

# The Effect of Sleep Disordered Breathing on Olfactory Functions: Analysis by Apnea-Hypopnea Index

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**Objectives.** One hypothesis of obstructive sleep apnea syndrome (OSAS) is that long-standing snoring vibrations and hypoxia of the nerves cause a local neuropathy in the upper airway during sleep. The aim of this study was to investigate olfactory function in subjects comprising snorers and untreated subjects with OSAS, and to correlate data with polysomnographic parameters.

**Methods.** Sixty-nine patients were evaluated for snoring from January 2010 to December 2013. The mild group (apnea-hypopnea index [AHI] < 15) consisted of 19 subjects, and the moderate-severe group (AHI ≥ 15) consisted of 50 subjects. Exclusion criteria were conductive olfactory dysfunction, previous tonsil or soft palatal surgery, central sleep apnea, and medications that are known to affect peripheral nerves. Nocturnal polysomnography and olfactory function test such as Korean version of Sniffin's stick test I, II (KVSS I, II) were performed.

**Results.** There was a significant difference in body mass index, average oxygen saturation (SaO<sub>2</sub>), lowest SaO<sub>2</sub>, average snoring duration, and KVSS I, II between the two groups. AHI was related to odor threshold score, and average SaO<sub>2</sub> was related to odor discrimination score. But, odor identification score showed no relation with AHI and average SaO<sub>2</sub> except for age. Average SaO<sub>2</sub> and AHI were closely related to the function of smell.

**Conclusion.** Hypoxia and low nasal airflow caused by OSAS may have an effect on the olfactory function. On comparison between the two groups, patients with a high AHI, especially those with OSAS, had an olfactory dysfunction. Also, low average oxygen is the main risk factor in determining the olfactory function. In people with OSAS, the possibility of olfactory dysfunction should be considered and an olfactory function test should be performed.

**Keywords.** *Obstructive Sleep Apnea; Polysomnography; Smell; Olfaction Disorders*

## INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) causes excessive daytime sleepiness, mood problems, poor neurocognitive performance, erectile dysfunction, and cardiovascular disorders [1-3].

In general, OSAS seems to be a progressive disorder whose

pathogenesis is not fully understood. One hypothesis is that long-standing snoring vibrations and hypoxia of the nerves cause a local neuropathy in the upper airway [4-7], which predisposes to obstructive events during sleep. Poor neurocognitive performance due to OSAS affects well known memory [8], new learning, attention, executive function, and cognitive function [1]. OSA is a risk factor for developing mild cognitive impairment [9] and the adult with severe OSA was more likely present cognitive deficits than those with mild or moderate OSA [10].

Olfaction is one of the special senses, and it plays a critical role in human life [11]. Olfactory function is reportedly influenced by cognitive impairment, as well as other main factors affecting head trauma, post-upper respiratory tract infection and sinonasal disease [11,12]. Olfaction scores were lower in pa-

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tients with mild cognitive impairment than in healthy comparison subjects [13]. And the other studies also found that olfactory impairment was associated mild cognitive impairment [14,15]. However, few studies had been reported on the relationship between the effect of olfactory function and degree of OSA.

The aim of this study was to determine among the subjects comprising snorers and untreated subjects with OSAS, classified by polysomnographic parameters such as apnea-hypopnea index (AHI), whether the moderate-severe group that has a high AHI ( $\geq 15/\text{hr}$ ) will have more severe olfactory dysfunction as compared to the mild group that have a low AHI ( $< 15/\text{hr}$ ) and to investigate the correlation between the influence of OSA and parameters of olfactory function.

## MATERIALS AND METHODS

### Subjects

Sixty-nine patients, who underwent a full-night respiratory recording in a sleep research laboratory because of snoring during sleep, were evaluated by an olfactory function test from January 2010 to December 2013. The inclusion criteria were as follows: age above 20 years; absence of neurologic, cardiovascular, pulmonary, or other chronic illness; no history of prior surgery on the nose and palate; no current history of drug intake; and no prior history of treatment of sleep-disordered breathing. Exclusion criteria were as follows: any previous history of treatment for snoring or OSAS, conductive olfactory dysfunction identified by computed tomography and endoscopic findings, sinonasal disease, central sleep apnea, previous history of oropharyngeal surgery excluding remote tonsillectomy, previous history of cerebrovascular accident, diabetes, any neuropathy or active neurologic disease, and a recent history of upper respiratory tract infection at the time of proposed investigation. The moderate-severe group included patients with  $\text{AHI} \geq 15/\text{hr}$  and the mild group included patients with habitual snoring verified by partners and  $\text{AHI} < 15/\text{hr}$  [16].

