

Evaluation of Cognitive Functions in Obstructive Sleep Apnea Syndrome

Obstrüktif Uyku Apne Sendromunda Bilişsel Fonksiyonların Değerlendirilmesi

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ABSTRACT

Aim: The aim of this study is to evaluate patients with Obstructive Sleep Apnea Syndrome (OSAS) in terms of various cognitive functions and determine the relationship between cognitive functions with anxiety and depression levels.

Material and Methods: This cross-sectional study was conducted between June 15, 2019 and December 15, 2019 and included 34 OSAS patients and 28 healthy volunteers between the ages of 18-65 with at least primary education. All participants underwent overnight recording of polysomnography. Patients were evaluated using sociodemographic data form, Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), Montreal Cognitive Assessment (MoCA) and the Stroop Color and Word Test (SCWT).

Results: There was no significant difference between the OSAS and control group in terms of age and gender. OSAS patients had significantly higher depression and anxiety scores compared to the control group. OSAS patients showed poor performance in naming, attention, abstract thinking, and delayed recalling compared to the control group. OSAS patients completed Stroop tests 1, 3, and 5 in a longer amount of time than the control group. Cognitive functions were found to have a significant negative correlation with apnea hypopnea index, BDI, and BAI scores.

Conclusion: OSAS was found to have a different effect on each subcomponents of cognitive function. Furthermore, it was determined that many negative factors caused by OSAS may play a role in cognitive involvement in OSAS. Further studies are warranted to shed light on the ethiopathogenesis of this subject.

Keywords: Stroop; attention; memory; abstract thinking; neurocognitive function.

ÖZ

Amaç: Bu çalışmanın amacı Obstrüktif Uyku Apne Sendromu (OUAS) hastalarını birçok bilişsel fonksiyon açısından değerlendirmek ve OUAS hastalarının bilişsel fonksiyonları ile anksiyete ve depresyon düzeyleri arasındaki ilişkiyi ortaya koymaktır.

Gereç ve Yöntemler: Bu kesitsel çalışmaya 15 Haziran 2019 ve 15 Aralık 2019 tarihleri arasında yapıldı ve 18-65 yaş arası en az ilkokul mezunu 34 OUAS hastası ve 28 sağlıklı gönüllü dahil edildi. Tüm katılımcıların bir gece boyunca polisomnografi kayıtları alındı. Tüm katılımcılara sosyodemografik veri formu, Beck Depresyon Ölçeği (BDÖ), Beck Anksiyete Ölçeği (BAÖ), Montreal Bilişsel Değerlendirme (MoCA) ve Stroop Renk ve Sözcük Testi (SCWT) uygulandı.

Bulgular: OUAS ile kontrol grubu arasında yaş, cinsiyet açısından anlamlı fark yoktu. OUAS hastalarının depresyon ve anksiyete ölçek puanları kontrol grubuna göre anlamlı şekilde daha yüksekti. OUAS hastalarının adlandırma, dikkat, soyut düşünme ve gecikmeli hatırlama performansları kontrol grubuna göre daha düşük idi. OUAS hastaları Stroop 1, 3 ve 5 testini kontrol grubundan daha uzun bir sürede tamamladı. Bilişsel fonksiyonların apne hipopne indeksi, BDÖ ve BAÖ skorları ile negatif yönde anlamlı bir korelasyonu olduğu bulundu.

Sonuç: OUAS'ın bilişsel fonksiyonların her bir alt birleşeni üzerinde farklı bir etkisinin olduğu saptandı. Ayrıca OUAS'daki bilişsel etkilenmenin altında, OUAS'ın neden olduğu birçok olumsuz faktörün rolü olabileceği tespit edildi. Bu konunun etyopatogenizinin daha açık hale gelmesi için ileri çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Stroop; dikkat; hafıza; soyut düşünme; nörokognitif fonksiyon.

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INTRODUCTION

Obstructive Sleep Apnea Syndrome (OSAS) is a disease characterized by obstructions in the upper respiratory tract causing cessations of breathing. Repeated pauses in breathing disrupt the integrity of sleep, preventing deep and restful sleep and causing excessive sleepiness during the day. At the same time, cessations in breathing often reduce oxygen saturation in the blood, causing emergence or aggravation of many diseases (1-4). One epidemiological study conducted in Switzerland reported that 50% of males between the ages of 49-68 were affected by OSAS (5). Peppard et al. (6) published a study evaluating the OSAS prevalence of two different periods, 1988-1994 vs. 2007-2010. This study asserted that 13% of men and 6% of women between the ages of 30-70 had moderate to severe OSAS. In addition, an increased risk of 48% for men and 44% for women compared to the 1988-1994 period was reported.

