





Original Research

Adherence to Mediterranean-Dietary Approaches to Stop Hypertension Intervention for Neurodegenerative Delay Diet in Relation to Serum Brain-Derived Neurotrophic Factor Concentrations and Metabolic Health Status in Adults



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ABSTRACT

Background: There is a lack of data regarding the Mediterranean-Dietary Approaches to Stop Hypertension Intervention for Neurodegenerative Delay (MIND) diet and metabolic health.

Objectives: This study assessed the relation between MIND diet and metabolic health status relative to serum brain-derived neurotrophic factor (BDNF) concentrations.

Methods: This was a cross-sectional study of 527 adults (286 males and 241 females) recruited from 20 schools in 6 different educational districts of Isfahan, Iran. Dietary intakes of participants were collected by a validated 168-item food frequency questionnaire, and MIND diet score was estimated. Anthropometric indices, blood pressure, biochemical parameters, and BDNF concentrations were assessed for all participants. The metabolically unhealthy (MU) phenotype was determined based on blood pressure, glycemic and lipid profiles, chronic inflammation, and insulin resistance.

Results: The frequency of MU phenotype among obese/overweight and normal-weight individuals was 79.5 % and 20.5 %, respectively. After adjustment for confounders, individuals in the top tertile of the MIND diet scores had 58 % lower odds of having the MU phenotype than individuals in the bottom tertile (odds ratios [ORs]: 0.42; 95 % confidence interval [CI]: 0.20, 0.90). In the fully adjusted model, females and normal-weight individuals had 81 % (OR: 0.19; 95 % CI: 0.04, 0.83) and 89 % (OR: 0.11; 95 % CI: 0.02, 0.69) lower chance of developing the MU phenotype, respectively. In addition, significant inverse associations between adherence to the MIND diet and high-blood pressure and hypertriglyceridemia were found. No significant association was found between adherence to MIND diet and odds of low BDNF concentrations.

Conclusions: Adherence to MIND diet is inversely associated with odds of MU phenotype, especially among women and normal-weight individuals. BDNF concentration is not associated with MIND diet and MU status.

Keywords: metabolic health status, MIND diet, brain-derived neurotrophic factor

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Abbreviations: ANCOVA, analysis of covariance; ANOVA, analysis of variance; BDNF, brain-derived neurotrophic factor; BP, blood pressure; DASH, Dietary Approaches to Stop Hypertension; FBG, fasting blood glucose; FFQ, food frequency questionnaire; hs-CRP, high-sensitivity C-reactive protein; MD, Mediterranean diet; MHNW, metabolically healthy normal weight; MHOW, metabolically healthy obese/overweight; MIND, Mediterranean-DASH Intervention for Neurodegenerative Delay; MU, metabolically unhealthy; MUNW, metabolically unhealthy normal weight; MUOW, metabolically unhealthy; OR, odds ratio; TG, triglyceride.

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Metabolic status is characterized by the absence or existence of cardiometabolic risk factors, such as dyslipidemia, hypertension, and hyperglycemia [1]. Accordingly, subjects with abnormal metabolic parameters are categorized as having a metabolically unhealthy (MU) phenotype, and in contrast, those with favorable metabolic profiles are considered to have a metabolically healthy phenotype [1]. Although excessive body weight has a contributing role in progression of MU status, all individuals in various weight categories are prone to metabolic disorders [2]. In this regard, it has been estimated that more than half of overweight/obese and about one-third of normal-weight adults in Iran suffer from MU status [3]. Considering the ascending trend of MU phenotype and its related consequences on physical and mental health of individuals [4], preventive and therapeutic approaches through modifiable effective factors, such as diet, are crucial.

Because people do not get nutrients on their own, but rather obtain them as part of a diet, assessment of dietary patterns could be a better predictor of metabolic health status [5]. Several studies have evaluated dietary patterns, including the Mediterranean diet (MD) and Dietary Approaches to Stop Hypertension (DASH) [6] in relation to metabolic disorders [7,8]. A recently proposed dietary pattern named Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND), which is a hybrid dietary pattern of the MD and DASH with some modifications, has also received a great deal of attention [9]. MIND diet has been developed to protect against mental disorders; however, it has also been suggested to be associated with metabolic disorders due to its antioxidant and anti-inflammatory nature [10]. A recent cohort study showed an inverse association between MIND diet and MU phenotype in both normal and overweight/obese subjects [11]. MIND diet was inversely associated with hypertriglyceridemia and low HDL cholesterol in a number of studies [12,13]. However, no significant associations were found with hypertension, hyperglycemia, other abnormal lipid profiles, and cardiometabolic parameters in several investigations [14,15].