This study was approved by the Ethics Committee of Konkuk University Hospital (KUH1110018).

### HIGHLIGHTS

- Objective olfactory function (KVSS II) score was significantly associated with apnea-hypopnea index (AHI) and average SaO<sub>2</sub>.
- Threshold (T) and discrimination (D) test scores were significantly correlated with AHI and average SaO<sub>2</sub>, respectively.
- Decreased olfactory function was more frequently seen in patients with moderate-to severe AHI.

### Polysomnography

All of the subjects with an initial evaluation who met the inclusion criteria underwent nocturnal polysomnography (PSG). PSG study was performed using an Embla N7000 (Embla, Reykjavik, Iceland). The following variables were monitored: electroencephalogram, electrooculogram, chin electromyogram, leg electromyogram, heart rate (modified V2 lead), and body position. Respiration was evaluated with a nasal cannula/pressure transducer system, polygraphic recording with measurement of esophageal pressure (PES), thoracic bands, abdominal bands, pulse oximetry, and neck microphone. Apnea was defined as the complete cessation of airflow for at least 10 seconds, whereas hypopnea was defined as a substantial reduction in airflow (50%) for at least 10 seconds or a moderate reduction in airflow (30%) for at least 10 seconds associated with electroencephalographic arousal or oxygen desaturation ( $> 4\%$ ). The AHI was defined as the total number of apneas and hypopneas per hour of sleep [16]. Snoring components included relative snoring time (%), average snoring episode duration (minutes), longest snoring episode duration (minutes), total snoring time (minutes), and number of snoring episodes. These components were automatically calculated during PSG.

### Olfactory function test

Olfactory function test included Korean version of Sniffin's stick test I, II (KVSS I, II), which was performed by the same examiner. KVSS I test is an identification test which is performed with 8 different odorant pens. There are tampons with an odorant substance in each pen so that when the examiner opens the lid and shakes it horizontally, it is set up to make the odor with equal concentration. The KVSS II offers an extensive test of olfactory deficits. It consists of three different sets, namely KVSS II threshold, discrimination, and identification tests. In brief, threshold is defined as the concentration at which n-butanol (highest concentration 4%, 1:2 serial dilutions to 16 steps) is correctly identified four times in a row from two blanks. For discrimination testing, triplets of odorants (two of them are identical, one is different) are presented and subjects have to choose the odd odorant. KVSS II identification test is a 16-item odor identification test [17,18]. All of the odors used in the test are familiar to Koreans. Subjects are supposed to choose one out of the four odors even though they do not know the correct one, and the number of correct answers is recorded. The result of each test is recorded as a score, ranging from 0 to 16, and the sum of the three tests is presented as a composite KVSS II score. Total scores of 0–20 are defined as anosmia, 21–27 as hyposmia, and 28–48 as normosmia [19]. Patients with a KVSS II score  $< 28$  were diagnosed as having olfactory dysfunction in this study. PSG and olfactory function test were performed on the same day.

### Statistical analysis

Analysis were performed using IBM SPSS ver. 20.0 (IBM Co.,

Armonk, NY, USA). The Wilcoxon signed rank test and Fisher exact test were used to evaluate the differences between the moderate-severe group and the mild group. Univariate analyses were performed using logistic regression to identify risk factors for olfactory dysfunction. A value of  $P < 0.05$  was considered to indicate a statistically significant result.

## RESULTS

### Demographics

Sixty-nine patients were recruited for this study (56 men, 13 women; mean age,  $43.86 \pm 14.16$  years). The number of patients in the mild group was 19 (28%), and the number of patients in the moderate-severe group was 50 (73%). The variables such as demographic distribution, body mass index (BMI), basic PSG parameters, and olfactory function test are summarized in Table 1. BMI, sex, average oxygen saturation (SaO<sub>2</sub>), lowest SaO<sub>2</sub>, average snoring episode duration, and KVSS II score were significantly different between the two groups. Otherwise, no statistically significant difference was observed in age, snoring time, longest snoring duration, and KVSS I. Regarding olfaction, 88% of patients (61/69) demonstrated olfactory dysfunction on testing. Among all patients, 68% of patients in the mild group (13/19) and 96% of patients in the moderate-severe group (48/50) demonstrated olfactory dysfunction on testing.