It has been theorized that the primary and secondary outcomes of obstructive breathing during sleep lead to changes in the control of cognition, emotion, learning, memory, and executive functions (7,8). Following this theory, few studies have shown that cognitive functions are affected in OSAS patients. On the other hand, the extent to which cognitive functions are affected has yet to be clarified (9,10).

Although some theories about cognitive impairment in OSAS have been proposed, the pathogenesis of this association has not been fully elucidated (9). Depression and anxiety are also known to have negative effects on cognitive function (11-13). Higher rates of depression and anxiety have been reported in OSAS patients compared to healthy control subjects (14-17).

This study aims to conduct a multifaceted evaluation of cognitive functions and determine the relationship between anxiety and depression levels and cognitive functions in OSAS patients.

MATERIAL AND METHODS

This cross-sectional case-control study was conducted simultaneously at the neurology and pulmonary diseases outpatient clinics of Yozgat Bozok University Medical School between January 15 and December 15, 2019. The study was conducted in accordance to the principles of the Helsinki Declaration and written informed consent was obtained from all participants. Yozgat Bozok University Local Ethics Committee approved the study protocol (Protocol Number: 2017-KAEK-189_2019.06.26_06 and Date: 26.06.2019).

Study Population

A total of 34 OSAS patients and 28 healthy volunteers between the ages of 18-65 were included in the study. People with at least primary education, and mental capabilities to complete the questionnaires and comprehend the scope of the study were included.

People with alcohol-substance and caffeine addiction, chronic physical disease, shift workers, pregnant and breastfeeding women, those with neurologic disease other than OSAS, lung diseases, infectious disease, and endocrine and systemic diseases were excluded from the study. OSAS patients who were receiving Continuous Positive Airway Pressure (CPAP) therapy were also excluded from the study.

The control group consisted of 28 healthy volunteers who were age and gender-matched with the OSAS group. The control group was also subjected to the exclusion criteria listed above; and also subjects with apnea/hypopnea index (AHI) of 5 and higher in polysomnography (PSG) was excluded from the study.

Detailed clinical history of the patients and the control group was obtained. Systemic physical and neurological examinations were performed. Height and weight measurements were recorded and body mass indexes (BMI) were calculated. PSG was performed on all participants. According to PSG results, participants were divided into two groups: OSAS patients and healthy volunteers.

Polysomnography (PSG) Evaluation

Patients who report snoring, witnessed apnea, and daytime sleepiness are evaluated for OSAS. These patients are asked to undergo overnight PSG in order to diagnose OSAS. PSG was performed using 31-channel ALICE 6 LDe (Respironics, PA, USA) at the sleep laboratory of the pulmonary department of the tertiary hospital.

The PSG recordings included electroencephalograms, electrooculograms, electromyograms for chin and leg movements, electrocardiograms, body position via thoracic belt, snoring sounds, oronasal airflow, arterial oxygen saturation via pulse oximetry, and respiratory efforts via chest and abdominal belts.

Sleep stages, movement events and respiratory parameters were scored according to the standard criteria of the American Academy of Sleep Medicine (AASM) version 2.5 published in 2018 (18). Sleep was scored manually in 30-second epochs. Drop in airflow amplitude $\geq 90\%$ relative to the basal amplitude lasting ≥ 10 seconds was defined as apnea while hypopnea was accepted as a $\geq 30\%$ decrease in airflow amplitude relative to the baseline values for ≥ 10 seconds with either an associated oxygen desaturation $\geq 3\%$ or arousal. The AHI was calculated using the total number of apneas and hypopneas divided by total sleep time in hours. AHI $< 5/h$ was accepted as the control group while AHI $\geq 5/h$ was accepted as having OSAS. The OSAS group was divided into three subgroups as mild ($5 \leq \text{AHI} < 15$), moderate ($15 \leq \text{AHI} < 30$), and severe ($\text{AHI} > 30$).

Data Collection Tools

Both groups were administered sociodemographic data form, Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), Montreal Cognitive Assessment (MoCA), and the Stroop Color and Word Test (SCWT).

Sociodemographic Form: The data collection form was developed by the researchers for study purposes and included questions related to the life stories of the participants. It included general information of patient and control groups. The form was applied at initial admission and collected data related to age, sex, marital status, education level, place of residence, habits, and medications used by the participants.

