Psychiatry and Behavioral Sciences 2018;8(4):147-57
https://doi.org/10.5455/PBS.20180530034643

ORIGINAL ARTICLE

Effect of Comorbid Metabolic Syndrome and Related Components on Cognition in Patients with Schizophrenia

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Objective: The aim of the present study is to compare the cognitive functions of patients with and without metabolic syndrome (MetS) in schizophrenia and schizoaffective disorder, and to investigate the relationship between the clinical symptomatology and MetS-related components with cognitive functions.
Methods: This cross-sectional study included 79 patients diagnosed with schizophrenia/schizoaffective disorder. All participants were assessed using the Positive PANSS and a neurocognitive battery to assess memory, attention and executive function.
Results: In the study group, 35 (44.30%) patients met the criteria for MetS. The MetS group performed worse than those without MetS on verbal memory subtests. There was no difference in attention and executive functioning of the Mets and non-MetS groups. Multiple regression analyses showed that, elevated HDL were significantly associated with better scores for verbal memory, visual memory, and executive functions. In contrast, a higher BMI was significantly associated with poorer scores on visual memory, verbal memory, attention and executive functioning. Unexpectedly, a greater waist circumference was associated with better scores for executive functioning.
Discussion: MetS and related components are associated with impaired cognitive functioning in patients with schizophrenia/schizoaffective disorder. Early interventions such as reducing risk related BMI values or increasing HDL levels, may reduce risk factors for MetS and have positive effects on cognitive functioning in patients with schizophrenia.
Keywords: Attention, cognitive function, executive function, metabolic syndrome, memory, schizophrenia, verbal memory

INTRODUCTION

Schizophrenia is a chronic, debilitating mental disorder, which has profound impacts on both the affected individual and society (1). Schizophrenia has been associated with an increased risk of cardiac morbidity and mortality (2). In addition, metabolic syndrome (MetS) and other cardiovascular risk factors are more prevalent in patients with schizophrenia (1). MetS is diagnosed if a person has at least three of five metabolic factors; which are abdominal obesity, high triglycerides, low high-density lipoprotein (HDL), hypertension, and hyperglycemia (3). According to Adult Treatment Protocol (ATP-III) criteria, the prevalence of MetS in patients with schizophrenia ranges from 19 to 63% in different ethnic groups (2). In a study by Lee et al., the prevalence of MetS in patients with schizophrenia was two to four times higher than in healthy individuals (4).

Schizophrenia has been associated with significant and persistent cognitive impairment (5), with schizophrenia patients showing impairments in many cognitive domains, including psychomotor speed, attention, vigilance, verbal learning, working memory, and executive function (4).

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Received: May 30, 2018 Accepted: December 21, 2018

Citation: Celikbas Z, Yildiz M, Batmaz S, Yalçınkaya Alkar Ö, Kocakaya H. Effect of Comorbid Metabolic Syndrome and Related Components on Cognition in Patients with Schizophrenia. Psychiatry and Behavioral Sciences 2018;8(4):147-57.
https://doi.org/10.5455/PBS.20180530034643

The aforementioned cognitive functions have important implications for interpersonal relationships, social problem solving, practical problem solving in everyday life, and quality of life (4). A previous study concluded that the severity of cognitive impairment was the best predictor of social functioning in the community (6). Thus, in recent years, cognitive impairment has been in the focus of much research (7). Cognitive deficits are thought to occur before the onset of psychosis, and are stable throughout the course of the illness in most patients (8). However, one study concluded that cognitive decline may continue in a subset of patients after the onset of psychosis (7).

