Posttraumatic olfactory dysfunction: MR and clinical evaluation.

D M Yousem, R J Geckle, W B Bilker, D A McKeown and R L Doty

Posttraumatic Olfactory Dysfunction: MR and Clinical Evaluation

David M. Yousem, Rena J. Geckle, Warren B. Bilker, Donald A. McKeown, and Richard L. Doty

PURPOSE: To evaluate the sites of injury in patients with posttraumatic olfactory deficits and to compare damage with findings on clinical olfactory tests. **METHODS:** Twenty-five patients with posttraumatic olfactory dysfunction were examined by means of olfactory testing, endoscopy, and MR imaging. MR surface-coil scans through the olfactory bulbs and tracts and head-coil scans of the temporal lobes were evaluated. Quantitative and qualitative gradings of damage to the olfactory bulbs, tracts, subfrontal region, hippocampus, and temporal lobes were compared with results on tests of odor identification, detection, memory, and discrimination. **RESULTS:** Twelve patients were anosmic, eight had severe impairment, and five were mildly impaired. Injuries to the olfactory bulbs and tracts (88% of patients), subfrontal region (60%), and temporal lobes (32%) were found, but these did not correlate well with individual olfactory test scores. Volumetric analysis showed that patients without smell function had greater volume loss in olfactory bulbs and tracts than did those posttraumatic patients who retained some sense of smell. Qualitative and quantitative assessments of damage showed few significant correlations with olfactory tests, probably because of multifocal injuries, primary olfactory nerve damage, and the constraints of a small sample size on the detection of clinically significant differences. **CONCLUSION:** MR imaging shows abnormalities in patients with posttraumatic olfactory dysfunction at a very high rate (88%), predominantly in the olfactory bulbs and tracts and the inferior frontal lobes.

Index terms: Brain, magnetic resonance; Head, injuries; Nerves, olfactory (I)

Posttraumatic anosmia occurs in approximately 31% of patients who have sustained major closed head injuries, as defined by posttraumatic amnesia for more than 24 hours (1). However, even in persons whose head injuries are not accompanied by loss of consciousness or in whom amnesia lasts less than 1 hour, the frequency of anosmia ranges from 3% to 8% (1). The exact cause of olfactory dysfunction is unclear, although many mechanisms have been

proposed. Shearing injuries at the cribriform plate that lacerate the primary olfactory nerves extending from the nasal cavity to the olfactory bulb are believed to be one of the common mechanisms involved in posttraumatic smell loss (1–5) (N. D. Zasler, R. M. Costanzo, P. G. Heywood, "Neuroimaging Correlates of Olfactory Dysfunction after Traumatic Brain Injury," *Arch Phys Med Rehabil* 1990;71:814, abstract). Alternatively, direct injury to the olfactory bulbs or tracts, intracerebral hematomas compressing these structures, injury to the septal nuclei in the inferior frontal region, orbitofrontal cortex injuries, or medial temporal lobe lacerations have been postulated as events that can precipitate posttraumatic olfactory deficits (1–5) (Zasler et al, "Neuroimaging Correlates"). Several postmortem neuropathologic studies have been performed in this regard (1, 3, 5).

As part of a broader study of smell and taste disorders, we examined 25 patients with olfactory dysfunction resulting from head trauma by using both surface-coil and head-coil magnetic resonance (MR) imaging to analyze injuries to

the olfactory-eloquent structures. We sought to determine what portions of the olfactory pathway are injured more frequently than others and whether certain locations of injury are more likely than others to produce deficits in smell detection, identification, discrimination, or memory. Since the olfactory system in the brain has been incompletely mapped, we hoped to gain a better understanding of the smell pathway by correlating sites of injury with olfactory deficits. To study these issues, we analyzed qualitative and quantitative measures of brain injury and clinical olfactory tests that look at odor detection, identification, discrimination, and memory.

Subjects and Methods

Twenty-five patients with olfactory dysfunction after head injuries were referred for smell testing to the Smell and Taste Center of the University of Pennsylvania. An extensive review of these patients' clinical histories was carried out to ascertain the origin of their olfactory dysfunction. All patients noticed the olfactory decline within 7 days of the head injury. Because some patients had altered consciousness at the time of their injury, the report of smell dysfunction was not immediate in some cases. These findings are in keeping with a report by Schecter and Henkin (6) in which 83% of patients experiencing posttraumatic smell loss did so immediately after the trauma, while the remainder noticed the deficits within 3 weeks to 4 months after the injury. No patient in our series reported olfactory deficits that predated the head trauma.

The study group included 14 men and 11 women who were 16 to 51 years old (mean, 36 years; SD, 9.8). The traumatic event occurred 3 to 183 months before the MR examination, with a mean of 23 months (SD, 37 months) and a median of 12 months. No patient was examined in the acute phase of the injury. All patients signed approved consent forms for participation in this study.