Recently, the metabolic role of brain-derived neurotrophic factor (BDNF) hormone, as a component of neurotrophic factor family, has been taken into account [16]. In addition to the main function of this protein in survivability and development of neurons in the brain, it has also been shown to be involved in metabolic health status by regulating energy and macronutrient hemostasis [17]. Some investigations revealed an inverse association between serum concentrations of BDNF and likelihood of cardiometabolic disorders [18,19]. It has also been reported that environmental factors, especially diet, could influence BDNF concentrations; some dietary factors have been previously assessed in relation to BDNF concentrations [20,21]. For example, the results of an interventional study indicated that polyphenols, which are abundant in MIND diet, could significantly improve BDNF concentrations [21]. Therefore, BDNF may be considered as a mediator through which diet could control metabolic status of individuals.

So far, few studies have examined the relationship between MIND diet and metabolic health of adults, and the results have been conflicting. Additionally, to the authors' knowledge, no investigation has assessed BDNF in relation to metabolic health status and MIND diet in Iranians. Thus, this study aimed to evaluate the association of MIND diet with metabolic health status in Iranian adults. The link between the dietary pattern and serum concentrations of BDNF was also investigated in a secondary analysis.

Methods

Study design and participants

This cross-sectional study was performed among a somewhat representative sample of Iranian adults aged 20-65 y. The sample size was calculated according to a previous study that reported the prevalence of MU status among Iranian adults [3]. To determine the minimum required sample size, a power of 80 %, type I error of 0.05, desired CI of 0.95, and precision of 4.5 % were taken into account. The sample size was calculated to be 474 individuals. Participants were selected from adults who worked in schools in 6 different educational districts of Isfahan by a stratified multistage cluster sampling approach. In total, 20 schools, 3-4 schools from each education district, were selected for participant recruitment. After the agreement of the schools' administrators, the study was conducted on all adult members working in these schools in various job categories [22]. Subjects were not eligible if they: 1) were following a specific diet plan; 2) had a previous history of chronic diseases, such as type 1 diabetes mellitus, cardiovascular diseases, stroke, and malignancy; or 3) were pregnant or lactating females. Among 600 invited individuals, 543 agreed to cooperate in the current study (response rate = 90.5 %); 527 individuals were included in the analysis. Sixteen individuals were excluded from the study because they: 1) left >70 items of the food frequency questionnaire (FFQ) unanswered (n = 4); 2) reported a total energy intake outside the range of 800–4200 kcal/d [23] (n = 3); 3) had missing blood pressure (BP) concentrations (n = 8), and 4) did not accept blood sampling for biochemical tests (n = 1) (Supplementary Figure 1). A signed written informed consent was obtained from each participant before study initiation. The study was conducted according to guidelines expressed in the declaration of Helsinki and was approved by the Ethics Committee of Isfahan University of Medical Sciences (no. 240278).

Dietary assessment and MIND diet score calculation

A validated Willet-format semiquantitative 168-item FFQ was used to estimate the usual dietary intake of participants [24]. This questionnaire provides a reasonably valid measure of common food intake among Iranian adults. A reasonable correlation was found between food intake determined from this FFQ and amounts determined from multiple 24-h dietary recalls by a prior validation study. Based on the results of the study, correlation coefficients for nutrients from FFQ and 24-h dietary recalls ranged from 0.24 to 0.71 in males and from 0.11 to 0.60 in females [24]. The study participants were requested to record the frequency and amount of each food item consumed during the previous year. To convert portion sizes of consumed foods to grams per day, household measures were used [25]. Finally, the daily intake of all nutrients and energy was estimated by Nutritionist IV software.

Data obtained from the FFQ were used to estimate the MIND diet score. The components of the MIND diet used in this study are shown in Supplementary Table 1. In the estimation of MIND diet score, 15 dietary parameters were considered [9]. Ten of

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these dietary parameters, comprising green leafy vegetables, other vegetables, nuts, berries, beans, whole grains, fish, poultry, olive oil, and wine were known as brain healthy food groups. Five other nutritional parameters, including red meat, butter and margarine sticks, cheese, pastries and candies, and fried/fast food were considered as brain unhealthy food groups. All these food groups, except for wine, were used in the construction of MIND diet in the present study. Intake of wine was not included in the score, due to the religious restriction and lack of required information. Individuals in the lowest, middle, and highest tertile of brain healthy food groups were given scores of 0, 0.5, and 1, respectively. Conversely, individuals in the lowest, middle, and highest tertile of brain unhealthy food groups were given scores of 1, 0.5, and 0, respectively. A total MIND diet score was calculated by summing the score of all dietary components. Therefore, each participant had a score between 0 and 14.

Assessment of anthropometric indices and cardiometabolic risk factors: anthropometric indices were measured by a trained nutritionist (KL) while subjects stood with no shoes and in light clothing. Weight (kg) was measured (to the nearest 0.1 kg) with a body composition analyzer (Tanita MC-780MA), and height was measured (to the nearest 0.1 cm) with a tape measure. Waist circumference was measured (to the nearest 0.1 cm) by measuring halfway between the lower rib margin and iliac crest at the end of a normal respiratory cycle using a nonstretchable tape measure [26]. BMI (kg/m²) was estimated by dividing weight by the height squared. BP was measured in the sitting position after a 5-min resting using a digital sphygmomanometer (OMRON, M3, HEM-7154-E). BP measurement was repeated twice for each subject with a 5-min rest interval, and the mean of 2 measurements was used for data analyses.

