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Olfactory testing in clinical settings - is there additional benefit from unilateral testing?*

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SUMMARY

In clinical settings, olfactory testing is usually performed bilaterally; thus, unilateral olfactory loss may go unnoticed. The aims of this study were to evaluate 1) whether patients presenting with self-reported olfactory disorders demonstrate significant side differences in odour perception, depending on the prevalance of measured unilateral disorder, and 2) to evaluate the existing testing procedure. In 518 patients presenting with olfactory disorders, olfactory testing was performed using the "Sniffin' Sticks" test battery (consisting of a threshold, discrimination, and odour identification test) examining each nostril separately. According to the history and results from the clinical examination, olfactory disorders were classified as related to trauma, sinunasal disease, upper respiratory tract infection (URTI), tumour, congenital, idiopathic, and other. A difference of three or more points in one of the subtests or six or more points in the composite olfactory test score was considered a side difference. In almost one quarter of all presenting patients (23.4%), a side difference was detected. To not to miss lateralized disorders, we recommend testing each nostril separately. Depending on the presence or absence of a significant difference, testing then can be continued birhinally or separately for each nostril.

Key words: lateralized, olfactory disorder, olfactory testing, birhinal

INTRODUCTION

In a typical clinical setting, the sense of smell is routinely tested in a bilateral fashion. One reason is that testing each nostril separately requires more time. Another reason might be the fact that few patients – if any – complain about unilateral olfactory loss. This is not surprising since humans are almost unable to lateralize olfactory perception [(1)]. The prevalence of olfactory disorders in the population is between 5% (functional anosmia) and 13 -16% (hyposmia) [(2,3)]; however, many patients often are not aware of the disorder and frequently are unable to describe their overall olfactory function precisely [(4)].

Complaints about unilateral disorders are rare. Nevertheless, lateralized olfactory differences have been described in left- and right-handed subjects [(5)], or in patients suffering from schizophrenia [(6)] or Parkinson's disease [(7)]. Frasnelli et al. [(8)] compared lateralized and birhinal olfactory thresholds and found no major difference for detection thresholds obtained for the best nostril compared to both nostrils. This result is not surprising considering that patients rarely can detect a unilateral reduction in smell. In everyday-life, one would have to voluntary hold one nostril and smell an odorant deliberately with one nostril alone and then with the other nostril to compare the function of either nostril and possibly detect an unilateral disorder. In fact, significant side differences of odour perception were found in 32% of patients suffering from a tumour, in 25% of patients suffering from chronic rhinosinusitis, and in 15% of healthy subjects [(9)]. These findings suggest that side differences might be more common than assumed and might be a sign of a serious cause of smell dysfunction.

We aimed 1) to investigate the prevalence of lateralized olfactory disorders, 2) to examine whether specific etiologies of olfactory loss produce a distinctive pattern in the results from olfactory tests by examining a large number of patients with olfactory dysfunction, and 3) to discuss a possible recommendation for the clinician about whether testing each nostril separately may be of advantage. To this end, we used the extended "Sniffin' Sticks" test battery including tests for odour threshold, discrimination, and identification applied separately for each nostril.

METHODS

Participants

The study was performed in accordance with the declaration of Helsinki on Biomedical Research involving human subjects. It was approved by the Ethics Committee of the University of Basel. All patients who visited our ENT clinic from 2001 until 2008 complaining about an olfactory disorder (n = 518) were examined. All patients with hyp- or anosmia were included in the study,

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while all patients with bilateral normosmia were excluded [10]. Exact medical histories were obtained including questions about current medications, smoking habits, and former nasal / paranasal surgeries, as well as allergies and previous head trauma. All patients underwent nasal endoscopy after decongestion and had an extensive smell test consisting of the "Sniffin' Sticks" battery. If necessary, further examination (e.g., magnetic resonance tomography / computer-assisted tomography, neurological examination) was performed to establish diagnosis.

According to the patients' histories and results of the clinical examinations, the olfactory disorders were classified into one of the following etiologies: upper respiratory tract infection (URTI), traumatic, sinunasal (disorders of the nose and/or the paranasal sinuses, either inflammatory (rhinosinusitis) or non-inflammatory (anatomical)), idiopathic, tumour, congenital, and others (e.g., postoperative or toxic).

Olfactory test

The olfactory test ("Sniffin' Sticks" test battery [11-13]) consists of a non-verbal threshold test, a non-verbal discrimination test, and a verbal identification test. For threshold (T) testing, *n*-butanol was presented in a dilution series, starting with 4% *n*-butanol. Sixteen serial dilutions were made starting at 1:2. Using a triple forced choice staircase paradigm, detection thresholds for *n*-butanol were determined. Scores ranged from 1 to 16. Odour discrimination (D) was tested using 16 triplets of pens with two containing the same odorant and a third containing a different odorant. Subjects had to determine which of the three odour-containing pens smelled differently. Since 16 triplets were tested, the subjects' D-scores ranged from 0-16. Throughout both threshold and discrimination tests, the subjects were blindfolded. Odour identification (I) was assessed using 16 commonly known odours. Using a multiple forced choice task, individual odours were identified from a list of four descriptors. Again, the score ranged from 0 to 16.

