



Evaluation of Thought and Language Functions in Patients with Obstructive Sleep Apnea Syndrome

Obstrüktif Uyku Apne Sendromlu Hastalarda Düşünce ve Dil Fonksiyonlarının Değerlendirilmesi

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Abstract

Objective: Patients with obstructive sleep apnea syndrome (OSAS) could display disorders in cognitive areas including attention, long-term visual and verbal memory, structural abilities, and executive functions. There are contradictory results regarding language ability and psychomotor functions. We evaluated the thought and language functions of patients with OSAS and their relationship with disease severity.

Methods: Patients who applied to the sleep disorders center with a preliminary diagnosis of OSAS were included in the study. According to the polysomnographic (PSG) results, 95 patients diagnosed with OSAS were accepted as the patient group, and 31 patients without OSAS were accepted as the control group. All patients were administered the thought-language index (TLI) by a psychologist. TLI scores were calculated and the differences between patient and control groups were evaluated. It was also examined the relationship between rapid eye movement (REM)-related OSAS and TLI scores.

Results: There was no significant difference between the patient and control groups regarding total TLI score. However, the "poverty of speech" score, which is a subcategory of TLI, was found to be significantly higher in the control group than in the patient group ($p=0.266$, $p=0.025$ respectively). No patient scored in the category of thought disorder. There was also no significant relationship between the severity of OSAS and TLI score, poverty of speech, weakening of purpose, and perseveration ($p=0.846$, $p=0.111$, $p=0.839$, $p=0.059$ respectively). When the patient group was classified as REM-related and non-REM-related OSAS, no significant.

Conclusion: In the evaluation of patients with OSAS through TLI, no impairment was found regarding thought and language functions. The poor performance of individuals who were diagnosed with OSAS were excluded in terms of "poverty of speech" may be related to snoring and accompanying arousal and excessive daytime sleepiness. No negative effect of REM-related OSAS on thought and language functions was detected. Further studies are required to evaluate thought and language functions in patients with OSAS.

Keywords: Obstructive sleep apnea, thought and language functions, cognitive functions



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Öz

Amaç: Obstrüktif uyku apne sendromlu (OUAS) hastaların dikkat, uzun süreli görsel ve sözel bellek, yapısal yetenekler ve yürütücü işlevleri de içeren kognitif alanlarda bozukluklar sergiledikleri bilinmektedir. Dil yeteneği ve psikomotor fonksiyonlar ile ilgili ise çelişkili sonuçlar mevcuttur. Bu çalışmada OUAS'li hastaların düşünce ve dil fonksiyonlarının değerlendirilmesi ve hastalık şiddeti ile ilişkisinin araştırılması amaçlanmıştır.

Yöntem: Hastanemiz uyku bozuklukları merkezine OUAS ön tanısı ile başvuran hastalar çalışma için değerlendirmeye alındılar. Polisomnografi (PSG) sonucuna göre OUAS tanısı alan 95 kişi hasta grubu ve OUAS tanısı dışlanan 31 kişi ise kontrol grubu olarak çalışmaya kabul edildi. Tüm hastalara bir psikolog tarafından düşünce-dil ölçeği (DDÖ) uygulandı. DDÖ skorları hesaplanarak, hasta ve kontrol grubu arasındaki fark ve OUAS şiddeti ile ilişkisi değerlendirildi. Ayrıca hızlı göz hareketi (REM)-ilişkili OUAS ve DDÖ skorları arasındaki ilişkide incelendi.