MetS has negative effects both on cognitive performance and the structure of the brain, and it is also known to increase the risk of dementia (9). MetS and its components are also implicated in cognitive impairment encountered in schizophrenia (7), although studies have reported discordant results. A number of studies reported that MetS was associated with cognitive impairment (10-12), but others found no such associations (13-15). However, in a meta-analysis by Bora et al. (7), co-morbidity associated with MetS was linked to more severe cognitive deficits in schizophrenia (d=0.28). In terms of specific MetS-related factors and cognitive function, studies reported poorer cognitive scores in patients with hypertension (11, 16, 17), high triglycerides (10, 11, 14, 18), low HDL (10), and abdominal obesity (10, 11, 14, 18, 19), and hyperglycemia (18, 20-23). Other studies reported unexpected results. For example, in a study by Wysokinsi et al. (18), elevated blood pressure was associated with improvements in all cognitive domains, and the CATIE study pointed to better cognitive functioning in patients with elevated cholesterol and triglyceride levels (24). In addition, hyperglycemia was reported to be associated with higher scores on a subset of neurocognitive tests (17).

Based on the aforementioned literature, we can assume that there is a complex relationship between MetS-related components and cognitive dysfunction in schizophrenia patients. A better understanding of this relationship will shed light on cognitive impairment, which is one of the main deficits in schizophrenia patients, and aid the development of treatment modalities.

In the present study, we aimed to compare the cognitive functions of patients with and without MetS in schizophrenia and schizoaffective disorder and to examine the relationship between the clinical symptomatology and MetS-related components with cognitive functions. We hypothesized that patients with MetS and components of MetS would perform worse than patients without MetS.

METHODS

Participants

This cross-sectional study was conducted at Gaziosmanpaşa University, School of Medicine, Department of Psychiatry between December 2015 and April 2016. Patients with schizophrenia or schizoaffective disorder aged 18–65 years who were in symptomatic remission, defined as a score of <60 on the Positive and Negative Syndrome Scale (PANSS) and on a stable dose of antipsychotics for at least 4 weeks (25), were screened for inclusion in the study. As the cognitive functions of patients were to be assessed, a Mini Mental State Examination score > 24 was required to rule out other potential reasons for cognitive impairment. The exclusion criteria were as follows: mental retardation; a history of head trauma; a history of alcohol or substance abuse in the last 6 months; degenerative neurological disorders; unstable cardiovascular, renal, gastrointestinal, or hepatic diseases; and unregulated diabetes mellitus. Pregnant women and breastfeeding women were also excluded. Eighty-two patients with schizophrenia or schizoaffective disorder diagnosed according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (26) were evaluated. Two patients stated that they did not wish to participate in the study, and MetS-related blood parameters were missing on one patient. Thus, these patients were removed from the sample. Finally, 79 patients were included in the study.

This study was approved by Gaziosmanpaşa University Ethics Comitee with 15-KAEK-182 project

number in December 2015, and written informed consent was obtained from all the participants prior to the commencement of the study. The study was conducted in accordance with the Declaration of Helsinki.

Procedure

After completing a sociodemographic data form, the PANSS and Calgary Depression Scale for Schizophrenia (CDSS) were used to determine the clinical status of the participants. MetS and its components were defined according to NCEP-Adult Treatment Protocol Adult Treatment Panel (ATP) III criteria (27). Routine blood tests of the patients in the last 6 months were used to record MetS-related parameters. Blood pressure, height, and weight and waist circumference measurements were taken by the same physician. Body mass index (BMI) values were grouped according to the classification system of the World Health Organization (WHO) (28). According to the WHO classification system, BMI values <18.5 denote underweight, 18.5–24.9 normal weight, 25–29.9 overweight (class I obese), 35–39.9 class II obese, and ≥40 kg/m^2 class III obese (morbid obesity).

The patient group was divided into two groups: MetS and non-MetS. The cognitive status of the participants was evaluated to assess attention, memory, and executive functions. Briefly, the Oktem Verbal Memory Process Test (VMPT) was used for verbal memory, the Wechsler Memory Scale-R (WMS-R) subscales were used for visual and logical memory, the Visual Aural Digit Span Test Form B (VADS-B) was used for attention and short-term memory, and the Stroop Test was used for evaluating executive function. Details on the tests are provided in Section 2.3.

