Original Article

Access this article online

Quick Response Code:

Website: www.jehp.net

DOI: 10.4103/jehp.jehp_82_23

Association between cognitive capacity and metabolic indices in patients with neuropsychiatric disorders

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Abstract:

BACKGROUND: Although previous studies suggested the relationship between metabolic indices and cognitive capacity, results have been conflicting. The prevalence of metabolic and cognitive disorders is high in patients with neuropsychiatric disorders. We aimed to assess the relationship between laboratory metabolic indices and specific areas of cognitive capacity.

MATERIALS AND METHODS: This was a retrospective review of the medical records of 423 from 452 patients with neuropsychiatric disorders who were admitted to the neuropsychiatry unit, Ayatollah Kashani Hospital, Isfahan, Iran, from September 1, 2018, to September 30, 2022. We extracted demographic factors, laboratory metabolic indices, and scores of the Neuropsychiatry Unit Cognitive Assessment tool (NUCOG). We utilized a generalized linear model (GLM) to demonstrate the effect of metabolic indices on the risk of reduction in cognitive domains. Due to the presence of missing data in the metabolic indices, we used the multiple imputation method.

RESULTS: The regression coefficient of NUCOG total score and subscale scores for metabolic indices using GLM after multiple imputation method demonstrated that among the metabolic indicators, fasting blood sugar (FBS) had the reverse relationship with the total score of NUCOG (β = -.05). Among the NUCOG subscales, executive functioning had the strongest relationship with FBS (β = -.01). Also, there was a negative relationship between patients' age and the total score of NUCOG (β = -.38). Educational level had a positive relationship with the total NUCOG score (β =10.2).

CONCLUSIONS: The main metabolic factors that might reduce cognitive capacity were higher FBS.

Keywords:

Cholesterol, cognition, neuropsychiatry, thyroid stimulating hormone

Introduction

As a brain function, cognitive capacity (CC) comprises attention, visual-spatial abilities, memory, language, and executive function.[1-3] CC is the basis of higher-order functions of brain, like decision-making, goal-setting, planning, and judgment.[4-6] It has received increasing attention in various disciplines such as medicine, neuroscience, psychology, health, sociology, and management.[7-9] It is an undisputed fact that CC changes from birth to death.[7-9] Currently, as people age, cognitive impairment has become one of serious health problems worldwide.[1,10-12] Studies have predicted that the number of persons with the major neurocognitive disorders will rise from 57.4 million patients worldwide in 2019 to 152.8 million patients in 2050.[2,12] According to the World Health Organization, people with cognitive disorders double every 20 years, and most live in developing countries.[2] In Iran, similar to other developing countries, the prevalence of cognitive impairment is increasing.[10] Numerous risk factors contribute to cognitive decline that comprise

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Received: 17-01-2023
Accepted: 11-03-2023
Published: 31-08-2023

How to cite this article: Rajabi F, Rahimi S, Maracy MR, Barekatain M. Association between cognitive capacity and metabolic indices in patients with neuropsychiatric disorders. J Edu Health Promot 2023;12:292.

health related behaviors, like smoking, social isolation, and diet.[1,10] Metabolic disturbances may be another risk factor for cognitive impairment.[1,10,13]

There is consensus on the relationship between cognitive health and components of metabolic homeostasis, which is partly explained by the correlation of the metabolic risk factors for vascular etiologies of neurodegeneration.[14-16] However, there has been a lack of consistency in the findings of a correlation between specific metabolic risk factors and discrete cognitive domains.[16] Impaired vascular reactivity, increased carotid artery stenosis or intima-media rigidity, neuroinflammation, accelerated proteinopathy, abnormal brain lipid metabolism, and other endothelial dysfunction have been reported as possible mechanisms that contribute to brain degeneration, especially white matter damage, and accompany cognitive decline.[17]