Bulgular: Hasta ve kontrol grubu arasında total DDÖ skoru açısından anlamlı farklılık izlenmezken, bir DDÖ alt kategorisi olan "konuşmanın fakirliği" puanı, kontrol grubunda hasta grubuna göre istatistiksel olarak anlamlı yüksek tespit edildi ($p=0,266$, $p=0,025$ sırasıyla). Hiçbir hasta düşünce bozukluğu kategorisinden puan almadı. OUAS şiddetine göre yapılan değerlendirmede hastalık şiddeti ile DDÖ toplam puanı, konuşmanın fakirliği, amacın zayıflaması ve perseverasyon arasında anlamlı farklılık izlenmedi ($p=0,846$, $p=0,111$, $p=0,839$, $p=0,059$ sırasıyla). Hasta grubu REM ilişkili ve non-REM ilişkili OUAS olarak gruplandırıldığında, DDÖ skorları açısından gruplar arasında anlamlı farklılık izlenmedi ($p=0,253$).

Sonuç: DDÖ ile yapılan değerlendirmede OUAS'li hastaların düşünce ve dil fonksiyonlarında bozukluk tespit edilmemiştir. OUAS dışlanan bireylerin "konuşmanın fakirliği" yönünden daha olumsuz bir performans sergilemesi, horlama ve buna eşlik eden ara suallar ve gündüz aşırı uykuluk hali, ile ilişkili olabilir. REM ilişkili OUAS'nin düşünce ve dil fonksiyonları üzerinde olumsuz bir etkisi izlenmemiştir. OUAS hastalarda düşünce ve dil fonksiyonlarının değerlendirilmesi için ileriye yönelik çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Obstrüktif uyku apne, düşünce ve dil fonksiyonları, kognitif fonksiyonlar

Introduction

Sleep is one of the most principle needs of the body in terms of physiological, mental, and cognitive aspects⁽¹⁾. Obstructive sleep apnea syndrome (OSAS) is a very common chronic disease characterized by recurrent airway obstruction during sleep and an accompanying decrease in oxygen saturation and arousal⁽²⁾. OSAS is associated with cognitive and emotional dysfunctions and cardiovascular diseases⁽³⁾. The pathophysiology of cognitive impairment observed in patients with OSAS is quite complex and is the result of multifactorial causes; fragmented sleep structure, inflammation, hypoxia, cerebral blood flow, changes in neurotransmitter and neuronal regulation, and anoxic brain damage are some of the reasons suggested⁽⁴⁾. In meta-analyses, strong evidence has been demonstrated that OSAS affects attention and alertness, long-term verbal and visual memory, and visual-spatial or structural abilities. In clinical terms, cognitive losses in patients with OSAS are in the form of memory problems, lack of attention, difficulty in focusing, and decreased ability to plan and make decisions⁽⁵⁾. Previous studies on language skills and psychomotor functions in patients with OSA obtained conflicting results. While some studies suggest that OSAS does not affect these functions some studies suggest that psychomotor retardation is the most sensitive cognitive area^(6,7). In a study conducted by Andreou and Agapitou⁽⁸⁾, it was determined that the language and verbal abilities of adolescents who snore and were diagnosed with

OSAS decreased compared with the controls. Researchers suggested that this result could be explained by the fact that OSAS causes some changes that may lead to dysfunction of the prefrontal cortex, which plays an active role in language and verbal skills⁽⁹⁾. Prefrontal cortex damage is associated with impaired verbal fluency and recovery, which also affects the speed and ease of verbal production⁽⁹⁾.

Thought and language index (TLI) is a semi-structured interview form developed mainly to detect thought disorders in schizophrenia and to be used in clinical studies^(10,11). Thought disorder is not specific to schizophrenia and can also be seen in manic episodes of bipolar disorder⁽¹²⁾. In both delusional and thought process disorders, language loses its function of conveying the intended content. Therefore, thought process disorders are generally evaluated together as "thought and language disorders"⁽¹³⁾. It is not possible to completely separate language and semantic disturbance⁽¹⁴⁾.

In view of this information, in this study, it was aimed to evaluate the thought and language functions of patients with OSAS by applying TLI.

