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Specific metabolic syndrome components predict cognition and social functioning in people with type 2 diabetes mellitus and severe mental disorders

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Abstract

Objective: Obesity and metabolic diseases such as metabolic syndrome (MetS) are more prevalent in people with type 2 diabetes mellitus (T2DM), major depressive disorder (MDD), bipolar disorder (BD), and schizophrenia (SZ). MetS components might be associated with neurocognitive and functional impairments in these individuals. The predictive and discriminatory validity of MetS and its components regarding those outcomes were assessed from prospective and transdiagnostic perspectives.

Methods: Metabolic syndrome components and neurocognitive and social functioning were assessed in 165 subjects, including 30 with SZ, 42 with BD, 35 with MDD, 30 with T2DM, and 28 healthy controls (HCs). A posteriori, individuals were classified into two groups. The MetS group consisted of those who met at least three of the following criteria: abdominal obesity (AO), elevated triglycerides

(TG), reduced high-density lipoprotein cholesterol (HDL), elevated blood pressure (BP), and elevated fasting glucose (FPG); the remaining participants comprised the No-MetS group. Mixed one-way analysis of covariance and linear and binary logistic regression analyses were performed.

Results: Cognitive impairment was significantly greater in the MetS group (n = 82) than in the No-MetS group (n = 83), with small effect sizes ($p < 0.05$; $\eta^2 p = 0.02 – 0.03$). In both groups, the most robust associations between MetS components and neurocognitive and social functioning were observed with TG and FPG ($p < 0.05$). There was also evidence for a significant relationship between cognition and BP in the MetS group ($p < 0.05$). The combination of TG, FPG, elevated systolic BP and HDL best classified individuals with greater cognitive impairment ($p < 0.001$), and TG was the most accurate ($p < 0.0001$).

Conclusions: Specific MetS components are significantly associated with cognitive impairment across somatic and psychiatric disorders. Our findings provide further evidence on the summative effect of MetS components to predict cognition and social functioning and allow the identification of individuals with worse outcomes. Transdiagnostic, lifestyle-based therapeutic interventions targeted at that group hold the potential to improve health outcomes.

KEYWORDS

cognition, metabolic syndrome, severe mental disorder, social functioning, type 2 diabetes mellitus

1 | INTRODUCTION

Obesity and metabolic problems have reached pandemic proportions in recent decades, representing an increased socioeconomic burden that in turn is associated with increased morbimortality.[1] For instance, people with type 2 diabetes mellitus (T2DM) and severe mental illness (SMI), such as major depressive disorder (MDD), bipolar disorder (BD), and schizophrenia (SZ), have a higher prevalence of metabolic syndrome (MetS) than the general population.[2,3] MetS is a cluster of certain medical conditions, such as abdominal obesity (AO), elevated triglycerides (TG), low- and high-density lipoprotein cholesterol (HDL), elevated fasting plasma glucose (FPG), and elevated blood pressure (BP).[4,5] Unhealthy lifestyle behaviors, including smoking, poor eating habits and diet quality and reduced physical activity, are major drivers of the increase in MetS among individuals with SMI and T2DM.[6,7] All these factors are strongly associated with poor quality of life, poor treatment adherence, and increased mortality in these populations.[8] Moreover, treatment with psychopharmacological medications, especially certain mood stabilizers and antipsychotics, may cause weight gain and further increase the risk of metabolic disorders.[9,10]

Significant outcomes

- Metabolic syndrome is linked with neurocognitive decline across somatic and psychiatric disorders over time.
- Specific metabolic syndrome components predict cognition and social functioning.
- Abdominal obesity did not play any significant role for neurocognitive performance and social functioning.

Limitations

- High experimental mortality at one-year follow-up.
- Relatively small sample size.
- Not information about dietary habits.

In recent years, the importance of a multimorbidity view that brings together the effects of mental and physical health has been increasingly recognized.[11,12] Indeed, recent reviews highlight that abnormal metabolic pathways promote the onset of several SMI, such us SZ, and it is related to increased early morbimortality.[13,14] MetS

diagnosis allows the identification of individuals at a higher risk of developing chronic conditions. MetS components, such as FPG levels and especially the combination of elevated TG and reduced HDL, predict the risk of developing T2DM.[15] Likewise, a recent study found that individuals with SMI who meet the criteria for MetS suffer from multiple comorbidities in comparison with healthy controls (HCs).[16] Moreover, individuals with SMI and MetS have a more severe condition, a worse response to pharmacological treatments and a worse prognosis than individuals without MetS.[17,18] On the other hand, recent studies have reported that MetS is significantly associated with cognitive impairment in individuals with SMI, which could in turn contribute to a decline in social functioning.[19,20] Other studies have suggested that BP, HDL, and TG are important predictors of cognition in individuals with SMI, whereas AO is one of the predictors of cognitive impairment and quality of life.[21] These relationships also apply to several nonpsychiatric conditions, including cardiometabolic illnesses.[22] Indeed, individuals with T2DM who meet the criteria for MetS have worse cognitive performance and poorer quality of life than individuals without MetS.[23,24] Likewise, metformin treatment has been associated with decreased cardiovascular risk and improved neurocognitive outcomes in patients with T2DM.[25] In summary, increasing evidence supports the notion that MetS and its components are relevant risk factors or predictors of neurocognitive and social dysfunction across common noncommunicable diseases. Therefore, it is likely that the former represents a transdiagnostic component with implications for relevant outcomes.

To our knowledge, no study has evaluated the contribution of MetS and its components to both neurocognitive and social functioning in people with SMI and T2DM. Moreover, the great heterogeneity of possible combinations of MetS components makes it difficult to estimate the risk of developing impaired cognitive or social functioning. No previous studies have been conducted to determine whether some combinations of MetS components predict cognitive performance and social functioning better than others in individuals with or without MetS diagnosis across T2DM and SMI. While MetS components might aid in the early detection of neurocognitive and functional impairment in at-risk populations, evidence supporting their potential application in clinical practice is scarce. To our knowledge, the discriminatory ability of MetS components for classifying individuals with greater cognitive impairment has not been tested. Therefore, research using samples of individuals with T2DM, MDD, BD, and SZ may help to determine the risk of neurocognitive and social dysfunction associated with MetS more effectively in these populations.

