The Journal of Laryngology & Otology

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Investigation of smell and taste function in patients with obstructive sleep apnoea syndrome

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Abstract

Objective. This study investigated the relationship between disease severity and taste and smell functions in patients with obstructive sleep apnoea syndrome.

Methods. A total of 65 patients with recurrent upper airway obstruction during sleep were included. Participants were divided into four groups according to apnoea-hypopnoea index, obtained on polysomnography. Smell and taste tests were performed on these patients.

Results. A significant difference was observed between the smell thresholds of the groups for the identification test ($p = 0.016$). In the taste test, significant differences were observed between the groups in terms of sweet, sour, salty and bitter taste test thresholds ($p = 0.029$, $p = 0.0005$, $p = 0.001$ and $p = 0.017$, respectively).

Conclusion. As sleep apnoea severity increased (according to the apnoea-hypopnoea index) in obstructive sleep apnoea syndrome patients, the taste and smell thresholds decreased due to the effect of neuropathy and inflammation in the upper respiratory tract.

Main Article

Dr A Yenigun takes responsibility for the integrity of the content of the paper

Cite this article: Yenigun A, Degirmenci N, Goktas SS, Dogan R, Ozturan O. Investigation of smell and taste function in patients with obstructive sleep apnoea syndrome. *J Laryngol Otol* 2019;**133**:376–379. https://doi.org/10.1017/S0022215119000768

Accepted: 3 January 2019
First published online: 22 April 2019

Key words:
Obstructive Sleep Apnea Syndrome; Sense of Smell; Taste Sense; Inflammation

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Introduction

The apnoeic episode in obstructive sleep apnoea syndrome (OSAS) begins with the collapse of the upper respiratory tract during sleep, and is relieved by stimuli produced by brief arousal during apnoea and the airway is reopened. Often, OSAS is progressive over time, and its prevalence increases with age.[1,2] Old age, anatomical differences, alcohol use, gender and obesity are important factors that play a role in OSAS development.[3] Polysomnography is necessary for OSAS diagnosis, and selection and regulation of positive airway pressure therapy.[4]

Taste occurs by taste receptor cells embedded in taste buds distributed along the tongue surface. As the highest tasting densities are found on the front, back and sides of the tongue, the tongue has a slightly lower sensitivity to dorsum taste stimuli.[5] The most common causes of taste disorders are idiopathic (34 per cent), post-traumatic (24 per cent) and post-operative (15 per cent). Taste disorder is relatively rare compared to olfactory disorders.[6] The quantitative taste function can be measured by psychophysical tests, which have been described previously.[7] Qualitative taste disorders can only be assessed via patients' own reports.[6]

It is known that exposure to long-term, low-frequency vibrations in humans causes peripheral nerve damage.[8] Sensorial neuropathy, which is the result of long-term vibrations, is not only due to thermal stimulation but also mechanical stimulation.[9,10] In the pathogenesis of OSAS, it has been suggested that neuropathy occurs in upper respiratory tract tissues as a result of neurogenic damage caused by prolonged snoring and apnoea-induced vibrations.[11] It is also reported that inflammatory markers are increased in OSAS, and this increase is related to OSAS severity and hypoxia duration.[12] This study investigated the effects of OSAS severity on taste and smell associated with these neuropathic and inflammatory processes.

Materials and methods

This prospective study was approved (on 20 July 2016; decision number 2016/135) by the Ethical Board for Clinical Research at the Faculty of Medicine, Bezmialem Vakif University, Istanbul. The written informed consent of all patients was obtained.

The study included 65 patients, comprising 23 females (35.4 per cent) and 42 males (64.6 per cent), who presented with snoring, daytime sleepiness and/or apnoea symptoms, as reported by their relatives, between June and December 2016.