Materials and Methods

Consecutive patients aged 30-70 years who applied to the sleep disorders center of our hospital between August 2018 and January 2019 with complaints of snoring, witnessed apnea, and/or excessive daytime sleepiness (EDS) and who underwent polysomnographic (PSG) examination with a

preliminary diagnosis of OSAS were included in the study. Patients who had a history of neurological and psychiatric diseases such as schizophrenia, Alzheimer's, dementia, bipolar disorder, had sleep disorders other than OSAS, shift workers, and did not want to participate in the study were excluded from the study. Demographic information and additional disease histories of the patients were recorded.

PSG examination results of the patients were obtained from their files. According to the PSG results, 95 patients diagnosed with OSAS were accepted as the patient group and 31 patients without OSAS were accepted as the control group. The diagnosis of OSAS was made in accordance with the ICSD-3 criteria⁽¹⁵⁾. Afterwards, a psychologist interview, which would last about 15 min, was planned with the patients, and the thought language index was applied. The psychologist who conducted the interview was not informed about the sleep test results of the patients.

TLI consists of two main categories, impoverishment of thought and disorganization of thought, and 8 items. The thought impoverishment category includes the poverty of speech, weakening of purpose, and repetition of thought (perseveration). The disturbance of thought category includes dissociation, peculiar word use, peculiar sentence structure, peculiar logic, and distractibility. The test material consists of a set of 8 pictures selected from the thematic perception test, numbered on the reverse side, in a fixed order⁽¹⁶⁾. Eight pictures were presented sequentially for 1 min each, and the participants were asked to talk about each picture. If the person stopped speaking before the minute was over, a nondirective prompt (e.g. "Can you say more?") was given. At the end of the minute, the interviewer asked the person tested to explain any odd or unusual utterances made during the minute. After this enquiry phase, during the minute. After this enquiry phase, the next picture was presented. The entire procedure lasted approximately 15 min. The interview was recorded on an audiotape and subsequently scored according to the TLI manual. Each error regarding thought and language impairment was scored⁽¹¹⁾. A validity and reliability study of the Turkish version of the TLI was performed by Ulaş et al.⁽¹⁷⁾.

In our study, the difference between the patient and control groups in terms of TLI scores and the relationship between the severity of OSAS and TLI scores were evaluated. In addition, patients diagnosed with OSAS were grouped as repeat eye movement (REM) related OSAS and non-NREM (NREM) related OSAS, and it was examined whether there were

differences between the groups in terms of TLI scores and PSG parameters. REM apnea-hypopnea index (AHI)/NREM AHI >2 was required for the diagnosis of REM-related OSAS.

Ethics Committee approval of the study was obtained from the Non-Interventional Ethics Committee of the University of Health Sciences Turkey, İzmir Tepecik Health Practice and Research Center (decision no: 2018/8-16, date: 11.07.2018).

Statistical Analysis

The data were evaluated in IBM-SPSS 25.0 package program. For categorical data, cross tables were created, and chi-square analysis was performed. The concordance of numerical variables with a normal distribution was evaluated with the Shapiro-Wilk test. For normal distributions, Student t-test was used to compare two groups, and more than two-group comparisons were made with the ANOVA test. If the ANOVA test was significant, pairwise comparisons were made with the Bonferroni test. In the variables that did not show normal distribution, comparison of two groups was made with Mann-Whitney U test, and comparison of more than two groups was made with Kruskal-Wallis analysis. If the Kruskal-Wallis analysis was significant, pairwise comparisons were made with the Dunn test. Statistical significance was assumed when $p < 0.05$.

Results

A total of 126 patients, 81 (64.3%) male and 45 (45.7%) female, were included in the study. The mean age was 50.7 ± 11.3 years. The most common comorbidities were hypertension (37.3%) and diabetes mellitus (23.8%). The sociodemographic characteristics of the study population are shown in Table 1. When the results of the questionnaire were evaluated, the mean scores were determined as 9.36 ± 6.5 for Epworth sleepiness scale (ESS) and 5 ± 1.48 for STOP-Bang. The total TLI score was 4 (2-8.75). The total TLI score and subcategory scores of the study group are presented in Table 2. Since none of the patients scored in the "difficulty of thought" category, this category is not included in the table.