To evaluate biochemical markers, a 12-h fasting venous blood sample was collected from each subject in the morning before the completion of questionnaires. An autoanalyzer (BioSystems) was used to measure serum concentrations of fasting blood glucose (FBG), HDL cholesterol, and triglyceride (TG) in the same day. The remaining serum was kept at -80° C to measure other biochemical variables. Commercial kits were used to measure serum concentrations of insulin (Monobined Inc.) and high-sensitivity C-reactive protein (hs-CRP) (turbidimetry kit, latex enhanced turbidimetric method, Delta.DP). HOMA-IR was evaluated by the following formula: HOMA-IR = [fasting insulin (mU/L) × FBG (mg/dL)]/405 [27]. To measure serum concentrations of BDNF, an ELISA kit (Zellbio) was used, and the first decile of serum BDNF concentration was defined as low serum BDNF values.

Defining metabolic health status

Individuals were classified into 4 groups of metabolic health, including metabolically healthy normal-weight (MHNW), metabolically healthy obese/overweight (MHOW), metabolically unhealthy normal-weight (MUOW), and metabolically unhealthy obese/overweight (MUOW), based on the definition presented by Wildman et al. [28]. According to Wildman et al.'s [28] definition, normal-weight (18.5 \leq BMI < 25) and overweight/obese individuals (BMI \geq 25) with 2 or more of the subsequent risk factors were considered as MUNW and MUOW, respectively: 1) FBG \geq 100 mg/dL; 2) HDL cholesterol <40 mg/dL in men and HDL cholesterol <50 mg/dL in women; 3) TG \geq 150 mg/dL; and 4) BP \geq 130/85 mmHg, 5) HOMA-IR >90th

percentile or HOMA-IR >3.99; and 6) hs-CRP >90th percentile or >6.14 mg/L. Normal-weight and overweight/obese participants with <2 of the mentioned risk factors were respectively considered as MHNW and MHOW.

Assessment of other variables

Basic demographic data, including sex, age, smoking, marital status, and education were gathered using a self-reported questionnaire. In addition, socioeconomic status of participants was evaluated using a validated questionnaire [29]. The questionnaire assessed the number of family members, home ownership, number and type of car, number of laptops/computers and traveling in the past year. A pretested questionnaire was applied to collect data regarding dietary habits of subjects (including eating rate, regular eating pattern, and intrameal fluid intake) [30].

Physical activity was assessed using the validated International Physical Activity Questionnaire-short form [31]. This questionnaire contains 7 questions about the frequency and duration of physical activity during the previous week. Data collected by the questionnaire were converted to metabolic equivalents of task in minutes per week.

Statistical analysis

Normal distribution of quantitative variables was evaluated using the Kolmogorov-Smirnov test. Continuous and categorical variables were reported as mean \pm SD/SE and percentages, respectively. Individuals were distributed in tertiles of MIND diet score (T₁: <6.50, T₂: 6.50–7.50, and T₃: >7.50). Continuous and categorical variables were compared among tertiles of MIND diet score by χ^2 test and one-way analysis of variance (ANOVA). Analysis of covariance (ANCOVA) was used to report age, sex, and energy-adjusted dietary intakes of participants among MIND diet score tertiles. To evaluate the association between MIND diet score and MU phenotype and its components, binary logistic regression was used to report odds ratios (ORs) and 95 % CIs in crude and multivariable-adjusted models; the first tertile was considered as the reference category in these analyses. In model 1, age, sex, and energy intake were controlled. Physical activity, smoking, marital status, educational status, socioeconomic status, and dietary habits were adjusted in model 2. The effect of BMI was additionally adjusted in model 3. MIND diet score tertiles were considered as continuous variables in logistic regression models to determine trends. Stratified analyses were performed based on sex (males compared with females) and BMI categories (normal-weight compared with overweight/obese). Crude and multivariable-adjusted ORs and 95 % CIs were also used to estimate odds of low BDNF in tertiles of MIND diet scores. In model 1, age and sex were controlled. The effects of physical activity, high FBG, TG, and BP were adjusted in model 2. All statistical analyses were performed using the Statistical Package for Social Sciences version 20 (SPSS Inc.), and P values of <0.05 were considered statistically significant.

