The Evaluation of Olfactory Function in Individuals With Chronic Halitosis

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Abstract

Halitosis and olfactory dysfunction may disrupt an individual’s quality of life remarkably. One may ask whether halitosis has effects on olfactory functions or not? Thus, the aim of this study was to evaluate the olfactory abilities of subjects with chronic halitosis evaluated using the measurements of volatile sulfur compounds. This study was carried out in 77 subjects, with a mean age of 40.1 ± 13.3 years, ranging from 18 to 65 years. Forty-three participants were diagnosed as halitosis according to the gas chromatography results and constituted the halitosis group. Also, a control group was created from individuals without a complaint of halitosis and also who had normal values for volatile sulfur compounds. Each subject’s orthonasal olfactory and retronasal olfactory functions were assessed using “Sniffin’ Sticks” and retronasal olfactory testing. The results showed that odor threshold scores were lower in participants with halitosis compared with controls. Also, hyposmia was seen more common in the halitosis group than in controls. Moreover, a significant negative correlation was found between odor threshold scores and volatile sulfur compounds levels, particularly with hydrogen sulfide and dimethyl sulfide levels. The results suggest that the chronic presence of volatile sulfur compounds may have a negative effect on olfactory function.

Key words: gas chromatography, halitosis, hyposmia, olfaction

Introduction

Halitosis, also called bad breath or malodor, is a symptom in which a conspicuously offensive and unpleasant odor is present in the exhaled breath (Tonzetich 1977). The majority of pathologies causing halitosis arise from the oropharynx and a bacterial formation of odorous volatile sulfur compounds (VSCs), including hydrogen sulfide (HS) and methyl mercaptan (MM). Oropharyngeal pathologies include gingivitis, periodontitis, tonsillitis, and tongue coating (Kazor et al. 2003). In addition, 10–15% of patients have an extraoral cause for halitosis, which is often due to the presence of dimethyl sulfide (DMS) in the breath. Upper and lower respiratory tract infections, gastrointestinal system disorders, and systemic diseases, such as diabetes and serious liver disease, are examples of extraoral causes of halitosis (Tonzetich 1977; Tangerman 2002; Quirynen et al. 2009; Tangerman and Winkel 2010).

Olfaction plays an important role in our daily lives, such as by warning us against or attracting us toward odorous items, influencing food intake, and affecting interpersonal relations (Frasnelli and Hummel 2005). Halitosis is a social problem and a reason for social anxiety, causing embarrassment with all its consequences (Zaitsu et al. 2011). Subjects with halitosis
present themselves to a doctor because their relatives usually tell them that their breath smells bad (Yaegaki and Coil 2000; Falcão et al. 2012). They are frequently unaware of their malodor, which may be partly explained by olfactory desensitization. Olfactory desensitization reduces the perceived intensity of and behavioral responses toward this odor, and it increases the detection threshold and reaction time (Stuck et al. 2014). However, to the best of our knowledge, there is no literature about the olfactory abilities of subjects with chronic (pathologic) halitosis who are subject to odorous VSCs of his or her own origin. The aim of this study was to evaluate the olfactory abilities of subjects with chronic halitosis by using the “Sniffin’ Sticks” olfactory test and retronasal olfactory testing (Heilmann et al. 2002; Hummel et al. 2007).

Material and methods

Study design

This study was approved by the Clinical Research Ethical Committee of Istanbul Haydarpasa Numune Training and Research Hospital (2013-107) and conducted at the otorhinolaryngology and neurology clinics of GATA Haydarpasa Training Hospital and Istanbul Surgery Hospital. Also, all participants provided written consent after having been informed of the procedures and aims of the study. The study was conducted according to the Declaration of Helsinki on Biomedical Research Involving Human Subjects.

Only subjects with chronic (pathologic) halitosis were included in the study. For example, individuals with a complaint of morning bad breath (also called physiologic halitosis), those who were considered halitophobic, or patients with pseudohalitosis were not included in the study (Falcão et al. 2012).