According to the PSG results, 31 subjects with AHI <5/h were included in the study as the control group, and 95 subjects with AHI ≥ 5 /hour were included in the study as the study group. When the patient and control groups were compared in terms of demographic characteristics and TLI scores, no statistically significant difference was observed between the groups in terms of total TLI score, but a significant difference was found regarding poverty of speech ($p=0.266$, $p=0.025$, respectively). There was no

significant difference between the two groups in terms of age, gender, and comorbidities (Table 3). When the patients were classified as mild, moderate, and severe OSA according to AHI, 14 (11.1%) patients were evaluated as mild OSA, 29 (23%) patients as moderate OSA, and 52 (41.3%) patients as severe OSA. There was no statistically significant difference between the mild, moderate, and severe OSAS groups in terms of total TLI score, poverty of speech, weakening of purpose, and perseveration ($p=0.846$, $p=0.111$, $p=0.839$, $p=0.059$, respectively).

Table 1. Demographic features of the study population (n=126)

Age, year	50.7±11.3
Male gender, n (%)	81 (64.3)
BMI, kg/m ²	31.5±5.67
Smoker, n (%)	50 (39.7)
Co-morbidities	
Hypertension, n (%)	47 (37.3)
Diabetes mellitus, n (%)	30 (23.8)
CAD, n (%)	13 (10.3)
Hypothyroidism, n (%)	12 (9.5)
Arrhythmia, n (%)	11 (8.7)
Depression, n (%)	9 (7.9)
Working status	
The active worker, n (%)	56 (44.3)
Retired, n (%)	37 (29.4)
Housewife, n (%)	33 (26.2)
Sleep-related symptoms	
Snoring, n (%)	116 (92.1)
Witness apnea, n (%)	102 (81)
EDS, n (%)	106 (84.1)
Insomnia, n (%)	3 (2.4)
BMI: Body mass index, CAD: Coronary artery disease, EDS: Excessive daytime sleepiness	
Data are depicted as mean ± standard deviation or number (percentage)	

Table 2. Thought and language index total and sub scores (n=126)

TLI total score	4 (2-8.75)
Thought impoverishment	
Poverty of speech	0.75 (0-7)
Weakening of purpose	0.75 (0-2.25)
Perseveration	0.25 (0-1)
TLI: Thought and language index	
Data are depicted as median (minimum-maximum)	

Table 4 shows the results obtained from the OSA patients when they were grouped as REM- and non-REM - related OSAs. No statistically significant difference was determined between the groups in terms of total TLI score, poverty of speech, weakening of purpose and perseveration ($p=0.253$, $p=0.253$, $p=0.850$, $p=0.483$, respectively). A statistically significant difference was observed between the two groups in terms of apnea number and oxygen desaturation index (ODI) ($p<0.001$, $p=0.029$, respectively).

Discussion

In the present study, which was conducted to evaluate the thought and language functions of patients with OSAS, no impairment was found that could be detected by TLI in OSAS patients. Surprisingly, individuals who were diagnosed with OSAS were excluded from the study performed worse in terms of "poverty of speech" compared to individuals diagnosed with OSAS.

This result is contrary to our expectations. It can be clearly seen that the patient and control groups are quite similar in terms of demographic characteristics in this study. However, the reason for the worse performance of the control group in terms of "poverty of speech" compared to the OSA patients group may be related to the selection of the control group. In our study, patients who applied to the sleep center with complaints of snoring, witnessed apnea, and/or EDS were included, and a control group was obtained from patients whom diagnosis of OSAS was excluded by PSG examination. Although the diagnosis of OSAS was excluded, the acceptance of these patients as healthy controls may have led to a potential bias. In a study by Smith et al.⁽¹⁸⁾ showed that the frequency of snoring rather than AHI better predicts both cognitive and behavioral problems in young children, and it was emphasized that snoring status should be evaluated when performing cognitive and behavioral examinations. Even if it is not accompanied by OSAS, snoring is associated with adverse health outcomes such as increased cardiovascular disease, stroke, and endothelial damage in adults^(19,20). In addition, another study revealed that there was a relationship between snoring severity, arousal, daytime sleepiness, and psychological problems⁽²¹⁾. There are also studies reporting that fragmented sleep, rather than short sleep duration, may be more correlated with cognitive functions in adults⁽²²⁾. Even though the diagnosis of OSAS was excluded, our control group may have had worse results in terms of "poverty of speech" due to snoring and accompanying fragmented sleep and arousal.