Results

In general, 527 Iranian adults (286 males and 241 females) with a mean age of 42.66 y and an average BMI of 26.91 were included in this study. The prevalence of MU status in the overall sample was 42.5 %. The prevalence of MU phenotype among

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TABLE 1

General characteristics and cardiometabolic factors of study	dy participants across tertiles of MIND diet score
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	MIND diet score tertiles			
	T1 (<i>n</i> = 178) (<6.50)	T2 ($n = 168$) (6.50–7.50)	T3 (<i>n</i> = 181) (>7.50)	
MIND score	5.07 ± 0.91	7.05 ± 0.39	9.01 ± 0.99	< 0.001
Age (y)	39.23 ± 9.69	$\textbf{42.44} \pm \textbf{11.28}$	$\textbf{46.23} \pm \textbf{11.44}$	< 0.001
Sex (%)				
Males	62.4	49.4	50.8	0.03
Females	37.6	50.6	49.2	
Marital status (%)				
Single	18.1	13.9	16.7	0.69
Married	81.4	84.2	81.	
Divorced or widowed	6.0	1.8	1.7	
Education status (%)				
Diploma or lower	14.6	10.8	7.9	0.13
Higher than diploma	85.4	89.2	92.1	
Socioeconomic status (%) ³				
Low	43.0	26.0	31.0	0.01
Moderate	28.9	37.8	29.1	
High	28.1	38.7	42.7	
Weight (kg)	$\textbf{76.79} \pm \textbf{14.68}$	$\textbf{75.52} \pm \textbf{14.29}$	75.01 ± 14.79	0.49
BMI (kg/m^2)	26.73 ± 4.59	26.98 ± 4.05	$\textbf{27.01} \pm \textbf{4.63}$	0.81
Waist circumference	92.56 ± 11.73	92.67 ± 11.19	92.76 ± 11.59	0.99
Smoking (%)				
Nonsmoker	95.7	91.2	93.8	0.53
Exsmoker	1.9	4.1	3.7	
Current smoker	2.5	4.7	2.5	
Physical activity (MET min/wk)	928.68 ± 103.62	777.92 ± 79.63	1062.96 ± 95.15	0.10
Regular eating pattern (%)				
Regular	52.4	55.6	63.4	0.10
Irregular	47.6	44.4	36.6	
Eating rate (%)				
Fast	13.6	8.8	9.1	0.26
Moderate	77.5	76.3	80.0	
Slow	8.9	15.0	10.9	
Intrameal fluid intake (%)				
Moderate	56.3	62.8	77.0	< 0.001
More	43.7	37.2	23.0	
BDNF (ng/mL)	1.11 ± 0.49	1.25 ± 0.61	1.39 ± 2.72	0.30
Systolic blood pressure (mmHg)	120.11 ± 14.82	121.21 ± 15.80	123.58 ± 16.98	0.11
Diastolic blood pressure (mmHg)	82.26 ± 9.60	82.20 ± 10.25	83.30 ± 9.57	0.49
Fasting blood glucose (mg/dL)	91.41 ± 17.97	92.27 ± 16.52	93.20 ± 21.58	0.67
Triglycerides (mg/dL)	156.59 ± 43.51	152.21 ± 40.27	150.91 ± 38.49	0.39
HDL cholesterol (mg/dL)	$\textbf{54.87} \pm \textbf{9.71}$	55.50 ± 9.92	55.80 ± 10.34	0.67
hs-CRP (>90 th percentile) (mg/L)	3.05 ± 2.83	3.47 ± 3.39	3.04 ± 2.49	0.30
HOMA-IR index (>90 th percentile)	1.59 ± 2.53	1.43 ± 1.69	1.86 ± 2.90	0.24

Abbreviations: BDNF, brain-derived neurotrophic factor; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment of insulin resistance; hs-CRP: high-sensitivity C-reactive protein; MET, metabolic equivalent of task; MIND, Mediterranean-DASH Intervention for Neuro-degenerative Delay.

¹ Values are mean \pm SD (except for physical activity, which is reported as mean \pm SE), unless otherwise indicated.

² Obtained from 1-way analysis of variance and χ^2 test for quantitative and categorical variables, respectively. All significant values are represented by bold font.

³ Socioeconomic status score was evaluated based on job, family size, having a car in the family, having a computer/laptop, and traveling, using a validated questionnaire.

obese/overweight individuals was 79.5 %, whereas 20.5 % of normal-weight individuals had an MU phenotype. General features of the study population across tertiles of MIND diet scores are presented in Table 1. The range of MIND scores was from 2 to 12 in entire population, and the mean MIND score was 5.07 ± 0.91 , 7.05 ± 0.39 , and 9.01 ± 0.99 in tertiles 1, 2, and 3, respectively. A significant difference was observed between tertiles of MIND diet score in terms of age (P < 0.001), sex (P = 0.03), socioeconomic status (P = 0.01), and intrameal fluid intake (P < 0.001). However, no significant difference was observed regarding other variables (P > 0.05).