The patients underwent a battery of psychophysical olfactory tests designed to ascertain the specific nature of their olfactory deficits. All tests were administered to each side of the nose separately and included the University of Pennsylvania Smell Identification Test (UPSIT) (20 items to each side); a 16-item odor discrimination test; a 12-item odor memory test (with retention intervals of 0, 30, and 60 seconds); and a single-staircase odor detection threshold test using the odorant phenylethyl alcohol (7–10). The results of these smell tests were used to determine the severity of the chemosensory deficit. The UPSIT is the most widely used test of odor identification in the world and is the standard for determining whether a patient can identify smells. The other tests determine whether a patient can distinguish one odor from another (odor discrimination), remember an odor and recognize it later (odor

memory), and detect varying concentrations of an odor, from very weak to very strong (odor detection threshold).

To assure that the cognitive capacity of the patients would not preclude psychophysical testing, we also administered the 40-item Picture Identification Test (PIT) and the 30-item Mini-Mental Status Examination (MMSE) (11, 12). The pictures used in the PIT are of the sources of the smells that are used in the scratch-and-sniff UPSIT (ie, a picture of a peanut is shown to ensure the patient knows the word *peanut* to identify the peanut odor when it is presented). In addition, the patients underwent sinonasal endoscopy to exclude obstructive or inflammatory causes of smell dysfunction. The sinonasal examination was scheduled during the same week as the smell testing and the MR study.

MR images of the olfactory bulbs and tracts were obtained with a 12.7-cm, round, general-purpose surface coil centered on the nasion. After a sagittal localizing scan, coronal images with parameters of 500/15/2 (repetition time/echo time/excitations) were obtained with 3-mm interleaved scans and a 256 × 256 matrix with a 12-cm field of view (Fig 1). These coronal scans were followed by 3-mm interleaved coronal fast spin-echo T2-weighted images through the same anatomy with scan parameters of 2000/84/2 and a matrix of 256 × 192. With the use of high-resolution surface-coil imaging, one can be quite confident of the location of the olfactory bulbs and tracts and can trace the tracts to the entrance to the brain near the septal nuclei.

The head-coil examination consisted of a sagittal localizing scan followed by coronal T1-weighted scans (600/11/1) with 3-mm contiguous sections, a 25-cm field of view, and a 256 × 256 matrix through the temporal lobes. These were followed by 5-mm interleaved T2-weighted scans (3000/90/1) in the axial plane using a fast spin-echo technique through the entire brain. No contrast agents were used in the surface-coil or head-coil studies.

Volumetric analysis based on tracing, threshholding, and three-dimensional volumetric processing of the right and left olfactory bulb/tract system and temporal lobes was performed by two independent researchers on an ISG technologies workstation. The olfactory bulb is located at the anterior cribriform plate, and the olfactory tract extends posteriorly to enter the brain below the rostrum of the corpus callosum—both these structures were included in measurements of the volume of the olfactory bulbs and tracts. To assess intraobserver and interobserver reliability, intraclass correlation coefficients were performed for pairs of interpretations done by a single examiner and for interpretations between examiners of the volumes of the right and left temporal lobes and of the right and left olfactory bulb-tract. The percentage of difference between the two observers' volume determinations was computed.

Areas of the olfactory system were also graded qualitatively for volume loss/damage on a scale from 0 to 3 (0 = none, 1 = minimal, 2 = moderate, 3 = marked) by one neuroradiologist (D. Y.) with the most experience in this area. Grades were assigned for the right and left olfactory bulbs, the right and left olfactory tracts, the right and left
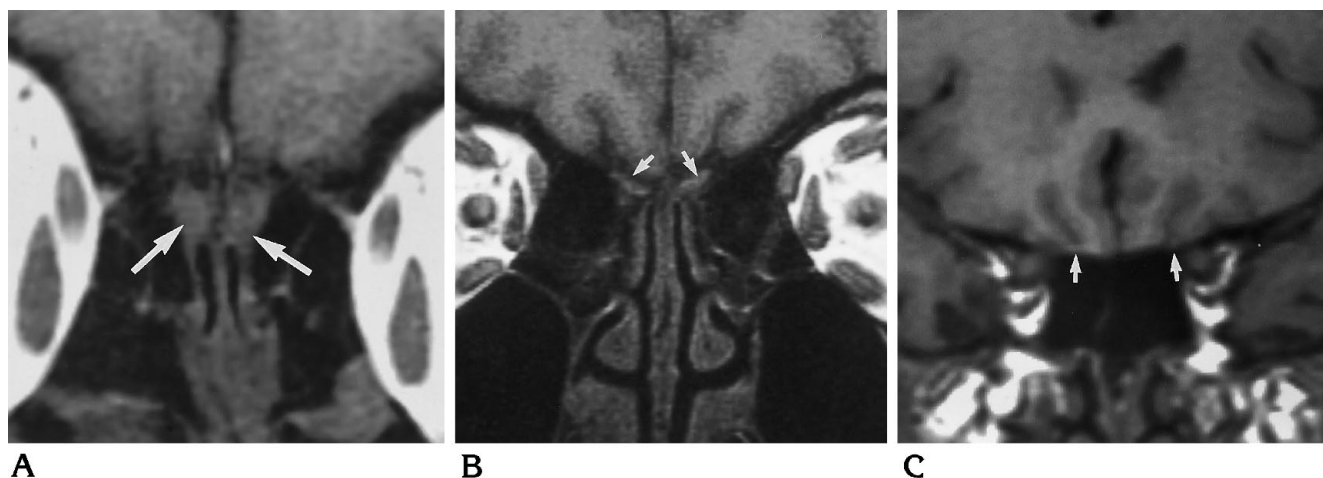
Fig 1. Grade 0 (no volume loss) in three patients through various parts of the anatomy.

