiting recovery of olfactory function and vice versa.

METHODS

Investigations were performed according to the Declaration of Helsinki on Biomedical Studies Involving Human Subjects.12 The study design was approved by the ethics committee of the Medical Faculty of the University of Dresden Medical School, Dresden, Germany. All subjects attended our Smell and Taste Clinic for detailed diagnostic evaluation. They received an otorhinolaryngological investigation including nasal endoscopy, olfactory testing, and a MRI of the brain between October 2003 and March 2004 (time 1) and again after 13 to 19 months (time 2) (mean interval, 15 months).

PARTICIPANTS

A total of 20 randomly selected patients participated. Fourteen of the patients had postinfectious olfactory deficits (mean [range] age, 65 years [50-76 years]; 10 women and 4 men), 6 had posttraumatic olfactory loss (mean...
[range] age, 59 years [23-72 years]; 2 women and 4 men). Duration of olfactory deficits at the time of the first examination ranged from 3 months to 6 years. Ten patients with postinfectious smell deficits, and 1 patient with posttraumatic olfactory dysfunction reported parosmia (mean [range] age, 63 years [50-76 years]; 8 women and 3 men; mean [range] duration of olfactory deficits, 10 months [3 months to 3 years]).

**Olfactory Testing**

Following a physical examination by an experienced ear, nose, and throat specialist, olfactory function was assessed in all individuals by means of the validated “Sniffin’ Sticks” test kit, which comprises 3 individual tests of olfactory function (phenyl ethyl alcohol odor threshold, odor discrimination, and odor identification). The scores of the individual tests were summarized to the so-called TDI (threshold, discrimination, and identification) score, which is a reliable means to estimate the degree of olfactory function.

**Magnetic Resonance Imaging**

The volume of the OB was determined using MRI (Figure 1). All examinations were performed on a 1.5-T system (Magnetom Vision; Siemens, Erlangen, Germany) using the circularly polarized head coil. To visualize the OB, a 3-dimensional CISS (constructive interference in steady state) sequence was applied, with slice selection gradients oriented coronally and perpendicularly to the frontal skull base or the cribiform plate. Depending on the size of the head, a slice thickness of 0.5 to 0.7 mm was used. The in-plane resolution varied between 0.5 × 0.2 mm and 1.0 × 0.2 mm. As previously described, volumetric measurements were performed by an experienced radiologist (A.R.) who was blind to the olfactory test data by manual segmentation of the coronal slices through the OBs on both sides separately. The change of diameter at the beginning of the olfactory tract was used as the proximal demarcation of the OB.

**Statistical Analysis**

Data were analyzed using SPSS 12.0 (SPSS Inc, Chicago, Illinois) statistical software for Windows. For analyses, the “best” volume was used, meaning the larger of the left- or right-side OB volume. This approach was chosen because results from birhinal olfactory tests typically reflect function of the better of the 2 sides of the nose, and thus, the OB with the largest volume was assumed to reflect the function of the best nostril. Comparisons were performed using t tests for paired samples. Correlation analyses were performed controlling for the patients’ age. The α level was .05.

**Results**

In general, change of OB volume in this study was not significantly related to age and sex of the individuals or to the occurrence of parosmia.

At time 1, 7 of the 20 patients presented with anosmia and 13 were hyposmic. When testing individuals for the second time, 6 of them had anosmia and 14 presented with hyposmia (for total results, see Table). Correlation analyses between the change in olfactory sensitivity and in OB volume during the testing interval were made separately for hyposmic and anosmic patients. In initially hyposmic patients (3 with posttraumatic and 10 with postinfectious smell loss), changes in OB volume were found to correlate significantly with odor threshold changes ($r = 0.82; P = .001$) (Figure 2), indicating that subjects with improving olfactory function also exhibited an increase of OB volume. However, no such correlations were found for odor discrimination or odor identification. In addition, the length of the interval between the tests showed a negative correlation with OB volume ($r = -0.57; P = .05$), which, however, missed the criterion for significance.

**Comment**

The main outcome of the present longitudinal study was that in hyposmic patients, changes in OB volume...
correlated with changes in odor threshold. Thus, the results from the present study demonstrate that OB volumes reflect olfactory function in patients with olfactory loss.

The present findings also support research in experimental animals on changes of OB volume in relation to input from the olfactory epithelium. This correlation between structure and function is most likely due to the high plasticity found in the synaptogenesis of the OB.\(^9\)\(^,\)\(^10\) In addition, there is a continuous stream of neurons to the OB, which is a unique phenomenon in the central nervous system.\(^11\)

The present investigation revealed correlations between OB volume and odor thresholds, but not between OB volume and suprathreshold measures of olfactory function (ie, smell discrimination and identification abilities). Provided that odor thresholds are more closely related to peripheral function,\(^20\)\(^-\)\(^22\) these results support the idea that OB volume is more directly related to peripheral input than to higher central nervous processing of olfactory information. It is also possible that the relatively small sample size investigated in this study accounts, at least in part, for the missing correlations between changes of suprathreshold functions and changes of OB volume. Nevertheless, the present data argue that the correlation between changes of OB volume and changes of odor thresholds may be stronger than that the correlation between changes of odor identification scores and changes of OB volume. The present results also are in line with previous research,\(^8\) exhibiting significant correlations between odor thresholds and OB volume but not between OB volume and odor identification or odor discrimination scores for orthonasal testing.

The correlation between OB volume and olfactory function may potentially be used in combination with other factors influencing olfaction such as remaining olfactory function, age, and duration of olfactory loss\(^23\) as a means to provide patients with individual information on the prognosis of their disease. Hypothetically, a multifactorial approach could be applied to eventually come up with a formula that would allow a more precise prognosis of olfactory function. Especially since therapeutic options in patients with olfactory loss are limited,\(^24\) at present, this type of information is of high clinical significance.

In conclusion, the present study emphasizes that OB volume correlates with olfactory function, and our data support the evidence that the human OB is a highly plastic structure.\(^9\)\(^,\)\(^10\)

Submitted for Publication: July 20, 2007; final revision received October 5, 2007; accepted October 10, 2007.

Correspondence: Thomas Hummel, MD, Department of Otorhinolaryngology, University of Dresden Medical School, Fetscherstrasse 74, 01307 Dresden, Germany (thummel@rcs.urz.tu-dresden.de).

Author Contributions: All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Hummel. Acquisition of data: Haehner, Rodewald, Gerber, and Hummel. Analysis and interpretation of data: Haehner and Hummel. Drafting of the manuscript: Haehner and Hummel. Critical revision of the manuscript for important intellectual content: Haehner, Rodewald, and Gerber. Statistical analysis: Hummel. Administrative, technical, and material support: Rodewald, Gerber, and Hummel. Study supervision: Haehner and Hummel.

Financial Disclosure: None reported.

Additional Contributions: Katja Lill, MD, helped with some of the psychophysical olfactory tests and Rudiger von Kummer, MD, provided suggestions with regard to earlier versions of the manuscript.

**REFERENCES**


**Figure 2.** Changes of best olfactory bulb (OB) volumes plotted against changes of phenyl ethyl alcohol (PEA) odor threshold testing in 13 hyposmic subjects indicating that subjects with improving olfactory function (higher threshold score) also exhibit an increase of OB volume.