Dietary intakes of the study population across tertiles of MIND diet scores are summarized in Table 2. Individuals in the highest tertile of MIND diet scores had a higher intake of energy, green leafy vegetables, other vegetables, nuts, berries, whole grains, beans, fish, poultry, and olive oil (P < 0.05), whereas they consumed a lower amount of butter and margarine, cheese, fast/fried foods, pastries, and sweets (P < 0.05). However, no significant difference was observed across tertiles of MIND diet scores regarding red meat intake (P > 0.05).

Crude and multivariate-adjusted ORs and 95 % CIs for MU status across tertiles of MIND diet scores are reported in Table 3.

TABLE 2

Dietar	y intakes (energy	and food	groups)	of study	particip	ants across	tertiles	of MIND	diet score ¹	
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	MIND diet score tertiles					
	T1 (<i>n</i> =178) (<6.50)	T2 ($n = 168$) (6.50–7.50)	T3 (n =181) (>7.50)	P value ²		
Energy, kcal/d	$2063.52{\pm}50.58$	2293.79±50.87	2471.29±49.98	< 0.001		
Green leafy vegetables, g/d	39.68±4.40	56.44±4.35	81.87±4.34	< 0.001		
Other vegetables, g/d	227.43±14.33	$293.52{\pm}14.17$	387.55 ± 14.13	< 0.001		
Berries, g/d	4.45±0.74	$6.16{\pm}0.73$	$8.65 {\pm} 0.73$	< 0.001		
Nuts, g/d	$8.61 {\pm} 0.96$	$11.18{\pm}0.95$	$15.62{\pm}0.95$	< 0.001		
Whole grains, g/d	$23.90{\pm}3.64$	42.37±3.60	55.45±3.59	< 0.001		
Fish, g/d	$2.36{\pm}0.47$	$3.71 {\pm} 0.47$	6.70±0.47	< 0.001		
Beans, g/d	$28.23 {\pm} 2.65$	$35.62{\pm}2.63$	45.66±2.62	< 0.001		
Poultry, g/d	$24.53{\pm}\ 2.35$	$29.00{\pm}2.32$	39.26±2.31	< 0.001		
Olive oil, g/d	1.00 ± 0.30	$1.82{\pm}0.30$	$2.72{\pm}0.30$	0.001		
Butter, margarine, g/d	$10.65{\pm}~0.89$	$7.38{\pm}0.88$	$7.71 {\pm} 0.88$	0.021		
Cheese, g/d	34.41 ± 2.11	$26.65 {\pm} 2.09$	$21.05 {\pm} 2.09$	< 0.001		
Red meat and products, g/d	$73.20{\pm}~3.50$	67.09±3.47	62.07±3.45	0.093		
Fast fried foods, g/d	27.11 ± 1.75	26.11 ± 1.73	20.57±1.72	0.02		
Pastries and sweets, g/d	144.94±7.79	127.65±7.71	89.01±7.68	< 0.001		

Abbreviation: MIND, Mediterranean-DASH Intervention for Neurodegenerative Delay.

 1 Values are mean \pm SE. Energy intake was adjusted for age and sex; all other values were adjusted for age, sex and energy intake.

 2 P value obtained from analysis of covariance for adjustment of energy intake. All significant values are represented by bold font.

No significant association was found between MIND diet score and MU phenotype in the crude model (OR: 1.11; 95 % CI: 0.73, 1.48). However, after adjustment for covariates, individuals in the third tertile of MIND diet scores had 58 % lower odds of MU phenotype than individuals in the first tertile (OR: 0.42; 95 % CI: 0.20, 0.90). Stratified analysis by sex showed no significant associations between MIND diet score and MU phenotype among males in the crude (OR: 1.37; 95 % CI: 0.79, 2.39) or fully adjusted (OR: 0.48; 95 % CI: 0.18, 1.27) models (Table 3). In females, no significant relationship was observed between MU phenotype and MIND diet score in the crude model (OR: 1.01; 95 % CI: 0.52, 1.95). However, after controlling for covariates, a significant inverse association was found between MU phenotype and MIND diet score among females, such that females in the top tertile of MIND diet scores had 81 % lower odds of MU phenotype than those in the bottom tertile (OR: 0.19; 95 % CI: 0.04, 0.83).

Stratified findings based on BMI showed no significant relationship between MU phenotype and MIND diet score in obese/ overweight subjects in the crude (OR: 1.04; 95 % CI: 0.63, 1.72) or fully adjusted (OR: 0.57; 95 % CI: 0.23, 1.39) models (Table 3). In normal-weight participants, no significant relationship was found between MU phenotype and MIND diet score in the crude model (OR: 1.06; 95 % CI: 0.48, 2.35). However, after controlling for confounding variables, a significant inverse association was found between MU status and MIND diet score among normal-weight participants (OR: 0.11; 95 % CI: 0.02, 0.69).