A, Coronal T1-weighted MR image shows normal-sized olfactory bulbs (*arrows*) bilaterally.

B, Proximal olfactory tracts (*arrows*) show normal volume on this T1-weighted image. Patient was anosmic (UPSIT score, 9/40).

C, Distal olfactory tract (*arrows*) on the left side is better seen than the one on the right side.

inferior frontal/septal regions, the right and left temporal lobes, and the right and left hippocampal/parahippocampal/amygdaloid regions. Spearman correlations were used to evaluate the relationship among these grades, the quantitative assessments of volume, and the olfactory tests for the patients who could smell. We used Wilcoxon's scores to determine whether there was a difference in the volumes of the temporal lobes and the olfactory bulbs and tracts between anosmic and nonanosmic patients.

A control population (six women and two men, with a slightly older age range of 43 to 70 years) with no history of head trauma, no reported olfactory deficits, and olfactory test results in the normal range was also examined. A Mann-Whitney test, which is a nonparametric alternative to the two-sample *t* test for independent samples, was used to compare UPSIT scores and mean volumes of the olfactory bulb/tract system and the temporal lobes among the control subjects, the posttraumatic anosmic patients, and the posttraumatic nonanosmic patients.

Results

Cognitive and Endoscopic Testing

Twenty-four of 25 patients had perfect scores on the 40-item PIT, with one patient getting one picture incorrect. Only one patient scored below 28 on the MMSE. These data suggest that the patients had sufficient cognitive skills to follow the directions adequately on the specific olfactory tests. No patient had findings at endoscopy that were sufficient to account for severe smell deficits. Therefore, for the purposes of this study, all 25 patients were included in the analysis of the relationship of olfactory system damage to olfactory test scores.

Olfactory Testing

Twenty-four patients had olfactory dysfunction as measured by the UPSIT. Twelve were anosmic (UPSIT score < 18), 8 were severely impaired (UPSIT score ≥ 18, ≤ 25), and 4 were mildly impaired (UPSIT score ≥ 27, ≤ 34). Despite subjective claims of a distortion in the sense of smell, one patient had normal smell function on the basis of standardized UPSIT norms (her UPSIT score was 35, which is the lower limit of normal) (7, 8). This patient did have deficits in odor memory and in phenethyl alcohol odor-detection threshold, so she was included in the data analysis. Another patient with mild impairment had an UPSIT score that was 5 items better on the right than the left; otherwise the deficits were seen to be bilateral and symmetric.

None of the olfactory test scores showed any relationship to the time interval between the traumatic event and the MR study. The interval from event to MR imaging for the patients with mild to unimpaired olfactory ability ranged from 3 to 62 months (mean, 27 months); for the anosmic group, the interval ranged from 5 to 183 months (mean, 29 months).

The mean normal value for persons without olfactory impairment on the bilateral 24-item odor memory test is 16 (SD, 2.8). Only 6 of our 25 patients scored above 10 on the 24-item odor memory test, and none of these patients was anosmic by UPSIT criteria. Three patients were mildly impaired and 3 were severely im-

Fig 2. Olfactory bulb and tract damage.

A, While the right olfactory bulb (*arrow*) is present in this patient, the left one cannot be seen. Despite this asymmetry on imaging, a symmetric olfactory deficit was noted on UPSIT responses (UPSIT score for left side, 9/20; UPSIT score for right side, 9/20).

B, In a different patient, bilateral inferior frontal lobe damage (right greater than left) is noted with poor visibility of both olfactory bulbs (UPSIT for right side, 5/20; UPSIT for left side, 7/20 = bilateral anosmia).

A   B
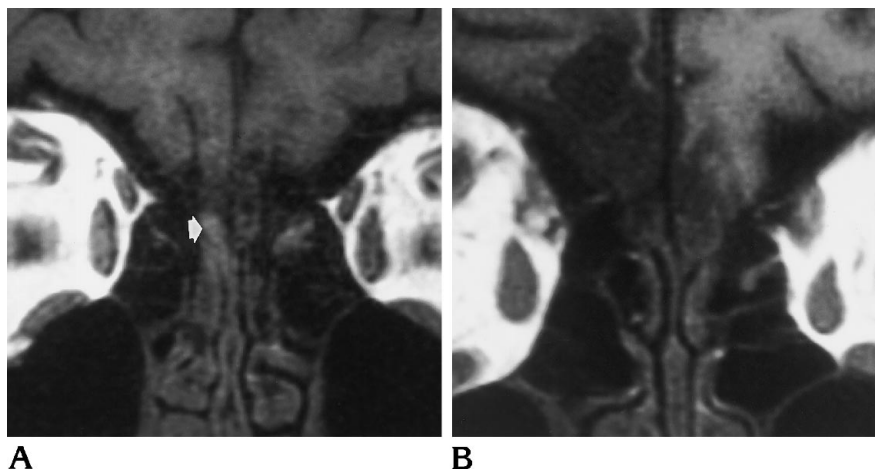
paired on the basis of UPSIT scores. The patient with "normal" smell function correctly remembered 9 of 24 odors presented (a score of 6 on the left and 3 on the right).