Table 3. Comparison of the patient and control groups regarding demographic characteristics, questionnaire results, and TLI scores

	AHI<5 (n=31)	AHI≥5 (n=95)	P value
Age, year	50.1±12.8	50.9±10.4	0.093
Male gender, n (%)	19 (61.3)	62 (65.3)	0.689
BMI, kg/m ²	31.4±5.6	31.6±5.7	0.724
Hypertension, n (%)	9 (29)	57 (40)	0.273
Diabetes mellitus, n (%)	8 (25.8)	22 (23.2)	0.764
Snoring, n (%)	28 (90.3)	88 (92.6)	0.680
Witness apnea, n (%)	22 (71)	80 (84.2)	0.103
EDS, n (%)	24 (77.4)	82 (86.3)	0.239
ESS	9.42±6.2	9.3±6.6	0.827
STOP-Bang score	4.61±1.58	5.13±1.43	0.182
TLI total score	4.25 (2.5-8.25)	3.75 (2-8.75)	0.266
The poverty of speech	1.5 (0-6.25)	0.75 (0-7)	0.025
Weakening of purpose	0.75 (0-2.25)	0.75 (0-2.25)	0.846
Perseveration	2 (0.25-3.50)	2 (0.75-4)	0.052

OSAS: Obstructive sleep apnea syndrome, AHI: Apnea-hypopnea index, BMI: Body mass index, EDS: Excessive daytime sleepiness, ESS: Epworth sleepiness score, TLI: Thought and language index
Data are depicted as mean ± standard deviation, median (minimum-maximum) or number (percentage)

Table 4. Comparison of REM-related OSAS and NREM-related OSAS groups regarding polysomnographic findings and TLI scores

	REM-related OSAS (n=21)	NREM-related OSAS (n=74)	P value
AHI, (event/h)	36.9 (7.8-126.9)	30.7 (9.3-84.3)	0.622
Apnea, (n)	7.5 (0-57)	49 (0-639)	<0.001
Hypopnea, (n)	87 (6-244)	89 (1-639)	0.451
Minimum StO ₂ , (%)	81.7±7.1	79.4±10.7	0.378
Average StO ₂ , (%)	94±1.09	92.9±4.1	0.059
ODI	22.6 (0.3-68)	36 (0.1-166)	0.029
TLI total score	4.25 (2.5-6.25)	3.75 (2-8.75)	0.253
The poverty of speech	1.125 (0-3.75)	0.75 (0-7)	0.253
Weakening of purpose	0.75 (0-2)	0.625 (0-2.25)	0.850
Perseveration	2 (1.25-3.50)	2 (0.75-4)	0.483

OSAS: Obstructive sleep apnea syndrome, AHI: Apnea-hypopnea index, ODI: Oxygen desaturation index, StO₂: Oxygen desaturation, TLI: Thought and language index, REM: Rapid eye movement, NREM: Non-rapid eye movement
Data are depicted as mean ± standard deviation, median (minimum-maximum) or number (percentage)

At this point, upper airway resistance syndrome (UARS), which is characterized by cortical arousal and sympathetic activation, could be considered as another pathology that should be excluded⁽²³⁾. In the control group, although OSAS was ruled out with PSG, there could be patients with simple snoring only and patients with UARS as well. This situation may have had a negative impact on TLI scores. Additionally, EDS was reported in 77.4% of our control group patients. It

should be kept in mind that EDS, which can be seen in 9% to 28% of the general population, is associated with increased cardiovascular, neurological, and psychiatric diseases⁽²⁴⁾.