Crude and multivariate-adjusted ORs and 95 % CIs for components of metabolic health status across tertiles of MIND diet scores are described in Table 4. There were no significant associations between MU characteristics and MIND diet scores in the crude model. However, following controlling for confounders, individuals in the highest tertile of MIND diet represented lower odds of high BP (OR: 0.43; 95 % CI: 0.19, 0.94) and hypertriglyceridemia (OR: 0.46; 95 % CI: 0.21, 1.00) than those in the first tertile. Mean BDNF values in tertiles 1, 2, and 3 of MIND diet scores were respectively 1.11, 1.25, and 1.38 ng/mL (P = 0.29). Crude and multivariate-adjusted ORs and 95 % CIs for low BDNF among tertiles of MIND diet scores are reported in Table 5. In the fully adjusted model, 34 % nonsignificant reduced odds for low BNDF values were found in participants in the highest tertile of MIND score compared with those in the first tertile (OR: 0.66; 95 % CI: 0.32, 1.35). Mean BDNF values were not significantly different in those with metabolic health and those with MU status (1.24 compared with 1.27 ng/mL; P = 0.81).

Discussion

In this study, adherence to MIND diet was inversely associated with odds of MU status among a sample of Iranian adults. This association was especially substantial among females and normal-weight subjects. Additionally, inverse associations were observed between MIND diet scores and the likelihood of hypertension and hypertriglyceridemia, although no significant association was found between serum BDNF concentrations and MIND diet score or MU status.

The MD and DASH diet, 2 healthy dietary patterns, have previously been assessed in relation to metabolic disorders. A prior study conducted on older Spanish adults examined adherence to MD and longitudinal changes in transition between different obesity phenotypes; each 2-point increment in MD adherence in the mentioned study was associated with 14 % lower risk of shifting toward an unhealthy phenotype [32]. A cross-sectional study among American adults also demonstrated an inverse relationship between the MD and DASH diet and MU profile of both normal-weight and obese subjects [33]. Nevertheless, several studies revealed contradictory findings. In a Chinese investigation, the DASH diet, but not MD, was associated with increased chance of metabolic health status among individuals with obesity [34]. On the other hand, inverse associations were found between the DASH diet and cardiometabolic factors among the Philippines population rather than Malaysian

TABLE 3

Multivariable-adjusted odds ratios and 95 % CIs for metabolically unhealthy status across tertiles of MIND diet score¹

	MIND diet score tertiles			P-trend
	T1 (<6.50)	T2 (6.50–7.50)	T3 (>7.50)	
All participants				
Participants/Cases (n)	178/78	168/62	181/84	
Crude	1	0.75 (0.49, 1.15)	1.11 (0.73, 1.48)	0.61
Model 1 ²	1	0.61 (0.38, 0.98)	0.72 (0.45, 1.17)	0.19
Model 2 ³	1	0.71 (0.35, 1.42)	0.47 (0.22, 0.97)	0.04
Model 3 ⁴	1	0.57 (0.28, 1.19)	0.42 (0.20, 0.90)	0.03
Males				
Participants/Cases (n)	111/54	83/41	92/52	
Crude	1	1.03 (0.58, 1.82)	1.37 (0.79, 2.39)	0.27
Model 1 ²	1	0.73 (0.40, 1.35)	0.82 (0.44, 1.52)	0.50
Model 2 ³	1	1.09 (0.42, 2.80)	0.55 (0.22, 1.42)	0.25
Model 3 ⁴	1	0.85 (0.31, 2.28)	0.48 (0.18, 1.27)	0.14
Females				
Participants/Cases (n)	67/24	85/21	89/32	
Crude	1	0.59 (0.29, 1.19)	1.01 (0.52, 1.95)	0.87
Model 1 ²	1	0.45 (0.21, 0.95)	0.56 (0.26, 1.19)	0.17
Model 2 ³	1	0.27 (0.08, 0.92)	0.21 (0.05, 0.85)	0.03
Model 3 ⁴	1	0.21 (0.06, 0.79)	0.19 (0.04, 0.83)	0.03
Normal-weight participants				
Participants/Cases (n)	63/19	56/11	51/16	
Crude	1	0.57 (0.24, 1.33)	1.06 (0.48, 2.35)	0.96
Model 1 ²	1	0.44 (0.17, 1.15)	0.83 (0.33, 2.08)	0.72
Model 2 ³	1	0.48 (0.08, 2.95)	0.11 (0.02, 0.69)	0.02
Overweight/obese participants				
Participants/Cases (n)	115/59	112/51	130/68	
Crude	1	0.79 (0.47, 1.34)	1.04 (0.63, 1.72)	0.85
Model 1 ²	1	0.70 (0.40, 1.23)	0.69 (0.39, 1.23)	0.21
Model 2 ³	1	0.58 (0.25, 1.37)	0.57 (0.23, 1.39)	0.21

Abbreviation: MIND, Mediterranean-DASH Intervention for Neurodegenerative Delay.

¹ All values are odds ratios and 95 % CIs. All significant values are represented by bold font.