Patients who were smokers, alcohol users, or had hypertension or diabetes mellitus, were excluded from the study. Patients with cardiac insufficiency and coronary artery disease, systemic inflammatory disease, severe anaemia or haematological disease, chronic liver and kidney disease, or malignancy, and those receiving anticoagulation and anti-inflammatory treatment, or using systemic corticosteroids, were excluded. As our patients

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were only at the stage of diagnosis, we included patients who had not used continuous positive airway pressure (CPAP) before.

Patients with a preliminary diagnosis of OSAS, who were scheduled to undergo polysomnography, underwent a thorough otorhinolaryngology examination. In the endoscopic examination, the patients who were thought to have nasal problems such as choanal atresia, nasal polyps, septum deviation or turbinate hypertrophy were excluded from the study. A skin prick test was performed on patients with signs and symptoms of allergic rhinitis. Patients with a positive skin prick test result were excluded from the study. Patients who had received systemic steroid treatment in the past three months were excluded from the study. Patients who had undergone ear surgery that may have affected the chorda tympani were also excluded from the study.

Patients were followed up overnight with an 18-channel polysomnography (Sleep Screen; Viasys Healthcare, Höchberg, Germany). Polysomnography is characterised by electroencephalography, electrooculography, chin and leg electromyography, electrocardiography, airflow measurement with an oronasal thermistor, assessments of chest and abdominal respiration movements, oxygen saturation measurements with a fingertip pulse oximeter, and snoring assessment with a longitudinally placed tracheal microphone. The body position was also recorded. Sleep stages were scored according to standard criteria of Rechtschaffen and Kales.[13]

Apnoea was considered to be a complete stop in airflow for 10 seconds or longer. Hypopnoea was defined as a 3 per cent decrease in oxygen saturation for 10 seconds or more, or at least a 50 per cent reduction in airflow with arousal development. Apnoea-hypopnoea index was defined as the number of apnoeas and hypopnoeas per hour.[14] According to the results, those with an apnoea-hypopnoea index of less than 5 were allocated to the control group (group 1), and those with an apnoea-hypopnoea index of 5 or more to an OSAS group. The OSAS patients were classified as having mild OSAS (apnoea-hypopnoea index = 5–14.9) (group 2), moderate OSAS (apnoea-hypopnoea index = 15–29.9) (group 3) or severe OSAS (apnoea-hypopnoea index of 30 or more) (group 4).

Taste function evaluation

Taste testing was performed in each patient using a validated test (Taste Strips; Burghart, Wedel, Germany).[7] It consists of 8 cm filter paper strips with an impregnated tip area of 2 cm^2. Each side of the anterior part of the tongue was tested with 16 Taste Strips. Four taste types were tested in four different concentrations: (1) 'sweet' – 0.4, 0.2, 0.1 and 0.05 g/ml sucrose; (2) 'sour' – 0.3, 0.165, 0.09 and 0.05 g/ml citric acid; (3) 'salty' – 0.25, 0.1, 0.04 and 0.016 g/ml sodium chloride; and (4) 'bitter' – 0.006, 0.0024, 0.0009 and 0.0004 g/ml quinine hydrochloride. For each tongue side and taste type, a value of 0–4 was attributed, with 1 point given for each correctly identified taste. All scores were transferred to a table, and total scores were calculated for the right and left sides of the tongue.

Olfactory function evaluation

The Connecticut Chemosensory Clinical Research Center olfaction test was conducted, as described elsewhere.[15] This test consists of an n-butanol smell threshold test and a smell identification test. The olfactory tests were applied individually and were scored out of 7 (0 = worst olfaction, 7 = best olfaction). The mean score was calculated as the total Connecticut Chemosensory Clinical Research Center test score. Test scores were categorised as previously defined, and the patients were evaluated as anosmic, severely hyposmic, moderately hyposmic, mildly hyposmic or normosmic.[15]

Statistical analysis

Based on power analysis conducted before starting the research, we planned for 65 individuals to be surveyed. With a 95 per cent confidence level, 80 per cent power, 130 units of the mean difference and 85 units for the standard deviation, the power analysis indicated that a minimum of 17 cases was appropriate for each group.