Prior to the onset of the study, data were registered for each participant individually, including age, sex, medical history, tobacco use, and a list of current medications. Nasopharyngeal endoscopy, oropharyngeal examination, and endoscopic laryngeal examination were also performed. The exclusion criteria included patients with a history of upper respiratory infections within the past 3 weeks, as well as those with taste and smell disorders, sinonasal disorders (nasal polyps, chronic rhinosinusitis, allergic rhinitis, severe septum deviation), asthma, malignancy, head trauma, neurologic and psychiatric disorders (Alzheimer’s disorder, Parkinson’s disease, epilepsy, schizophrenia), metabolic and endocrine disorders (diabetes mellitus, hypogonadism, liver disease, kidney disease), or a habit of smoking. After performing gas chromatography for a measurement of sulfur compounds in the breath, 43 subjects were considered to have halitosis according to the individual cutoff level of each of the 3 VSCs; they constituted the halitosis group. The cutoffs for halitosis were 112 ppb for HS, 26 ppb for MM, and 8 ppb for DMS (Hanada et al. 2003; Dadamio et al. 2013). The age- and sex-matched control group was built from people who were admitted to the otolaryngology clinic for other reasons and met the above criteria. The gas chromatography measurements for all the volunteers were found to be normal.

After the study groups had been identified, all participants completed the orthonasal and retronasal olfactory testing process and nobody was excluded from the study due to his or her olfactory testing results.

Measurement of sulfur compounds

The HS, MM, and DMS levels were measured using a portable gas chromatograph (OralChroma, AbiMedical), which had been previously validated for clinical studies (Hanada et al. 2003; Murata et al. 2006; Awano et al. 2008 2011; Tangerman and Winkel 2008; Dadamio et al. 2013). Briefly, a 1-mL disposable syringe was inserted into the oral cavity through the lips and teeth with the piston fully inserted. Subjects were instructed to keep their mouths closed and to breathe through their nose for 30 s before the analysis. It was important to avoid contact between the syringe and the tongue. After waiting 30 s, the syringe aspirated 1 mL of mouth air. Immediately, 0.5 mL of mouth air from the sample was injected into the OralChroma.

After 8 min, the process was completed and the concentrations of the 3 gases were displayed in either ng/10 mL or ppbv (nmol/mol) (OralChroma Data Manager, AbiMedical). A software packet is available, OralChroma Data Manager (OralChroma Data Manager, AbiMedical), which collects the data from the OralChroma and graphically displays the sensor responses on a computer screen via a chromatogram (Tangerman and Winkel 2008).

All subjects received a letter with instructions before the examinations. One day before their appointment, the participants avoided garlic, onions, and spicy food. Twelve hours before the measurements, the participants also refrained from drinking alcohol or coffee and from smoking. On the morning of the appointment, the use of chewing gum, mints, drops, scents, and mouth rinses was not allowed. On the other hand, the participants could perform normal oral hygiene (tooth brushing) and had breakfast in order to avoid confusion between pathologic halitosis and bad morning breath (physiologic or transient halitosis). All measurements were recorded in the morning between 8:30 and 11:30 (before lunch) and at least 2 h after eating or drinking and oral hygiene. The cutoffs for halitosis were 112 ppb for HS, 26 ppb for MM, and 8 ppb for DMS, which are modified from a previous study (Hanada et al. 2003; Dadamio et al. 2013). Therefore, each of the 3 VSCs was categorized according to the individual cutoff level.

Orthonasal olfactory testing

Psychophysical testing of olfactory function was performed using the validated “Sniffin’ Sticks” test, where odorants were presented in commercially available felt-tip pens.
Retronasal olfactory testing

For retronasal olfactory testing, a standardized, validated test was used (Heilmann et al. 2002). The test is based on the identification of odorized powders or granules presented to the oral cavity (spices, instant drinks, and instant soups including ginger, grapefruit, bread, milk, strawberry, vanilla, orange, onion, cocoa, celery, mushroom, paprika, coffee, smoked ham, cloves, garlic, nutmeg, curry, cinnamon, and raspberry). The substances were applied to the midline of the tongue on fenestrated plastic sticks. Subjects were free to sample as much stimulant as needed for identification. This approach also minimized the need to standardize the area of stimulation or the differences in tongue or oral cavity size. In a typical trial, the researcher placed approximately 0.05 g on the middle of the tongue inside the oral cavity. Nostrils were not closed during the application of powders on the tongue. After administration of each powder, participants rinsed their mouths with water.