Neuropsychiatry patients, in addition to taking the drugs they receive to control their symptoms like antipsychotics, due to impaired judgment, may undergo dietary changes that lead to increase in carbohydrate consumption and decrease in intake of microelements and the risk of occurrence and exacerbation of metabolic disorder increases.[14,15] Numerous studies in non-neuropsychiatric individuals showed the association between cognitive function and metabolic indices.[11,13,18,19] But in some studies conducted in the clinical environment, no relationship was observed.[20-22]

Our hypothesis was that there is a relationship between metabolic indices and CC domains. In previous studies, limited metabolic indices were used, and metabolic indices were compared with the total cognitive score, but in the present study, different metabolic indices were entered, and their relationship with different cognitive domains was measured. Also, NUCOG was used in this study, which can measure different dimensions of cognitive function separately. Therefore, the purpose of this research is to investigate the relationship between cognitive function and various components of cognitive function using biochemical and metabolic indices.

Materials and Methods

Study design and setting

This research was a cross-sectional study of the medical records of 452 patients with neuropsychiatric disorders. This study was conducted in Ayatollah Kashani Hospital, Isfahan, Iran. The patients' medical records data comprised a patient's neuropsychiatry and medical history, laboratory testing, neuropsychological assessments, and treatment details, which have been completed under the supervision of the neuropsychiatry fellow and an attending neuropsychiatrist.

Study participant and sampling

The studied population included people who were admitted to the neuropsychiatry unit from September 1, 2018, to September 30, 2022. A neuropsychiatrist evaluated and screened the patients' medical records. Patients with the misusing drugs/substances or an acute psychiatric disorder affecting cognition or intellectual disability and patients who were not fluent in Persian and had the inability to perform the Neuropsychiatry Unit Cognitive Assessment tool (NUCOG) were excluded from the research. Base on the inclusion and exclusion criteria, all the files of eligible patients were included, which shows that, finally, 423 patient files were selected for this study.

Data collection tool and technique

First demographic information on age, sex, marital state, educational level, and medications were collected based on medical records. The Persian version of NUCOG was used to investigate the patients' cognitive performance of 423 patients.

NUCOG is a cognitive screening test with high internal consistency (Cronbach's alpha = 0.919) and confirmed content validity.[23] This test can evaluate cognition in five domains of attention, visual constructional capacity, memory, executive function, and language. Each of the five domains has a maximum score of 20, and the full total score is 100.[23] The Persian version of NUCOG separates the healthy individuals from people with a mild neurocognitive disorder (at 86.5/100 with a specificity of 87.5%) and people with a major neurocognitive disorder from a healthy individuals (at 75/100 with specificity of 100%).[23]

During hospitalization, blood samples were taken from the patients. Analysis of the patients' laboratory biochemical and metabolic indices were done in the Department of laboratory in Kashani hospital. Theses indices, including HbA1C, serum fasting blood sugar (FBS), triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), thyroid stimulating hormone (TSH), and uric acid (UA) were in normal range 70–99 mg/dl, <5.7%, <200mg/dl, 40–59mg/dl, <100mg/dl, <150mg/dl., 5–5 MIU/L, 3.5–7.2mg/dl, respectively.

Statistical analyses were did in the SPSS version 20. The Spearman correlation method was used for the primary data analysis. The distribution of the variable's attention, memory, and executive function was normal. However, the variables of visuoconstruction, language, and the total score of NUCOG were not normal distributions. The factors such as sex, age, marriage, education, and medication were controlled in the model. We used a

GLM to identify whether metabolic disturbances were related to an increased risk of cognitive deterioration, both total and within subclass divisions of cognitive domains. *P* value of less than 0.05 was considered significant.

It should be noted we did not have any missing data for the NUCOG and its domains, but the metabolic indices in our study had missing data as follows:

Table 1: Demographic characteristics of the study population (*n*=423)

Variables	Value
Age (year) [mean±SD*]	56±17
Sex [*n* (%)]	
Male	210 (49.6)
Female	213 (50.3)
Unmarried	63 (14.8)
Married	360 (85.1)
Education level [*n* (%)]	
Illiterate	58 (13.7)
Primary studies	191 (45.1)
Diploma and associative degree	131 (31)
Bachelor of science and higher degree	43 (10.1)
Drugs taken [*n* (%)]	
No	338 (79.9)

*SD=Standard deviation

The percentage of missing data about UA, HbA1C, LDL-C, HDL-C, total cholesterol, TG, TSH, and FBS included 66.4%, 61,9%, 35,9%, 35%, 31.7%, 27%, 17%, and 6.9%, respectively.