Although there is strong evidence that OSAS negatively affects cognitive functions, not every patient with OSAS has impaired cognitive functions⁽²⁵⁾. At this point, beyond the classification of OSA depending on AHI, perhaps the

recently identified phenotypic features (high loop gain, low respiratory threshold, poor pharyngeal muscle response during sleep, and upper airway anatomy) may gain importance. Different clinical phenotypes may lead to different clinical manifestations of sleep apnea syndrome.

Studies evaluating the relationship between OSAS severity and the severity of cognitive impairment have not found consistent evidence supporting this relationship⁽⁵⁾. Consistent with these studies, in our study, no significant relationship was found between OSAS severity and thought and language functions. To the best of our knowledge, our study is the first in which TLI was applied to patients with OSAS. Studies evaluating the relationship between OSAS and language disorders are mostly concentrated in the pediatric age group. It has been found that delay in the diagnosis and treatment of OSAS is associated with a delay in the verbal skill acquisition in children. Most phonetic sounds are acquired between the ages of 3 and 7 years, which is the period when tonsil hypertrophy and childhood OSAS peak⁽²⁶⁾.

REM-related sleep apnea syndrome is a very interesting phenotype regarding its relationship with both cardiovascular diseases and neurocognitive disorders, in which respiratory events are mostly observed in REM sleep⁽²⁷⁾. Compared with NREM sleep, REM sleep is associated with increased sympathetic activity and cardiovascular instability in both healthy and OSAS persons⁽²⁸⁾. REM sleep is closely related to cognitive functions such as memory, attention, executive functions, and dreams⁽²⁹⁾. In our study, no significant difference was found in terms of thought and language functions in patients with REM-related and NREM-related OSAS. Patients with REM-related OSAS exhibited similar findings to patients with NREM-related OSAS regarding EDS, although they were associated with milder disease severity. In a recent study, patients with REM-related and NREM-related OSAS were evaluated and it was shown that although NREM AHI was two times higher than REM AHI, both groups showed similar results in terms of ESS and EDS⁽³⁰⁾. In another study evaluating cognitive functions in patients with REM-related and NREM-related OSAS, no significant difference was found between the groups regarding cognitive functions⁽²⁹⁾.

Study Limitations

This study has some limitations that must be addressed. As mentioned above, our results may have been affected by the selection of control group. We could not make analyzes related to arousal and snoring severity because it was not included in the study protocol. Since the data on

the education and socioeconomic levels of the participants were not recorded, an evaluation could not be made in this respect. However, there was no difference between the groups in terms of working status. Additionally, it should be kept in mind that given the complex neuropathology of OSAS, it is likely that the snapshot value of a particular function or ability, assessed by cognitive tests, does not fully account for its fluctuation over time and various daytime requirements⁽⁴⁾.

Conclusion

In the evaluation of patients with OSAS through TLI, no impairment was found regarding thought and language functions. The poor performance of individuals who were diagnosed with OSAS in terms of "poverty of speech" may be related to snore and accompanying arousal and EDS. No negative effect of REM-related OSAS on thought and language functions was detected. Further studies are required to evaluate thought and language functions in patients with OSAS.

Presentation: This study was presented as an oral presentation at the 7th UTSAK Congress on 28-29 August 2021.

Ethics

Ethics Committee Approval: Ethics Committee approval of the study was obtained from the Non-Interventional Ethics Committee of the University of Health Sciences Turkey, İzmir Tepecik Health Practice and Research Center (decision no: 2018/8-16, date: 11.07.2018).

Informed Consent: Patient consent was obtained.

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Authorship Contributions

Concept: B.O.A., Z.Z.U., Design: B.O.A., Z.Z.U., Data Collection or Processing: B.O.A., E.A., Analysis or Interpretation: B.O.A., Z.Z.U., E.A., Literature Search: B.O.A., E.A., Writing: B.O.A.

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