Beck Depression Inventory (BDI): The BDI was developed by Beck et al. (19) in order to evaluate bodily, emotional, cognitive, and motivational symptoms observed in depression. Total score ranges between 0-63, in which 0-9 indicates minimal, 10-16 mild, 17-29 moderate, and 30-63 severe depression. The scale's Turkish validity and reliability study was conducted by Hisli N. (20).

Beck Anxiety Inventory (BAI): The BAI was developed by Beck et al. (21) to measure the person's frequency of anxiety symptoms. Total score ranges between 0-63, in which 8-15 indicates mild anxiety, 16-25 moderate anxiety, and 26-63 severe anxiety. The scale's Turkish validity and reliability study was conducted by Ulusoy et al. (22).

Montreal Cognitive Assessment (MoCA): The MoCA test was developed as a fast screening test for mild cognitive impairment. MoCA evaluates various cognitive domains including attention and concentration, executive functions, memory, language, visuo-construction skills, abstract thinking, calculations, and orientation. Maximum test score is 30. Cut-off score of 21 and higher is considered normal. Selekler et al. (23) conducted the Turkish validity and reliability study.

Stroop Color and Word Test (SCWT): The SCWT is used to evaluate attention and mental control, shift in reaction mechanism, and ability to resist interference. The Stroop test uses four white cards. The first card contains color names printed in black letters over a white background. The second card shows color names printed in different colors that are inconsistent to the color name; for example, the word "red" is printed in yellow. This card is the main stimulus and the most critical part of the test. The third card consists of 0.4 cm diameter circles printed in different colors. The fourth card contains neutral words (much, thin, if, middle, etc.) printed in different colors. The Stroop test is based on stimuli and responses of the participant to these stimuli. The first and second cards assess reading and information-processing speed; the second, third, fourth and fifth cards assess focused attention; the fourth and fifth cards assess selective attention; and the fifth card measures executive functions of locking and inhibition. At the end of the test, number of errors, number of self-corrections, and test completion time are determined (24). The Stroop test is used to evaluate executive functions. Its fundamental purpose is to measure the perceptive configuration and capability to shift response when under an impairing effect. Other measured attributes include information-processing speed and attention. This test is accepted as the most selective test to evaluate the inhibition of mis-matched stimulus and is sensitive to damage to the left frontal lobe, especially the orbitofrontal cortex. The Turkish validity and reliability study of the test has been conducted (25).

Statistical Analysis

Statistical analysis was performed using the SPSS® 22.0 package program. Descriptive statistics of the data were calculated. Shapiro-Wilk test was used to assess normality distribution. Student's t-test was used to compare normally distributed data between two groups. Mann-Whitney U test was used in two group comparisons of data without normal distribution. Chi-square test was used to compare categorical variables. Pearson's correlation test was used to assess data with normal distribution and Spearman's correlation test was used for data without normal distribution. A p value of less than 0.05 was considered statistically significant.

RESULTS

There was no significant difference between the OSAS (n=34) and control group (n=28) according to age, gender, or BMI. The OSAS group had significantly higher BDI

and BAI scores compared to the control group (p=0.005 and p=0.019, respectively). Sociodemographic and psychological test results of the OSAS and control groups are presented in Table 1.

According to AHI classification, 35.3% (n=12) of OSAS patients had mild OSA, 38.2% (n=13) moderate OSA, and 26.5% (n=9) severe OSA. Polysomnographic data and results of the OSAS patients and control group are presented in Table 2.

Table 1. Sociodemographic characteristics and psychological test results of the OSAS patients and control group

	Control (n=28)	OSAS (n=34)	P
Age, years	41.57±10.14	44.88±8.04	0.157
Gender, n (%)			
Female	8 (28.6)	10 (29.4)	0.942
Male	20 (71.4)	24 (70.6)	
Education, years	9.89±3.37	10.82±3.13	0.308
	11 (3) [5-15]	11 (7) [5-15]	
BMI	31.33±5.11	30.49±3.98	0.467
Smoking, n (%)	13 (46.4)	16 (47.1)	0.961
BDI	5.61±4.96	10.35±7.50	0.005
	5.5 (6.5) [0-23]	9.5 (7.5) [0-34]	
BAI	6.29±5.65	11.09±8.69	0.019
	5.5 (7.5) [0-24]	8.5 (10.5) [0-40]	