In retrospective studies, some data may be incomplete, and it is not possible to access them. In these cases, the multiple imputation method is used to place the missing data.[24]

Ethical consideration

This study has been approved by the Bioethics Committee of Isfahan University of Medical Sciences (registration number: IR.MUI.MED.REC.1401.220) and was performed with the support of Isfahan University of Medical Sciences.

Results

Table 1 showed the demographic characteristics.

Table 2 showed cognitive and metabolic variables.

The correlation between metabolic parameters and cognitive subscales was extracted using the Spearmen correlation method. The results are shown in Table 3. FBS and HbA1C were negatively correlated with attention

Table 2: Patients' laboratory metabolic indices and cognitive profile

Variables	Mean (SD)*	Median (IQR)**	Mean (SD) Impute missing data	Median (IQR) Impute missing data
Attention	9.06 (4.9)	9 (5–15)	-	-
Visuoconstruction	13.1 (4.1)	9 (5–13)	-	-
Memory	9.7 (4.5)	9.5 (6–13)	-	-
Executive function	9.7 (5.2)	10 (5.5–14))	-	-
Language	16.02 (4.1)	17.5 (14–19)	-	-
Total score	57.7 (20.6)	58.5 (43–75)	-	-
TSH (MIU/L)	2.6 (6.5)	1.6 (1–2.6)	3.36 (6.5)	1.8 (1–3.47)
FBS (Mg/dl)	108.8 (42.6)	99 (87–115)	109 (42)	99 (87–115)
HbA1C (%)	6.2 (1.3)	6 (5.5–6.5)	6 (1.2)	6 (5.4–6.7)
TG (Mg/dl)	149.5 (82.5)	129 (93–178)	149.5 (81)	130 (93–185.8)
Total cholesterol (Mg/dl)	169.5 (44)	167 (140–194)	168.5 (44.3)	167 (138–194)
LDL (Mg/dl)	96.7 (35)	93.4 (70.2–116)	97.3 (35.2)	94 (72.2–120.4)
HDL (Mg/dl)	46.7 (11.4)	45 (38–53)	47 (11)	46 (39–53)
Uric acid (Mg/dl)	5.6 (1.3)	5.6 (4.7–6.4)	5.6 (1.3)	5.5 (4.5–6.4)

SD=Standard deviation*; *IQR=Inter quartile range

Table 3: Result of Spearman correlation analysis on metabolic parameters and cognitive scores of study patients

Variables	Attention	Visuoconstruction	Memory	Executive function	Language	Total score
TSH	0.005	-0.02	-0.003	0.003	-0.03	-0.009
FBS	-0.16*	-0.13*	-0.18*	-0.18*	-0.14*	-0.18*
HbA1C	-0.17*	-0.13*	-0.2*	-0.17*	-0.11*	-0.18*
TG	-0.01	-0.02	-0.09	-0.05	-0.05	-0.05
Total cholesterol	-0.02	-0.02	-0.05	0.01	0.02	-0.02
LDL	-0.03	-0.05	-0.04	0.003	0.02	-0.03
HDL	0.002	-0.02	0.004	0.01	0.01	-0.003
Uric acid	0.02	0.03	-0.009	0.003	0.0003	0.01

*P<0.05

(P = -0.16), (P = -0.17); visual constructional capacity (P = -0.13), (P = -0.13); memory (P = -0.18), (P = -0.2); executive function (P = -0.18), (P = -0.17); language (P = -0.14), (P = -0.11); and the total score of the NUCOG test (P = -0.18), (P = -0.18).

Table 4 showed the association between demographic characteristics and cognition with the use of the *t* test and Mann–Whitney test.

