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WILEY
Characteristics of Olfactory Disorder With and Without Reported Flavor Loss

Simona Negoias, MD, PhD; Benjamin Meves; Yunpeng Zang, MD; Antje Haehner, MD, PhD; Thomas Hummel, MD, PhD

OBJECTIVES/HYPOTHESIS: Quality of life related to olfactory disorder (OD) depends on the perceived impairment. It is not known why some patients with OD report smell and flavor loss while others report smell loss only. In order to understand this, we compared the two clinical presentation forms in terms of demographics, clinical features, and orthonasal olfaction test results.

STUDY DESIGN: Observational, analytic, cross-sectional study.

METHODS: A total of 401 patients with measured orthonasal OD presenting at a tertiary referral center were divided in 2 groups according to their subjective reports (smell loss only = 129 patients vs. smell and flavor loss = 272 patients). Groups were compared in terms of demographic (age, sex), clinical features (duration of disease, type of onset, etiology, degree of impairment due to the disorder) and test results (taste and orthonasal olfaction).

RESULTS: Groups did not differ in terms of age, sex distribution, orthonasal olfactory, or taste function. Patients reporting smell and flavor loss were characterized by a mainly sudden onset of the disorder and a predominance of postinfectious olfactory loss. They also have a shorter disease duration and a higher disease impairment. For patients reporting smell loss only, disease duration is longer, they feel less impaired, the onset of the disorder is to a higher degree protracted and the main cause is idiopathic.

CONCLUSIONS: Patients with orthonasal OD reporting smell and flavor loss feel more impaired and present significant different clinical features compared to patients reporting smell loss only. Future studies measuring retronasal olfaction are necessary to fully understand flavor perception in OD.

KEY WORDS: Smell disorder, flavor, orthonasal, retronasal, olfaction.

LEVEL OF EVIDENCE: 4

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INTRODUCTION

Olfactory disorder (OD) is a common health issue especially in older people, with an estimate of 20% of the general population exhibiting a certain degree of dysfunction. The most common causes are sinonasal disease, followed by postinfectious and posttraumatic dysfunction. Quality of life can decrease significantly in this group of patients and a strong association with depression has been described. Nevertheless, not everybody notices the disorder and not everybody feels impaired enough though as to address the health issue, the level of impairment depending on the individual importance of olfaction.

Patients with OD generally report problems in their daily life, like lack of ability to detect hazards (gas, fire, or rotten food), problems with cooking and eating, as well as enjoying environmental and body odors. This is related to the existence of two pathways for olfaction, orthonasal, through the nostrils and retronasal, through the nasopharynx. While orthonasal olfaction loss is noticed when snifing and identified by patients as smell loss, retronasal olfaction is related to eating and drinking and plays a very important role in the multisensory flavor perception together with taste and trigeminal sensations. Because retronasal olfactory stimuli are typically food-related, they are referred to the mouth. Consequently, retronasal olfactory loss is reported by patients as flavor or even taste loss. In terms of disease distress, retronasal olfaction seems to be a better predictor of distress than orthonasal olfaction.

Although it would be trivial to assume that OD affects both orthonasal and retronasal pathways and patients report both smell and flavor loss, some studies as well as clinical observations suggest the contrary. While most of the patients with OD report indeed smell and flavor loss, some report occasionally smell loss only with intact flavor perception. One explanation is that some patients with OD seem to maintain a certain degree of functionality or even an intact retronasal olfaction, supporting the idea that orthonasal and retronasal olfaction are processed differently. On the other side, a recent
study showed that patients with OD reporting intact flavor perception have actually also an impaired retronasal olfaction,\(^\text{17}\) and are therefore unaware of their deficit. Authors suggested that retronasal olfaction might be retrieved in this group of patients by unconscious memory recall from previous crossmodal sensory interactions within flavor perception. Consequently, in patients with OD who report smell loss only, flavor perception is either preserved in some rare cases or is affected but remains unnoticed in others. It is unclear why this is the case or what the exact level of retronasal olfaction is. While ideally all patients presenting with OD should receive testing of both olfactory pathways, time constrains in clinical routine, and lengthy testing methods, lead to retronasal olfaction testing being very limited. In the present study, we aimed therefore to answer the first question and characterize patients with OD reporting smell loss only as compared to patients reporting smell and flavor loss, in terms of clinical features (degree of dysfunction, type of onset, cause and duration of the OD) as well as perceived impairment caused by the dysfunction. We studied a large population of patients with measured orthonasal OD presenting at a tertiary referral center. We hypothesized that differences between the two groups would be mainly due to a gradual or a sudden onset of the disorder. This was based on the assumption that, in gradual OD, the retronasal olfactory deficit during eating or drinking is compensated by other components of flavor perception as texture, gustatory function, temperature, fattiness, astringency, spiciness etc. We further on hypothesized that patients with reported smell and flavor loss would suffer more as a consequence of the dysfunction as patients reporting smell loss only.