OSAS: Obstructive Sleep Apnea Syndrome, BMI: Body Mass Index, BDI: Beck Depression Inventory, BAI: Beck Anxiety Inventory, descriptive statistics given as mean±standard deviation and median (interquartile range) [minimum-maximum]

Table 2. Polysomnographic data and results of the OSAS patients and control group

	Control (n=28)	OSAS (n=34)
Total Recording time, (minutes)	385.32±53.04	406.87±46.16
Total Sleep Time, (minutes)	311.69±77.33	324.67±62.27
Sleep Efficiency, (%)	80.96±13.99	79.64±11.62
Sleep Latency, (minutes)	12.64±12.99	17.15±15.08
REM Latency, (minutes)	123.78±69.03	133.12±76.62
Wake Time During Sleep Period	60.98±54.24	65.02±39.22
Sleep Stage 1, (minutes)	8.25±3.16	11.19±4.67
Sleep Stage 2, (minutes)	199.75±60.81	210.23±66.56
Sleep Stage 3, (minutes)	67.02±26.75	51.73±28.25
REM Stage, (minutes)	34.01±21.99	40.51±23.49
Right side sleep time, (minutes)	108.29±99.51	90.06±83.39
Left side sleep time, (minutes)	52.84±60.56	80.79±69.68
Supine sleep time, (minutes)	120.16±85.92	135.03±94.22
Prone sleep time, (minutes)	15.47±26.00	9.29±26.46
AHI Total, (n/hour)	2.48±1.28	27.52±22.19
AHI REM, (n/hour)	4.46±6.48	30.98±26.07
AHI NREM, (n/hour)	2.34±1.45	29.07±23.86
LEFT AHI, (n/hour)	2.09±3.16	21.18±24.98
RIGHT AHI, (n/hour)	1.16±1.56	11.30±16.32
PRONE AHI, (n/hour)	0.08±0.39	7.17±22.52
SUPINE AHI, (n/hour)	2.92±2.66	40.73±33.96
Minimum O ₂ Saturation, (%)	86.53±4.89	79.12±10.74
Mean O ₂ Saturation, (%)	92.74±3.02	91.25±4.57
Oxygen Saturation Index, (%)	5.69±4.98	34.51±24.59

OSAS: Obstructive Sleep Apnea Syndrome, AHI: Apnea Hypopnea Index

Mean overall MoCA score was 21.38 ± 5.01 for the OSAS patients and 25.32 ± 3.28 for the healthy control group; there was a significant difference between the groups ($p=0.001$). According to MoCA subdomains, OSAS patients had significantly lower naming, attention, abstract thinking, and delayed recall scores compared to the control group ($p=0.028$, $p<0.001$, $p=0.047$ and $p<0.001$, respectively). The OSAS patients had lower executive, language, and orientation scores compared to the control group, but these differences were not statistically significant ($p=0.088$, $p=0.402$ and $p=0.242$, respectively). MoCA scores of the OSAS patients and control group are presented in Table 3.

Comparison of the OSAS and control groups according to Stroop times showed that OSAS patients had longer Stroop 2 and 4 times but these differences were not statistically significant ($p=0.090$ and $p=0.099$, respectively). Stroop 1, 3 and 5 times were significantly longer in OSAS patients compared to the control group ($p=0.028$, $p=0.008$ and $p<0.001$, respectively). There was no significant difference between the OSAS group and control group according to correction and error results. Stroop test results of the OSAS and control groups are presented in Table 4. There was a statistically significant low negative correlation between MoCA total score and AHI ($r=-0.404$,

$p=0.001$). MoCA total score were found to have a statistically significant moderate negative correlation with BDI ($r=-0.568$, $p<0.001$) and BAI ($r=-0.530$, $p<0.001$) scores. There was a moderate positive correlation between Stroop 5 time and AHI ($r=0.510$, $p<0.001$). Stroop 5 time was found to have a statistically significant low positive correlation with BDI ($r=0.487$, $p<0.001$) and BAI ($r=0.407$, $p=0.001$) scores. Correlation analysis of AHI, BDI, BAI, MoCA and Stroop test is presented in Table 5.