The results of regression coefficients of the NUCOG total score and subscale for metabolic indices of patients using a generalized linear model (GLM) with actual data are demonstrated in Table 5.

Among the metabolic indices, TC, HDL-C, and LDL-C had the strongest relationship with memory, and with an increase of one mg/dl in the level of total cholesterol, the memory score decreased by 1 (B = -1). With an increase of one mg/dl in the level of LDL or HDL, the memory score increased by 1. (B = 1), (B = .9).

The results of the regression coefficients of the NUCOG total score and subscale for metabolic indices of patients using a GLM after performed multiple imputation methods and missing data replacement are demonstrated in Table 6.

Among the metabolic indicators, FBS had the reverse relationship with the total score of NUCOG (B = -.05); so, by controlling the intervening variables, with an increase of one mg/dl in the level of FBS, the total score of the cognitive performance decreased by .05.

Among the NUCOG subscales, executive functioning had the strongest relationship with FBS (B = -.01), and with an increase of one mg/dl in the level of FBS, executive function decreased by .01.

Also, age had a negative relationship with the total score of NUCOG (B = -.38), so that with every one-year increase in age, the total NUCOG score decreased by 0.38. Education level had a positive relationship with the total NUCOG score (B = 10.2), and for each higher level of education, the total score increased by 10.2.

Discussion

This cross-sectional study investigated the association between metabolic indices and cognitive function either as a whole concept or isolated cognitive domains. In this study, increased FBS was associated with a worse overall cognitive score. Among the NUCOG subscales, executive functioning had the strongest relationship with FBS.

Our results were in agreement with Casagrande *et al*., in 2021, who found that adults with diabetes and increasing

Table 4: Association between demographic characteristic and cognition

Variable	Attention*		Visuconstcruction**		Memory*		Executive function*		Language**		Total score**	
	Mean (SD)	*P*	M (IQR)	*P*	Mean (SD)	*P*	Mean (SD)	*P*	M (IQR)	*P*	M (IQR)	*P*
Gender												
Female	9 (5)	0.94	13 (10–16.5)	0.18	9.8 (4.7)	0.6	10.1 (5.2)	0.15	17.5 (14–19)	0.6	59.5 (42.5–76.5)	0.8
Male	9 (5)		13.75 (11–16.5)		9.6 (4.3)		9.4 (5.1)		17 (13.5–19)		57.5 (45.5–73)	
Age	-0.31	<0.001	-0.33	<0.001	-0.42	<0.001	-0.38	<0.001	-0.37	<0.001	-0.4	<0.001
Education												
Illiterate	4.8 (3.4)	<0.001	10 (8–11.5)	<0.001	6.1 (2.9)	<0.001	5.8 (3.8)	<0.001	13 (11–15)	<0.001	38.2 (31–48)	0.0001
Primary education	7.8 (4.1)		12.5 (10–15)		9 (4)		9 (4.7)		16.5 (13.5–18.5)		53 (42.5–67)	
Diploma, associative degree	11.5 (4.6)		15.5 (12.5–17.5)		11.4 (4.4)		11.5 (5)		19 (17–20)		72 (55–80.5)	
Bachelor or higher degree	12.7 (4.2)		17 (15–18)		12.4 (5)		13.1 (5.2)		19 (18–20)		79 (58.5–88.5)	
Marital status												
Single	10.4 (5.1)	0.01	14.5 (11.5–17)	0.03	11.5 (4.6)	<0.001	11.5 (5)	<0.001	18.5 (15.5–20)	<0.001	70 (51–81.5)	0.001
Married	8.8 (4.8)		13 (10–16.5)		9.3 (4.4)		9.4 (5.1)		17 (13.5–19)		56.2 (42.5–73.5)	
Drug												
No	9.2 (4.9)	0.25	13.5 (10.5–16.5)	0.9	9.6 (4.5)	0.7	9.8 (5.2)	0.55	17.25 (14–19)	0.5	58.7 (43.5–75)	0.6
Yes	8.5 (4.7)		13.5 (10–16.5)		9.8 (4.4)		9.5 (5)		17.5 (14–19)		58.5 (42.5–73.5)	