² Model 1: adjusted for age, sex, and total energy intake. In stratified analysis by sex, adjusted for age and total energy intake.

³ Model 2: additionally adjusted for eating rate, regular eating pattern, intrameal fluid intake, physical activity, smoking, marital status, educational status, and socioeconomic status.

⁴ Model 3: additionally adjusted for BMI.

TABLE 4

Multivariable-adjusted odds ratios and 95 % CIs for metabolic components across tertiles of MIND diet score¹

	MIND diet score te		P-trend	
	T1 (<6.50)	T2 (6.50–7.50)	T3 (>7.50)	
High-blood pressure				
Age, sex, and energy-adjusted model	1	0.60 (0.37, 0.96)	0.73 (0.45, 1.19)	0.21
Fully adjusted model ²	1	0.47 (0.22, 1.01)	0.43 (0.19, 0.94)	0.03
High fasting blood glucose				
Age, sex, and energy-adjusted model	1	0.78 (0.44, 1.41)	0.68 (0.37, 1.22)	0.19
Fully adjusted model ²	1	0.50 (0.20, 1.23)	0.80 (0.34, 1.92)	0.65
High triglyceride				
Age, sex, and energy-adjusted model	1	0.98 (0.63, 1.54)	0.67 (0.42, 1.08)	0.09
Fully adjusted model ²	1	0.92 (0.45, 1.88)	0.46 (0.21, 1.00)	0.05
Low HDL cholesterol				
Age, sex, and energy-adjusted model	1	0.83 (0.40, 1.69)	1.22 (0.61, 2.45)	0.53
Fully adjusted model ²	1	1.27 (0.44, 3.65)	1.20 (0.39, 3.68)	0.75
High HOMA-IR				
Age, sex, and energy-adjusted model	1	0.63 (0.28, 1.42)	1.33 (0.70, 2.71)	0.38
Fully adjusted model ²	1	0.52 (0.17, 1.62)	1.36 (0.50, 3.68)	0.52
High hs-CRP				
Age, sex, and energy-adjusted model	1	0.82 (0.40, 1.67)	0.62 (0.30, 1.33)	0.22
Fully adjusted model ²	1	1.11 (0.42, 2.92)	0.36 (0.11, 1.14)	0.11

Abbreviations: HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment of insulin resistance; hs-CRP, high-sensitivity C-reactive protein; MIND, Mediterranean-DASH Intervention for Neurodegenerative Delay.

¹ All values are odds ratios and 95 % CIs. All significant values are represented by bold font.

² Fully-adjusted model: Adjusted for age, sex, total energy intake, eating rate, regular eating pattern, intrameal fluid intake, physical activity, smoking, marital status, educational status, socioeconomic status, and BMI.

TABLE 5

Multivariable-adjusted	l odds ratios and	1 95 % CIs for	low BDNF va	lues across terti	les of MIND diet score ¹
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	MIND diet score tertile	MIND diet score tertiles				
	T1 (<6.50)	T2 (6.50–7.50)	T3(>7.50)			
Low BDNF						
Crude	1	0.75 (0.38, 1.48)	0.69 (0.35, 1.36)	0.27		
Model 1 ²	1	0.73 (0.36, 1.45)	0.69 (0.34, 1.40)	0.29		
Model 2 ³	1	0.70 (0.35, 1.41)	0.66 (0.32, 1.35)	0.25		

Abbreviations: BDNF, brain-derived neurotrophic factor; MIND, Mediterranean-DASH Intervention for Neurodegenerative Delay.

¹ All values are odds ratios and 95 % CIs.

² Model 1: adjusted for age and sex.

³ Model 2: additionally adjusted for physical activity, high fasting blood glucose, high triglyceride, and high-blood pressure.

people [35]. Because the MIND diet is a combination of these 2 dietary patterns, it could provide valuable information regarding metabolic health of individuals.

Our results suggested that highest adherence to MIND diet was associated with reduced odds of MU phenotype in Iranian adults. The finding was in agreement with a previous cohort study on metabolically healthy Tehranian adults, which revealed that higher compliance with the MIND diet was related to lower risk of developing MU status [11]. Moreover, a cross-sectional survey among Italian adults aged 30-60 y illustrated an inverse association between the MIND diet and hypertriglyceridemia and low HDL cholesterolemia, whereas no significant relationship was seen with regard to hyperglycemia [12]. The same results were also found for TG and HDL cholesterol in a cross-sectional investigation among Kurdish adults in Iraq [13]. However, a prospective survey on 2706 Iranian individuals with a wide age range of 20-79 y showed that the MIND diet was not substantially associated with likelihood of hypertension [14]. Similarly, no significant associations were observed for BP, FBG, TG, HDL cholesterol, and HOMA-IR in a cross-sectional study on obese adults [15]. According to conflicting results of the mentioned studies, additional well-organized investigations are necessary.