DISCUSSION

The primary finding of this observational study was that OSAS had a negative effect on cognitive functions and this effect had different degrees of extent on different domains of cognition. In addition, OSAS patients were found to have higher rates of depression and anxiety compared to the control group. Impaired cognitive function showed correlation with AHI as well as depression and anxiety. Hypoxia due to OSAS has been found that it could cause major damage to the central nervous system. Reduced oxygen saturation may result in decreased protective vascular mechanisms and increased vasoconstriction, which may lead to the development of structural and functional changes in the brain (26,27). The anterior frontal cortex, which is highly susceptible to hypoxia,

Table 3. MoCA scores of the OSAS patients and control group

	Control (n=28)				OSAS (n=34)				P
	Mean±SD	Median	IQR	Min-Max	Mean±SD	Median	IQR	Min-Max	
Executive	4.07±0.85	4	1.75	2-5	3.61±1.04	4	1.25	2-5	0.088
Naming	2.61±0.49	3	1	2-3	2.26±0.62	2	1	1-3	0.028
Attention	4.77±1.23	6	1	2-6	3.94±1.13	4	2	2-6	<0.001
Language	1.96±1.14	2	2	0-3	1.76±1.10	2	2	0-3	0.402
Abstract thinking	1.53±0.69	2	1	0-2	1.09±0.9	1	2	0-2	0.047
Delayed recall	3.93±1.05	4	2	2-5	2.82±0.97	3	2	1-5	<0.001
Orientation	5.96±0.89	6	0	5-6	5.88±0.32	6	0	5-6	0.242
Total MoCA	25.32±3.28	25	5	19-30	21.38±5.01	21.5	7.75	11-29	0.001

MoCA: Montreal Cognitive Assessment, OSAS: Obstructive Sleep Apnea Syndrome, SD: Standard Deviation, IQR: Interquartile Range, Min: Minimum, Max: Maximum

Table 4. Stroop test results of the OSAS patients and control group

	Control (n=28)				OSAS (n=34)				P
	Mean±SD	Median	IQR	Min-Max	Mean±SD	Median	IQR	Min-Max	
Stroop 1 (Time)	11.35±2.75	11.5	2.75	7-20	12.56±2.12	12.5	3	9-20	0.028
Stroop 1 (Error)	0.07±0.38	0	0	0-2	0.15±0.44	0	0	0-2	0.261
Stroop 1 (Correction)	0.00±0.00	0	0	0-0	0.03±0.17	0	0	0-1	0.364
Stroop 2 (Time)	12.21±4.56	11.5	5.75	7-25	13.09±2.44	13	4	9-18	0.090
Stroop 2 (Error)	0.07±0.26	0	0	0-1	0.12±0.41	0	0	0-2	0.787
Stroop 2 (Correction)	0.04±0.19	0	0	0-1	0.08±0.29	0	0	0-1	0.406
Stroop 3 (Time)	13.14±4.34	12	5	7-25	15.32±2.81	15.5	3.5	10-21	0.008
Stroop 3 (Error)	0.11±0.42	0	0	0-2	0.29±0.52	0	1	0-2	0.059
Stroop 3 (Correction)	0.11±0.41	0	0	0-2	0.24±0.49	0	0	0-2	0.155
Stroop 4 (Time)	20.50±6.56	19	10	10-35	23.71±7.27	24	13.25	10-37	0.099
Stroop 4 (Error)	0.68±1.02	0	1.75	0-3	0.76±0.92	1	1	0-4	0.457
Stroop 4 (Correction)	0.57±0.92	0	1	0-3	0.65±0.73	0.5	1	0-2	0.389
Stroop 5 (Time)	26.57±8.65	27.5	14.75	10-41	35.82±10.10	38	12.5	12-50	<0.001
Stroop 5 (Error)	2.07±2.39	1.5	2.5	0-10	2.35±1.39	2	2.25	0-6	0.094
Stroop 5 (Correction)	1.39±1.61	1	2	0-6	1.71±1.19	2	1.25	0-5	0.155

OSAS: Obstructive Sleep Apnea Syndrome, SD: Standard Deviation, IQR: Interquartile Range, Min: Minimum, Max: Maximum