*Two sample *t*-test: for data with normal distribution, **Mann Whitney *U*-test: for data with abnormal distribution

Table 5: Association between cognition and metabolic parameter in the study population based on GLM with actual data

Variable	β** (CI† 95%)	β (CI 95%)				
	Attention (0–20)	Visuoconstruction (0–20)	Memory (0–20)	Executive function (0–20)	Language (0–20)	Total score (0–100)
Marriage	0.72 (-4.2–5.6)	2.2 (-2.7–7.2)	2.5 (-2.3–7.3)	1 (-4.4–6.6)	2.6 (-2.8–8)	8.1 (-16–32.3)
Sex	1.4 (-1.1–4.1)	2 (-0.21–4.1)	1.5 (-1–4)	0.30 (-2.6–3.3)	0.56 (-2–3.2)	6.8 (-2.8–16.5)
Age	-0.06 (-0.15–0.01)	-0.06 (-0.13–0.01)	-0.09 (-0.17–-0.006)*	-0.08 (-0.18–0.006)	-0.04 (-0.13–0.04)	-0.35 (-0.71–0)
Education	1.7 (0.4–3.1)*	2.2 (-0.93–3.4)*	1.3 (-0.05–2.66)	2 (0.53–3.63)*	1.4 (0.005–3)*	11.5 (5.6–17.3)*
TSH	0.003 (-0.12–0.13)	0.006 (-0.08–0.09)	0.03 (-0.08–0.16)	0.05 (-0.08–0.2)	0.01 (-0.1–0.14)	0.16 (-0.28–0.61)
FBS	0.002 (-0.04–0.04)	-0.01 (-0.04–0.02)	-0.005 (-0.04–0.03)	-0.01 (-0.05–0.03)	-0.02 (-0.06–0.02)	-0.05 (-0.21–0.1)
HbA1C	-0.22 (-1.6–1)	0.71 (-0.67–2.1)	0.48 (-0.9–1.8)	0.1 (-1.4–1.7)	1 (-0.55–2.7)	2.7 (-3.4–9)
TG	0.11 (-0.04–0.28)	0.13 (-0.07–0.35)	0.18 (0.02–0.35)*	0.14 (-0.04–0.32)	0.1 (-0.1–0.32)	0.72 (-0.33–1.7)
Total cholesterol	-0.61 (-1.45–0.21)	-0.74 (-1.8–0.32)	-1 (-1.8–0.16)*	-0.72 (-1.6–0.21)	-0.5 (-1.6–0.48)	-3.7 (-9–1.4)
LDL	0.6 (-0.23–1.4)	0.72 (-0.35–1.7)	1 (0.16–1.8)*	0.70 (-0.23–1.6)	0.57 (-0.5–1.6)	3.6 (-1.5–8.9)
HDL	0.6 (-0.21–1.4)	0.80 (-0.26–1.8)	0.9 (0.09–1.7)*	0.71 (-0.2–1.6)	0.61 (-0.46–1.6)	3.9 (-1.3–9.1)
Uric acid	-0.73 (-1.5–0.09)	0.36 (-0.41–1.1)	-0.49 (-1.3–0.31)	-0.25 (-1.1–0.67)	0.2 (-0.67–1)	0.65 (-2.7–4)
Medication	-0.16 (-2.5–2.2)	1 (-1.1–3.15)	0.61 (-1.7–2.9)	0.8 (-1.8–3.5)	1 (-1.4–3.5)	3.1 (-6.5–12.8)