**MATERIALS AND METHODS**

**Study Population and Sampling**

Charts of all consecutive patients presenting at the specialized smell and taste clinic of the University of Dresden Medical School between January and October 2019 were reviewed for inclusion in this retrospective study. Before proceeding with the examination, patients were asked to fill in a structured medical interview assessing disease-specific and general clinical details. Firstly, patients were asked to indicate whether they have any problems with their smell, perception of flavor, or taste. In the case of a positive answer, they were asked to specify the exact problem by choosing one or more answers from the following 3 possibilities: 1) problem with smell, 2) problem with flavor perception, and 3) problem with taste perception (sweet, sour, bitter, salty). To avoid confusions between flavor and taste, the 4 most known taste qualities were specified in brackets. After completing the questionnaire, patients underwent a thorough clinical interview with the examining physician. This included revisiting the items of the questionnaire and revising any open questions, especially regarding potential confusions between smell, flavor, and taste. For the purpose of the present study, we focused on patients who opted for both smell and flavor problems (group 1) and patients who opted for smell problem only (group 2). No patients reporting taste impairments were included. Further on, patients indicated the duration of the dysfunction at the moment of presentation, the type of dysfunction onset (suddenly, gradual, since always, unknown), and self-rated the impairment caused by the dysfunction on a 6-point scale, from 0 – “not at all impaired” to 5 – “extremely impaired”. Further history of upper airway infection, head trauma, presence of other neurologic, rheumatologic or sinonasal symptoms (rhinorrhea, nasal blockage, face pain), current or past medication, current or past diagnosis, and operations were further inquired or retrieved from patients history charts. All patients underwent a thorough ENT clinical examination, including nasal endoscopy, sensory testing, and whenever needed, imaging or complimentary examinations (e.g., neurological). After completion of diagnostic steps, the most probable cause of disorder was identified, as previously reported:\(^\text{18}\): upper-airway infection (postinfectious olfactory loss), trauma (posttraumatic olfactory loss), sinonasal disease, congenital olfactory loss, dysfunction due to central nervous causes like stroke, tumors etc (termed central), neurodegenerative causes, idiopathic, and others.

**Sensory Testing**

Patients’ olfactory function was assessed as previously described with the standardized and validated Sniffin’ Sticks test battery (Burghart, Wedel, Germany) consisting of measurements of odor thresholds, discrimination, and identification based on pen-like odor dispensers.\(^\text{19-21}\) The maximum score of each test (threshold, discrimination, and identification) is 16 points and the sum of all 3 tests constitutes into the TDI-Score (threshold, discrimination, and identification score), with a maximum of 48 points. Taste function was screened with taste sprays containing suprathreshold sweet, sour, salty, and bitter solutions.\(^\text{22}\) While some of the patients received retronasal olfactory testing, the majority did not, so no retronasal olfactory results were considered for this study.

**Statistical Analysis**

For statistical analysis, SPSS 25 (IBM) was used. Statistical comparisons between groups were conducted with Chi-square test for categorical variables and independent sample t-tests for continuous variables. P-value was set at <0.05.

**Ethics**

The retrospective study was performed according to the “Declaration of Helsinki on research involving human subjects”, and approved by the local ethics committee of University of Dresden Medical School (EK122032011).

**RESULTS**

Charts of a total of 491 consecutive patients were reviewed. Patients reporting isolated taste loss (3), isolated aroma loss (13), combined aroma and taste loss (5), smell and taste loss (14), or smell taste and aroma loss (55) were excluded. We included the remaining 401 patients (236 female and 165 male) that reported either smell and flavor loss (272 patients, 67.8\%, group 1), or smell loss alone (129 patients, 32\%, group 2). The two groups were comparable in terms of age (group 1: mean age 56.2 ± 14.9, range 16–85 years, group 2: mean age 55.6 ± 17.8, range 11–83 years, T(399) = 0.33, P = .74) and sex distribution (group 1: 111 men, 161 women, group 2: 54 men, 75 women, \(\chi^2(1) = 0.04, P = .84\)).

