

Contribution of Components of Metabolic Syndrome to Cognitive Performance in Middle-Aged Adults

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Abstract

Introduction: Metabolic syndrome (MetS) has been associated with impaired cognition in different cognitive domains. This study investigated the association between MetS and cognitive functioning in middle-aged Bulgarians across different definitions of MetS severity.

Material and Methods: Our cross-sectional sample included 112 participants (67 free of MetS and 45 with MetS) with a mean age of 50.04 ± 3.31 years. The following MetS variables were considered—presence of MetS, continuously measured MetS components, dichotomized MetS components, number of MetS components present, and Metabolic Syndrome Severity Score (MSSS). Participants' cognitive performance was assessed using the Consortium to Establish a Registry for Alzheimer's Disease Neuropsychological Battery (CERAD-NB). We employed multivariate regression models to investigate the associations between different measures of MetS severity and CERAD-NB total and subtest scores.

Results: Bivariate analyses showed that the CERAD-NB total score was significantly higher in women, participants with a university degree, those with normal blood pressure, normal waist circumference, and low triglyceride levels, compared with their counterparts. MetS participants had lower CERAD-NB total score (78.87 ± 6.89 vs. 84.97 ± 7.84) and specifically performed poorer on the subtest Word List Recall (7.16 ± 1.52 vs. 7.99 ± 1.52). These findings persisted after controlling for age, gender, and education. Next, generalized linear regression indicated that the CERAD-NB total score was lower in participants with MetS ($\beta = -4.86$; 95% confidence interval [CI]: $-7.60, -2.11$), those with more MetS components ($\beta = -8.31$; 95% CI: $-14.13, -2.50$ for fours vs. 0 components) and with an increase in MSSS ($\beta = -3.19$; 95% CI: $-4.67, -1.71$). Hypertension independently contributed to lower CERAD-NB total score ($\beta = -4.00$; 95% CI: $-6.81, -1.19$).

Conclusions: Across several definitions, MetS was associated with lower cognitive functioning, and MetS severity appeared to be a better predictor than most MetS components. Recognizing and reducing severity of MetS components might be helpful in supporting cognitive functioning. Further longitudinal research is needed to shed more light on the relationship between MetS and cognitive functioning across the life span.

Keywords: Alzheimer's disease; Cardiovascular disease; Mild cognitive impairment; Cerebrovascular disease/accident and stroke

Introduction

Metabolic syndrome (MetS) is a complex disorder defined as a clustering of cardiovascular risk factors: abdominal obesity, arterial hypertension, high blood levels of triglycerides, low levels of high-density lipoprotein (HDL) cholesterol, and hyperglycemia (Alberti et al., 2009). In the United States alone, it affects 35% of all adults and 50% of those aged 60 years or more (Aguilar, Bhuket, Torres, Liu, & Wong, 2015). On a global scale, one quarter of the adult population has MetS, which accounts for a substantial economic burden (Boudreau et al., 2009; Marangos, Okamoto, & Caro, 2010). In the modern society, the components of MetS are not only highly prevalent, but also contribute to the development of other diseases (Taylor & Mac Queen, 2007). MetS is widely recognized as a major risk factor for adverse health outcomes such as Type 2 diabetes, cardiovascular disease, and even cancer (O'Neill & O'Driscoll, 2015).

Recent years have seen growing recognition that MetS is also associated with impaired cognitive functioning in different cognitive domains such as memory, attention, and information processing. These findings remain inconsistent in terms of the extent of cognitive decline and the domains affected, as discussed by Alcorn and colleagues (2019). MetS components have been identified as important modifiable risk factors for mild cognitive impairment (Liu et al., 2015), vascular dementia (Frisardi et al., 2010), and Alzheimer's disease (Vanhanen et al., 2006). Given the aging of the population and raising numbers of adults with cognitive impairment/dementia, especially in those with an underlying metabolic disorder, investigation of this association is highly warranted (Assuncao, Sudo, Drummond, de Felice, & Mattos, 2018).