We discovered an inverse association between MIND diet adherence and MU status among subjects with normal weight, but not in those with overweight/obesity. This might be the result of diverse physiological responses of humans in different BMI categories to external stimuli, including diet, to prevent metabolic disorders. Also, underestimation of total energy in overweight/obese individuals due to lack of accurate food reporting could affect the results. Our findings also revealed that this association was especially significant among females. It has been documented that females have a healthier dietary intake than males and also are more interested in consuming plantbased foods, which is the basis of MIND diet [36,37]. Furthermore, estrogen, as a pivotal hormone in premenopausal women, could be a major contributor for maintaining cardiometabolic health status [38]. The different number of cases in each subgroup or limited number of individuals in subgroups might be another explanation for observing nonsignificant association in subjects with obesity/overweight or males. However, further large-scale studies are needed to confirm the accuracy of these hypotheses.

The positive association between MIND diet and healthier metabolic status could be justified by its features. MIND diet consists of plant-based foods with low glycemic indexes and high fiber and water contents, which effectively facilitate weight reduction and thereby regulate the cardiometabolic parameters related to extra fat accumulation, including hypertension, hyperglycemia, and abnormal lipid profile [39,40]. In addition, although MIND diet includes only berries among fruits, berries are rich sources of phytochemicals, such as flavonoids, tannins, phenolic acids, and lignans, which have potent antioxidant properties [41]. It has been documented that oxidative stress has a complex relationship with metabolic disorders [42]. Therefore, berries in the MIND diet could have a protective effect against metabolic disorders by reducing reactive oxygen species and their detrimental damage to the body. In addition, vegetables and fruits contain adequate quantities of potassium, which has a restorative effect on high BP [43]. Furthermore, the favorable impacts of this dietary pattern on metabolic profile may be attributed to consumption of olive oil as the main source of dietary fat. High amounts of polyphenols in olive oil contribute to regulating oxidative stress, HDL cholesterol concentrations, and insulin sensitivity [44,45].

So far, a number of studies have investigated the association between dietary factors and BDNF concentrations [21]. A clinical trial study in Sweden indicated an increase in BDNF concentrations after consumption of kernel-based whole grain [46]. Another intervention study among Spanish adults showed that adherence to the MD plus nuts was related to improvement in BDNF concentrations [47]. However, serum concentrations of BDNF have not been previously assessed in relation to the MIND diet. In this study, we found no significant association between BDNF and the MIND diet. This result could be explained by insufficient population size; the sample size was not calculated based on this hypothesis, due to financial constraints. Further well-designed studies with larger sample sizes are needed to examine this association.

As an important global health concern, metabolic disturbances are related to developing odds of cardiovascular disease, type 2 diabetes, cancers, and consequently, decreased life expectancy among adults suffering from these conditions [48,49]. Furthermore, individuals with unhealthy metabolic profiles are prone to various mental disorders such as depression and anxiety [50]. The relationship between adherence to MIND diet and reduced risk of psychological disorders has been reported previously [51–53]. We additionally found an inverse association between MIND diet compliance and the odds of MU phenotype in our investigation. Therefore, providing nutritional education to adults through the health care system to follow healthy diets, including the MIND diet, can be considered a useful way to reduce the risk of adverse metabolic status and correlated complications including psychological abnormalities.

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There are multiple strengths to the present investigation. To our knowledge, this is the first study that examined adherence to the MIND diet and odds of MU status, in addition to considering the role of BDNF, among a somewhat representative sample of adults in a large central city of Iran. Moreover, using validated questionnaires and adjusting for several plausible confounders strengthened our study. However, several limitations should also be noted. Taking the cross-sectional design of the study into account, no causal relationships could be identified. In addition, we were unable to use the complete MIND diet scores in our analyses, due to lack of information on wine or alcohol intake in our FFQ. Because of using self-reported FFQ to collect information regarding dietary intakes, potential biases, such as measurement errors and misclassification of subjects were inevitable. Furthermore, despite adjusting for covariates, the effects of residual confounding variables could not be eliminated.

In conclusion, this study suggested that higher adherence to MIND diet is inversely associated with MU phenotypes but not with BDNF concentrations in a sample of Iranian adults. These associations should be assessed in further longitudinal investigations along with considering various underlying variables to confirm the results.

Authors' contributions

The authors' responsibilities were as follows – SAT: conceptualized, designed the methodology of the study, formally analyzed the study, acquired funding, wrote the original draft; DP: investigated the study, wrote the original draft; FS: investigated the study; KL, ZH, PR: investigated and curated the data; PS: conceptualized, designed the methodology of the study, supervised the study, collected the resources, formally analyzed the study, acquired the funding, edited and reviewed the manuscript; and all authors: reviewed and commented on subsequent drafts of the manuscript and read and approved the final manuscript.

Conflict of interest

The authors report no conflicts of interest.

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Data availability

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

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cdnut.2024.102082.

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