**β=Regression coefficient; †CI=Confidence interval; **P*<0.05

HbA1C had poorer performance in cognitive function.[13] Also, our results were consistent with Teixeira *et al*., in 2020, which showed that diabetes was related to a decrease in the total cognitive score and executive function domain and also, unlike our study, with the domains of memory and language. Also, older age and lower education level in Monika *et al*. are associated with poorer cognitive performance.[18] This was also consistent with the study by Zhang *et al*.,[25] in 2019, which showed that increased HbA1C is associated with the total cognitive score and, contrary to our study, is associated with memory domain. Also, our results concordant with Callisaya *et al*.,[11] in 2019, showed that type 2 diabetes was associated with lower score in total cognitive score, but unlike our study, the domains that were most affected were attention processing speed, verbal fluency, and verbal memory. It has been postulated that the possible mechanisms associated with diabetes and cognitive impairment are duration and uncontrolled hyperglycemia. Uncontrolled blood sugar status and high HbA1c are associated with cognitive decline, which is proposed to be due to small vessels disease, the presence of infarcts, and oxidative stress, which may impair neuronal function.[26] Another possible mechanism is chronic inflammation that, in many patients with diabetes and insulin resistance, is related to increased levels of inflammatory cytokines, which high levels of inflammatory cytokines can be related to the deterioration of cognitive function in patients with diabetes.[27] This result was not in line with Ravona *et al*.,[20] in 2012, who found that diabetes was not related to the rate of cognitive decline in the non-demented population.

We also found that thyroid stimulating hormone and UA levels were not associated with the scores of cognitive profile. This was congruent with Van Vliet *et al*., in 2021, who showed no consistent relations were observed between thyroid dysfunction and cognitive impairment.[21] This was also concordant with Hu *et al*., 2016, who displayed that there was no observed association between TSH and cognitive function.[22] This was not similar to Elbadawy *et al*.[28] in 2020, who found that a rise in TSH level is associated with a decreased total cognitive score. This was concordant with Monique M, in 2009, who showed that serum UA levels were not associated with cognitive decline.[29] Also, our result was not in agreement with Niu, who showed that a high level of serum UA was associated with cognitive decline.[30] Our study was not concordant with Suzuki *et al*.,[31] 2016, who showed that the patients in the highest quartiles of UA levels were found to be at a significantly higher risk of cognitive decline than those in the lowest quartiles. According to the difference in the results of the studies, some studies revealed that has a neuroprotective attribute against cognitive disorder by its antioxidant capability. On the other hand, other studies mentioned that UA causes cognitive impairment by the increase of vascular risk factors.[12]

Also, we found that according to GLM with actual data, there was a positive and considerable relationship between TG, HDL, and LDL and memory, and there was an important inverse relationship between total cholesterol and memory. This was concordant with Lee *et al*.,[32] in 2021, who showed that there was a positive association of total cognitive score with LDL and HDL. TG and TC did have no meaningful relationship with cognition in the mentioned study. Our result was in agreement with Mefford *et al*.,[33] in 2021, who found members with higher versus lower time-averaged LDL-C had a lower score in the language domain. This was in concordance as this was incompatible with Parthasarathy *et al*.,[34] in 2017, who showed that

Table 6: Generalized linear model analysis of the association between cognition and laboratory metabolic parameters after imputing missing data