Table 5. Correlation analysis of AHI, BDI, BAI, MoCA and Stroop test

		AHI	BDI	BAI
Executive	r	-0.154	-0.453	-0.337
	p	0.232	0.001	0.007
Naming	r	-0.383	-0.479	-0.489
	p	0.002	<0.001	<0.001
Attention	r	-0.398	-0.501	-0.449
	p	0.001	<0.001	<0.001
Language	r	-0.133	-0.340	-0.309
	p	0.302	0.007	0.015
Abstract thinking	r	-0.370	-0.460	-0.448
	p	0.003	<0.001	<0.001
Delayed recall	r	-0.419	-0.391	-0.378
	p	0.001	0.002	0.002
Orientation	r	-0.215	-0.434	-0.530
	p	0.094	<0.001	<0.001
MoCA total	r	-0.404	-0.568	-0.530
	p	0.001	<0.001	<0.001
Stroop 1 time	r	0.211	0.568	0.510
	p	0.100	<0.001	<0.001
Stroop 2 time	r	0.142	0.346	0.023
	p	0.273	0.006	0.289
Stroop 3 time	r	0.280	0.510	0.398
	p	0.028	<0.001	0.001
Stroop 4 time	r	0.284	0.560	0.420
	p	0.025	<0.001	0.001
Stroop 5 time	r	0.510	0.487	0.407
	p	<0.001	<0.001	0.001
AHI	r	----	0.452	0.368
	p		<0.001	0.003
BDI	r	0.452	---	0.899
	p	<0.001		<0.001
BAI	r	0.368	0.899	---
	p	0.003	<0.001	

AHI: Apnea Hypopnea Index; BDI: Beck Depression Inventory; BAI: Beck Anxiety Inventory; MoCA: Montreal Cognitive Assessment

seems to be the most affected region of the brain (28). In addition, grey matter volume loss in basal ganglia has been identified in OSAS patients (29,30). Reduced information processing and psychomotor speed, difficulty switching between tasks, and difficulty in preventing predominant responses in OSAS patients was also reported (31). It is noteworthy that studies showing the neuroanatomical regions affected in the literature from the above sentences also coincide with studies showing clinical results. Our study found that Stroop 1, 3, and 5 times were longer in OSAS patients compared to the control group, while Stroop 5 time had the highest correlation with AHI value. The fundamental feature of the Stroop test is that it measures the perceptive configuration of cognition under impairment, the capability to shift response, and the speed of information processing. Stroop test is also highly sensitive to frontal cortex damage. Evaluation of information in the literature in conjunction with our study results suggests that our findings are indicative of damage in the frontal region. Although increasing evidence over the past decade confirms our findings, it should be noted that the underlying pathophysiology linking OSAS and cognitive involvement is still controversial (32).

Depression and anxiety are common among OSAS patients (33,34). On the other hand, Gupta et al. (35) showed increased prevalence of OSAS in individuals with

major depressive disorder and post-traumatic stress disorder. Clinical studies have indicated that the relationship between OSAS and depression is multifactorial (36). Inanç et al. (37) showed that BDI and BAI scores of the patients with OSAS were higher than the healthy control group. However, there are also studies that did not find an association between the OSAS with anxiety and depression (17,38). Depression, even in its mildest forms, has been associated with reduced cognitive functions (12,39). Depending on its duration and severity, anxiety has been known to cause cognitive disorders including deficits in cognitive flexibility and decision-making (40,41). Our study found higher levels of anxiety and depression in OSAS patients compared to the control group and also detected a correlation between cognitive functions and anxiety and depression. When evaluated in this regard, the results of our study may suggest that anxiety and depression associated with OSAS may be the cause of poor cognitive performance.

In addition, it should not be forgotten that OSAS patients have excessive daytime sleepiness. Sleepiness plays a role in the development of cognitive dysfunction, especially attention and executive functions (42,43). It is also noteworthy that daytime sleepiness may have contributed to the low cognitive performance of our patients. It has been reported that even short-term CPAP treatment has shown a positive effect on neurocognitive functions in OSAS patients (44,45). On the other hand, it also indicates that structural damage is not a single factor.

CONCLUSION

In conclusion, the results of this study imply that OSAS has different effects on various domains of cognitive function and that many negative factors caused by OSAS may play a role in cognitive involvement associated with OSAS. It should be kept in mind that further studies are warranted to more clearly illustrate the ethiopathogenesis of this subject. In addition, we believe long-term follow-up of cognitive status before and during CPAP therapy will provide significant contributions to our understanding of the irreversibility and extent of reversibility of cognitive involvement in OSAS.

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REFERENCES

1. Daurat A, Sarhane M, Tiberge M. Obstructive sleep apnea syndrome and cognition: A review. *Neurophysiol Clin.* 2016;46(3):201-15.
2. Gagnon K, Baril AA, Gagnon JF, Fortin M, Décary A, Lafond C, et al. Cognitive impairment in obstructive sleep apnea. *Pathol Biol (Paris).* 2014;62(5):233-40.