Groups were comparable in terms of measured gustatory and orthonasal olfactory function (Table I) with no significant difference in any of the subtests.
Significant differences were seen between groups in terms of disease duration, subjective impairment, type of onset, and cause of disorder. Firstly, patients reporting smell and flavor loss showed a shorter disease duration ($t(382) = 2.51, P = .012$) and a higher subjective impairment ($t(385) = 2.93, P = .004$), as compared to patients reporting olfactory loss only (Table I, Fig. 1).

Further on, the type of disorder onset was significantly different between groups ($\chi^2(3) = 12.91, P = .003$). Specifically, a predominant sudden onset was seen in patients reporting smell and flavor loss, whereas patients reporting olfactory loss only showed a higher incidence of idiopathic and postinfectious onset conditions (Table I, Fig. 1).

### Table I

<table>
<thead>
<tr>
<th></th>
<th>Patients Reporting Smell and Flavor Loss</th>
<th>Patients Reporting Smell Loss Only</th>
<th>Group Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>M</td>
<td>SD</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>272</td>
<td>56.17</td>
<td>14.89</td>
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<tr>
<td>Duration (mo)</td>
<td>264</td>
<td>43.52</td>
<td>71.82</td>
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<td>Impairment</td>
<td>262</td>
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<td>0.98</td>
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<tr>
<td>Threshold</td>
<td>271</td>
<td>2.49</td>
<td>2.41</td>
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<tr>
<td>Discrimination</td>
<td>272</td>
<td>7.58</td>
<td>3.18</td>
</tr>
<tr>
<td>Identification</td>
<td>272</td>
<td>6.87</td>
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<tr>
<td>TDI-score</td>
<td>271</td>
<td>16.94</td>
<td>7.48</td>
</tr>
<tr>
<td>Taste sprays</td>
<td>244</td>
<td>3.70</td>
<td>0.76</td>
</tr>
</tbody>
</table>

Bold values represent significant values ($p < .05$).

Fig. 1. (A) Pie diagram depicting the distribution of the etiology of olfactory loss (percent and number of patients) for patients reporting smell and flavor loss (left) and patients reporting smell loss only (right). (B) Mean duration of olfactory disorder with standard error bars and (C) Mean impairment due to olfactory disorder with standard error bars for patients reporting smell and flavor loss (orange) and patients reporting smell loss only (blue). Note: the star (*) represents a $P$-value $< .05$, the double star (**) represents a $P$-value of $< .01$. 

Laryngoscope 130: December 2020 Negoias et al.: Olfactory Disorder With and Without flavor Loss
with smell and flavor loss (53.5%), followed by gradual (33.1%) and unknown (10.8%) as compared to patients with olfactory loss only (35.9%), where a more gradual onset (39.8%), followed by unknown onset (20.3%) was seen.

Finally, reflecting the type of onset, the distribution of disease causes was also different between groups ($\chi^2(7) = 37.31, P < .001$). For patients with olfactory and flavor loss, the dysfunction was most frequently caused by an infection of the upper respiratory airways (35%), followed by idiopathic causes (24%), head trauma (20%) and sinunasal disorders (17%). Most patients with olfactory loss only suffered from an idiopathic dysfunction (39%), followed by sinunasal disorder and infection of the upper respiratory airways (19% each) (Fig. 1).

**DISCUSSION**

The most important results of this study were:

1. No difference in orthonasal olfactory function or taste function was seen between patients reporting smell and flavor loss and patients reporting smell loss alone.
2. Patients reporting smell and flavor loss show a predominantly sudden disease onset and a different distribution pattern of causes of disease as compared to patients reporting smell loss only.
3. Patients reporting smell and flavor loss show a higher impairment caused by the disorder as compared to patients reporting smell loss alone.

Ever since the observation of Rozin that olfaction is a dual system, multiple studies explored differences between the two pathways. Nevertheless, this has not been mirrored at clinical level, since only few studies exist and they show a slightly controversial picture. Two explanations emerged as to why some patients with OD report no flavor dysfunction: either they do not have it, or they are not aware of it.