Variable	β (CI 95%)					
	Attention (0–20)	Visuoconstruction (0–20)	Memory (0–20)	Executive function (0–20)	Language (0–20)	Total score (0–100)
Marriage	0.51 (-0.86–1.89)	0.86 (-.43–2.1)	0.83 (-.45–2.1)	0.96 (-0.53–2.4)	0.62 (-0.68–2)	3.7 (-2.4–10)
Sex	-0.47 (-1.29–0.34)	0.17 (-.54–.89)	-0.50 (-1.2–.25)	-1 (-1.9–0.13)*	-0.44 (-1.1–0.3)	-2 (-5.2–1.3)
Age	-0.05 (-.08–-0.02)*	-0.06 (-.09–-0.03)*	-0.09 (-.12–-0.07)*	-0.09 (-0.12–0.06)*	-0.06 (-0.08–-0.03)*	-0.38 (-0.51–-0.25)*
Education	2.6 (2.9–3.1)*	2 (1.5–2.4)*	1.6 (1.2–2.1)*	1.9 (1.4–2.4)*	1.7 (1.2–2.3)*	10.2 (8–12.3)*
TSH	0.01 (-.04–.07)	-0.01 (-.05–.02)	0.01 (-.04–.07)	0.01 (-0.05–0.07)	-0.004 (-0.05–0.04)	0.008 (-0.19–0.21)
FBS	-0.01 (-.02–.001)	-0.006 (-.01–.003)	-0.007 (-.01–.003)	-0.01 (-0.02–-001)*	-0.009 (-0.02–0.0008)	-0.05 (-0.1–-0.01)*
HbA1C	0.01 (-0.4–.43)	0.14 (-.22–.51)	-0.11 (-.5–.27)	0.2 (-0.25–0.65)	0.15 (-0.22–0.54)	0.96 (-0.72–2.6)
TG	0.004 (-.001–.01)	0.003 (-.001–.009)	0.0006 (-0.004–0.006)	0.004 (-0.002–0.01)	0.0002 (-0.005–0.005)	0.01 (-0.007–0.04)
Total cholesterol	-0.004 (-.02–.01)	-0.008 (-.02–.008)	0.002 (-0.01–0.02)	-0.01 (-0.031–0.009)	0.001 (-0.1–0.01)	-0.03 (-0.11–0.04)
LDL	0.0006 (-.02–.02)	0.002 (-.01–.02)	-0.001 (-0.02–0.01)	0.01 (-0.01–0.03)	0.0006 (-0.01–0.02)	0.02 (-0.06–0.11)
HDL	0.01 (-.02–.05)	0.003 (-.03–.03)	0.001 (-0.03–0.04)	0.03 (-0.01–0.07)	-0.006 (-0.04–0.02)	0.04 (-0.11–0.19)
Uric acid	0.07 (-.23–.38)	0.12 (-.14–0.4)	0.09 (-0.019–0.38)	0.17 (-0.15–0.51)	0.14 (-0.14–0.43)	0.68 (-0.56–2)
Medication	0.26 (-.77–1.3)	0.58 (-.32–1.4)	1.3 (0.37–2.31)*	0.71 (-0.41–1.8)	0.71 (-0.22–1.6)	2.6 (-1.4–6.7)

TG levels were inversely correlated with executive functioning, but no association was observed with memory. This discrepancy may be due to differences in the normal expected range of lipid profile assessment, study design, and sample participants' characteristics. Further studies are needed to identify the lipid profile cognition link. Both types of physical activities (aerobic and resistance) were effective to reduce HbA1c values. Exercise helped to lower insulin resistance in previously sedentary older adults with abdominal obesity at risk for diabetes. It is reasonable to recommend patients with an impaired metabolic state, especially higher FBS and hemoglobin A1C level, to obtain dietary changes and increase their physical activity to prevent probable cognitive decline.[35]

The current study had numerous strengths. Unlike preceding studies that evaluated the association of a limited number of metabolic indices with one or two cognitive subscale, we assessed the association of many metabolic indices with five cognitive domains. The other strengths of this study were the large sample size, reliable data gathering from our database, and using GLM with multiple imputation methods to deal with missing data.

Limitation and recommendation

This study had multiple limitations. The dominant limitation of our study is the cross-sectional analysis. Future studies should perform longitudinal research to find the causal relationship between metabolic indices and cognitive impairment. Due to the retrospective quiddity of the study, missing data were unavoidable. All data were gathered from the patient's medical records at a referral hospital; therefor, the sample may not be representative of patients with neuropsychiatric disorders in the community. It is recommended to conduct more studies in different geographical and cultural areas.

Conclusion

The main metabolic factors that might reduce CC were higher FBS. We suggest that in patients with metabolic disorders, regular evaluation of cognitive function be considered as a part of routine assessments. It is also suggested that preventive cognitive rehabilitation be included in intervention programs; for patients with established clinical cognitive decline, therapeutic group/individual cognitive rehabilitation sessions can be administered.

Acknowledgement

We would like to thank Isfahan University of Medical Sciences and Isfahan Kashani hospital. (Registration number: IR.MUI.MED.REC.1401.220).

Financial support and sponsorship
Founded by Medical University of Isfahan.

Conflicts of interest
There are no conflicts of interest.

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