MetS components are considered risk factors in and of themselves and each component has been found to adversely influence cognitive function—impaired glucose metabolism (McCrimmon, Ryan, & Frier, 2012), obesity (Dahl et al., 2013; Gunstad et al., 2007), high blood pressure (Novak & Hajjar, 2010), and dyslipidemia (Koch & Jensen, 2016). Therefore, it is challenging to disentangle their independent contributions and it is likely that all components have a synergistic effect on cognition. Current MetS diagnostic criteria are binomial (present vs. nonpresent), dichotomized at a specific cutoff value. This makes it difficult to assess the severity of the underlying process. In an attempt to overcome this weakness, continuous MetS scores have been developed (Kahn, Buse, Ferrannini, & Stern, 2005). One such composite measure is the Metabolic Syndrome Severity Score (MSSS) developed by Gurka, Lilly, Oliver, & DeBoer (2014). Its potential to predict MetS progression and development of cardiovascular complications or Type 2 diabetes was later confirmed in a number of studies (Guo et al., 2018; Gurka, Filipp Stephanie, Pearson Thomas, & DeBoer Mark, 2018). However, the only measure of MetS severity used so far in earlier cognitive functioning research is the number of MetS components (Alcorn et al., 2019; Vishnu, Gurka, & DeBoer, 2015).

Given the infancy of this field of inquiry and disparate results of earlier research, the present study aimed to investigate the association between MetS and cognitive functioning in middle-aged Bulgarians across different definitions of MetS severity, compared against an omnibus definition of MetS. That is, we hypothesized that a composite measure like MSSS would predict cognitive performance above and beyond individual MetS components considered in isolation.

Material and Methods

Study Design and Sampling

This cross-sectional study was conducted between 2014 and 2016 in the District of Plovdiv, Bulgaria. Participants were recruited at the Clinics of Endocrinology and Neurology, “St George” University Hospital, Plovdiv. We included literate volunteers aged between 45 and 55 years. Exclusion criteria were: chronic diseases other than hypertension and diabetes, psychiatric disorders, dementia, drug addiction, and heavy or problematic alcohol use. The initial selection was done mostly on exclusion criteria—if not present, then the volunteers were deemed eligible. Their MetS status was assessed after they were included. Thus, the analysis sample consists of 67 subjects free of MetS and 45 with MetS.

The participants were asked to complete a questionnaire about basic demographic, lifestyle, and health-related factors. They also underwent a neuropsychological evaluation and physical examination. The study protocol adhered to the Declaration of Helsinki and was approved by the Ethics Committee at the institution of the principal investigator. Informed consent was obtained from all participants prior to their participation in the study.

MetS Assessment

We looked at associations between MetS and its components and cognitive functioning. The following MetS variables were considered: presence of MetS, continuously measured MetS components, dichotomized MetS components, number of MetS components present, and MSSS. MetS was defined after the International Diabetes Federation diagnostic criteria (Alberti et al., 2009), that is, as meeting three or more of the following: systolic ≥ 130 mmHg and/or diastolic blood pressure ≥ 85 mmHg, waist

circumference ≥ 94 cm for men and ≥ 80 cm for women, fasting plasma glucose ≥ 5.6 mmol/L, triglyceride levels ≥ 1.7 mmol/L, HDL cholesterol levels < 1 mmol/L for men and < 1.3 mmol/L for women. Biochemical tests were performed on morning venous blood samples obtained between 8.00 and 10.00 a.m. after an overnight fast. Systolic and diastolic blood pressure was measured using a standard sphygmomanometer in a sitting position after a 5-min rest (Muntner et al., 2019). Waist circumference was measured in centimeters at the midpoint between the last palpable rib and the upper margin of the iliac crest at minimal respiration to the closest 1 cm (World Health Organization, 2011).

MSSS was calculated using the equations proposed by Gurka and colleagues (2014). A previous study supported its validity and reliability in middle-aged Bulgarians (Dimitrov et al., 2016).