TDI-Score

Results of the three subtests of the "Sniffin' Sticks" (i.e., threshold, discrimination, identification) were analyzed as a composite TDI-score, which was derived from the sum of the results obtained for threshold, discrimination, and identification. The TDI-score ranged from 1 to 48. A TDI-score of less than 16 was defined as functional anosmia, and a TDI-score of less than 31 as hyposmia [13].

"Sniffin' Sticks" testing was performed separately for each nostril. In the case of visible lateralized endonasal pathology, testing started at the narrower side, which was assumed to be worse in terms of olfactory function. The patients closed the other nostril with the thumb. Threshold testing was performed first. Then, followed by a short break of 5-10 minutes, discrimination was performed alternating right and left nostril. Again followed by a short break, odour identification was performed, first on the side with the poorer threshold and then the other nostril.

Statistical analysis

Data were analyzed using SPSS 15.0 for Windows (SPSS Inc. Chicago, IL, USA). The analysis focused on lateralized differences in olfactory testing. According to Gudziol et al. [9], a significant side difference in one of the subtests (threshold, discrimination, or identification) was defined as a difference of three or more points. In the composite TDI-score, a difference of six or more points was considered a significant side difference. One-way analysis of variance (ANOVA) was used to investigate the influence of etiology, the results from olfactory testing, and the influence of age. Correlations were performed according to Pearson. The results are shown as means and standard errors of means (SEM) in both the results section as well as in all figures.

RESULTS

A total of 518 patients were examined (235 female and 283 male). Mean age was 50.4 years (range: 9 - 93 years). According to the causes of olfactory disorders, patients were classified as posttraumatic (34.2%; n = 177), post-URTI (18.7%; n = 97), sinunasal (11.4%; n = 59), idiopathic (16.2%; n = 84), congenital (3.1%; n = 16), tumour (1.4%; n = 7, olfactory groove meningioma, lateralized n = 2, bilateral n = 2; falx meningioma, lateralized, n = 1, esthesioneuroblastoma, lateralized n = 1, all localized endocranially; tumour of unknown histology on the upper part of septum, bilateral, n = 1, localized exocranially), and other (15.1%; n = 78).

Overall, in 23.4% (n = 121) of patients, a significant difference in the TDI-score was detected. Looking at the different etiologies of disorders, a lateralized disorder was present in 23.7% of all post-URTI disorders, in 22.6% of posttraumatic disorders, in 25.4% of sinunasal disorders, in 21.4% of idiopathic disorders, in 57.1% of tumour disorders, in 12.5% of congenital disorders, and in 24.4% of other disorders. Comparing the three most common olfactory disorders, post-URTI, posttraumatic, and sinunasal olfactory disorders, differences in threshold were more frequent in patients with post-URTI olfactory loss compared to those with loss after trauma ($F = 4.87$, $p = 0.008$; Figure 1). Comparing all different etiologies, the largest side difference was seen in tumour patients, and the lowest in subjects with congenital anosmia (Figure 2). A side difference in odour thresholds correlated with a side difference in discrimination ($r_{518} = 0.15$, $p < 0.001$), in identification ($r_{518} = 0.18$, $p < 0.001$), and in the composite TDI-score ($r_{518} = 0.51$, $p < 0.001$). There were no statistically significant differences between smoking and non-smoking patients, men or women, or related to age.

DISCUSSION

The data from the present study show that 1) side differences are present in 23.4% of our patients presenting with an olfactory disturbance; 2) among the most common disorders, only post-URTI and posttraumatic disorders differ in regard to threshold differences; and 3) a difference in threshold testing correlates positively with a difference in discrimination, identification, and the TDI-score.

Of all patients, almost one-quarter presented with a lateralized difference in olfactory sensitivity. This number is surprisingly high

and is in line with data from Gudziol et al., [9] who used an olfactory screening test that revealed similar numbers. These deficits are usually not detected in routine clinical testing since in birhinal testing, the results obtained reflect the better nostril [14]. Regarding the different etiologies, an unilateral deficit is not at all surprising in a patient with a tumour in which pathology is usually restricted to one side. Other disorders compatible with unilateral olfactory differences are known, e.g., unilateral cerebellar lesions [15] or other localized intracranial lesions like those resulting from temporal lobectomy [16]; even systemic diseases may present at certain stages with lateralized olfactory loss, e.g., schizophrenia [6,17] or Parkinson's disease [7].

