Recovery of Olfactory Function Following Closed Head Injury or Infections of the Upper Respiratory Tract

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Objective: To investigate the outcome of olfactory function in patients with olfactory loss following infections of the upper respiratory tract (post-URTI) or head trauma.

Design: Retrospective patient-based study.

Setting: Smell and Taste Outpatient Clinic at a university hospital.

Patients: A total of 361 patients (228 women, 133 men) were included.

Main Outcome Measures: Olfactory function was assessed using the “Sniffin’ Sticks” test battery, which resulted in a threshold, discrimination, and identification score. The mean interval between first and last visit was 14 months.

Results: In comparing the overall threshold, discrimination, and identification scores between the last and first visit, olfactory function improved in 26% of the patients whereas it decreased in 6%. The cause of olfactory impairment had a significant effect on the recovery rate of olfactory function. Within the post-URTI group (n=262), 32% of the patients improved, but in the posttraumatic group (n=99) only 10% improved. In patients with post-URTI olfactory loss, a negative correlation was found between age and recovery of olfactory function. In general, the factor “sex” had no significant effect on recovery of smell function.

Conclusions: To our knowledge, the series of patients presented herein is the largest in the literature to date in which standardized testing methods were used to assess the progression of impaired olfaction. It showed that the rate of improvement of olfactory function was significantly higher in patients with post-URTI dysosmia compared with patients with posttraumatic dysosmia. During an observation period of approximately 1 year, more than 30% of patients with post-URTI olfactory loss experienced improvement, whereas only 10% of patients with posttraumatic olfactory loss experienced improvement. Furthermore, age plays a significant role in the recovery of olfactory function.


Olfactory disorders occur at a much higher rate than previously thought, as demonstrated in recent population-based studies.\(^1\,^2\) The frequency of a decreased olfactory function was as high as 16% in one studied population, with at least 5% of the general population being functionally anosmic.\(^3\) In another study, the prevalence of impaired olfaction was 25% in adults 50 years and older.\(^4\) These surveys report that upper respiratory tract infections (URTIs) and trauma are among the most frequent causes of dysosmias.\(^5\) In contrast to a slowly progressive decrease of olfactory function, patients with post-URTI and posttraumatic dysosmia experience sudden olfactory loss. This has been reported to have a more severe impact on quality of life\(^6\) compared with progressive olfactory loss, which may go unrecognized.\(^2,^6\) Apart from the psychological strain in these patients, most of them experience hazardous events.\(^7\) Because no therapy has yet been proven to be effective in post-URTI and posttraumatic smell disorders, correct information on the nature of the disorder and its prognosis appears to be essential in the counseling of these patients. Until now, only few studies have addressed long-term changes of olfactory function in patients with post-URTI or posttraumatic smell disorders, often in relatively small samples. Thus, the aim of this retrospective study was to investigate the change of olfactory function in a large group of patients with the use of standardized testing methods with strict criteria.

METHODS

PATIENTS

All participants were evaluated at the Smell and Taste Clinic of the Department of Otorhinolaryngology of the University of Dresden Medical School, Dresden, Germany. A total of 361 patients were included (228 women [63.2%] and
133 men (36.8%). The mean ± SEM age was 55.3 ± 0.7 years (range, 17-82 years). The patients were thoroughly examined by experienced otorhinolaryngologists, including an endoscopic investigation of the nasal cavity. Depending on the clinical examination and the detailed, structured history, olfactory dysfunction was classified as either postinfectious or posttraumatic, following an infection of the upper respiratory tract or a closed head injury, respectively. The “postinfection group” comprised 262 patients (187 women and 75 men; mean ± SEM age, 38 years), and the “posttraumatic group” comprised 99 patients (41 women and 58 men; mean ± SEM age, 48.1 years). Because the presentation of the patients to our clinic is dependent on their subjective degree of complaint and on the often ignoring attitude of clinicians and the social environment toward olfaction and its problems, the time span between appearance of olfactory disturbance and first visit varied from 1 to 216 months (mean ± SEM, 17.4 ± 1.7 months). The mean ± SEM interval between the first and last visit was 13.6 ± 0.6 months.

**OLFACTORY TESTING**

Olfactory testing was performed using the “Sniffin’ Sticks” test kit, which involves tests for odor threshold, odor discrimination, and odor identification. With the use of commercially available felt-tip pens, the odorants were presented approximately 2 cm in front of both nostrils for 2 seconds. Phenylethyl alcohol odor threshold was assessed by a single-staircase, 3-alternative, forced-choice procedure. Three pens were presented to the patient in a randomized order, 2 containing an odorless solvent (propylene glycol) and the other containing the odorant in a certain dilution. The patient’s task was to indicate the pen with the odorant. Concentration was increased if one of the blanks was chosen and decreased if the correct pen was identified twice. The mean of the last 4 of 7 reversal points was used as detection threshold. The second subtest assessed the ability of the patient to discriminate different odors. Therefore, 16 triplets of pens were offered, each including 2 identical and 1 different odor. The patient’s task was to indicate the pen that had a different smell. Threshold and discrimination testing were performed with the patient being blindfolded. For testing odor identification, 16 pens containing common odors were offered. The patient had to identify each of the odorants from a list of 4 descriptors. The sum of the 3 subtests resulted in the threshold, discrimination, and identification (TDI) score, with a maximum of 48 points. As defined in Hummel et al and Kobal et al, a score of 32 points or more indicates normosmia, a score between 16 and 32 points indicates reduced olfactory function in terms of hyposmia, and a score of less than 16 points indicates functional anosmia.