Measures

PANSS (Positive and Negative Syndrome Scale): This instrument measures symptom severity in patients with schizophrenia (29). The scale consists of 7 positive symptom items, 7 negative symptom items, and 16 general psychopathology items. All individual items are scored on a 7-point Likert scale, ranging from 1 to 7. The reliability and validity of the Turkish version of the scale was conducted by Kostakoglu et al. (30).

CDSS (Calgary Depression Scale for Schizophrenia): This is the most widely used scale to assess the level of depression in schizophrenia patients (31). The scale consists of 9 items, and all items are scored on a 4-point Likert scale, ranging from 0 to 3. The reliability and validity of the Turkish version of the scale was conducted by Aydemir et al. (32).

VMPT (Verbal Memory Processing Test): This instrument evaluates the processes of working memory, learning or acquiring knowledge, retention of information, and recall (33). In the evaluation, immediate memory, complete learning, total learning, highest learning, and long-term recall scores are recorded. The scale was developed by Öktem based on the Verbal Learning Test developed by Rey (34).

WMS-R IV (Weschler Memory Scale-Revised IV): Immediate and delayed verbal memory and immediate and delayed visual memory were measured by 13 WMS-R subtests. The test also provides measurements of attention related to memory processes and concentration (35). The reliability and validity of the Turkish version of the WMS-R was conducted by Karakas and Kafadar (36). In this study, only visual production I and II and logical memory I and II subtests were applied to the participants.

VADS-B (Visual Auditory Digit Span-B): This is a standardized test to assess attention and short-term memory (37). VADS-B consists of four subtests, in which numeric sequences (numbered 1 through 9) are used as stimuli. The standardization and validation of the Turkish version of the test was conducted by Karakas and Yalin (38).

The Stroop Color and Word Test (SCWT): The Stroop Color and Word Test (SCWT) is a neuropsychological test extensively used for both experimental and clinical purposes. The Stroop test was first developed by Stroop (39), and various forms of the test were later developed. The Stroop test evaluates a subject's attention and executive function. The four stimulus cards and related tasks used in the Stroop Test include all of the cards and tasks that led to the three factors obtained for the Stroop Effect in the study of Jensen (40). Factor 1 color naming, Factor 2 deteriorating effect and Factor 3 named speed factor. Standardization

of the test for a Turkish population was done by Karakaş et al. (41).

Statistical Analysis

IBM SPSS for Windows, Version 19.0 (42) was used for all statistical analyses. The demographic and clinical data of the participants were analyzed by descriptive statistics. In significance testing, when comparing the mean of quantitative variables in the two groups, the difference between the two averages was used. Cross-tabulation and chi-square tests were conducted to assess whether there was a relationship between qualitative variables.

Prior to the series of regression analysis, three composite scores for the Stroop test, factor 1, factor 2, and factor 3, were calculated (40). Then, correlations between the neuropsychological and psychiatric measures of the study were examined (Table 3). To identify the predictors of the neuropsychological measures eight hierarchical regression analyses were performed. In these analyses, the dependent variables were the neurocognitive test scores, and the predictors were the MetS-related components. In the regression analyses performed with dependent variables that were correlated with PANSS and CDSS scores, PANSS and CDSS scores were controlled at the first step.