The mean score for persons with no olfactory impairment on the bilateral 32-item odor discrimination test is 21.8 (SD, 2.8). Three of our patients scored 20 or higher on the combined 32-item odor discrimination test. These 3 patients had the 3 highest UPSIT scores (35, 33, and 28, respectively). Two of these 3 also scored above 10 on the odor memory test.

Odor detection thresholds for phenethyl alcohol are measured in logarithmic dilutions, with −2.0 the strongest odor concentration and −10.0 the weakest concentration. On average, persons with normal smell function can detect a −6.3 dilution of phenethyl alcohol (SD, 1.6). Seventeen of the 25 patients studied scored a −2.0 on at least one side of the nose. The −2.0 value is the maximum concentration and the value expected of anosmic persons.

Imaging Findings

Because the earliest MR study was performed 3 months after the traumatic event, the imaging findings in our population represent the late changes one finds in patients with posttraumatic olfactory deficits. Twenty-two of the 25 patients had damage (ie, volume loss) to the olfactory system (olfactory bulbs, olfactory tracts, inferior frontal region, hippocampi, or temporal lobes). All 22 had injury to the olfactory bulbs or tracts, and in all but 2 the injury was bilateral (Fig 2). The damage to the olfactory bulbs or tracts was moderate to severe in

15 of the 22 patients, and mild in the other 7. Frontal lobe injury occurred in 15 patients (moderate to severe in 12) and 13 had bilateral inferior frontal damage. Temporal lobe injury occurred unilaterally in 5 patients and bilaterally in 3 patients; 1 patient had isolated right hippocampal trauma. Four patients had moderate to severe temporal lobe injury and 4 had mild injury (Fig 3).

Of the anosmic patients, only 1 did not have olfactory bulb or tract damage. The single patient with no smell impairment by UPSIT had mild bulb damage on the right side but no other areas of volume loss by inspection. The olfactory bulbs and tracts had minimal to no damage in 4 of the 5 patients who could smell but in just 3 of the 12 anosmic patients. Of the 4 patients who showed a differential between right and left UPSIT, odor memory, or odor discrimination scores who could definitely smell (UPSIT score > 27), only 1 had asymmetric damage (more disease was present ipsilateral to the nostril with the larger deficit). Only 1 patient in whom temporal lobe injury was evident on MR images could smell: his odor memory and odor discrimination deficits were the worst among the mildly impaired or unimpaired patients.

The volume of the olfactory bulbs and tracts ranged widely, from what appeared to be no damage to complete destruction of the bulbs and tracts. The mean volume of the left olfactory bulbs and tracts for the 25 patients was 73.2 mm^3 (SD, 48.6 mm^3; range, 0 to 171.3 mm^3). The mean volume of the right olfactory bulbs and tracts was 80.9 mm^3 (SD, 45.7 mm^3; range, 0 to 147.2 mm^3). The average volume of the right and left olfactory bulbs and tracts was
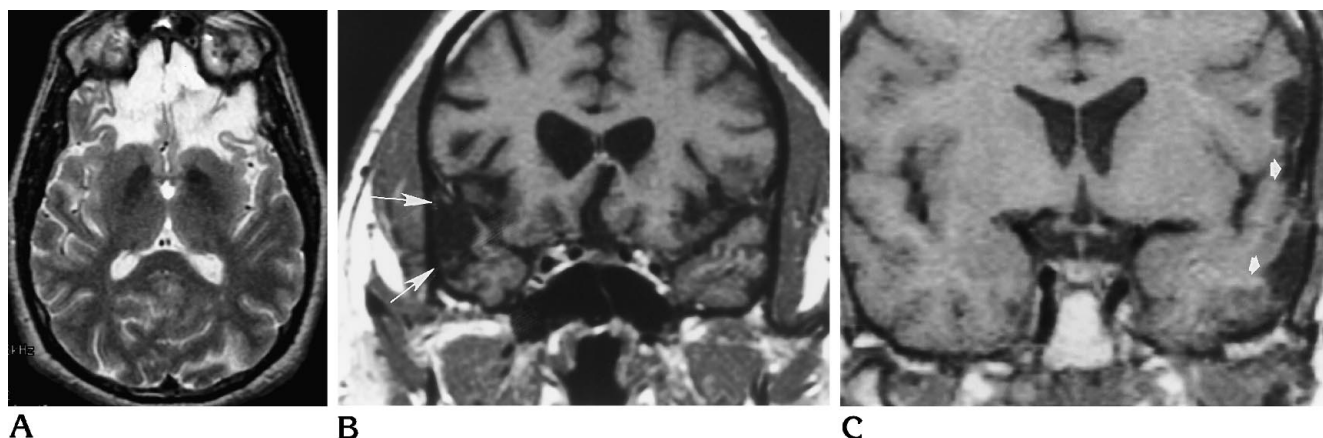
Fig 3. Cortical damage in three patients.