To categorize progression of olfactory function, an increase of more than 6 points in the TDI score was regarded as a clinically significant improvement of olfactory function. In contrast, a significant decrease of olfactory function was assumed if the TDI score decreased by more than 6 points.

The “Sniffin’ Sticks” test has been used in many patients and subjects to assess olfactory performance since it was developed in 1996. Its correlation with previously established tests of olfactory function (eg, the 12-item Cross-Cultural Smell Identification Test [CC-SIT, a subtest of the University of Pennsylvania Smell Identification Test “UPSIT”] and the Connecticut Chemosensory Clinical Research Center Test [CCCRC] has been demonstrated in various studies).

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Total (SD)</th>
<th>Female (SD)</th>
<th>Male (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>99</td>
<td>41</td>
<td>58</td>
</tr>
<tr>
<td>Age, y</td>
<td>48.1 ± 1.5</td>
<td>52.1 ± 2.4</td>
<td>45.2 ± 1.9</td>
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<tr>
<td>TDI score: first visit</td>
<td>13.6 ± 0.7</td>
<td>11.9 ± 0.9</td>
<td>14.8 ± 1.0</td>
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<tr>
<td>TDI score: last visit</td>
<td>13.9 ± 0.7</td>
<td>12.7 ± 0.9</td>
<td>14.8 ± 1.0</td>
</tr>
<tr>
<td>Time between first and last visit, mo</td>
<td>13.4 ± 0.9</td>
<td>12.8 ± 1.3</td>
<td>13.7 ± 1.2</td>
</tr>
<tr>
<td>Time between infection and first visit, mo</td>
<td>18.2 ± 2.6</td>
<td>19.4 ± 5.5</td>
<td>17.3 ± 2.1</td>
</tr>
</tbody>
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**STATISTICAL ANALYSIS**

For statistical analyses, SPSS version 12.0 (SPSS Inc, Chicago, Ill) was used. Comparisons between the first and last visit were performed using the t test for paired samples. Correlation analyses were performed according to Pearson. The α level was set at .05.

**RESULTS**

Of the 361 patients, 93 (25.8%) exhibited an increase in having a TDI score of more than 6 points, indicating significant improvement of olfactory function, whereas 22 patients (6.1%) exhibited a decrease in olfactory function. Descriptive statistics for the patients with post-URTI or posttraumatic olfactory loss are given in the Table.

**PATIENTS WITH POST-URTI OLFACTORY LOSS**

Of the 262 patients with post-URTI olfactory loss, 83 performed significantly better at the second visit (ie, 31.7% of the patients exhibited improved olfactory function). However, a significant decrease of the TDI score was observed in 15 subjects (5.7%), and 164 patients...
(62.6%) exhibited no change. Across all subjects, the mean±SEM TDI score changed by 3.8±0.4 points. This change, as well as differences in each of the subtests (threshold, discrimination, and identification) were statistically significant ($P < .001$) (Figure 1).

The mean±SEM interval between the first and last visit was 13.7±0.8 months. The time between infection and first visit varied from 1 to 204 months (mean±SEM, 17.1±1.4 months). Patients with a shorter duration of olfactory loss had a higher chance to exhibit improvement of overall olfactory function, expressed as the change of TDI score ($r_{262} = -0.17; P = .006$). In contrast, no significant correlation could be found between the interval between first and last visit and improvement of olfactory function ($r_{262} = 0.11; P = .08$).

There were more women among patients with post-URTI olfactory loss than men (187 women vs 75 men). However, the factor “sex” had no significant effect on recovery ($P = .34$) (Figure 2).

To investigate the effect of age on recovery from olfactory loss, patients were divided into 5 age groups (<40 years [$n=17$; 6.5%]; 40–49 years [$n=31$; 11.8%]; 50–59 years [$n=76$; 29.0%]; 60–69 years [$n=110$; 42.0%]; and >69 years [$n=28$; 10.7%]). The number of patients exhibiting recovery decreased continuously with age (<40 years, 47.1%; 40–49 years, 35.5%; 50–59 years, 34.2%; 60–69 years, 32.7%; and >69 years, 7.1%) (Figure 3). This also resulted in a significant negative correlation between the patients’ age and recovery rate ($r_{262} = -0.18; P = .003$).

**Figure 1.** Threshold, discrimination, and identification (TDI) scores of the first and last visit of patients with olfactory loss following infections of the upper respiratory tract.