3. Kısabay Ak A, Sarı ÜS, Oktan B, Korkmaz T, Dinç Horasan G, Selcuki D, et al. Evaluation of cognitive function using objective and subjective tests in the obstructive sleep apnea syndrome. *J Turk Sleep Med.* 2017;4(3):76-83.
4. Hamamcı M, Alpua M, Ergün U, Inan LE. Obstructive sleep apnea syndrome and neurology. *Bozok Med J.* 2018;8(Special Issue):20-5.
5. Heinzer R, Vat S, Marques-Vidal P, Marti-Soler H, Andries D, Tobback N, et al. Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study. *Lancet Respir Med.* 2015;3(4):310-8.
6. Peppard PE, Young T, Barnett JH, Palta M, Hagen EW, Hla KM. Increased prevalence of sleep-disordered breathing in adults. *Am J Epidemiol.* 2013;177(9):1006-14.
7. Verstraeten E. Neurocognitive effects of obstructive sleep apnea syndrome. *Curr Neurol Neurosci Rep.* 2007;7(2):161-6.
8. Goel N, Rao H, Durmer JS, Dinges DF. Neurocognitive consequences of sleep deprivation. *Semin Neurol.* 2009;29(4):320-39.
9. Olaithe M, Bucks RS, Hillman DR, Eastwood PR. Cognitive deficits in obstructive sleep apnea: insights from a meta-review and comparison with deficits observed in COPD, insomnia, and sleep deprivation. *Sleep Med Rev.* 2018;38:39-49.
10. Bucks RS, Olaithe M, Eastwood P. Neurocognitive function in obstructive sleep apnoea: A meta-review. *Respirology.* 2013;18(1):61-70.
11. Demir Akça AS, Saraçlı Ö, Emre U, Atasoy N, Güdül S, Özen Barut B, et al. Relationship of cognitive functions with daily living activities, depression, anxiety and clinical variables in hospitalized elderly patients. *Noro Psikiyatı Ars.* 2014;51(3):267-74.
12. Pantzar A, Laukka EJ, Atti AR, Fastbom J, Fratiglioni L, Bäckman L. Cognitive deficits in unipolar old-age depression: a population-based study. *Psychol Med.* 2014;44(5):937-47.
13. Bierman EJ, Comijs HC, Rijmen F, Jonker C, Beekman AT. Anxiety symptoms and cognitive performance in later life: results from the longitudinal aging study Amsterdam. *Aging Ment Health.* 2008;12(4):517-23.
14. Karaaslan Ö. Obstructive sleep apnea syndrome and psychiatry. *Bozok Med J.* 2018;8(Special Issue):34-8.
15. Doherty LS, Kiely JL, Lawless G, McNicholas WT. Impact of nasal continuous positive airway pressure therapy on the quality of life of bed partners of patients with obstructive sleep apnea syndrome. *Chest.* 2003;124(6):2209-14.
16. Kerner NA, Roose SP. Obstructive sleep apnea is linked to depression and cognitive impairment: evidence and potential mechanisms. *Am J Geriatr Psychiatry.* 2016;24(6):496-508.
17. Fidan F, Ünlü M, Sezer M, Pala E, Geçici Ö. Relationship between obstructive sleep apnea syndrome and anxiety or depression. *Turk Thorac J.* 2006;7(2):125-9.
18. Berry RB, Albertario CL, Harding SM, Loyd RM, Plate DT, Quan SF, et al. for the American Academy of Sleep Medicine. The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications. Version 2.5. Darien, IL: American Academy of Sleep Medicine; 2018.
19. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry.* 1961;4(6):561-71.
20. Hisli N. A study on the validity of Beck Depression Inventory. *Turk Psychol J.* 1988;6(22):118-26.
21. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. *J Consult Clin Psychol.* 1988;56(6):893-7.
22. Ulusoy M, Hisli Sahin N, Erkmen H. Turkish version of the Beck Anxiety Inventory: psychometric properties. *J Cogn Psychother.* 1998;12(2):163-72.
23. Selekler K, Cangöz B, Uluç S. Power of discrimination of Montreal Cognitive Assessment (MOCA) Scale in Turkish patients with mild cognitive impairment and Alzheimer's disease. *Turk J Geriatr.* 2010;13(3):166-71.
24. Stroop JR. Studies of interference in serial verbal reactions. *J Exp Psychol.* 1992;121(1):15-23.
25. Karakaş S, Erdoğan E, Soysal Ş, Ulusoy T, Yüceyurt Ulusoy İ, Alkan S. Stroop test TBAG form: standardisation for Turkish culture, reliability and validity. *J Clin Psychiatry.* 1999;2(2):75-88.
26. Aloia MS, Arnedt JT, Davis JD, Riggs RL, Byrd D. Neuropsychological sequelae of obstructive sleep apnea-hypopnea syndrome: a critical review. *J Int Neuropsychol Soc.* 2004;10(5):772-85.
27. Zimmerman ME, Aloia MS. A review of neuroimaging in obstructive sleep apnea. *J Clin Sleep Med.* 2006;2(4):461-71.
28. Beebe DW, Gozal D. Obstructive sleep apnea and the prefrontal cortex: towards a comprehensive model linking nocturnal upper airway obstruction to daytime cognitive and behavioral deficits. *J Sleep Res.* 2002;11(1):1-16.
29. Castronovo V, Scifo P, Castellano A, Aloia MS, Iadanza A, Marelli S, et al. White matter integrity in obstructive sleep apnea before and after treatment. *Sleep.* 2014;37(9):1465-75.
30. Joo EY, Tae WS, Lee MJ, Kang JW, Park HS, Lee JY, et al. Reduced brain gray matter concentration in patients with obstructive sleep apnea syndrome. *Sleep.* 2010;33(2):235-41.
31. Olaithe M, Bucks RS. Executive dysfunction in OSA before and after treatment: a meta-analysis. *Sleep.* 2013;36(9):1297-305.
32. Devita M, Zangrossi A, Marvisi M, Merlo P, Rusconi ML, Mondini S. Global cognitive profile and different components of reaction times in obstructive sleep apnea syndrome: Effects of continuous positive airway pressure over time. *Int J Psychophysiol.* 2018;123:121-6.
33. Rezaeitalab F, Moharrari F, Saberi S, Asadpour H, Rezaeitalab F. The correlation of anxiety and depression with obstructive sleep apnea syndrome. *J Res Med Sci.* 2014;19(3):205-10.
34. Sharafkhaneh A, Giray N, Richardson P, Young T, Hirshkowitz M. Association of psychiatric disorders and sleep apnea in a large cohort. *Sleep.* 2005;28(11):1405-11.
35. Gupta MA, Simpson FC. Obstructive sleep apnea and psychiatric disorders: a systematic review. *J Clin Sleep Med.* 2015;11(2):165-75.