RESULTS

Patient characteristics

Of the 79 participants, 67 (84.8%) had a diagnosis of schizophrenia, and 12 (15.2%) had a diagnosis of

Table 1: Sociodemographic and Clinical Variables of Patients with MetS and Non-MetS

Variables	Metabolic Syndrom				Statistic	p
	Non-MetS		MetS			
Diagnosis	n	%	n	%		
Schizophrenia	36	(81.8)	31	(88.6)	0.690	0.406
Schizoaffective Disorder	8	(18.2)	4	(11.4)		
Gender						
Female	19	(43.2)	15	(42.9)	0.001	0.977
Male	25	(56.8)	20	(57.1)		
Marital Status						
Married	18	(40.9)	16	(45.7)		
Single	20	(45.5)	14	(40)	0.250	0.885
Divorced/Widowed	6	(13.6)	5	(14.3)		
	Mean	SD	Mean	SD		
Age	39.05	11.49	39.77	10.54	0.289	0.773
Education (years)	10.18	3.72	I0.03	3.85	0.179	0.858
Age at onset of illness	24.64	7.35	25.51	8.29	0.498	0.620
Waist circumference (cm)	93.14	13.52	108	9.35	5.763	<0.001
Systolic blood pressure (mm Hg)	118.86	8.92	127.31	14.75	2.983	0.004
Diastolic blood pressure (mm Hg)	73.32	7.54	76.66	9.28	1.765	0.082
HDL (mg/di)	48.98	16.59	38.13	13.36	3.141	0.002
Triglycerides (mg/di)	132.61	97.29	225.5	92.76	4.303	<0.001
Fasting Glucose (mg/di)	92.36	15.36	104.75	28.36	2.327	0.024
BMI (kg/m^2)	27.44	5.46	32.17	4.85	4.017	<0.001
PANSS Total	42.59	7.13	44.6	7.35	1.227	0.224
CDSS Total	0.57	1.13	0.51	1.04	0.218	0.828

HDL: High Densitiy Lipoprotein, BMI: Body Mass Index, PANSS: Positive and Negative Syndrome Scale, COSS: Calgary Depression Scale for Schizophrenia

Table 2: Comparison of cognitive test scores between MetS and non-MetS groups

Variables	Metabolic Syndrome		t	p
	Non-metS	MetS		
VMPT immediate memory	4.41±1.4	4.49±1.5	0.234	0.816
VMPT maximum learning	10.36±2.55	10.8±2.77	0.726	0.470
VMPT farulty learning score	1.82±2.8	0.74±1.07	2.344	0.023
VM PT perseveration	1.34±2.19	0.43±1.44	2.225	0.029
VMPT total recall	13.3±2.72	l3.91±2.48	1.045	0.299
VM PT false recognition	1.7±2.69	1.11±2.47	1.004	0.318
WMS-R IV visual reproduction I	1.5±1.5	1.43±1.4	0.216	0.829
WMS-R IV visual reproduction II	1.2±1.4 7	1.37±1.37	0.515	0.608
WMS-R IV visual memory total score	3.75±2.43	3.91±2.39	0.300	0.765
WMS-R IV logical memory subtest	4.28±2.92	4.97±3.54	0.946	0.347
Data was shown as mean±standard deviation. Independent samples t test was used				
Stroop Interference	18.02±12.37	22.77±18.06	1.384	0.170
VADS B Total score	21.73±4.88	22.57±4.13	0.817	0.417

VMPT: Verbal Memory Processing Test, WMS-R: Weschler Memory Scale-Revised, VADS: Visual Auditory Digit Score

schizoaffective disorder. There were 45 (57%) males and 34 (43%) females in the sample. The mean (SD) age was 39.4±10.95 years. The mean PANSS and CDSS scores of the participants were 43.43±7.22 and 0.54±1.08, respectively. The distribution of the sociodemographic and clinical variables of the participants is shown in Table 1.

MetS and related components

In the study, 35 (44.30%) of the participants had MetS according to NCEP-ATP III criteria. The rate of MetS was 44.44% in males (20/45) and 44.11% in females (15/ 34). Regarding MetS-related components, the mean values were as follows: waist circumference: 99.76±13.85 cm, systolic blood pressure: 122.70±12.46 mmHg, diastolic blood pressure: 74.93±8. 49 mmHg, HDL cholesterol: 44.02±16.05 mg/dl, triglycerides: 174.42±104.97 mg/dl, low-density lipoprotein cholesterol: 124.23±36.08 mg/dl, fasting glucose: 97.6±22.74 mg/dl, and BMI: 29.53±5.64 kg/m^2. There were significant differences in the waist circumference, systolic blood pressure, triglyceride, fasting blood glucose, HDL, and BMI values of the MetS and non-MetS groups.