The procedure was self-timed. Each substance was identified by means of a closed set with 4 verbal items using a forced-choice procedure. The test result was a sum score of the correctly identified stimuli.

Statistical analysis

Data analyses were performed using the Statistical Package for Social Sciences 21.0 (SPSS; SPSS Inc.). The normal distribution of the considered variables was first evaluated using the Shapiro–Wilk test. The data are presented as the mean ± standard deviation for the continuous variables, and the number of cases was used for the categorical variables. The differences between the groups were analyzed by t- or chi-square test, as appropriate. To explore olfactory function in relation to the continuous variables measured in this study, data were submitted to a multivariate analysis of variance using the general linear model. Correlational analyses were calculated according to the Pearson’s test, and the level of significance was set at 0.05.

Table 1  Descriptive statistics of the study groups

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Halitosis group (n = 43)</th>
<th>Control group (n = 34)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>39.5 ± 14.4</td>
<td>40.8 ± 11.9</td>
<td>0.65</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>28/15</td>
<td>20/14</td>
<td>0.37</td>
</tr>
<tr>
<td>Odor threshold score</td>
<td>7.05 ± 2.3</td>
<td>12.8 ± 1.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Odor discrimination score</td>
<td>12.9 ± 0.9</td>
<td>13.3 ± 0.9</td>
<td>0.07</td>
</tr>
<tr>
<td>Odor identification score</td>
<td>12.6 ± 1.2</td>
<td>13.1 ± 1.1</td>
<td>0.08</td>
</tr>
<tr>
<td>TDI score</td>
<td>32.5 ± 3.7</td>
<td>39.1 ± 3.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Retronasal olfactory test scores</td>
<td>14.4 ± 1.6</td>
<td>14.9 ± 1.1</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Halitosis group: participants with a complaint of persistent halitosis; Control group: participants without a complaint of halitosis.

Results

This study was carried out in 77 subjects, with a mean age of 40.1 ± 13.3 years, ranging from 18 to 65 years. According to the gas chromatography results, 43 participants were diagnosed with halitosis; they constituted the halitosis group. In addition, a control group was created from individuals without a complaint of halitosis who had normal values for HS, MM, and DMS according to the OralChroma gas chromatograph. There was no difference between the groups in terms of age and sex. Table 1 gives the descriptive statistics of each of the variables of the study groups.

As shown in Table 1, the differences in odor threshold scores were significant between the groups, whereas no significant change was detected between them in terms of odor identification and discrimination scores, despite the decreases in the halitosis group when compared with the control group. Overall, there was a significant difference between the study groups in terms of the “Sniffin’ Sticks” composite scores (TDI). With regard to retronasal olfaction, the groups did not differ.

In addition, according to the TDI scores with a cutoff between normosmia and hyposmia at 30.3, 15 participants in the halitosis group were hyposmic and 28 were normosmic. In contrast, all participants in the control group were normosmic, with the difference between the groups being significant (P < 0.001).

When the gas chromatography results were examined in detail for the halitosis group, we found that HS levels alone were above the cutoff level in 12 people, whereas MM levels were above in 2 people and DMS levels were above in 8 people. However, we found that 2 of the 3 sulfur compounds were found to be above the cutoff levels in 18 people and MM levels increased together with HS levels in the majority of cases (n = 11 people). Also, all the measured VSCs were above the cutoff levels in 3 people. As shown in Table 2, there were significant differences between the participants in the halitosis group and those in the control group in terms of VSC levels.
Halitosis group; $P_{\text{Tonzetich}} < 0.001$ for control group < 0.001. Table 2: Gas chromatography results (ppb) according to the study groups.

<table>
<thead>
<tr>
<th>VSC</th>
<th>Halitosis group</th>
<th>Control group</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HS</td>
<td>404±559</td>
<td>17.1±22.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MM</td>
<td>99.6±195</td>
<td>2.6±5.5</td>
<td>0.002</td>
</tr>
<tr>
<td>DMS</td>
<td>15.8±24.3</td>
<td>0.3±1.2</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The cutoffs for halitosis were 112 ppb for HS, 26 ppb for MM, and 8 ppb for DMS.