In KVSS II, odor threshold test and discrimination test scores were significantly worse in moderate-severe group. Otherwise, odor identification score showed no difference between the two groups.

### Correlation of olfactory function and OSAS

KVSS I test score was significantly correlated with age ( $P < 0.001$ ). Also, KVSS II test score (threshold, discrimination, identi-

fication [TDI]) was significantly associated with AHI ( $P = 0.022$ ) and average SaO<sub>2</sub> ( $P = 0.024$ ). We found that AHI and average SaO<sub>2</sub> were more closely related to the olfactory function test scores than snoring time and longest snoring episode (Table 2, Fig. 1). Snoring time and longest snoring episode showed no significant association with olfactory function test scores. In KVSS II test, threshold (T) test score was significantly correlated with AHI ( $P = 0.005$ ). Therefore, AHI was more strongly associated with odor threshold score than average SaO<sub>2</sub>. Discrimination (D) test score was significantly correlated with average SaO<sub>2</sub> ( $P = 0.042$ ). Average SaO<sub>2</sub> was related to odor discrimination score than AHI. Identification (I) test score was significantly associated with age ( $P < 0.001$ ). Odor identification score showed no significant relation with AHI and average SaO<sub>2</sub> (Table 3, Fig. 2).

## DISCUSSION

In this study, we found that olfactory dysfunction was much more frequent in the moderate-severe group than in the mild group and the AHI had a significant negative correlation with

**Table 2.** Correlation between polysomnographic parameters and olfactory function test score

Variable	KVSS I		KVSS II	
	$r^a$	$P$ -value <sup>b)</sup>	$r^a$	$P$ -value <sup>b)</sup>
Age (yr)	-0.408	<0.001 <sup>c)</sup>	-0.216	0.075
Apnea-hypopnea index (/hr)	0.151	0.214	-0.275	0.022 <sup>c)</sup>
Average oxygen saturation (%)	-0.019	0.878	0.271	0.024 <sup>c)</sup>
Snoring time (min)	-0.078	0.526	0.078	0.527
Longest snoring episode (min)	-0.150	0.216	0.065	0.598

KVSS, Korean version of Sniffin's stick test.

<sup>a)</sup>Pearson correlation coefficient. <sup>b)</sup>Univariate regression test. <sup>c)</sup>Statistically significant.

**Table 1.** Comparison of baseline variables between the moderate-severe group and the mild group

Variable	Moderate-severe group (n=50)	Mild group (n=19)	$P$ -value <sup>a)</sup>
Age (yr)	$44.6 \pm 13.8$	$41.8 \pm 15.4$	0.267
Sex (female:male)	6:44	7:12	0.037 <sup>b,c)</sup>
Body mass index (kg/m <sup>2</sup> )	$29.1 \pm 5.7$	$24.6 \pm 2.3$	<0.001 <sup>c)</sup>
Average oxygen saturation (%)	$94.5 \pm 2.2$	$96.6 \pm 1.4$	<0.001 <sup>c)</sup>
Low oxygen saturation (%)	$79.8 \pm 7.3$	$85.3 \pm 9.1$	<0.001 <sup>c)</sup>
Snoring time (min)	$98.1 \pm 69.6$	$68.0 \pm 37.1$	0.094
Average snoring duration (min)	$0.7 \pm 0.5$	$2.6 \pm 3.7$	0.034 <sup>c)</sup>
Longest snoring duration (min)	$10.8 \pm 10.3$	$10.5 \pm 8.3$	0.773
KVSS I	$5.1 \pm 1.6$	$5.5 \pm 1.6$	0.334
KVSS II	$21.4 \pm 4.6$	$25.5 \pm 5.8$	0.021 <sup>c)</sup>
Threshold	$3.6 \pm 2.1$	$5.4 \pm 3.2$	0.013 <sup>c)</sup>
Discrimination	$8.4 \pm 3.1$	$10.4 \pm 3.0$	0.030 <sup>c)</sup>
Identification	$9.5 \pm 2.5$	$10.2 \pm 1.8$	0.300

KVSS, Korean version of Sniffin's stick test.

<sup>a)</sup>Wilcoxon rank-sum test. <sup>b)</sup>Fisher exact test. <sup>c)</sup>Statistically significant.