Comparison of sociodemographic (age, gender, marital status, and education level) and clinical variables (age at onset of illness, PANSS scores, and CDSS scores) of the MetS and non-MetS groups revealed no significant between-group differences. The demographic and clinical characteristics of the MetS groups are presented in Table 1.

MetS and cognitive test performance

The MetS group performed worse on two subscales of the VMPT: "false recognition" (p=0.023) and "perseveration" (p=0.029) as compared to the non-MetS group. There were no significant between-group

Table 3: Correlations between the neuropsyehological and psychiatric measures of the study

	PANSS	CDSS
CDSS	.32**	
VMPT immediate memory	-.46***	.08
VMPT total recall	-.36**	-.01
WMS-R IV Logical Memory subtest immediate recall	-.35**	.07
WMS-R IV Logical Memory subtest delaved memory	-.37**	.07
V ADS B total score	-.32**	.08
ST factor I	.08	-.06
ST factor 2	.03	-.03
ST factor 3	.20	-.12

*p<.05, **p<.01, ***p<.001
PANSS: Positive and Negative Syndrome Scale, CDSS: Calgary Depression Scale for Schizophrenia, VMPT: Verbal Memory Processing Test, WMS-R: Weschler Memory Scale-Revised, V ADS 8: Visual Auditory Digit Span B, ST: Swoop Test

differences in the findings of the WMS-R subscales, VADS-B form, and Stroop tests. The cognitive test performances of the Mets and non-MetS groups are shown in Table 2.

Correlation analysis

There was a negative correlation between the PANSS and VMPT immediate memory and total recall, WMS R IV logical memory immediate and delayed memory subtests, VADS B total scores. There was no correlation between PANSS scores and Stroop subtest scores.

Regression analysis

For the first six regression analyses PANSS and CDSS scores entered into the regression to control their effect on criterion variables, VMPT-immediate memory, VMPT-total recall, WMS-R IV Logical Memory subtest immediate recall, WMS-R IV Logical Memory subtest delayed memory, and VADS-B (Table 4). The results of the regression models showed that variables entered to the regression analysis accounted for the 29% of the variance in VMPT-immediate memory, 30% of the variance in VMPT-total recall, 21 % of the variance in WMS-R IV Logical Memory subtest immediate recall, 23% of the variance in WMS-R IV Logical Memory subtest delayed memory, and 24% of the variance in VADS-B, 17% of the variance in ST factor 3 scores significantly. However, regression analyses were not significant for the ST factor 1 and ST factor 2. Regression analyses showed that lower PANSS scores predicted higher scores on VMPT

Table 4: Regression analysis: Predictors of neuropsychological measures

Model	B	Beta β	t	p	Model R^2
DV					
IV					
VMPT immediate memory					
PANSS	-.10	-.50	-4.72***	.000	.29
VMPT total recall					
PANSS	-.14	-.40	-3.84***	.000	.30
Waist circimference	.08	41	2.37*	.020	
HDL	.05	.30	2.56*	.013	
BMI (kg/m^2)	.21	-.45	-2.82*	.006	
WMS-R IV logical Memory subtest immediate recall					
PANSS	-.24	-.41	-3.70***	.000	.21
Waist circimference	.12	.39	2.11*	.038	
WMS-R IV Logical Memory subtest delayed memory					
PANSS	-.24	-.44	-4.03***	.000	.23
Waist circimference	.12	.43	2.36*	.021	
VADS B total score					
PANNS	-.23	-.36	-3.32**	.001	.24
Waist circimference	.15	.46	2.54*	.013	
BMI (kg/m^2)	-.42	-.52	-3.19**	.002	
ST Factor 1					
Not significant					.07
ST Factor 2					
Not significant					.09
ST Factor 3					
BMI (kg/m^2)	.49	.40	2.38*	.020	.17