Estimated apnoea-hypopnoea index variability was taken as the reference value. The Number Cruncher Statistical System ('NCSS'; 2007) and Power Analysis and Sample Size ('PASS'; 2008) statistical software programs (NCSS; Kaysville, Utah, USA) were employed for data evaluation. As well as evaluating the data using descriptive statistics (mean, standard deviation), the one-way analysis of variance (ANOVA) test and Tukey's honest significant difference test were used to compare the quantitative data and the normally distributed parameters between groups. The significance levels were set at $p < 0.001$ and $p < 0.05$.

Results

The study included 65 patients, comprising 23 females (35.4 per cent) and 42 males (64.6 per cent). There were no statistically significant differences between the groups in terms of mean age and sex ($p = 0.533$ and $p = 0.491$ respectively).

In the smell test, there was no significant difference between the groups for the n-butanol test ($p = 0.654$). A significant difference was observed between the olfactory thresholds of the groups in the smell identification test (one-way ANOVA test, $p = 0.016$). The smell threshold in group 4 (severe OSAS group) was significantly lower than that in group 1 (control group) (Tukey honest significant difference test, $p = 0.044$) (Table 1 and Figure 1).

In the taste test, one-way ANOVAs showed significant differences between groups in terms of sweet, sour, salty and bitter taste test thresholds ($p = 0.029$, $p = 0.0005$, $p = 0.001$ and $p = 0.017$, respectively). The sweet taste threshold in group 4 was significantly lower than that in group 1 (Tukey honest significant difference test, $p = 0.032$). The sour taste thresholds in group 3 (moderate OSAS) and group 4 were significantly lower than that in group 1 (Tukey honest significant difference test, $p = 0.001$ and $p < 0.001$ respectively). The salty taste thresholds in groups 3 and 4 were significantly lower than that in group 1 (Tukey honest significant difference test, $p = 0.008$ and $p = 0.008$ respectively). The bitter taste thresholds in groups 3 and 4 were significantly lower than that in group 1 (Tukey honest significant difference test, $p = 0.035$ and $p = 0.047$ respectively) (Table 1 and Figure 2).

Discussion

In this study, the relationship between OSAS severity (according to apnoea-hypopnoea index classification) and smell and taste functions, was evaluated in patients with OSAS without mucosal or systemic disease. Obstructive sleep apnoea syndrome is a widespread disease that is becoming increasingly prevalent. This disease is characterised by recurrent intermittent hypoxia. Intermittent hypoxia has been reported to

https://doi.org/10.1017/S0022215119000768 Published online by Cambridge University Press

Table 1. Demographic and laboratory data of the groups

Variables	Group 1 (control)	Group 2 (mild OSAS)	Group 3 (moderate OSAS)	Group 4 (severe OSAS)	*P*-value
Sex ratio (male:female)	10:6	12:6	10:6	10:5	0.491
Age (mean ± SD; years)	44.06 ± 9.09	45.12 ± 5.09	49.83 ± 7.70	48.81 ± 10.72	0.533
BMI (mean ± SD; kg/m^2)	30.54 ± 6.16	33.97 ± 6.79	33.53 ± 6.66	36.15 ± 6.63	0.20
AHI	<5	5–14.9	15–29.9	>30	
Total sleep time (mean ± SD; minutes)	357.30 ± 87.64	408.51 ± 78.13	392.13 ± 120.91	380.36 ± 105.73	0.473
Total sleep time activity (mean ± SD; %)	70.94 ± 13.23	80.39 ± 11.11	81.47 ± 8.95	76.74 ± 17.34	0.254
Epworth Sleepiness Scale score (mean ± SD)	8.62 ± 4.20	10.56 ± 6.27	9.93 ± 6.31	10.06 ± 5.86	0.793
Taste test threshold (mean ± SD)					
– Sweet	3.26 ± 0.70	2.75 ± 0.68	2.38 ± 1.14	2.25 ± 1.29	0.029*
– Sour	3.53 ± 0.51	2.75 ± 0.68	2.22 ± 1.11	2.00 ± 1.26	0.0005†
– Salty	3.53 ± 0.51	3.25 ± 0.68	2.22 ± 1.39	2.18 ± 1.51	0.001†
– Bitter	3.46 ± 1.06	3.00 ± 0.73	2.16 ± 1.68	2.18 ± 1.55	0.017*
Smell test threshold (mean ± SD)					
– n-Butanol	6.79 ± 0.70	6.62 ± 1.02	6.77 ± 0.94	6.68 ± 1.01	0.654
– Identification	6.60 ± 0.50	6.62 ± 1.02	5.83 ± 1.09	5.37 ± 1.96	0.016*