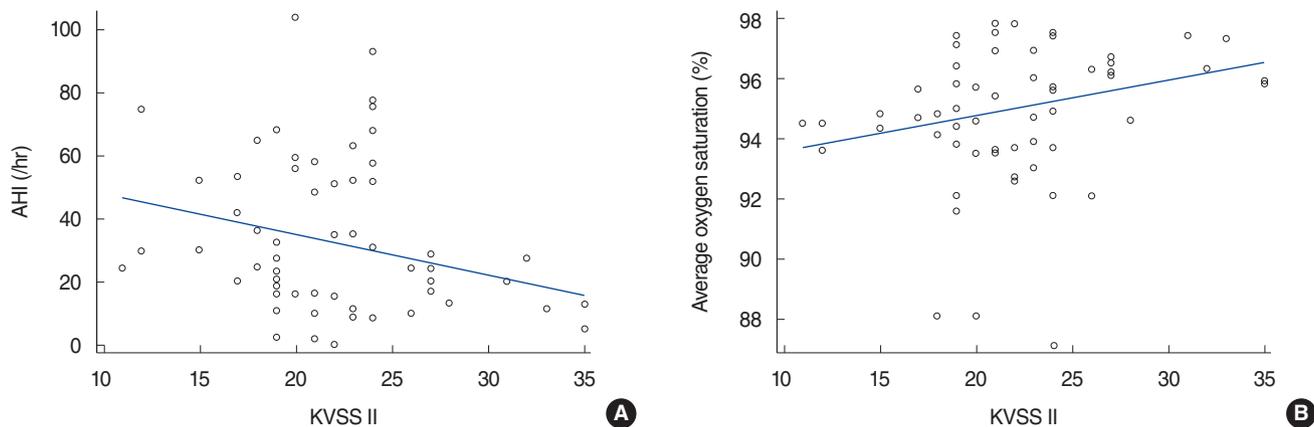


Fig. 1. (A) Scatter plot showing a significant negative association of apnea-hypopnea index (AHI) with Korean version of Sniffin's stick test II (KVSS II) score (Spearman rank correlation,  $-0.275$ ;  $P=0.022$ ). Regression line and lines for the 95% confidence interval (CI) are shown. (B) Scatter plot showing a significant positive association of average oxygen saturation with KVSS II score (Spearman rank correlation,  $0.271$ ;  $P=0.024$ ). Regression line and lines for the 95% CI are shown.

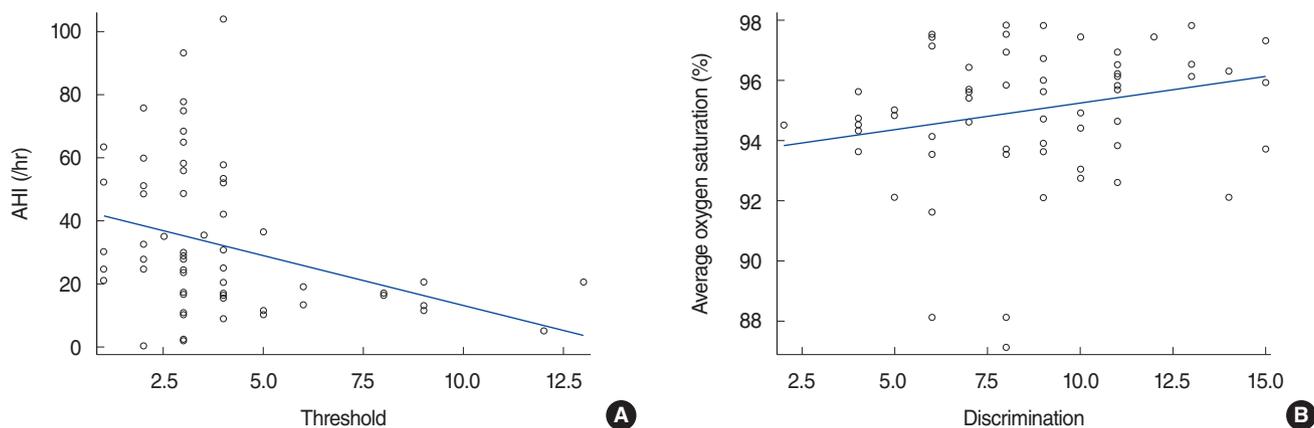


Fig. 2. (A) Scatter plot showing a significant negative association of apnea-hypopnea index (AHI) with threshold test score (Spearman rank correlation,  $-0.336$ ;  $P<0.01$ ). Regression line and lines for the 95% confidence interval (CI) are shown. (B) Scatter plot showing a significant positive association of average oxygen saturation with discrimination test score (Spearman rank correlation,  $0.246$ ;  $P=0.042$ ). Regression line and lines for the 95% CI are shown.