1.1 | Aims of the study

The aims of this study were threefold: (a) to explore whether baseline MetS components are significant predictors of cognitive performance and social functioning at the one-year follow-up, (b) to examine the discriminatory ability of specific MetS components for classifying individuals with greater cognitive impairment, and (c) to analyze the differences between specific MetS components, cognitive performance, and social functioning in people with or without MetS diagnosis across T2DM and SMI.

2 | MATERIALS AND METHODS

2.1 | Study design and ethical considerations

This article is part of a project aimed at identifying and validating peripheral biomarkers for neurocognitive deficits in MDD, BD, SZ, and T2DM. This prospective and comparative cohort project was conducted between April 2015 and January 2018, and it investigated the association and evolution of certain peripheral blood biomarkers and neurocognitive impairments in a unique longitudinal cohort of individuals with somatic and psychiatric disorders. Demographic and clinical data, neurocognitive and social functioning data, and biomarkers of peripheral blood were collected at baseline (T1) and after one year (T2). Individuals with SMI were recruited from mental health units (MHUs) in several towns in the province of Valencia, Spain (Foios, Catarroja, Paterna, and Sagunto); the psychiatry outpatient clinic and endocrinology department of the University Hospital Dr. Peset; and the Miguel Servet MHU in Valencia City. HCs were residents of the same areas as the individuals with SMI. Participants were demographically matched. All participants provided informed consent after the study procedures were explained. The ethical committees or an institutional review board at each participating center approved the study protocol, and the study was conducted in accordance with the ethical principles of the Declaration of Helsinki. For this article, only those variables related to this study aims were included in the analyses.

2.2 | Participants

SZ, BD, and MDD were diagnosed based on the criteria of the Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM 5).[26] T2DM was diagnosed based on the Standards of Care criteria of the American Diabetes Association.[27] Participants with MDD and BD had to meet

the remission criteria[28] of an acute affective episode, and individuals with SZ had to be clinically stable.[29] Individuals with T2DM had to be free of severe diabetic neuropathy and kidney disease (serum creatinine <1.5 mg/dl) and, at baseline and at 1-year follow-up, FPG levels were previously checked in this group to reduce possible biases due to overlapping of the glycemic pathway between HC and those with T2DM. For HC recruitment, the absence of physical illness, pharmacological treatments, and family history of SMI in first-degree relatives was required. An ability to understand study procedures and willingness to give written consent were required for participation. General exclusion criteria for all groups included current hospitalization, documented cognitive impairment not secondary to psychiatric disorder (intellectual disability or major neurocognitive disorder, i.e., dementia), disability or inability that prevented understanding of the protocol, current substance abuse disorder (except for nicotine), pregnancy, intake of steroids, corticosteroids, antioxidants, antibiotics, and immunologic therapies, fever over 38°C, and history of vaccination within 4 weeks of the evaluation. The same inclusion and exclusion criteria were used at T1 and T2.

MetS diagnosis was assessed at both times following the revised criteria of the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III).[4,30] This diagnosis requires the presence of at least three of the following five criteria: AO, elevated TG, reduced HDL, elevated BP, and elevated FPG. NCEP ATP III cut-off values to define these alterations are as follows: (i) waist circumference (WC) >102 cm for men and >88 cm for women will hereafter be used as a measure of AO, (ii) TG ≥150 mg/dl or specific treatment for this lipid abnormality, (iii) HDL levels <40 mg/dl for men and <50 mg/dl for women or specific treatment for this lipid abnormality, (iv) systolic BP (SBP) ≥130 mmHg and diastolic BP (DBP) ≥85 mmHg or treatment of previously diagnosed hypertension, and (v) fasting FPG levels ≥100 mg/dl or previously diagnosed T2DM. Following this definition, the participants with alterations in at least three criteria were defined as having MetS, and the remaining participants were classified as not having MetS.

The following MetS components were collected as follows: weight (kg), height (m), WC (cm), TG, HDL, SBP/DBP (mmHg), and FPG. Body weight, height, and WC were measured by calibrated scales. WC was measured in the standing position at the end of normal expiration and at the midway between the inferior costal margin and the superior border of the iliac crest. BP was measured on the right arm using an automatic sphygmomanometer with participants in the sitting position after resting for 5 minutes. Average SBP and DBP values of at least two repeated measurements were calculated. Under aseptic conditions, fasting venous blood samples were collected between 8 and 9 am to measure TG, HDL and FPG levels. Individuals with diseases followed the prescribed pharmacological treatment throughout the study.

2.3 | Assessments

The assessments were conducted by the same experienced psychologists and psychiatrists of the research group. Sociodemographic data, including sex, age, years of education, occupational status and laterality (defined as manual, ocular and crural dominance), were collected.

Clinical evaluations were conducted using the following scales: (i) Kaplan–Feinstein Scale (KFS),[31] (ii) Charlson Comorbidity Index (CCI),[32] (iii) 17-item Hamilton Rating Scale for Depression (HRSD),[33] (iv) Young Mania Rating Scale (YMRS),[34] (v) Positive and Negative Syndrome Scale (PANSS),[35] and (vi) Clinical Global Impression (CGI) scale.[36] For smokers, current tobacco consumption, expressed as the number of cigarettes per day (CPD), and breath carboxyhemoglobin (COHb) level, a validated measure of smoke exposure, were collected.[37] The total number of prescribed psychopharmacological medications and other medications were also registered.

Cognitive performance was evaluated using a comprehensive battery of neuropsychological tests and subtests previously used by our group.[38-41] Seven cognitive domains were assessed: (i) *verbal learning and memory*: Complutense Verbal Learning Test (TAVEC) total immediate recall, short-term free recall and long-term free recall variables[42]; (ii) *cognitive flexibility*: Stroop Color and Word test (SCWT) color/word subtest[43] and Wisconsin Card Sorting Test (WCST) categories completed and perseverative errors[44]; (iii) *verbal fluency*: FAS and animal naming test for phonemic and semantic fluency, respectively[45]; (iv) *working memory*: Trail Making Test (TMT) Part B[45] and Wechsler Adult Intelligence Scale III edition (WAIS-III) digit span backwards[46]; (v) *short-term memory*: TAVEC immediate recall of the first learning trial and immediate recall of the interference list[42] and WAIS-III digit span forward[46]; (vi) *visual memory*: Rey-Osterrieth Complex Figure Test (ROCFT) figure two minutes after the copy (fRey2) and 20 minutes after the copy (fRey20)[47]; and (vii) *processing speed*: finger tapping test (FTT) left unimanual, right unimanual, left bimanual, right bimanual and average four scores,[45,48] WAIS-III digit symbol coding subtest,[46] SCWT color and word subtests[43] and TMT Part A.[45] A global cognitive score (GCS) was calculated by averaging the seven cognitive domain scores.