- MSSS for non-Hispanic White men = $-5.4559 + .0125 \times \text{Waist Circumference} - .0251 \times \text{HDL} + .0047 \times \text{SBP} + .8244 \times \ln(\text{Triglycerides}) + .0106 \times \text{Glucose}$
- MSSS for non-Hispanic White women = $-7.2591 + 0.0254 \times \text{Waist Circumference} - .0120 \times \text{HDL} + .0075 \times \text{SBP} + .5800 \times \ln(\text{Triglycerides}) + .0203 \times \text{Glucose}$

Consortium to Establish a Registry for Alzheimer's Disease Neuropsychological Battery

Participants' cognitive performance was assessed using the Bulgarian version of the Consortium to Establish a Registry for Alzheimer's Disease Neuropsychological Battery (CERAD-NB), developed to detect the primary cognitive manifestations of Alzheimer's disease (Moms et al., 1989). CERAD-NB is a sensitive, valid, and reliable measure of cognitive functioning (Welsh et al., 1994). Briefly, CERAD-NB comprises several subtests (e.g., Verbal Fluency, Boston Naming Test [BNT], Constructional Praxis, Word list recall, Word list recognition) tapping into different aspects of cognitive functioning. Each subtest was scored and then total score was calculated according to the method proposed by Chandler and colleagues (2005). This composite score has shown good sensitivity in distinguishing mild cognitive impairment in the European population (Seo et al., 2010). The neuropsychological evaluation was conducted at a hospital-based neurology department. Confirmatory factor analysis revealed that, in our sample, the seven subtests of the Bulgarian version of CERAD-NB loaded onto one latent factor: $\chi^2_{(13)} = 16.54$, $p = .221$; comparative fit index = .97; root mean square error of approximation = .05. However, the internal consistency of the scale was not outstanding (McDonald's omega = .57).

Other Covariates

A questionnaire was administered to collect data on participants' gender, age, education (secondary vs. university degree), smoking status (never vs. former/current smoker), and alcohol consumption (no vs. yes). These factors were considered plausible confounders based on literature precedent (Alcorn et al., 2019; Oh, Kim, Kang, Park, & Song, 2011).

Statistical Analyses

First, the dataset was inspected for missing values. Given the reasonable low percentage of missing data in some covariates ($< 10\%$) and that they were missing at random, they were replaced using the expectation maximization algorithm to make better use of the relatively modest sample size (Schlomer, Bauman, & Card, 2010). Next, we evaluated the distribution of the main outcome variables. According to D'Agostino-Pearson's K^2 normality test, the CERAD-NB total score was normally distributed. Some subtest scores deviated from normality but within reasonable limits; therefore, they were analyzed by parametric methods (Schmider, Ziegler, Danay, Beyer, & Bühner, 2010). Univariate associations between the variables were examined with Pearson's chi-squared tests, independent samples t -tests, and Spearman correlations. We used one-way ANOVA to calculate mean scores for the subscales of CERAD-NB adjusted for age, gender, and education.

In the multivariate analyses, we regressed the CERAD-NB total score on the following MetS predictors: Presence of MetS (reference group: absence) (Model 1); continuously measured MetS components, as a set (Model 2); dichotomized MetS components, as a set (Model 3); number of MetS components present (Model 4); and MSSS (Model 5). A separate generalized linear regression model was fitted to test each of the five models. In line with precedent, these models were adjusted for age, gender (except Model 5), education, smoking status, and alcohol consumption; the MetS components in Models 2 and 3 were also mutually adjusted for each other (Alcorn et al., 2019). We did not detect multicollinearity according to tolerance ($> .2$) and Variance Inflation Factor (< 5) values. As a sensitivity analysis, the relationship between MSSS and the CERAD-NB total score was tested for deviation from linearity using restricted cubic splines with four knots (Orsini, 2017).

Results were considered statistically significant at the $p < .05$ level (two tailed). Statistical analyses were conducted with the Statistical Package for the Social Sciences (SPSS) v. 17 (SPSS Inc., Chicago, IL).

Table 1. Participant characteristics in relation to MetS status ($N = 112$)