Analysed using Tukey's honest significant difference test and the one-way analysis of variance test. *$p < 0.05$; †$p < 0.01$. OSAS = obstructive sleep apnoea syndrome; SD = standard deviation; BMI = body mass index; AHI = apnoea-hypopnoea index

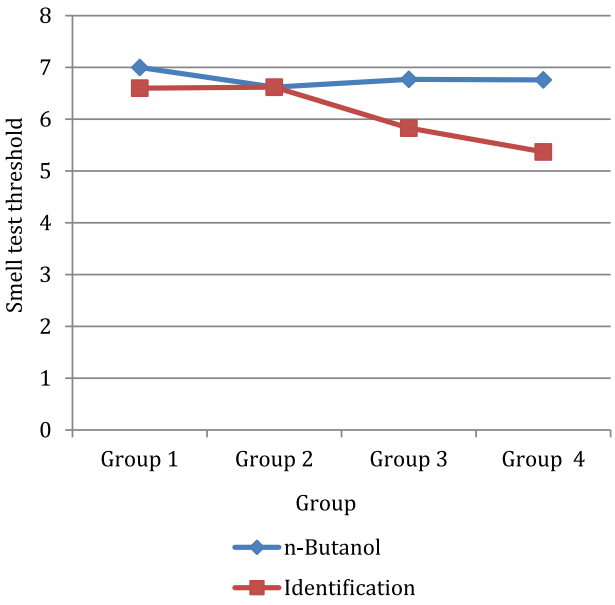

Fig. 1. Smell test results of the control, mild, moderate and severe obstructive sleep apnoea syndrome groups (groups 1–4 respectively).

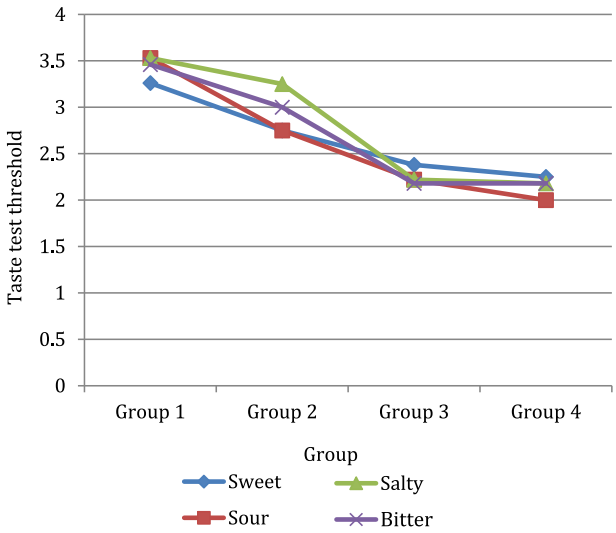

Fig. 2. Taste test results of the control, mild, moderate and severe obstructive sleep apnoea syndrome groups (groups 1–4 respectively).

increase inflammatory activity.[16] Obstructive sleep apnoea syndrome is associated with inflammation. It has been reported that inflammatory markers are increased in OSAS, and that this increase is related to OSAS severity and hypoxia duration.[12]

We hypothesised that patients with OSAS may have decreased taste and smell thresholds due to increased inflammation associated with OSAS severity and neuropathy in the upper respiratory tract. We wanted to investigate whether neuropathy occurring in the upper respiratory tract in patients with OSAS results in taste and smell disturbances.