*p<.05. **p<01. ***p<.001

DV: Dependent variable, IV: Independent variable, PANSS: Positive and Negative Syndrome Scale, HDL: High Density Lipoprotein, BMI (kg/m^2): Body Mass Index, VMPT: Verbal Memory Processing Test, WMS-R: Weschler Memory Scale-Revised, VADS B: Visual Auditory Digit Span B, ST: Stroop Test

immediate memory subtest. Lower PANSS scores, lower BMI, higher waist circumference and higher HDL were associated with better scores on VMPT total recall scores. Both WMS R IV visual memory immediate and delayed memory were predicted by lower PANSS scores and higher waist circumference. Lower PANSS scores, lower BMI and higher waist circumference predicted higher scores on VADS B total score. There was no association between ST Factor 1 and 2 scores and metabolic syndrome parametres but ST Factor 3 was significantly associated with increased BMI.

DISCUSSION

The objective of the present study was to compare the cognitive functions of patients with schizophrenia or schizoaffective disorder in the presence and absence of MetS. An additional aim was to determine the relationship between the clinical symptomatology of MetS-related components and cognitive functions. The results showed that MetS patients performed worse on the VMPT (verbal memory) subtest as compared to non-MetS patients. There were no between-group differences in the results of any of the other neurocognitive tests carried out in this study.

We enrolled 79 patients with a diagnosis of schizophrenia/ schizoaffective disorder.

Although our sample size was not high, it is moderately comparable to that of similar studies (11, 18, 43). In our study, males accounted for 57% of the study population. Although males outnumber females in the majority of schizophrenia studies in the literature the ratio of female to male patients with schizophrenia is reported to be equal in society (44). As compared to the literature (10, 12, 14), the present study was more balanced in terms of gender distribution. According to NCEP-ATP III criteria, the prevalence of MetS in the present study was 44%. The prevalence of MetS based on NCEP-ATP III criteria in patients with schizophrenia and schizoaffective disorder range between 19 and 63% (2). Other studies performed in Turkey reported a rate of 32% (45) and 37% (2). The higher prevalence of MetS in our study may be due to the male/female ratio. The prevalence of MetS in female schizophrenia patients has been reported to be higher than that of male patients, both in Turkey and elsewhere (2, 14).

In the present study, the mean PANSS and CDSS scores were 43.43±7.22 and 0.54±1.08, respectively. Other studies that used clinical assessment scales, such as the PANSS, to examine the relationship between MetS and cognitive functions reported PANSS scores between 44 and 75 (14, 18, 43, 46). A few of these studies examined depressive symptomatology based on clinical rating scales (14, 15, 17). The PANSS and the CDSS scores of our study were lower than those of the aforementioned studies. Previous studies reported that the negative effects of psychotic and depressive symptoms on cognitive functions depended on the severity of the symptoms (47, 48). The relatively low scale scores on PANSS and CDSS in this study may enhance the reliability of the results regarding cognitive functions.

In the present study, as expected, the waist circumference, systolic blood pressure, triglyceride, fasting blood glucose, HDL, and BMI values of the MetS and non-MetS groups were significantly different. There were no other between-group differences with regard to other sociodemographic (age, gender, marital status, and education level) and clinical variables (age at onset of illness, PANSS scores, and CDSS scale scores), which made it easier to compare the two groups.