Social functioning was evaluated using (i) the Functional Assessment Short Test (FAST),[49] (ii) the Short Form-36 Health Survey questionnaire (SF-36),[50] and (iii)

the World Health Organization Quality of Life brief scale (WHO-QoL-Bref).[51] A global social functioning score (GSFS) was calculated by averaging the total scores on the three scales.

2.4 | Statistical analyses

Data were analyzed using Statistical Package for Social Sciences (SPSS) version 26.0 for Windows.[52] Descriptive analyses were conducted using Student's t-tests for independent samples for continuous variables and chi-square tests for categorical variables. Normality was assumed for all continuous variables because the sample was sufficiently representative of the target population, which was statistically verified. This fact guarantees that the variables are distributed in a normalized way. The differences between groups for MetS components, cognitive performance, and social functioning at T1 and T2 and their evolution overtime were assessed using a mixed one-way analysis of covariance (ANCOVA), with diagnosis (SMI and T2DM) and sex as covariables. It was adjusted for diagnosis and sex because these factors were differentially distributed between the two groups and were a confounding variable. The direct scores obtained for GCS and GSFS were transformed into Z-scores. For the calculation of the Z-scores, the mean and standard deviation of the individuals without MetS (No-MetS) at T1 were taken as reference values. Thus, a valid measure was obtained to contrast the objective condition of the study (exposure or not to MetS). To test the predictive capacity of MetS components at baseline to explain the variance in cognitive performance and social functioning at T2, a linear regression analysis was performed using a predictive model that included only MetS components that were significant for each MetS group. Other variables relevant to cognitive performance and social functioning were not included because the MetS components were optimal predictors per se. Likewise, to test the ability to discriminate individuals with greater cognitive impairment at T2 from MetS components at T1, a binary logistic regression was performed using a predictive model that included only MetS components that were significant for each group. Greater cognitive impairment was defined by scores greater than one standard deviation below the mean on the GCS. Subsequently, a receiver operating characteristic (ROC) curve was generated for the variables identified in the binary logistic regression as explanatory factors of cognitive performance. From this curve, optimal performance levels were delimited based on sensitivity and specificity values for each of the selected variables. For all analyses, $p < 0.05$ was considered statistically significant. The procedure to create the predictive models was as follows: first, a predictive analysis was performed with MetS components one by one, then predictive models were generated that included and combined the statistically more powerful variables; finally, the optimal predictive combination was obtained. No more than five variables were included in each model, thus guaranteeing the correct performance of the analysis.

3 | RESULTS

3.1 | Sample description

At T1, the sample consisted of 165 persons, including 30 with SZ, 42 with BD, 35 with MDD, 30 with T2DM, and 28 HCs. The total sample was classified into two groups: 83 in the No-MetS group (T2DM = 4, MDD = 27, BD = 22, SZ = 8 and HC = 22) and 82 in the MetS group (T2DM = 26, MDD = 8, BD = 20, SZ = 22 and HC = 6).

Forty participants were lost to follow-up at T2 (retention rate: 75.7%). The sample consisted of 70 individuals in the No-MetS group (T2DM = 3, MDD = 18, BD = 18, SZ = 12 and HC = 19) and 55 individuals in the MetS group (T2DM = 22, MDD = 7, BD = 11, SZ = 15 and HC = 0).

A summary of the sociodemographic and clinical characteristics of the participants is presented in Table 1. Women represented half of the total sample (48%). The mean age of the whole sample was 49.9 (SD: 10.2) years. The MetS group was characterized by a significantly lower percentage of women than the No-MetS group. Age, mean number of years of education and laterality were similar in both groups. Moreover, the MetS group had significantly higher levels of multimorbidity and use of medications other than psychopharmacological agents.

3.2 | Between-group comparisons of MetS components, cognitive performance and social functioning at T1 and T2

MetS components at T1 and T2 for both groups are shown in Table 2. Overall, at T1, MetS components were significantly higher in the MetS group ($p < 0.01$; $\eta^2p = 0.03$ to 0.26). Similar findings were observed at T2 ($p < 0.0001$; $\eta^2p = 0.11$ to 0.32). At both assessments, moderate effect sizes were observed for all MetS components when compared between groups. As expected, individuals with MetS had significantly higher WC than those without MetS ($p < 0.0001$; $\eta^2p = 0.12$). Furthermore, HDL was significantly lower in the MetS group ($p < 0.0001$; $\eta^2p = 0.15$). The within-group presence of MetS components did not significantly differ over time.

TABLE 1 Sociodemographic and clinical characteristics of the sample at T1

Variables[a]	No-MetS ($n = 83$)	MetS ($n = 82$)	Statistical analyses t or χ^2 (p)[i,j]
Sociodemographic			
Sex[b]	53 (64%)	26 (32%)	17.0***
Age	48.8 (9.2)	51.1 (11.2)	NS
Years of education	12.4 (4.8)	12.5 (4.6)	NS
Dependent status[c]	18 (22%)	23 (28%)	NS
Occupation status[d]	50 (60%)	54 (66%)	NS
Laterality[e]	80 (96%)	77 (94%)	NS
Clinical			
Tobacco[f]	37 (44%)	32 (39%)	NS
COHb	0.9 (1.0)	1.1 (1.3)	NS
KFS	0.9 (1.5)	1.6 (1.9)	2.5**
CCI	0.7 (1.2)	1.3 (1.6)	2.9**
HRSD[g]	6.5 (6.5)	6.3 (5.9)	NS
YMRS[g]	1.8 (2.7)	2.8 (4.4)	NS
PANSS-P[g]	7.3 (1.4)	8.7 (3.9)	2.9**
PANSS-N[g]	8.7 (5.0)	11.7 (8.4)	2.7**
PANSS-G[g]	19.7 (8.0)	23.4 (11.2)	2.4**
CGI[g]	2.8 (1.4)	3.0 (1.5)	NS
Psychiatric medications[h]	2.0 (2.1)	2.2 (2.1)	NS
General medications[h]	3.0 (3.1)	4.3 (2.7)	2.6**

Abbreviations: CCI, Charlson Comorbidity Index; CGI, Clinical Global Impression; COHb, carboxihemoglobina; G, general; HRSD, Hamilton Rating Scale for Depression; KFS, Kaplan-Feinstein Scale; MetS, metabolic syndrome; N, negative; NS, not significant; P, positive; PANSS, Positive and Negative Syndrome Scale; T1, time 1; YMRS, Young Mania Rating Scale.