Characteristics	Without MetS ($n = 67$)	With MetS ($n = 45$)	p
Age (mean, SD)	49.87 (3.36)	50.29 (3.26)	.507
Men ($n, \%$)	18 (26.9)	24 (53.3)	.005
University education ($n, \%$)	52 (77.6)	30 (66.7)	.200
Smokers ($n, \%$)	40 (59.7)	26 (57.8)	.839
Alcohol drinkers ($n, \%$)	44 (65.7)	31 (68.9)	.723
Hypertension ($n, \%$)	22 (32.8)	31 (68.9)	<.001
High waist circumference ($n, \%$)	38 (56.7)	42 (93.3)	<.001
High glucose ($n, \%$)	15 (22.4)	25 (55.6)	<.001
Low HDL cholesterol ($n, \%$)	10 (14.9)	30 (66.7)	<.001
High triglycerides ($n, \%$)	5 (7.5)	32 (71.1)	<.001
Systolic blood pressure (mean mmHg, SD)	116.12 (12.52)	125.56 (10.67)	<.001
Diastolic blood pressure (mean mmHg, SD)	75.13 (8.14)	80.22 (8.12)	.002
Waist circumference (mean cm, SD)	89.06 (12.99)	102.06 (14.52)	<.001
Glucose (mean mmol/L, SD)	5.09 (.65)	6.07 (1.43)	<.001
HDL cholesterol (mean mmol/L, SD)	1.54 (.35)	1.12 (0.28)	<.001
Triglycerides (mean mmol/L, SD)	1.19 (.89)	2.36 (1.24)	<.001
MSSS (mean, SD)	-0.42 (.59)	0.91 (.68)	<.001
CERAD-NB (mean, SD)			
Total score	84.97 (7.84)	78.87 (6.89)	<.001
Verbal Fluency	19.00 (4.78)	18.60 (4.87)	.667
Modified BNT	14.78 (.49)	14.58 (.69)	.077
Word List Learning	21.06 (3.42)	19.96 (3.26)	.090
Constructional Praxis	9.66 (1.47)	9.51 (2.19)	.675
Word List Recall	7.99 (1.52)	7.16 (1.52)	.006
Word List Recognition Discriminability	9.82 (1.33)	9.60 (0.72)	.310
Constructional Praxis Recall	9.05 (2.09)	9.31 (1.88)	.509

Notes: Comparisons are made using independent samples t -tests and Pearson's chi-squared tests. CERAD-NB = Consortium to Establish a Registry for Alzheimer's Disease Neuropsychological Battery; HDL = high-density lipoprotein; MetS = metabolic syndrome; MSSS = Metabolic Syndrome Severity Score; BNT = Boston Naming Test.

Results

Overall, 112 participants were included in the study, with 40.2% meeting the criteria for MetS. Participants' mean age was 50.04 ± 3.31 years and the majority were women ($n = 70, 62.5\%$). Table 1 shows the participant characteristics depending on their MetS status. Those with MetS were more likely to be men and have higher blood pressure, waist circumference, glucose and triglyceride levels, and lower HDL cholesterol levels. MetS was associated with lower CERAD-NB total score, with the Word List Recall score, specifically, being lower in participants with MetS. The CERAD-NB total score was significantly higher in women (84.04 ± 8.28 vs. 79.98 ± 6.95 ; $p = .009$), participants with a university degree (83.94 ± 7.08 vs. 78.63 ± 9.22 ; $p = .002$), those with normal blood pressure (84.78 ± 7.63 vs. 80.00 ± 7.76 ; $p = .001$), waist circumference below the cutoff values (85.22 ± 7.31 vs. 81.44 ± 8.09 ; $p = .024$), and low triglyceride levels (83.81 ± 8.14 vs. 79.89 ± 7.18 ; $p = .014$), compared with their counterparts.

Controlling for participants' age, gender, and education, the mean CERAD-NB scores for cases and controls were as follows: Total score (79.60 ± 1.09 vs. $84.48 \pm .89$), Verbal Fluency ($19.00 \pm .72$ vs. $18.73 \pm .59$), Modified BNT ($14.56 \pm .09$ vs. $17.79 \pm .07$), Word List Learning ($20.32 \pm .50$ vs. $20.82 \pm .41$), Constructional Praxis ($9.51 \pm .27$ vs. $9.66 \pm .22$), Word List Recall ($7.28 \pm .23$ vs. $7.90 \pm .18$), Word List Recognition Discriminability ($9.63 \pm .17$ vs. $9.80 \pm .14$), and Constructional Praxis Recall ($9.42 \pm .32$ vs. $8.98 \pm .25$). In this case, we again observed a significant difference only for the subscale Word List Recall ($p = 0.039$) and a borderline significant difference for the Modified BNT ($p = 0.054$).

Table 2 shows Spearman correlations between the main continuous variables in the study. The CERAD-NB total score was associated with lower systolic and diastolic blood pressure, waist circumference, triglyceride levels, number of MetS components, and MSSS, and with higher HDL cholesterol.