A, Axial T2-weighted MR image shows bifrontal encephalomalacic change, which was symmetric in severity. The patient was anosmic and also had olfactory bulb and tract injury.

B, Bilateral temporal lobe injury was present in a different patient, more severe on the right side (*arrows*). No asymmetry in smell test scores was noted.

C, Unilateral temporal lobe damage (*arrows*) is present in this third patient who had a striking odor memory deficit (4 of 12 items recalled bilaterally).

77.1 mm^3. The mean volumes of the right and left temporal lobes of the 25 patients were 70 094 mm^3 and 69 635 mm^3, respectively (SD, 8216 mm^3 and 10 516 mm^3, respectively). Ranges from 45 028 mm^3 to 89 035 mm^3 were present for the temporal lobes. The average of the right and left temporal lobes was 69 864.5 mm^3.

Because the olfactory tracts are typically hyperintense on long-repetition-time pulse sequences obtained with a surface coil, the value of assessing signal-intensity abnormality on T2-weighted images was reduced; in fact, no areas of frankly abnormal signal intensity were identified in a bulb or tract that had normal volume.

Statistical Analysis: Reliability Data

Intraclass correlation coefficients were performed to assess the reproducibility of the quantitative measurements of the right and left olfactory bulbs and tracts and the temporal lobes for each examiner (each examiner having performed the quantitative volumetric analysis twice to determine intraobserver reliability). The intraclass correlation coefficients ranged from .90 to .96, signifying an outstanding degree of reproducibility for the two examiners (Table). The intraclass correlation coefficients are graded on the same scale as the κ statistic, with values above .80 regarded as "almost perfect" (13). When the values *between* examiners were analyzed, the intraclass correlation coefficients

Intraclass correlation coefficients within and between observers

Anatomic Region	Correlation Coefficient		
	Observer 1: Two Interpretations	Observer 2: Two Interpretations	Between Observers
L temporal lobe	.96	.95	.93
R temporal lobe	.90	.91	.93
L olfactory bulb/tract	.92	.92	.95
R olfactory bulb/tract	.94	.94	.90

were in the .90 to .95 range, again signifying "almost perfect" reliability between examiners.

We then assessed the percentage of difference between examiners' values by dividing the absolute difference between examiners' values by the most experienced examiner's values. This yielded a mean percentage of absolute difference between interpretations of 7.0% for the left temporal lobes, 7.5% for the right temporal lobes, 12.2% for the left olfactory bulbs and tracts, and 18.6% for the right olfactory bulbs and tracts. The degree of difference between the two interpretations of the same structure by the same person averaged 3.6% for the temporal lobes and 16.7% for the olfactory bulbs.

Anosmic (UPSIT < 18) versus Nonanosmic (UPSIT ≥ 18) Patients

There was a statistically significant difference between the volume of the left olfactory bulbs and tracts in the patients who were anosmic

(mean, 52.4 mm^3; SD, 55.7) and that of the nonanosmic patients (mean, 95.8 mm^3; SD, 36.4) ($P = .038$). Similarly, the volume of the right olfactory bulbs and tracts was smaller in anosmic patients (mean, 62.5 mm^3; SD, 45.9) than in those with residual smell function (mean, 105.8 mm^3; SD, 40.8) ($P = .032$). The volume of the temporal lobes in the anosmic patients (mean left and right temporal lobe volume of 68 285 mm^3 and 69 746 mm^3, respectively) was not significantly different from that of patients who could smell (mean left and right temporal lobe volume of 68 892 mm^3 and 68 273 mm^3, respectively). No differences in qualitative grades of damage were discovered between patients with and without residual olfaction.

Anosmic and Hyposmic Posttraumatic Patients versus Control Subjects

The UPSIT scores of the control subjects ranged from 35 to 40, with a mean of 37. These values were significantly different from those of patients with head trauma ($P < .0001$), whether they did ($P = .0006$) or did not ($P = .0002$) have residual olfactory function. The mean volume of the olfactory bulbs and tracts for the 8 control subjects was 126.6 mm^3 (SD, 38.4), and the mean volume of the temporal lobe was 70 319 mm^3 (SD, 11 139). The volumes of the olfactory bulbs and tracts differed statistically from those of all posttraumatic patients ($P = .029$) and from the posttraumatic anosmic patients ($P = .008$), but not from those of posttraumatic hyposmic patients ($P = .307$). There was no statistically significant difference in temporal lobe volumes between control subjects and patients with posttraumatic olfactory deficits (P values ranged from .839 to .901).