NS = $p > 0.05$; *$p \leq 0.05$; **$p \leq 0.01$; ***$p \leq 0.001$; ****$p \leq 0.0001$.

[a]Expressed as the mean (standard deviation) except when indicated.

[b]Female n (%).

[c]Dependent n (%).

[d]Not active n (%).

[e]Right-handers n (%).

[f]Yes n (%).

[g]Lower scores represent a better outcome.

[h]Number

[i]t-test for independent samples.

[j]Chi-square test.

Neurocognitive performance and social functioning at T1 and T2 for both groups are shown in Table 3. Individuals with MetS showed worse cognitive performance than individuals without MetS at T1 ($p < 0.05$; $\eta^2 p = 0.02$) and T2 ($p < 0.05$; $\eta^2 p = 0.03$). At both assessments, small effect sizes were observed for neurocognitive performance and social functioning when compared between groups. However, social functioning was similar ($p > 0.05$) at both assessments. The within-group cognitive performance and social functioning did not significantly differ over time.

3.3 | Predictive capacity of MetS components at T1 of neurocognitive performance and social functioning at T2

The results of the relative contributions of MetS components at T1 to explain the variation in GCS and GSFS scores at T2 are shown in Table 4. For individuals with MetS, TG alone was the most powerful predictor of GCS at T2 (12.6%), followed by the combination of SBP and DBP, which were the MetS components that explained 10.8% of GCS variance at T2. Moreover, the combination of TG and FPG significantly predicted GSFS at T2 and explained 19.1% of the variance.

For the No-MetS group, 12.5% of GCS variance at T2 could be explained by the combination of TG and FPG. Moreover, WC alone significantly predicted 14.3% of the variance in GSFS at T2, while the combination of TG, HDL, and FPG explained the largest percentage of variance (18.8%) of GSFS at T2.

3.4 | Discriminatory ability of MetS components at T1 to classify individuals with greater cognitive impairment at T2

The results regarding the ability of MetS components at T1 to discriminate individuals with greater cognitive impairment at T2 are shown in Table 5. The combination of four components (TG, FPG, SBP, and HDL) was the model that best classified these individuals, with a correct classification rate of 87.1%. Next, the combination of TG, SBP, and FPG (86.3%), the combination of TG and SBP (81.5%), and TG alone (75%) were successively the best classifiers. ROC curve analysis was performed to assess the diagnostic usefulness of TG, which, as seen in the binary logistic regression, proved to be the most useful component in the classification of individuals with greater cognitive impairment (Figure 1). The analysis showed that the area under the ROC curve for the identification of individuals with greater cognitive impairment was 83.9% with TG (95% CI = 0.77–0.91). As seen in the figure, the TG level that best discriminates individuals with greater cognitive impairment will likely be between those points of the curve, with sensitivity between the 0.75 and 0.80 values.

TABLE 2 Components related to metabolic syndrome at T1 and T2

	No-MetS		MetS		*Statistical analyses*				
Variables[a]	**T1 (*n* = 83)**	**T2 (*n* = 70)**	**T1 (*n* = 82)**	**T2 (*n* = 55)**	**T1 F (*p*)**[b]	**η^2p**[c]	**T2 F (*p*)**[b]	**η^2p**[c]	**T1-T2 F (*p*)**[b]
WC	92.9 (18.3)	94.9 (16.1)	107.3 (11.1)	110.0 (12.5)	23.4****	.12	15.1****	.11	NS
TG	94.5 (39.6)	100.9 (47.6)	160.0 (60.4)	191.7 (88.1)	58.2****	.26	57.7****	.32	NS
HDL	55.4 (12.2)	54.9 (12.8)	43.0 (9.9)	42.4 (10.3)	30.0****	.15	16.6****	.12	NS
SBP	119.3 (12.7)	118.4 (13.4)	133.3 (17.2)	136.4 (17.9)	25.5****	.13	24.4****	.16	NS
DBP	73.9 (10.3)	73.0 (9.5)	79.2 (9.9)	81.8 (10.0)	5.0**	.03	20.4****	.14	NS
FPG	94.5 (20.5)	96.2 (18.4)	121.7 (46.9)	128.9 (41.4)	24.2****	.13	33.6****	.21	NS

Abbreviations: ANCOVA, analysis of variance; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL, high-density lipoprotein; MetS, metabolic syndrome; NS, not significant; SBP, systolic blood pressure; T1, time 1; T2, time 2; TG, triglycerides; WC, waist circumference.

NS = $p > 0.05$; *$p \leq 0.05$; **$p \leq 0.01$; ***$p \leq 0.001$; ****$p \leq 0.0001$. Effect size: η^2p: small ≈ 0.02; moderate ≈ 0.15; large ≈ 0.35.

[a]Expressed as the mean (standard deviation).

[b]ANCOVA.

[c]Partial eta-squared (η^2p).

TABLE 3 Cognitive performance and social functioning at T1 and T2

	No-MetS		MetS		Statistical analyses				
Variables[a]	**T1 (*n*=83)**	**T2 (*n*=70)**	**T1 (*n*=82)**	**T2 (*n*=55)**	**T1 F (*p*)**[b]	**η^2p**[c]	**T2 F (*p*)**[b]	**η^2p**[c]	**T1-T2 F (*p*)**[b]
GCS	0.0 (1.0)	0.0 (0.9)	−0.3 (0.9)	−0.3 (0.9)	3.9*	.02	4.3*	.03	NS
GSFS	0.0 (1.0)	0.0 (1.0)	0.1 (0.9)	0.0 (1.0)	NS		NS		NS

Abbreviations: ANCOVA, analysis of covariance; GCS, global cognitive score; GSFS, global social functioning score; MetS, metabolic syndrome; NS, not significant; T1, time 1; T2, time 2.