Lateralized differences also are found in healthy subjects, for example, as reported by Gudziol et al. [9] and Good et al. [18]. Gudziol et al. [9] hypothesized that this unilateral deficit might reflect the beginning of an olfactory disorder. Interestingly, lateralized differences also were observed in patients suffering from olfactory disorders due to sinunasal diseases or post-URTI, both disorders in which pathophysiological changes are usually present bilaterally [19,20]. Thus, one can only speculate as to why such a pronounced lateralization of the disorder is present on one side of the affected patients

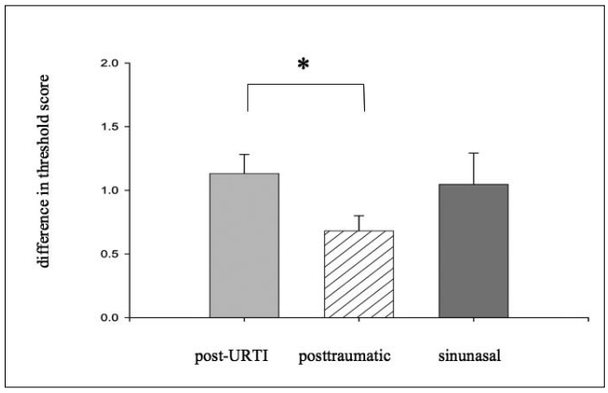

Figure 1. Differences in olfactory threshold in post-URTI olfactory loss, posttraumatic disorders, and sinonasal olfactory disorders are shown.

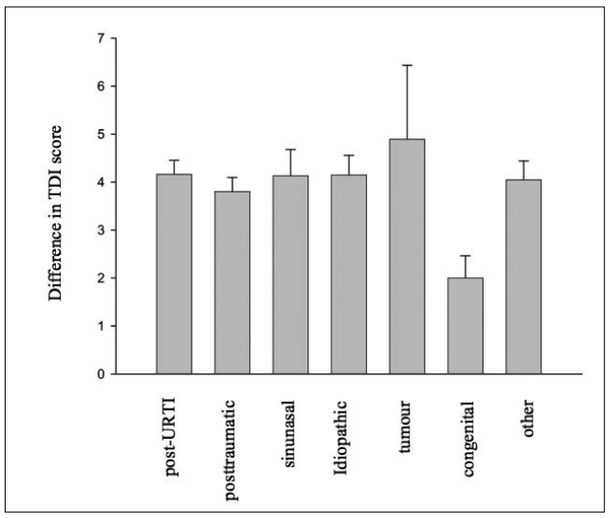

Figure 2. Side differences in TDI score of all etiologies are depicted.

Reden et al. [21] observed improvement of olfactory dysfunction in 32% of 262 patients with post-URTI smell disorders compared to only 10.1% of patients with posttraumatic disorders over a period of 14 months. Improvement might not always occur simultaneously on both sides. As is known for other sensory systems (e.g., bilateral vestibular disorders [22] or bilateral hearing disorders [23]), bilateral disorders do not necessarily recover simultaneously and might even persist unilaterally. Follow-up examinations in patients with olfactory disorders and significant side differences might provide valuable advice concerning the patients' prognosis.

Although we evaluated each nostril separately in a large number of patients, it was not possible to establish a certain "pattern" enabling the examiner to establish a diagnosis from the results in the different subtests alone. Other studies failed to do so as well [24]. Only posttraumatic and post-URTI disorders exhibited a significant difference in threshold testing, possibly indicating that recovery is a more dynamic process in patients with post-URTI olfactory loss.

Results from the threshold tests showed a significant correlation with other subtests from the "Sniffin' Sticks" test battery, which is the basis for the following testing recommendation in a clinical situation: we recommend starting with odour threshold testing separately for each nostril. If a side difference of more than three points is present, then testing should be continued for each nostril separately. If thresholds for both sides do not differ by more than three points, however, testing can be continued in a bilateral fashion. Testing in such a way will not increase the overall testing time significantly and may help to identify unilateral pronounced disorders.

CONCLUSION

In this study, patients with olfactory disorders due to different etiologies were examined using the extended "Sniffin' Sticks" test battery applied to each nostril separately. Differences of six or more points in the TDI-score between the right and left nostrils were found in almost one-quarter of all patients. Starting threshold testing in each nostril separately will aid in identifying unilateral disorders. In the absence of a side difference in the odour threshold, testing can be continued birhinally, while in the case of a side difference of at least three points in threshold testing, further subtests should be performed for each nostril separately to confirm this difference. If the etiology of the disorder does not explain the lateralized deficit, it might reflect various stages of recovery that may relate to the patients' prognosis.

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