The findings revealed a significant difference between the olfactory thresholds of the groups for the identification test (one-way ANOVA test, $p = 0.016$). In the taste test, there were significant differences between groups in terms of sweet, sour, salty and bitter taste test thresholds (one-way ANOVA tests; $p = 0.029$, $p = 0.0005$, $p = 0.001$ and $p = 0.017$, respectively). Patients with OSAS were grouped according to their apnoea-hypopnoea index. The severe OSAS group (group 4) showed statistically significant decreases in smell and taste thresholds compared to the control group (group 1) (Figures 1 and 2).

According to Svanborg's hypothesis of OSAS pathogenesis, long-term, snoring-induced vibrations lead to neurogenic lesions in the upper respiratory tract tissues, causing damage to the reflex circuits that allow the upper respiratory tract to remain open during inspiration.[11] This can result in serious relaxation, as muscle tone normally decreases during sleep. Some studies have supported this hypothesis by confirming neuropathy in the upper respiratory tracts of OSAS patients.[11,17,18] Other research groups have presented contributory data that support this hypothesis. These studies

https://doi.org/10.1017/S0022215119000768 Published online by Cambridge University Press

have used various methods to measure local sensory neuropathy, such as vibration, two-point palatal discrimination and air pressure pulse analysis.[19–21]

The correlation between soft palate sensory deficit grade and apnoea severity has not been evaluated before. Segmental demyelination and axonal degeneration of afferent neurons, such as alpha fibres, cause sensory disturbances. These lesions are responsible for the slowing of impulse transmissions.[22] Friberg *et al.* presented evidence of severe neuronal and local neurogenic lesions in OSAS patients.[11,23,24] Kimoff *et al.* reported histological findings that support the neuropathy hypothesis related to snoring.[19] Sunnergren *et al.* estimated snoring periods, and examined the degree of both sleep deprivation and deterioration of soft palate sensation objectively and showed a significant positive correlation.[25] Jeong *et al.* reported that long-lived snoring-induced vibrations cause soft palate deformed stiffness, and soft palate sensory changes may play a role in the pathological progression of OSAS. They reported a two-point discrimination threshold of 2.5 mm for the early diagnosis of probable soft palate peripheral neuropathy in OSAS patients.[26] We consider that the drying effect of mouth breathing may mean that odours do not dissolve in the saliva and mucus, and this may be another reason for taste disturbance.

There were several limitations to our study. It was a preliminary study, and we think that patients with severe OSAS may also be affected by hypoxia. Use of CPAP might affect smell and taste. For this reason, we included patients who had not used CPAP previously. In this study, the sample size was small and the results may not represent a true effect. Thus, further studies with larger numbers of patients are needed to confirm our findings. We performed a thorough nasal endoscopic examination in all patients. However, nasal endoscopy may not have allowed adequate evaluation of pathologies associated with the olfactory fossa.

- Obstructive sleep apnoea syndrome (OSAS) is characterised by recurrent upper airway obstruction and intermittent hypoxia during sleep
- Local neuropathy in OSAS is defined by damage to the reflex circuits that allow the upper respiratory tract to remain open
- Participants in the study were divided into four groups according to apnoea-hypopnoea index on polysomnography
- This study examined the effects of OSAS severity on taste and smell associated with neuropathic and inflammatory processes

Conclusion

The pathogenesis of OSAS is known to involve prolonged snoring and apnoea-induced vibrations. This could result in neuropathy in the upper respiratory tract tissues, causing neurogenic damage and increased inflammation associated with OSAS severity. In our study, as sleep apnoea severity increased (according to the apnoea-hypopnoea index) in OSAS patients, there was a significant decrease in taste and smell thresholds, associated with the effect of neuropathy and inflammation in the upper respiratory tract.

Competing interests. None declared

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