NS = $p > 0.05$; *$p \leq 0.05$; **$p \leq 0.01$; ***$p \leq 0.001$; ****$p \leq 0.0001$. Effect size: η^2p: small ≈ 0.02; moderate ≈ 0.15; large ≈ 0.35.

[a]Z-scores expressed as the mean (standard deviation).

[b]ANCOVA.

TABLE 4 Predictive MetS components at T1 of cognitive performance and social functioning at T2.

Dependent variables at T2	**Predictors at T1**	***β***	**95% CI**	***t***	**Percent of variance explained (adjusted R^2)**
Group: No-MetS					
GCS	TG	−0.29	−0.01 to 0.00	2.39*	12.5
	FPG	−0.19	−0.02 to 0.00	1.65*	
GSFS	WC	−0.37	−0.04 to 0.00	3.11***	14.3
	TG	−0.21	−0.01 to 0.00	1.77*	18.8
	HDL	0.28	0.00 to 0.04	2.33*	
	FPG	−0.23	−0.02 to 0.00	1.96*	
Group: MetS					
GCS	SBP	0.35	0.00 to 0.03	2.48**	10.8
	DBP	−0.32	−0.05 to 0.00	2.28*	
	TG	−0.35	−0.009 to −0.002	2.98**	12.6
GSFS	TG	−0.44	−0.01 to 0.00	3.71***	19.1
	FPG	−0.19	−0.008 to 0.001	1.60*	

Abbreviations: DBP, diastolic blood pressure; FPG, fasting plasma glucose; GCS, global cognitive score; GSFS, global social functioning score; HDL, high-density lipoprotein; MetS, metabolic syndrome; NS, not significant; SBP, systolic blood pressure; T1, time 1; T2, time 2; TG, triglycerides; WC, waist circumference.

NS = $p > 0.05$; *$p \leq 0.05$; **$p \leq 0.01$; ***$p \leq 0.001$; ****$p \leq 0.0001$.

TABLE 5 MetS components at T1 with ability to discriminate individuals with greater cognitive impairment at T2

Dependent variables at T2	Predictors at T1	β	Wald	Percent of variance explained	Global percentage correctly predicted
GCI	TG	0.02	26.9****	0.31 to 0.42	75.0
	TG	0.03	26.2****	0.44 to 0.58	81.5
	SBP	0.08	16.5****		
	TG	0.03	24.2****	0.51 to 0.68	86.3
	SBP	0.04	12.3****		
	FPG	0.07	11.9****		
	TG	0.03	19.9****	0.53 to 0.71	87.1
	FPG	0.05	12.1****		
	SBP	0.07	9.7***		
	HDL	−0.06	4.9*		

Abbreviations: FPG, fasting plasma glucose; GCI, greater cognitive impairment; HDL, high-density lipoprotein; MetS, metabolic syndrome; NS, not significant; SBP, systolic blood pressure; T1, time 1; T2, time 2; TG, triglycerides.

NS = $p > 0.05$; *$p \leq 0.05$; **$p \leq 0.01$; ***$p \leq 0.001$; ****$p \leq 0.0001$.

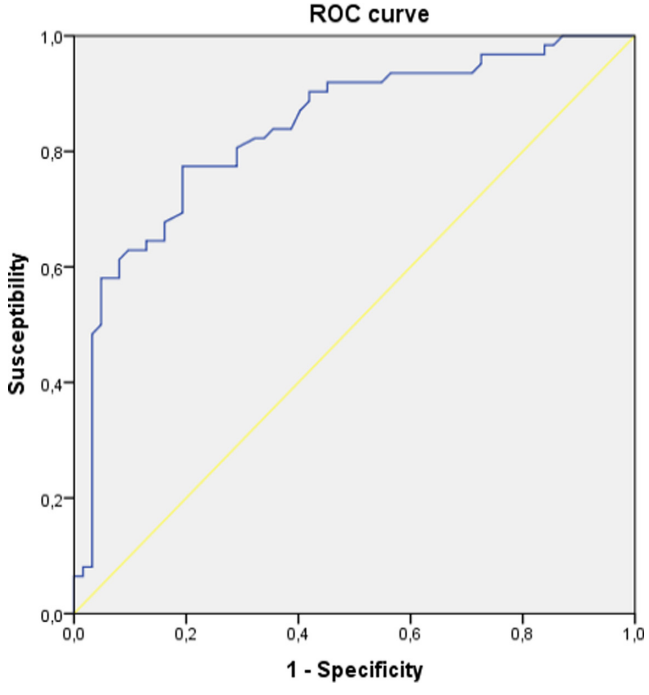

FIGURE 1 Identification of individuals with greater cognitive impairment based on TG levels

4 | DISCUSSION

The growing and dramatic impact of overweight/obesity and metabolic illnesses on physical and mental health is becoming increasingly well known. It is therefore crucial to determine the MetS components that play a key role in this relationship. To our knowledge, this is the first study to evaluate the predictive and discriminatory validity of MetS and its components regarding cognitive and social functioning across people with T2DM and SMI using a longitudinal design and a transdiagnostic perspective.