The multivariate regression models explained 17%–20% of the variance in the CERAD-NB total score (Table 3). More specifically, the presence of MetS was associated with lower CERAD-NB total score (Model 1), but when all MetS components were adjusted for each other, only hypertension was still associated with it according to standard criteria for statistical significance. The CERAD-NB total score was lower in participants with more MetS components (Model 3) and higher MSSS (Model 4).

Table 2. Spearman correlations between cognitive functioning (CERAD-NB) and MetS components

Variables	1.	2.	3.	4.	5.	6.	7.	8.	9.
1. CERAD-NB total	1	-.28*	-.21*	-.42*	-.17	.23*	-.32*	-.35*	-.43*
2. Systolic blood pressure		1	.66*	.45*	.09	-.24*	.39*	.44*	.52*
3. Diastolic blood pressure			1	.36*	.09	-.26*	.28*	.32*	.39*
4. Waist circumference				1	.16	-.38*	.42*	.59*	.67*
5. Glucose					1	-.03	.22*	.42*	.46*
6. HDL cholesterol						1	-.62*	-.60*	-.66*
7. Triglycerides							1	.72*	.81*
8. MetS components number								1	.84*
9. MSSS									1

Notes: CERAD-NB = Consortium to Establish a Registry for Alzheimer's Disease Neuropsychological Battery; HDL = high-density lipoprotein; MetS = metabolic syndrome; MSSS = Metabolic Syndrome Severity Score.

* $p < .05$

Table 3. Associations between MetS and cognitive functioning (CERAD-NB total score)

MetS predictors	β (95% CI)	p
Model 1: Presence of MetS	-4.86 (-7.60, -2.11)	.001
Model 2: Continuous MetS components		
Systolic blood pressure	-.15 (-0.31, .11)	.068
Diastolic blood pressure	.08 (-0.14, .31)	.594
Waist circumference	-1.00 (-0.22, .02)	.115
Glucose	-1.01 (-2.20, .17)	.095
HDL cholesterol	-.43 (-2.59, 2.73)	.788
Triglycerides	-.90 (-3.28, 5.07)	.674
Model 3: Dichotomized MetS components		
Hypertension	-4.00 (-6.81, -1.19)	.005
High waist circumference	-.44 (-3.69, 2.81)	.790
High glucose	-1.49 (-4.37, 1.39)	.312
Low HDL cholesterol	.26 (-2.81, 3.32)	.869
High triglycerides	-1.78 (-5.18, 1.62)	.304
Model 4: Number of MetS components		
0	Reference group	
1	-.86 (-5.24, 3.52)	.701
2	-.68 (-5.62, 4.25)	.786
3	-4.74 (-9.50, .02)	.051
4	-8.31 (-14.13, -2.50)	.005
5	-2.55 (-9.60, 4.50)	.479
Model 5: MSSS	-3.19 (-4.67, -1.71)	<.001

A separate linear regression model is fitted for each model. Coefficients are unstandardized linear regression coefficients (β) with their 95% CIs. Models are adjusted for age, gender (except Model 5), education, smoking status, and alcohol consumption; the MetS components in Models 2 and 3 are also mutually adjusted for each other. CERAD-NB = Consortium to Establish a Registry for Alzheimer's Disease Neuropsychological Battery, HDL = high-density lipoprotein; MetS = metabolic syndrome; MSSS = Metabolic Syndrome Severity Score.

Finally, testing of the nonlinear model did not indicate that the association between MSSS and CERAD-NB total score deviated from linearity ($p = .209$) (Fig. 1).

Discussion

To our knowledge, this was the first study in Bulgaria to investigate the association between MetS and cognitive functioning. Although MetS was associated with lower CERAD-NB total scores, when we looked into the contribution of specific MetS components, we found that only hypertension was statistically predictive of worse cognitive functioning. MetS severity, expressed by the calculated MSSS, emerged as a better predictor of lower CERAD-NB than most MetS components. Noteworthy, statistical significance does not necessarily correspond to clinical significance. The associations we found were weak; therefore, readers should cautiously consider their material importance.