**Figure 2.** Sex distribution and recovery rate in patients with olfactory loss following infections of the upper respiratory tract.

**Figure 3.** Age distribution and recovery rate in patients with olfactory loss following infections of the upper respiratory tract.

**Figure 4.** Threshold, discrimination, and identification (TDI) scores of first and last visit of posttraumatic patients.

A total of 99 patients had olfactory dysfunction following head trauma. There was no significant difference in mean±SEM TDI scores (0.3±0.47 points; $P = .52$) between the first and last visit for patients with head trauma (Figure 4). Of the 99 patients, 10 (10.1%) improved; 82 (82.8%) did not change in olfactory function; and 7 (7.1%) exhibited a decreased test result at their last visit. On average (mean±SEM), they consulted our clinic


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18.2 ± 2.6 months after the trauma and returned 41 ± 0.9 months after the trauma for the last visit. In these patients, neither sex nor age affected the recovery rate (sex-related difference in recovery; $P = .40$; correlation between age and recovery rate; $r_{95} = .05; P = .62$), nor was there a significant effect of the duration of olfactory loss (correlation between duration of head trauma and recovery rate; $r_{95} = .019; P = .054$).

**POST-URTI OLFACTORY LOSS**

Previous studies reported a wide range of patients with recovery of the sense of smell following URTI. Mori et al reported that 58% (n = 190) of patients with post-URTI olfactory dysfunction showed an improvement in terms of their olfactory sensitivity. However, olfactory function was not tested, but patients were only interviewed with regard to recovery of their sense of smell. These data may be biased by the fact that the patients’ self-assessments have been shown to be notoriously unreliable. Therefore, in the present study, subjective reports were not considered and only results from quantitative olfactory testing were taken into account.

Duncan and Seiden found in their long-term follow-up study of olfactory loss an improvement in 62% of the patients based on the patients’ ratings. When tested with the UPSIT, even more (66%) showed an increased score of 4 UPSIT points or more. Investigations were performed after a mean duration of disease of 36.9 months. It has to be kept in mind, however, that this study included only 21 subjects. In addition, the observation period was approximately 3 times longer than that in the present study, which might explain the higher recovery rate.

In contrast to these relatively high rates of recovery, Hendriks reported in his excellent summary of the literature up to 1988 that spontaneous recovery occurs in 35% of the patients over a period of approximately 12 months. Furthermore, an investigation on the effectiveness of lipooic acid in the treatment of smell dysfunction following a URTI (which has proven to be as effective as placebo [T.H., unpublished data, 2005]) showed that 35% of the patients exhibited a remarkable increase in olfactory function over an average period of 4 months. In line with these observations, the present study indicates that approximately one third (32%) of patients with post-URTI olfactory loss exhibit improvement over a period of approximately 1 year.

The effect of aging on the sense of smell has been investigated extensively, and it has been shown in many studies that olfactory function decreases as a function of age. In the present study, post-URTI olfactory loss was observed in more than 70% of the group aged 50 to 69 years, which confirms findings of previous studies. The decline of olfaction with age and the higher number of elderly patients in the post-URTI group indicate that age is among the most important factors in terms of recovery of smell function. Reasons for this may be found in the fact that regeneration of olfactory receptor neurons decreases with age, leading to a decreased number of olfactory receptor neurons. As a possible result, the size of olfactory epithelium decreases with aging. These pathophysiological findings explain, at least in part, why nasal mucosa and olfactory epithelium in elderly people are more vulnerable for infections and that the chance of recovery of olfaction in post-URTI olfactory loss becomes smaller with increasing age, which was already observed in 1930 by Bednár in a study of 27 post-URTI patients. The present results showed that 47% of patients younger than 40 years improved during approximately 1 year of observation. In contrast, only 7% of patients recovered if they were 70 years or older.

Another prognostic factor is the duration of disease. As reported previously, the likelihood for recovery decreases with the duration of olfactory loss. This can be confirmed by the negative correlation between duration of olfactory impairment and change in TDI score seen in the present data. To investigate this effect in greater detail, we divided the patients into 4 groups with regard to the duration of disease. This analysis revealed that 31.6% (n = 155) of the patients who showed up within 1 year after infection improved in terms of olfactory function; the percentage of recovery was 37.5% (21 of 56 patients) after 1 to 2 years, 36.8% (7 of 19 patients) after 2 to 3 years, and 18.8% (6 of 32 patients) after 3 years or later. Thus, within the first 3 years after infection, the proportion of patients who show improvement remains constant at about one third, whereas after 3 years we see an obvious decrease in the recovery rate. These data indicate that functional regenerative processes in peripheral and/or central regions may be effective not only within the first year but even after a relatively long latency.
The literature favors the hypothesis that shearing or tearing of the fila olfactoria is the most likely cause of olfactory loss, although little research has been done in this area. Investigations by Delank and Fechner35 indicate that the vulnerability of the fila varies. This seems to confirm reports by Sumner,36 who already observed changes in olfactory function. These data should also dem-

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