The results indicated that cognitive performance was significantly worse in individuals with MetS than in those without MetS, while social functioning was similar in both groups. In addition, TG and FPG were found to be key MetS components for predicting cognitive performance and social functioning across SMI and T2DM, regardless of MetS status. Moreover, BP was a significant predictor of cognitive function in individuals with MetS. Regarding discriminatory ability, TG seemed to be the most accurate MetS component for identifying individuals with greater cognitive impairment.[15,16,19,20]

These findings build upon growing evidence suggesting that individuals with SMI and T2DM, who also meet criteria for MetS, have worse cognitive performance than those without MetS.[20,23] Moreover, evidence indicates that individuals with SMI and T2DM have an unhealthy lifestyle that, in addition to psychopharmacological medication intake, increases the risk of developing MetS.[6,9] Thus, people with SMI and T2DM appear to be particularly vulnerable to cognitive and functional impairments linked to MetS. This could be explained by underlying pathophysiological pathways common to somatic and psychiatric diseases, such as immune-inflammatory processes, epigenetic regulatory mechanisms, or the microbiota-gut-brain system.[15,17]

These results have potential implications for the prevention and management of functional impairment in individuals with SMI and T2DM who meet criteria for MetS and individuals with MetS only. MetS is currently considered a major risk factor for the development of chronic diseases that involve high morbimortality, such as T2DM and SMI,[53] and therefore, early detection and

intervention for those at high risk of developing MetS is crucial. Based on the results of this study, it is proposed that some MetS components are especially useful to discriminate between individuals with disease and healthy individuals, thereby representing key elements for agile and accurate prevention. Thus, early detection of changes in those MetS components offers an opportunity to promote healthy lifestyle behaviors in individuals with SMI and T2DM, which in turn may reduce the risk of developing cardiometabolic complications. In this respect, we emphasize the importance of including MetS components as promising illness diagnostic markers for individuals with SMI and T2DM.[18] Furthermore, our findings converge with the current therapeutic strategy of increasing physical activity and improving the quality of the dietary patterns to address MetS. On the other hand, the recently issued Royal Australian and New Zealand College of Psychiatrists (RANZCP) clinical guidelines for depression place lifestyle-based interventions as the first step in the primary healthcare approach.[54] In keeping with current views that lifestyle is a multidimensional construct,[55] our results further emphasize the need to implement therapeutic interventions that are sensitive to lifestyle changes, thus encouraging regular physical exercise, restorative sleep patterns, improved diet quality, and increased social interaction, among others. Of note, all these behaviors are modifiable. The efficacy of lifestyle-based interventions is widely acknowledged for the prevention and treatment of several noncommunicable diseases and represents the grounds of lifestyle medicine.[56] The recent development of lifestyle psychiatry is gaining momentum.[57] Lifestyle modifications reportedly have a positive impact on symptom severity and neurocognitive function for individuals with SMI,[58,59] which goes beyond their known efficacy to treat metabolic comorbidities. Moreover, the negative impact of several MetS components on cognition might be prevented with nutritional and dietary interventions specifically designed to improve cognition in individuals with SMI and T2DM.[60,61] However, further studies are needed to determine whether lifestyle modifications have sustained, long-term effects in the SMI population.[62] This evidence should be urgently translated into clinical practice, given the poor literacy for nutritional and lifestyle medicine among healthcare professionals and trainees.[63,64]

This paper cannot be concluded without pointing out some of its limitations and strengths. Thus, the limitations of the study include its relatively small sample size, which reduces the generalization of the results to populations of individuals with clinical characteristics similar to those studied. Moreover, after a year of follow-up, high experimental mortality was observed. This may have led to a potential bias in the retention of individuals who completed the assessments and were thus in a presumably better clinical condition. Despite these limitations, this study is characterized by a novel transdiagnostic approach and a comprehensive assessment of cognitive and functional outcomes in individuals with or without MetS across populations with somatic and psychiatric disorders. Furthermore, being a multicenter study increases the external validity of the results.

Our current findings emphasize the need to promote lifestyle-based interventions for people with SMI and T2DM. The use of mobile health (m-health) technologies offers a promising opportunity to gather real-time data on lifestyle changes and self-care, which may be particularly useful for the prevention, tracking, and management of metabolic complications during the course of chronic illnesses. Further research is required to address the mental health effects derived from metabolic complications and changes in lifestyle. In this regard, studies that include more longer-term observations of concomitant lifestyle behaviors could serve to detect changes in metabolic conditions that allow the prevention of neurocognitive impairment among those with somatic and mental disorders. Therefore, considering lifestyle from a holistic perspective, rather than assessing individual behaviors in isolation, becomes essential to understanding the interactions between lifestyle and mental health. Additionally, rigorous further research on the identification of other clinical markers related to changes in lifestyle could not only improve our understanding of mental and physical health but also help to achieve excellence in clinical practice and improve precision psychiatry, which is likely to change the current compartmentalized mental health approach.

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CONFLICT OF INTERESTS

None.

AUTHORS' CONTRIBUTION

JVS-O, VB-M, PC-G, and RT-S: conception and design of the study; acquisition and analysis of data; drafting the manuscript and figures. GS-V, CS-M, VMV, IE-L, AH-M, JV-L, and BC-F: drafting the manuscript and figures. JV-F and RM-B: Formal analysis. All authors have read and agreed to the published version of the manuscript.