Results of this study corroborate earlier findings with the same battery (Oh et al., 2011; Song et al., 2015). In our study, only performance on the subtest Word List Recall showed differences between participants with and without MetS. Previously, as

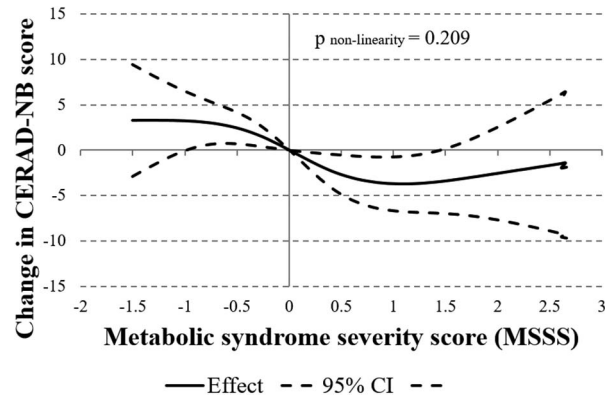


Fig. 1. Restricted cubic spline model of the association between MSSS and cognitive functioning (CERAD-NB). Coefficients are unstandardized linear regression coefficients with their 95% CIs and represent the change in CERAD-NB per 1 unit increase in MSSS. Models are adjusted for age, gender, education, smoking status, and alcohol consumption. The effect of MSSS on CERAD-NB is statistically significant when the bounds of the 95% CI do not cross the reference line (zero) on the y-axis. MSSS value of “0” is the reference point. CERAD-NB = Consortium to Establish a Registry for Alzheimer’s Disease Neuropsychological Battery; CI = confidence interval; MSSS = Metabolic Syndrome Severity Score.

reported by [Oh and colleagues \(2011\)](#), MetS participants scored lower on the Korean version of the Consortium to Establish a Registry for Alzheimer’s Disease—CERAD-K scales Verbal Fluency, Construction Recall, Word List Learning, and Trail Making B. In that study, participants’ age was more advanced compared with our sample (69.3 ± 4.4 vs. 50.20 ± 3.26) and this could explain the observed negative change in more cognitive domains. In support of this assumption are the results from a study on subjects similar in age to those studied by us ([Song et al., 2015](#)). The authors found lower total score in MetS participants, without significantly lower results in any particular subtest ([Song et al., 2015](#)).

In a study on MetS and cognition, [Dik and colleagues \(2007\)](#) reported that hyperglycemia was the most influential factor behind the association of MetS and impaired cognitive performance. They hypothesized two possible mechanisms for this effect: a direct pathway, which has not been established in other components of the MetS and a pathway related to vascular components and cerebrovascular disease. In that study, abdominal obesity, high triglycerides, and high blood pressure were not related to any of the tested cognitive variables. Another important issue to consider is the mechanism by which the negative effect on cognition is carried into effect. This mechanism is not fully understood. Neuroanatomical and neuroendocrine effects causing bodily dysregulation are discussed together with vascular impairments and inflammatory processes, among others ([Taylor & Mac Queen, 2007](#); [Yaffe, 2007](#)). A better understanding of the link between MetS and cognitive functioning at different ages may also help to elucidate the mechanisms of effect of the MetS as a whole and its individual elements on the cognitive system. Also of interest is whether MetS predicts cognitive impairment and how age modifies this process ([Komulainen et al., 2007](#)). Addressing these potential precursors of future cognitive impairment may help in dementia prevention efforts.

[Bae and colleagues \(2017\)](#) found gender differences in individual MetS components, which were differentially associated with risk of nonamnesic mild cognitive impairment. MetS has been associated with impaired reading, working memory, and attention among adolescents ([Rubens et al., 2016](#)). Adverse relationship between Digit symbol test scores and increasing numbers of MetS constituents has also been reported ([Tsai et al., 2016](#)). However, other studies did not observe an association between presence of MetS and cognitive performance in the older population ([Chen et al., 2016](#)).

Our results indicated low-to-moderate correlation between the CERAD-NB total score and all MetS components except for HDL cholesterol, where the correlation was positive. Glucose level was weakly associated with the CERAD-NB total score. In support of our hypothesis, we found a moderate negative correlation between the number of MetS components and the CERAD-NB total score ([Table 2](#)).