Qualitative versus Qualitative Ratings

We found statistically significant correlations between the qualitative degree of damage to the olfactory bulbs and that to the ipsilateral tracts ($P < .001$) and frontal lobe ($P < .001$), as well as that to the contralateral bulb ($P < .001$), tracts ($P < .001$), and frontal lobe ($P < .001$). These data suggest that the injuries sustained are often multifocal and will usually affect both bulbs, tracts, and frontal lobes. Only two patients had damage that was isolated to one site. Damage scores for frontal lobe injuries and

those for ipsilateral temporal lobe injuries ($P = .037$ and $P < .001$ for right and left frontal lobes, respectively) and for the left frontal and right temporal lobes ($P = .048$) also showed statistical significance. The relationship between the temporal lobe and hippocampal damage scores and those of other structures showed insignificant correlation.

Correlations between Tests

Spearman's rank correlation coefficients were calculated between the subsets of data for the qualitative assessment of volume loss, the quantitative assessment of the volume of the olfactory bulbs and tracts and temporal lobes, and the assessment of individual olfactory tests. We used a significance level of .05 to search for differences between groups. Only the 13 patients who could smell as determined by UPSIT scores were included to help establish the relationship between smell test scores and location of injury. A multiple comparisons adjustment devised by Hotchberg (14), which is a modified Bonferroni procedure that achieves the required type 1 error while achieving a lower type 2 error, was applied to the significance tests. With this modified Bonferroni correction applied, no correlations between smell tests and qualitative or quantitative gradings of olfactory-eloquent structures were noted. Because the smell tests differ in reliability, however, and because such tests are generally correlated with one another (15), we developed a composite olfactory test score based on a weighted average of the four tests administered so as to simplify data presentation and decrease the probability of a type 1 error. The test-retest reliability coefficients of these tests, used as weights within this composite, were proportioned to equal 1.0 (total UPSIT score, 0.316; phenethyl alcohol score, 0.302; odor memory, 0.234; and odor discrimination, 0.148) (15, 16). Again, there was no significant correlation between composite scores and the volume of the olfactory bulbs and tracts and temporal lobes.

Discussion

While smells are perceived in the upper nasal cavity by olfactory neuroepithelial receptors, the primary olfactory nerves pierce the cribriform plate to stimulate and synapse with olfactory bulb nuclei. From the olfactory bulb and

tract, fibers pass in the olfactory stria to septal nuclei at the base of the brain just inferior and anterior to the rostrum of the corpus callosum. From the medial and lateral septal nuclei, fibers extend to the limbic system with branches to the uncus, hippocampus, parahippocampal region, septum pellucidum, fornices, amygdala, and gyrus rectus regions.

Thus far, it is unclear which olfactory functions correspond to the various anatomic sites. The location of the source of olfactory dysfunction has been surmised from animal and human models. The nasociliary olfactory nerves, olfactory bulbs, and olfactory tracts are necessary for odor detection. Sectioning these nerves results in anosmia. With orbitofrontal or medial thalamic lesions, odor discrimination and odor quality recognition are affected, though in some instances odor detection may be unaffected or even more sensitive than that in control subjects (4). The ability to recognize, interpret, and remember odors is located more classically in the uncus and hippocampus, whereas the emotional response to smell is tied into the entire limbic system (B. E. Wexler, R. K. Fulbright, C. Greer, et al, "An fMRI Study of Human Brain Response to Attractant and Aversive Odors," Sarasota, Fla: Association for Chemoreception Sciences, April 22, 1995, abstract 219). We had hoped that this study of posttraumatic injuries of olfactory-eloquent regions would lead to a clearer understanding of anatomic-functional relationships as measured by smell tests.

The prevalence of posttraumatic anosmia ranges from 24% to 30% among patients who have sustained severe head injuries, 15% to 19% among those with moderate head injuries, and 0% to 16% among patients with mild head injuries (17). This disorder is commonly associated with blows to the frontal region or the occiput. Sumner (1) found that a blow to the occiput has five times the chance of inducing anosmia than does a blow to the forehead if posttraumatic amnesia is present (indicating a severe head injury). This may be due to contrecoup shearing effects at the cribriform plate and inferior frontal lobe region. Because frontal injuries are more common than occipital blows, posttraumatic anosmia is most often seen in the setting of a frontal contact injury (1, 18, 19). Fractures of the skull or face are seen in 45% to 68% of patients with bilateral posttraumatic anosmia (5, 19).

Most patients reporting olfactory dysfunction after head trauma are totally anosmic, but approximately one fourth may have hyposmia or parosmia (distortion of smells) (5, 18, 20). Retention of the sense of smell in one nostril is uncommon, occurring in fewer than 11% of posttraumatic patients examined for chemosensory abnormalities (3, 17–19). In patients who have partial or incomplete loss of olfactory function, the deficit may go completely unnoticed.