PEER REVIEW

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

1. Haase CL, Lopes S, Olsen AH, Satylganova A, Schnecke V, McEwan P. Weight loss and risk reduction of obesity-related outcomes in 0.5 million people: evidence from a UK primary care database. Int J Obes. 2021;45:1249-1258.
2. de Louw EJ, Paans NPG, Sonnenberg CM, et al. Metabolic syndrome rates in older patients with severe mental illness after five years of follow-up and the association with mortality. Int J Geriatr Psychiatry. 2019;34:333-336.
3. Pucci G, Alcidi R, Tap L, Battista F, Mattace-Raso F, Schillaci G. Sex- and gender-related prevalence, cardiovascular risk and therapeutic approach in metabolic syndrome: a review of the literature. Pharmacol Res. 2017;120:34-42.
4. Alberti KGMM, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome. Circulation. 2009;120(16):1640-1645. 10.1161/circulationaha.109.192644
5. Punthakee Z, Goldenberg R, Katz P. Definition, classification and diagnosis of diabetes, prediabetes and metabolic syndrome. Canadian J Diabetes. 2018;42:10-15.
6. Firth J, Solmi M, Wootton RE, et al. A meta-review of "lifestyle psychiatry": the role of exercise, smoking, diet and sleep in the prevention and treatment of mental disorders. World Psychiatry. 2020;19:360-380.
7. Singh VK, Karmani S, Malo PK, et al. Impact of lifestyle modification on some components of metabolic syndrome in persons with severe mental disorders: a meta-analysis. Schizophr Res. 2018;202:17-25.
8. Sotos-Prieto M, Ortolá R, Ruiz-Canela M, et al. Association between the Mediterranean lifestyle, metabolic syndrome and mortality: a whole-country cohort in Spain. Cardiovasc Diabetol. 2021;20:1-12.
9. Mazereel V, Detraux J, Vancampfort D, van Winkel R, De Hert M. Impact of psychotropic medication effects on obesity and the metabolic syndrome in people with serious mental illness. Front Endocrinol. 2020;11:479-573.
10. Hammoudeh S, Lawati HA, Ghuloum S, et al. Risk factors of metabolic syndrome among patients receiving antipsychotics: A retrospective study. Community Ment Health J. 2020;56:760-770.
11. Sánchez-Valle J, Tejero H, Fernández JM, et al. Interpreting molecular similarity between patients as a determinant of disease comorbidity relationships. Nat Commun Jun. 2020;11:28-54.
12. Tabarés-Seisdedos R, Baudot A. Editorial: Direct and inverse comorbidities between complex disorders. Front Physiol. 2016;7:1-2.
13. Garcia-Rizo C, Bitanihirwe BKY. Implications of early life stress on fetal metabolic programming of schizophrenia: a focus on epiphenomena underlying morbidity and early mortality. Prog Neuropsychopharmacol Biol Psychiatry. 2020;101:109-118.
14. Pillinger T, McCutcheon RA, Vano L, et al. Comparative effects of 18 antipsychotics on metabolic function in patients with schizophrenia, predictors of metabolic dysregulation, and association with psychopathology: a systematic review and network meta-analysis. Lancet Psychiat. 2020;7:64-77.
15. Meamar R, Amini M, Aminorroaya A, Nasri M, Abyar M, Feizi A. Severity of the metabolic syndrome as a predictor of prediabetes and type-2 diabetes in first degree relatives of type 2 diabetic patients: a 15-year prospective cohort study. World J Diabetes. 2020;11:202-212.
16. Barton BB, Zagler A, Engl K, Rihs L, Musil R. Prevalence of obesity, metabolic syndrome, diabetes and risk of cardiovascular disease in a psychiatric inpatient sample: results of the Metabolism in Psychiatry (MiP) Study. Eur Arch Psychiatry Clin Neurosci. 2020;270:597-609.
17. Bioque M, García-Portilla MP, García-Rizo C, et al. Evolution of metabolic risk factors over a two-year period in a cohort of first episodes of psychosis. Schizophr Res. 2018;193:188-196.
18. de la Fuente-Tomás L, Sierra P, Sanchez-Autet M, et al. A clinical staging model for bipolar disorder: longitudinal approach. Transl Psychiatry. 2020;10:37-45.
19. Bora E, McIntyre R, Ozerdem A. Neurococognitive and neuroimaging correlates of obesity and components of metabolic syndrome in bipolar disorder: a systematic review. Psychol Med. 2019;49:738-749.
20. Dimache AM, Şalaru DL, Sascău R, Stătescu C The role of high triglycerides level in predicting cognitive impairment: a review of current evidence. Nutrients. 2021;13(6):2118. 10.3390/nu13062118
21. Anjum S, Bathla M. A comparative study of prevalence and predictors of metabolic syndrome in various psychiatric disorders in state of Haryana: More than 30 years vs. less than 30 years. Diabetes Metab Synd Clin Res Rev. 2019;13:510-516.
22. Wali JA, Jarzebska N, Raubenheimer D, Simpson SJ, Rodionov RN, O'Sullivan JF Cardio-Metabolic Effects of High-Fat Diets