36. Flemons WW, Tsai W. Quality of life consequences of sleep-disordered breathing. *J Allergy Clin Immunol.* 1997;99(2):S750-6.
37. Inanç L, Ünal Y, Kutlu G, Semiz ÜB. The relationship between illness severity, anxiety and depressive symptoms in obstructive sleep apnea syndrome patients. *J Turk Sleep Med.* 2017;4(3):71-5.
38. Özkurt S, Öztürk E, Yıldız Aİ, Dursunoğlu N, Özdel O, Akdağ B, et al. Psychiatric evaluation in patients with obstructive sleep apnea syndrome. *Tuberk Toraks.* 2013;61(3):216-20.
39. Dotson VM, Resnick SM, Zonderman AB. Differential association of concurrent, baseline, and average depressive symptoms with cognitive decline in older adults. *Am J Geriatr Psychiatry.* 2008;16(4):318-30.
40. Park J, Moghaddam B. Impact of anxiety on prefrontal cortex encoding of cognitive flexibility. *Neuroscience.* 2017;345:193-202.
41. Eysenck MW, Derakshan N, Santos R, Calvo MG. Anxiety and cognitive performance: attentional control theory. *Emotion.* 2007;7(2):336-53.
42. Naismith S, Winter V, Gotsopoulos H, Hickie I, Cistulli P. Neurobehavioral functioning in obstructive sleep apnea: differential effects of sleep quality, hypoxemia and subjective sleepiness. *J Clin Exp Neuropsychol.* 2004;26(1):43-54.
43. Ohayon MM, Vecchierini MF. Daytime sleepiness and cognitive impairment in the elderly population. *Arch Intern Med.* 2002;162(2):201-8.
44. Kylstra WA, Aaronson JA, Hofman WF, Schmand BA. Neuropsychological functioning after CPAP treatment in obstructive sleep apnea: a meta-analysis. *Sleep Med Rev.* 2013;17(5):341-7.
45. Ferini-Strambi L, Baietto C, Di Gioia M, Castaldi P, Castronovo C, Zucconi M, et al. Cognitive dysfunction in patients with obstructive sleep apnea (OSA): partial reversibility after continuous positive airway pressure (CPAP). *Brain Res Bull.* 2003;61(1):87-92.