The existence of OD with preserved flavor perception is supported by some data presenting better retronasal than orthonasal olfaction in nasal polyposis. The same authors identified patients with absent or severely compromised orthonasal olfaction but normal or slightly altered retronasal tests also in the absence of chronic rhinosinusitis. Nevertheless, two recent studies show a strong correlation between orthonasal and retronasal measurements in chronic rhinosinusitis, although patients with anosmia were shown to identify certain ret-ronasal odors more often than expected.

On the other hand, Liu et al found patients with non-sinogenic orthonasal smell deficit claiming normal flavor perception, to be also retronasally dysosmic; therefore, being unaware of their retronasal deficit. They postulated that self-reports of flavor perception are unreliable and offered as an explaining mechanism memory retrieval of flavor patterns from previous experiences. Multiple studies show that patients with OD are often unaware of their olfactory deficits, even after controlling for cognitive function. Patients with severe OD are more aware of their dysfunction compared to hyp-osmic patients, while normosmic subjects rather evaluate the nasal patency when asked about their olfactory function. Nevertheless, patient-reported smell and taste metrics were shown to correlate stronger to orthonasal than retronasal olfaction. Generally, flavor perception awareness studies are rare, with most of the studies on olfactory deficit awareness and its relation to measured function based on orthonasal olfaction.

Time constrains in the clinical practice make comprehensive testing of retronasal olfaction in all patients with OD difficult, so, this study including, no big population data exist to assess and characterize the degree of retronasal dysfunction in patients with smell loss. Why some patients with smell loss may maintain flavor perception while others are unaware of the deficit remains unclear. Although no retronasal testing was performed, our data help, nevertheless, to better differentiate smell loss patients with and without flavor perception dysfunction, in terms of clinical characteristics and provides clarifying directions for future studies. As hypothesized, patients reporting smell loss alone show a higher degree of gradual onset of the disorder compared to patients with reported smell and flavor dysfunction, where sudden disease onset is dominating. The difference between groups in terms of disease onset is also reflected in the different distribution of disease etiology. Idiopathic olfactory loss, typically gradual in onset, was predominant in patients reporting smell loss alone, while postinfectious olfactory loss was the leading cause in patients reporting smell and flavor loss. Further on, patients reporting smell and flavor loss had a shorter disease duration than patients with smell loss alone. Based on these results it might be hypothesized that, a longer disease duration or a more gradual onset might facilitate adaptation to the dysfunction at flavor perception level. Specifically, it allows retronasal deficits, if existing, to get compensated by other components of flavor perception like texture, gustatory function, temperature, fattiness, astringency, spiciness etc., which then allows retrieval of memories associated with the food/drink.

This could in turn lead to a lower degree of distress. On the contrary, this adaptation is more unlikely to occur in the case of a sudden disease onset and/or shorter disease duration, maintaining dysfunction awareness at all levels (orthonasal and retronasal) and associating a higher disease distress. It may also be hypothesized that a longer disease duration allows regeneration processes in the posterior part of the olfactory cleft (OC) to occur, if we consider the hypothesis of differential damage and recovery of the anterior and posterior parts of the OC, which would place the anterior OC in a more vulnerable position. Our results should be interpreted with caution though, since it is still notable that ca. 25% of patients with smell loss only had a “sudden onset” etiology like post-traumatic and post-viral, while ca 25% of patients with smell and flavor loss have a “gradual onset” etiology like idiopathic. Consequently, onset type and etiology as well as disease duration are presumably only some of the factors playing a role in flavor perception and flavor perception awareness in OD. Future studies on large populations are necessary to elucidate the question of other determinants of flavor perception in OD besides the ones evaluated in this study, especially the level of retronasal olfaction.
This should be of interest if only because patients with reported smell and flavor loss exhibited higher levels of subjective impairment as compared to patients reporting smell loss only. Our results are hereby in line with conclusions of a recent study stating that retronasal olfactory function is better in predicting quality of life than orthonasal olfactory loss.14

In conclusion, patients with OD reporting smell and flavor loss exhibit a shorter disease duration, a predominately sudden disorder onset and a different distribution pattern of the causes of disorder as compared to patients reporting smell loss only. The former also seem to suffer more as a consequence of the dysfunction. Although these subtle differences in the patients history are only indicative and need to be integrated in the overall clinical context, they can help to prospectively better understand flavor loss in OD. They can also help the clinician to be more attentive toward those patients who require more support.

REFERENCES