A multivariate analysis was performed for evaluating the effects of independent variables (VSC levels) on dependent variables (“Sniffin’ Sticks” subtests and retronasal score). HS had a significant effect on odor threshold score, odor identification score, and TDI score ($P = 0.02$, 0.047, and 0.004, respectively), but not on odor discrimination and retronasal scores ($P = 0.08$ and 0.3, respectively). Additionally, there was a significant negative correlation between HS, odor threshold score, and TDI score ($P < 0.001$, $r = 0.5$ and $P < 0.001$, $r = 0.47$), whereas no similar correlation was found between HS and other olfactory scores.

The combined effect of HS and MM was also significant on all subtests of “Sniffin’ Sticks,” namely TDI ($P = 0.02$, 0.023, and 0.023, respectively), whereas there was no similar effect on retronasal olfactory score ($P = 0.3$). Furthermore, DMS levels had significant negative effects on odor threshold scores and TDI scores ($P < 0.001$, $r = 0.4$ and $P = 0.003$, $r = 0.3$). Our data did not show a correlation between DMS levels and other olfactory tasks.

### Discussion

In the current investigation, we tried to answer the question of whether potentially toxic sulfur compounds may cause olfactory dysfunction in individuals with a complaint of chronic (persistent or pathologic) halitosis. We designed a pilot study including individuals with a complaint of persistent halitosis as well as healthy controls. Our findings showed that, in particular, odor threshold scores were lower in participants with halitosis compared with the controls. In addition, hyposmia was seen more often in halitosis patients than in the controls. Moreover, a significant negative correlation was found between odor threshold scores and VSC levels, particularly HS and DMS levels.

However, the reasons for the results obtained in this study remain unclear. Little is known about the effects of chronic exposure at low concentrations of VSCs. The concentration and duration of toxic exposure may be important determining factors in the damage of the olfactory epithelium. It was demonstrated that the permeability of porcine nonkeratinized sublingual mucosa is increased by up to 75–103% following exposure to HS and MM, respectively (Ng and Tonzetich 1984). The authors of this study speculated that the increase in the permeability of the mucosa was dependent on both the time of exposure and the concentration of VSCs in the headspace.

HS is produced in small amounts by cells of the human body and has a number of biological functions (Tonzetich 1977; Kimura 2002). It acts as a vasodilator and has a role in the formation of memory. However, at high concentrations, HS is known to be a broad-spectrum toxin, which especially affects the nervous system. It has a characteristic smell commonly described as “rotten egg.” Similar to HS, MM and DMS can be found in the body at very low concentrations (Tangerman 2002). MM has a smell like “rotten cabbage or sewer gas,” and DMS has a characteristic smell that is highly disagreeable at even low concentrations and is commonly described as cabbage like. Both MM and DMS have a neurotoxic effect similar to HS (Tansy et al. 1981; Ng and Tonzetich 1984). The toxic effect of VSCs on olfactory epithelium is a matter to be investigated.

Participants with halitosis are typically unaware of their malodor. This situation can be explained by olfactory desensitization (Stuck et al. 2014), which may be lasting or temporary. This phenomenon is a conflicting issue in that subjects adapt more rapidly to malodors than to pleasant smells or vice versa (Jacob et al. 2003; Croy et al. 2013). Among other functions, olfactory adaptation serves to facilitate the perception of new or changing olfactory stimuli (Stuck et al. 2014). It is unclear whether this also generalizes to other odors.

One of the possible limitations of this study was the lack of organoleptic scoring (OLS) of the participants. However, current literature shows that the measurement of VSCs with a portable gas chromatograph is accepted as a gold standard for diagnosing halitosis and it has a high correlation with OLS (Hanada et al. 2003; Murata et al. 2006; Awano et al. 2008 2011; Tangerman and Winkel 2008; Dadamio et al. 2013).

### Conclusion

The relationship between chronic halitosis and olfactory dysfunction was not known prior to this study. Studies on olfactory perception conducted at pretreatment and post-treatment of halitosis are needed to understand the clinical relationship between halitosis and olfactory function better. Furthermore, controlled chemical exposure studies, particularly on animal subjects, may help in the understanding of the pathophysiology behind the results of this study.

### References


Halitosis and Hyposmia