The MetS patients performed worse on verbal memory (VMPT) subtests compared to the non-MetS patients. Despite this finding, there were no differences in the attention and executive function of the two groups. Two previous studies also reported no relationship between MetS and neurocognitive performance (13, 14). Similar to our results, Botis et al. (11) found that the performance of an MetS group on verbal memory was significantly worse than that of a non-MetS group. However, in their study, the MetS group also performed poorly on executive function tests. Another study also demonstrated that patients with MetS performed worse on IQ, immediate memory, delayed memory, recognition, processing speed, and vigilance compared to non-MetS group (12). In a study by Li et al. (46); attention, immediate memory, and delayed memory scores were lower in an MetS group. It was also shown that patients with MetS performed significantly worse on tests measuring

processing speed, attention/vigilance, working memory and problem solving/reasoning as compared with those of a non-MetS group (10).

Although the present study examined only three areas of cognitive functioning (i.e., attention, memory, and executive function), the results seem to be consistent with findings in the literature (11, 12, 46). As noted above, the results of the studies investigating the effect of MetS on cognitive functions suggest that memory functions are negatively affected in patients with MetS. With regard to attention and executive function, studies have reported inconsistent results (10, 11, 14, 46). The discord in the results of these studies might be due to differences in sample size, patient group selection (age, sex, and duration of illness), cognitive tests used, criteria used for the confirmation of MetS, and MetS prevalence rates.

There was a negative correlation between PANSS scores and verbal memory, visual memory, attention and short term memory. These findings show that severe symptomatology in patients with schizophrenia negatively effects neurocognitive performance on attention and memory.

Regression analysis demonstrated interesting results. First of all, higher PANSS scores predicted worse scores on VMPT immediate and total recall, WMS-R IV visual memory immediate and delayed recall and VADS-B scores. This finding is consistent with the literature on the fact that higher PANSS score are linked to lower performance on cognitive tests (47).

In the present study, higher HDL levels were associated with better performance on VMPT total recall but not on other tests. Most previous studies which conducted regression analyses found no association between HDL levels and cognitive functions (14, 17, 46). However, similar to the present study, one study found a positive effect of elevated HDL on cognitive function, with the authors showing that the HDL level was positively associated with scores for attention/vigilance (10). Both the present study and that of Lindenmayer et al. suggest that elevated HDL may be associated with positive effects on cognitive functioning, even in different cognitive domains.

In our study, higher BMI values was found negative predictor of verbal memory (VMPT total recall) and attention (VADS-B). Interestingly, increased BMI was a positive predictor of ST Factor 3 (speed factor). Previous studies of the association between BMI and cognitive functions reported different results. One study demonstrated that a BMI above 25 kg/ m^2 was associated with negative effects on delayed memory in patients with schizophrenia and healthy controls, although the results did not reach statistical significance (16). Another study found no significant associations between cognitive functions and BMI in patients with schizophrenia (15). However, in the same study, a higher BMI was significantly associated with lower scores for visual memory, attention, and IQ in patients with schizophrenia. The BMI is a simple reproducible measurement, which is commonly used to classify adults as obese. Although BMI is not a component of metabolic syndrome according to NCEP-ATP III criteria, it is considered a component of MetS in criteria adapted by the Chinese Diabetes Society for MetS (49). High BMI values are known to be strongly associated with obesity and MetS (50). In previous research, healthy individuals who were overweight or obese exhibited decreased cognitive functioning (51, 52). Based on the findings in the literature and those of the present study; providing medical or behavioral suggestions to reduce BMI values may contribute to improvements in the cognitive performance of patients with schizophrenia.