Recovery of olfactory function after head trauma is variable. Most large series report a return of olfactory function in 14% to 39% of patients who were initially anosmic (1, 5, 21), especially if the interval of posttraumatic amnesia is less than 24 hours. While 74% of patients recovering olfactory function do so within 12 weeks, one study reported that an additional 22% will regain function by the second year after the injury (1). However, reports of return of olfactory function as long as 7 years after injury have been published, although few studies have used quantitative tests of olfactory function (1, 5, 18). Olfactory neurons have the capacity for neurogenesis, allowing new receptor growth, so it is surmised that the late return of function may be related to a peripheral (olfactory nerves/bulbs/tracts) mechanism rather than a more central one (22). In hamsters, recovery of odor detection after unilateral olfactory nerve transection occurs in over half the cases (22). In humans, though, it is believed that there may be fibrotic scarring that occurs at the cribriform plate that may prevent regenerating axons from connecting to the secondary neurons of the olfactory bulb (23). In our study group, the rate of recovery of function was less than 10%, possibly because the mean time from evaluation to traumatic event was 23 months. However, we have not performed serial testing in this group.

The use of MR imaging in evaluating disorders of the olfactory system has been relegated to a few case-control studies involving patients with congenital anosmia or other olfactory disorders (24–31). MR imaging, with surface-coil technology, is ideally suited to examination of the small structures of the olfactory bulbs and tract. This is important in the setting of posttraumatic smell dysfunction, since the most common sites of injury after head trauma are at the skull base. Additionally, the cerebral abnormalities for central causes of olfactory dysfunction can be readily detected with MR imaging at the base of the skull, an area where beam-harden-

ing artifacts and partial volume effects often obscure computed tomographic (CT) studies. The usefulness of CT in the identification of the olfactory bulbs and tracts, let alone damage to these structures, is suspect, and we believe that MR imaging is the appropriate means for investigating these regions. Injuries to the gyrus rectus, subfrontal, and anteroinferior temporal regions are well seen on MR images. The gyrus rectus region is often lacerated as it scrapes along the anterior cranial fossa, whereas the anteroinferior temporal lobe is often traumatized by the greater or lesser wings of the sphenoid bone.

We have shown in this MR study that the most common sites of injury in patients with posttraumatic olfactory dysfunction are the olfactory bulbs and tracts followed by the inferior frontal lobes. The prevalence of temporal lobe and hippocampal injury is low. The finding that the volume of the olfactory bulbs and tracts in patients with anosmia is less than that of patients with residual smell function or control subjects suggests that the source of the olfactory deficit may be at the level of the olfactory bulbs and tracts or proximally in the olfactory neurons. The lack of a statistical difference between anosmic patients and persons with normal smell function (both control subjects and posttraumatic patients) in the volume of their temporal lobes and in the qualitative grade of injury at multiple intracerebral sites (frontal, temporal, or hippocampal regions) supports this hypothesis.

Why were no significant relationships found between individual olfactory tests and qualitative and quantitative measures of damage (as seen on MR images) to olfactory-eloquent regions of the brain? We believe that several factors account for this phenomenon. 1) Olfactory deficits may result from extraparenchymal injury at the ciliary nerve or olfactory epithelium level, which MR imaging cannot detect. 2) Injury occurs at multiple sites; only two of our patients had an injury that was isolated to one olfactory site (ie, usually the frontal lobes and olfactory bulbs were damaged together), making it difficult to correlate findings on smell tests with single anatomic sites. 3) Few (n = 13) of our patients could still smell, and those with severe deficits (n = 8) had unreliable scores on odor memory, discrimination, and threshold tests. 4) Recent work by Doty et al (15, 16) suggests that many olfactory tests are unreliable and may

actually be testing the same function. 5) With the modified Bonferroni corrections applied to as many tests as were performed, only a highly significant Spearman's rank score would show up as statistically significant. Performing our algorithm on a larger sample population of mildly impaired patients may help in this regard. We are continuing our efforts in this segment of the olfactory-impaired population. Alternatively, functional MR studies may be the route to take for location of olfactory function.

We did not compare the volume of the olfactory bulbs and tracts and temporal lobes in our patients who had posttraumatic olfactory dysfunction with that of posttraumatic patients with normal olfactory function. However, the volume difference between anosmic and hyposmic patients, between anosmic persons and control subjects with normal smell function, and between the combined anosmic-hyposmic group and subjects with normal smell function suggests that the volume loss seen in the olfactory bulbs and tracts may reflect a propensity for smell loss. One cannot presume cause and effect from our study. Most of the patients we saw were referred to the Smell and Taste Center; one would have to assess all head trauma patients with surface-coil examinations of the olfactory bulbs and tracts to produce a control population with documented damage to this system but without smell dysfunction. The prevalence of damage to olfactory bulbs and tracts and the frontal lobe would be expected to be greatest in patients with acceleration-deceleration injuries, in which the plane of impact was in an anteroposterior direction.

It is gratifying to note the high intraclass correlation coefficients obtained for the volumes of olfactory structures examined. These values (all above .90) suggest that our technique is both reliable and reproducible. We believe that the difference in volume of the olfactory bulbs and tracts between anosmic patients and those with normal olfaction is real. We further believe that the lack of significant correlation between individual olfactory tests and quantitative or qualitative grades of damage reflects the influence of the factors listed above as well as the small sample size rather than a deficiency in the method used. A study that includes more patients with residual olfactory function and/or limited damage to the olfactory bulbs and tracts would be required to obtain sufficient power to detect a clinically significant relationship be-

tween intracranial sites of injury and specific results on smell tests.