Table 3. Correlation between polysomnographic parameters and threshold, discrimination, identification test score

Variable	Threshold		Discrimination		Identification	
	$r^a$	$P$ -value <sup>b)</sup>	$r^a$	$P$ -value <sup>b)</sup>	$r^a$	$P$ -value <sup>b)</sup>
Age (yr)	0.040	0.744	-0.123	0.313	-0.475	<0.001
Apnea-hypopnea index (/hr)	-0.336	0.005 <sup>c)</sup>	-0.226	0.062	0.009	0.939
Average oxygen saturation (%)	0.218	0.071	0.246	0.042 <sup>c)</sup>	0.106	0.388
Snoring time (min)	0.020	0.872	-0.013	0.918	0.095	0.438
Longest snoring episode (min)	0.003	0.979	0.022	0.859	0.056	0.650

<sup>a)</sup>Pearson correlation coefficient. <sup>b)</sup>Univariate regression test. <sup>c)</sup>Statistically significant.

odor threshold and TDI scores; otherwise, average SaO<sub>2</sub> had a significant positive correlation with odor discrimination and TDI scores.

The comparison of baseline variables showed that the parameters of PSG, BMI, SaO<sub>2</sub> level (average and lowest), and snoring duration showed a significant difference between the moderate-

severe group and mild group. The figures obtained from this study correspond with those from other recent reports [20].

This study showed the negative effect of OSA on olfactory testing. We assessed olfactory function by the KVSS-I and KVSS-II. KVSS II score (TDI score), and not KVSS I score, showed a significant difference between the two groups. Results

of the present study confirm the findings of earlier studies, which reported that TDI scores were significantly decreased with increasing severity of OSA [20]. On comparison between the parameters of PSG and olfactory function test, AHI showed a negative correlation with KVSS II score (TDI score). Average SaO<sub>2</sub> level had a significant positive correlation with KVSS II score (TDI scores). Snoring time and longest snoring episode had no significant effects on olfactory function in OSA patients. Our findings imply that olfactory dysfunction in OSAS patients is influenced by apnea-hypopnea and blood oxygen level than long-standing vibration.

Among the TDI scores, odor threshold score had a significant negative correlation with AHI. Otherwise, odor discrimination score had a significant positive correlation with average SaO<sub>2</sub>. Odor identification score had no effects on the parameters of PSG in OSA patients. Previous reports showed a negative correlation between AHI and TDI scores and a positive correlation between mean SaO<sub>2</sub> and odor threshold and discrimination scores. In contrast to a previous study, we found that AHI had a negative correlation with odor threshold score and average SaO<sub>2</sub> had a positive correlation with odor discrimination score [20].

Although the mechanism underlying the correlation between OSAS and olfactory function is unclear, the previous study had proposed that intermittent hypoxia and sleep fragmentation can lead to neuronal loss in the hippocampus and prefrontal cortex, areas that are closely associated with memory function and executive function [20,21]. The effect of impairment of cognitive function on olfaction may produce a decrease in discrimination and identification function [22]. But, we found that AHI had no effect on the discrimination and identification tests. These results suggest that these tests used suprathreshold concentration of odorants [23].

It is well known that OSA is characterized by breathing cessation (apnea) or reduction of airflow (hypopnea) during sleep. The increase in AHI was related to the decrease in nasal airflow. Recently, Fu et al. [24] reported that alteration of nasal airflow affected the olfactory function, especially odor threshold. Therefore, negative correlations between AHI and odor threshold seem to indicate the alteration of nasal airflow in OSA patients.

This study has several limitations; first, the sample size was limited (e.g., few female patients) and analyses were done without a healthy control group. Second, this study was a retrospective study on hospital based-subjects and not the general population. Hence, future studies are needed to assess the effect of OSA treatment on olfactory function. Indeed, OSA is associated with olfactory functions. Olfactory dysfunctions were associated with intermittent hypoxia and alteration of airflow.

In conclusion, the current study demonstrated that low nasal airflow and hypoxia caused by OSAS may have an effect on the olfactory function. On comparing between the moderate-severe group and mild group, patients with a high AHI, especially those with OSAS, had negative effects on olfactory dysfunction, espe-

cially on threshold, and patients with a high SaO<sub>2</sub> had positive effects on olfactory discrimination function.

## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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