Contrary to expectations, a greater waist circumference was associated with better scores for verbal memory (VMPT immediate and total recall), visual and logical memory (WMS-R IV visual memory and logical memory subtests) and attention (VADS-B). Two previous studies found a negative association between waist circumference and cognitive functioning. In one study, abdominal obesity was associated with lower scores for reactive flexibility but not with lower scores for other measures of cognition, such as memory and executive function (53). In the other study, Lindenmayer et al. demonstrated that a greater waist circumference was associated with lower scores for attention/vigilance but not with lower scores for other measures of cognition (10). In contrast, other studies found no correlation between abdominal obesity and cognitive functions (17, 22, 46). Although the relationship between abdominal obesity and cognitive function is controversial, the unexpected finding of our study (i.e., the association of a greater waist circumference with better scores on

executive function tests) needs to be explained. Although Li et al. reported a negative effect of obesity on cognitive functions, another study demonstrated that overweight individuals performed better in tests of some cognitive domains (51, 54). The discord in the literature may be associated with differences in sample size, patient groups, cognitive tests, and different methods used to measure waist circumference.

In light of the current literature, it may be hypothesized that MetS and its components are associated with some deficits in cognitive functioning. However, it should also be considered that cognitive deficits per se may result in poor decision making and unhealthy lifestyle choices, both of which may ultimately contribute to MetS and its components (7).

The results of the present study must be interpreted within certain limitations. The relatively small sample size is the first limitation of our study, although the sample was comparable to that of other studies (11, 18). Second, the majority of the study group was composed of patients with schizophrenia (84.8%), and only a small number of patients with schizoaffective disorder were included in the study. This is a common limitation, as noted in similar studies (10, 17). Third, as we included only patients in symptomatic remission, the sample may not be representative of the entire population of patients with schizophrenia. Fourth, another limitation of the present study is this study had a cross-sectional design rather than a prospective design. Measuring cognitive levels in schizophrenic patients with premetabolic syndrome and observing changes in cognitive tests in follow-ups may lead to a better understanding of the effect of MetS and its components on cognitive functions. Fifth, the use of various MetS criteria in different studies is another limitation. Specific MetS-related components may have distinct effects on cognitive functions (7). As MetS is a categorical definition, it limits the inclusion of patients who are considered only to have premetabolic syndrome. We tried to overcome this problem by employing the most commonly used definition of MetS in the literature. Sixth, the present study applied cognitive tests to measure memory, attention, and executive function, and we did not measure all cognitive domains. The heterogeneity of cognitive tests used in different studies is a limitation. Finally, we did not collect information on the groups' dietary habits or physical exercise levels. As both these factors may contribute to the cognitive abilities of individuals (55), this may be another limitation. Differences in study designs, inclusion/exclusion criteria, sample selection (age, male/female ratio, and duration of illness), cognitive tools used for assessment, and drugs used (typical/atypical/combination) limit the comparison of the results with those of other studies. The strengths of the present study are as follows: (1) The male:female ratio was close to that reported for the incidence of schizophrenia in the community, (2) there were no significant differences in the sociodemographic and clinical variables of the MetS and non-MetS groups, and (3) the inclusion of patients who were in symptomatic remission contributed to a more reliable assessment of the cognitive test scores.

CONCLUSIONS

In conclusion, MetS patients performed worse on verbal memory compared to non-MetS patients. PANSS score was in negative correlation between verbal memory, visual memory and attention. BMI was found negative predictor of verbal memory while waist circumference and HDL were positive predictors. Visual memory, attention and short term memory were predicted positively by waist circumference. MetS remains widely underdiagnosed and undertreated among patients with schizophrenia (1). Delays in recognizing MetS and related components are associated with impaired cognitive functioning in patients. Early interventions, such as reducing the BMI or increasing HDL levels, may reduce risk factors for MetS and have positive effects on cognitive functioning in patients with schizophrenia. Prospective studies examining the cognitive functions before and during exposure to MetS and related components will provide a better understanding of the relationship between MetS and cognitive functions in patients with schizophrenia.

Ethics committee approval: This study was approved by the local clinical research ethics committee (Gaziosmanpaşa University), and written informed consent was obtained from all the participants prior to the commencement of the study. The study was conducted in accordance with the Declaration of Helsinki.

Conflict of Interest: There is no conflict of interest with any financial organization regarding the materials discussed in the manuscript.

Financial Disclosure: None declared.

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