The expected decrease of cognition scores with each additional MetS component was also confirmed ([Hassenstab, Sweat, Bruehl, & Convit, 2010](#)). On the other hand, [Falkowski, Atchison, DeButte-Smith, Weiner, & O’Byrant \(2014\)](#) did not find additive effects of the number of MetS components on cognition; participants with one or more components scored lower on the executive function test, but the mean score was not affected.

Here, results from cognitive testing were negatively related to severity of MetS (measured with the MSSS index). Our restricted cubic spline analysis showed that the effect of MSSS was statistically significant only when MSSS was moderate. If this finding was not a statistical artifact or due to uncontrolled for residual confounding, we can offer several explanations. For one, it is possible the contrasts in MSSS were not as pronounced that among individuals with MetS, preventing us from observing an effect. On the other hand, MSSS was initially developed as a composite of cardiovascular risk factors, with a view

to predicting future negative cardiovascular outcomes (Gurka et al., 2018). Being a specific cardiovascular risk tool, it could not achieve the same accuracy of predicting cognitive status. Also, other factors that are involved in cognitive functioning might not be taken into account by the MSSS.

We corroborated previous findings that high blood pressure was an important predictor of cognitive functioning (Del Brutto, Mera, & Zambrano, 2016; Dik et al., 2007; Hassenstab et al., 2010; Tournoy et al., 2010; Vieira et al., 2011; Yaffe, 2004). One explanation of this could be that mutually adjusting the MetS components obscures the effect of less influential components.

Nevertheless, addressing MetS risk factors at earlier stages is likely to be more beneficial. This finding is also supported by data for a higher incidence of MetS in patients with dementia in Alzheimer's disease, despite the divergent results for the individual components of MetS (García-Lara, Aguilar-Navarro, Gutiérrez-Robledo, & Avila-Funes, 2010). Timely identification of the risk associated with the MetS may open more opportunities for effective management of dementia. In any case, our cross-sectional findings offer no definitive explanation; so, this issue merits further investigation.

Limitations

We acknowledge several limitations with the present study. First, the cross-sectional design precludes us from drawing causal inferences about the observed associations. In addition, our findings cannot be extended to the general population due to the narrowly defined age group considered. Second, in light of growing concerns about the validity of conclusions based on dichotomized statistical significance interpretation (Amrhein, Greenland, & McShane, 2019), we acknowledge that some of the “nonsignificant” associations observed here could have been underestimated owing to the modest sample size. Still, the latter is comparable to that in several earlier studies (cf. Alcorn et al., 2019). Relatedly, individuals with serious complications of hypertension and diabetes were not included in the study. That could have resulted in more complicated or severe cases of MetS being underrepresented in the sample, thereby potentially attenuating the observed effects on cognitive functioning. On the other side, this gave us the opportunity to observe the effects of MetS in its initial, uncomplicated stage. Third, we only employed CERAD-NB for the present study, which does not capture executive functions for which pertinent findings have been reported (Alcorn et al., 2019). MSSS also has some inherent limitations—it does not account for all potential risk factors for cognitive impairment such as diastolic blood pressure (Novak & Hajjar, 2010), as it was originally developed to predict cardiovascular risk (Wiley & Carrington, 2016). Fourth, we only had crude information on dichotomized lifestyle covariates (alcohol consumption, smoking), which would be better expressed as continuous or more nuanced categories. Another limitation was the likely confounding by physical activity and diet on cognitive functioning, but we did not gather such detailed data. This has likely resulted in underestimating confounding by those factors. Another limitation was the likely correlation between MetS and other adverse behavioral or lifestyle factors (e.g., unhealthy nutrition, low physical activity). We could not account for such residual confounding. Finally, we decided not control for the increase in familywise error across the reported statistical analyses owing to concerns about raising type II error rate (Rothman, 1990; Perneger, 1998; Cabin & Mitchell, 2000).

Although we focused on a modest selective sample of patients, our study fills a gap in the literature from Eastern Europe, a region characterized by high prevalence of MetS and unsatisfactory clinical management of cardiometabolic risk factors (Ostrihoňová et al., 2017).

Conclusions

Across several definitions, MetS was associated with lower cognitive functioning, with MetS severity emerging as a better predictor than most MetS components. Recognizing and reducing severity of MetS components might be helpful in supporting cognitive functioning. Further longitudinal research is needed to shed more light on the relationship between MetS and cognitive functioning across the life span.

Conflict of Interest

None declared.

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