References

1. Sumner D. Post-traumatic anosmia. *Brain* 1964; 87:107–120
2. Costanzo RM, Heywood PG, Ward JD, Young HF. Neurosurgical applications of clinical olfactory assessment. *N Y Acad Sci* 1987; 510:242–244
3. Levin HS, High WM, Eisenberg HM. Impairment of olfactory recognition after closed head injury. *Brain* 1985;108:579–591
4. Potter H, Butters N. An assessment of olfactory deficits in patients with damage to prefrontal cortex. *Neuropsychologia* 1980;18: 621–628
5. Zusho H. Posttraumatic anosmia. *Arch Otolaryngol* 1982;108: 90–92
6. Schecter PJ, Henkin RI. Abnormalities of taste and smell after head trauma. *J Neurol Neurosurg Psychiatry* 1974;37:802–810
7. Doty RL, Shaman P, Dann M. Development of the University of Pennsylvania Smell Identification Test: A standardized microencapsulated test of olfactory function. *Physiol Behav* 1984;32: 489–502 (Monograph)
8. Doty RL, Ugrawal U, Frye RE. Evaluation of the internal consistency reliability of the fractionated and whole University of Pennsylvania Smell Identification Test (UPSIT). *Percept Psychophys* 1989;45:381–384
9. Smith RS, Doty RL, Burlingame GK, McKeown DA. Smell and taste function in the visually impaired. *Percept Psychophys* 1993; 54:649–655
10. Bromley SM, Doty RL. Odor recognition memory is better under bilateral than unilateral test conditions. *Cortex* 1995;31:25–40
11. Vollmecke TA, Doty RL. Development of the Picture Identification Test (PIT): A research companion to the University of Pennsylvania Smell Identification Test. *Chem Senses* 1985;10:413–414
12. Folstein MF, Folstein SE, McHugh PR. Mini-mental state. *J Psychiatr Res* 1975;12:189–198
13. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977;33:159–174
14. Hotchberg Y. A sharper Bonferroni procedure for multiple tests of significance. *Biometrika* 1988;75:800–803
15. Doty RL, McKeown D, Lee WW, Shaman P. Test-retest reliability of 10 olfactory tests. *Chem Senses* 1995;20:645–656
16. Doty RL, Newhouse MG, Azalina JD. Internal consistency and short-term test-retest reliability of the University of Pennsylvania Smell Identification Test. *Chem Senses* 1985;10:297–300
17. Costanzo RM, Zasler ND. Head trauma. In: Getchell TV, Doty RL, Bartoshuk LM, Snow JB Jr, eds. *Smell and Taste in Health and Disease.* New York, NY: Raven Press; 1991:711–730
18. Leigh AD. Defects of smell after head injury. *Lancet* 1943;1: 38–40
19. Symonds CP. Discussion on differential diagnosis and treatment of post-contusional states. *Proc Royal Soc Med* 1942;35:601–614
20. Mott AE, Leopold DA. Disorders in taste and smell. *Med Clin North Am* 1991;75:1321–1353
21. Varney NR. Prognostic significance of anosmia in patients with closed-head trauma. *J Clin Exp Neuropsychol* 1988;10:250–254
22. Costanzo RM. Neural regeneration and functional reconnection following olfactory nerve transection in hamster. *Brain Res* 1985; 361:258–266
23. Jafek BW, Eller PM, Esses BA, Moran DT. Post-traumatic anosmia: ultrastructural correlates. *Arch Neurol* 1989;46:300–304
24. Truwitt CL, Barkovich AJ, Grumbach MM, Martini JJ. MR imaging of Kallmann syndrome: a genetic disorder of neuronal migration affecting the olfactory and genital systems. *AJNR Am J Neuroradiol* 1993;14:827–838
25. Bick DP, Ballabio A. Bringing Kallmann syndrome into focus. *AJNR Am J Neuroradiol* 1993;14:852–854
26. Iida Y, Naito M, Asahina N, et al. Magnetic resonance imaging of the olfactory apparatus. *Arch Otolaryngol Head Neck Surg* 1994; 120:869–872
27. Knorr JR, Ragland RL, Brown RS, Gelber N. Kallmann syndrome: MR findings. *AJNR Am J Neuroradiol* 1993;14:845–851
28. Li C, Yousem DM, Doty RL, Kennedy DW. Imaging evaluation of olfactory deficits. *AJR Am J Roentgenol* 1994;162:411–418
29. Vogl TJ, Stemmler J, Heye B, et al. Kallman syndrome versus idiopathic hypogonadotrophic hypogonadism at MR imaging. *Radiology* 1994;191:53–57
30. Yousem DM, Turner WJD, Li C, Snyder PJ, Doty RL. Kallmann's syndrome: MR evaluation of olfactory system. *AJNR Am J Neuroradiol* 1993;14:839–843
31. Yousem DM, Geckle RJ, Bilker W, McKeown D, Doty RL. MR evaluation of patients with congenital hyposmia or anosmia. *AJR Am J Roentgenol* 1996;166:711–713