and Their Underlying Mechanisms—A Narrative Review. Nutrients. 2020;12(5):1505. 10.3390/nu12051505
23. Dembrowski GC, Barnes JW. Resolution of metabolic syndrome with reduction of visceral adipose tissue in a 47 year old patient with Type-2 Diabetes Mellitus. Diabetes Metab Syndrome Clin Res Rev. 2020;14:1001-1004.
24. Mallorquí-Bagué N, Lozano-Madrid M, Toledo E, et al. Type 2 diabetes and cognitive impairment in an older population with overweight or obesity and metabolic syndrome: baseline cross-sectional analysis of the PREDIMED-plus study. Sci Rep. 2018;31:1-9.
25. Zhang K, Yang W, Dai H, Deng Z. Cardiovascular risk following metformin treatment in patients with type 2 diabetes mellitus: Results from meta-analysis. Diabetes Res Clin Pract. 2020;160:108-120. 10.1016/j.diabres.2020.108001
26. American Psychiatric Association. (2014). Manual Diagnóstico y Estadístico de los Trastornos Mentales (DSM 5). Quinta edición. Madrid: Editorial Médica Panamericana.
27. Standards of Medical Care in Diabetes—2015 Abridged for Primary Care Providers. Clinical Diabetes. 2015;33(2):97-111. 10.2337/diaclin.33.2.97
28. Tohen M, Frank E, Bowden CL, et al. The international society for bipolar disorders (ISBD) task force report on the nomenclature of course and outcome in bipolar disorders. Bipolar Disorders. 2009;11(5):453-473. 10.1111/j.1399-5618.2009.00726.x
29. Andreasen NC, Carpenter WT, Kane JM, Lasser RA, Marder SR, Weinberger DR Remission in schizophrenia: proposed criteria and rationale for consensus. American Journal of Psychiatry. 2005;162(3):441-449. 10.1176/appi.ajp.162.3.441
30. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet. 2005;365:1415-1428.
31. Rosas-Carrasco O, González-Flores E, Brito-Carrera AM, et al. Evaluación de la comorbilidad en el adulto mayor. Revista Médica Del Instituto Mexicano Del Seguro Social. 2011;49:153-162.
32. Rius C, Pérez G, Martínez JM et al. An adaptation of Charlson comorbidity index predicted subsequent mortality in a health survey. J Clin Epidemiol. 2004;57:403-408.
33. Ramos-Brieva JA, Cordero-Villafáfila AA. Validación de la versión castellana de la Escala de Hamilton para la Depresión. Actas Luso Esp Neurol Psiquiatr Cienc Afines. 1986;14:324-334.
34. Colom F, Vieta E, Martínez-Arán A, et al. Versión española de una escala de evaluación de la manía: validez y fiabilidad de la Escala de Young. Medicina Clínica. 2002;119:366-371.
35. Peralta V, Cuesta MJ. Psychometric properties of the Positive and Negative Syndrome Scale (PANSS) in schizophrenia. Psychiatry Research. 1994;53(1):31-40. 10.1016/0165-1781(94)90093-0
36. Haro JM, Kamath SA, Ochoa S, et al. The clinical global impression-Schizophrenia scale: a simple instrument to measure the diversity of symptoms present in schizophrenia. Acta Psychiatrica Scandinavica. 2003;416:16-23. 10.1034/j.1600-0447.107.s416.5.x
37. Benowitz NL, Bernert JT, Foulds J, et al. Biochemical verification of tobacco use and abstinence: 2019 update. Nicotine Tob Res. 2020;12:1086-1097.
38. Aliño-Dies M, Sánchez-Ortí JV, Correa-Ghisays P, et al. Grip strength, neurocognition, and social functioning in people with Type-2 diabetes mellitus, major depressive disorder, bipolar disorder, and schizophrenia. Front. Psychol. 2020;11:525-231.
39. Correa-Ghisays P, Balanzá-Martínez V, Selva-Vera G, et al. Manual motor speed dysfunction as a neurocognitive endophenotype in euthymic bipolar disorder patients and their healthy relatives. Evidence from a 5-year follow-up study. J Affect Disord. 2017;215:156-162.
40. Correa-Ghisays P, Sánchez-Ortí JV, Ayesa-Arriola R, et al. Visual memory dysfunction as a neurocognitive endophenotype in bipolar disorder patients and their unaffected relatives. Evidence from a 5-year follow-up Valencia study. J Affect Disord. 2019;257:31-37.
41. San Martín-Valenzuela C, Borras-Barrachina A, Gallego JJ, Urios A, Mestre-Salvador V, Correa-Ghisays P. Motor and cognitive performance in patients with liver cirrhosis with minimal hepatic encephalopathy. J Clin Med. 2020;8:21-54.
42. Benedet MJ & Alejandre MA TAVEC. Test de Aprendizaje Verbal España-Complutense. TEA Ediciones; 2014.
43. Golden CJ. Test de Colores y palabras Stroop Manual. TEA Ediciones; 2001.
44. Grant DA, Berg EA. Test de clasificación de tarjetas Wisconsin Manual. TEA Ediciones; 2001.
45. Reitan RM, The WD, Test H-R & Battery: Theory and Clinical Interpretation Tucson, Arizona: Neuropsychology Press; 1985.
46. Weschler D Weschler Memory Scale – Third Edition. Escala de Inteligencia Wechsler para adultos-III. TEA Ediciones; 1999.
47. Rey A. Test de Copia y de Reproducción de Memoria de Figuras Geométricas Complejas. TEA ediciones S.A. 7ª edición; 1999.
48. Tabarés-Seisdedos R, Salazar J, Selva G, et al. Abnormal motor asymmetry only during bimanual coordination in schizophrenic patients compared to healthy subjects. Schizophr Res. 2003;61:245-253.
49. Rosa AR, Sánchez-Moreno J, Martinez-Aran A, et al. Validity and Reliability of the Functioning Assessment Short Test (FAST) in bipolar disorder. Clin Pract Epidemiol Ment Health. 2007;7:3-5.
50. Alonso J, Prieto L, Antó JM. The Spanish version of the SF-36 Health Survey (the SF-36 health questionnaire): an instrument for measuring clinical results. Med Clin (Barc). 1995;104:771-776.
51. Bobes J, Portilla MP, Bascarán MT, Saiz PA, Bousoño M. Banco de instrumentos básicos para la práctica de la psiquiatría clínica, 3rdªición. ed. Ars Médica; 2004.
52. Corp IBM. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. IBM Corp; 2019.
53. GBD. 2019 – Disease and Injury Incidence and Prevalence Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet. 2020;396:1204-1222.
54. Malhi GS, Bell E, Bassett D, et al. The 2020 Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders. Aust NZJ Psychiatry. 2021;55:7-117.
55. Balanzá-Martínez V, Kapczinski F, de Azevedo-Cardoso T, et al. The assessment of lifestyle changes during the COVID-19 pandemic using a multidimensional scale. Rev Psiquiatr Salud Ment. 2021;14:16-26.
56. Börnhorst C, Russo P, Veidebaum T, et al. The role of lifestyle and non-modifiable risk factors in the development of metabolic disturbances from childhood to adolescence. Int J Obes. 2020;44:2236-2245.

57. Firth J, Ward PB, Stubbs B. Editorial: lifestyle psychiatry. Front Psychiatry. 2019;26:5-9.
58. Bauer IE, Gálvez JF, Hamilton JE, et al. Lifestyle interventions targeting dietary habits and exercise in bipolar disorder: a systematic review. J Psychiatr Res. 2016;74:1-7.
59. Kennedy KG, Islam AH, Grigorian A, et al. Elevated lipids are associated with reduced regional brain structure in youth with bipolar disorder. Acta Psychiatr Scand. 2021;143:513-525.
60. Balanzá-Martínez V, Shansis FM, Tatay-Manteiga A, López-García P. Diet and neurocognition in mood disorders – an overview of the overlooked. Curr Pharm Des. 2020;26:2353-2362.
61. de Kluiver H, Jansen R, Milaneschi Y, et al. Metabolomic profiles discriminating anxiety from depression. Acta Psychiatr Scand. 2021;144:178-193.
62. Vancampfort D, Firth J, Correll CU, et al. The impact of pharmacological and non-pharmacological interventions to improve physical health outcomes in people with schizophrenia: a meta-review of meta-analyses of randomized controlled trials. World Psychiatry. 2019;18:53-66.
63. Ganis L, Christides T. Are we neglecting nutrition in UK medical training? A quantitative analysis of nutrition-related education in postgraduate medical training curriculums. Nutrients. 2021;16:1-13.
64. Mörkl S, Stell L, Buhai DV, et al. 'An apple a day'?: Psychiatrists, psychologists and psychotherapists report poor literacy for nutritional medicine: International survey spanning 52 countries. Nutrients. 2021;2:8-22.

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