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Does choline have an effect on Transient Global Amnesia (TGA)?

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Abstract

Background Choline was frequently reported to have some beneficial effects on memory function. However, the association of dietary choline with different types of amnesia is not well understood. The objective of this study was to examine the association between dietary intake of choline and transient global amnesia (TGA).

Methods This case–control study was carried out on 258 patients with TGA and 520 participants without amnesia. Data on dietary choline intake was collected using a validated food frequency questionnaire (FFQ). All participants were examined for amnesia by a neurologist according to the Kaplan and Hodges criteria.

Results There was an inverse association between TGA and dietary choline intake after adjustment for age and gender (OR: 0.98, CI 95% 0.96–0.98, P = 0.03). The association remained significant after additional adjusting for physical activity, body mass index (BMI), occupation, marital status, smoking, and drinking alcohol (OR: 0.98, CI 95% 0.96–0.99, P = 0.04) and after further adjustment for calorie and food groups intake (OR: 0.98, CI 95% 0.96–0.99, P = 0.03).

Conclusion The results of this study indicated that choline may have beneficial effects against TGA. Further longitudinal studies are warranted.

Keywords Transient Global Amnesia, Choline, Dietary intake

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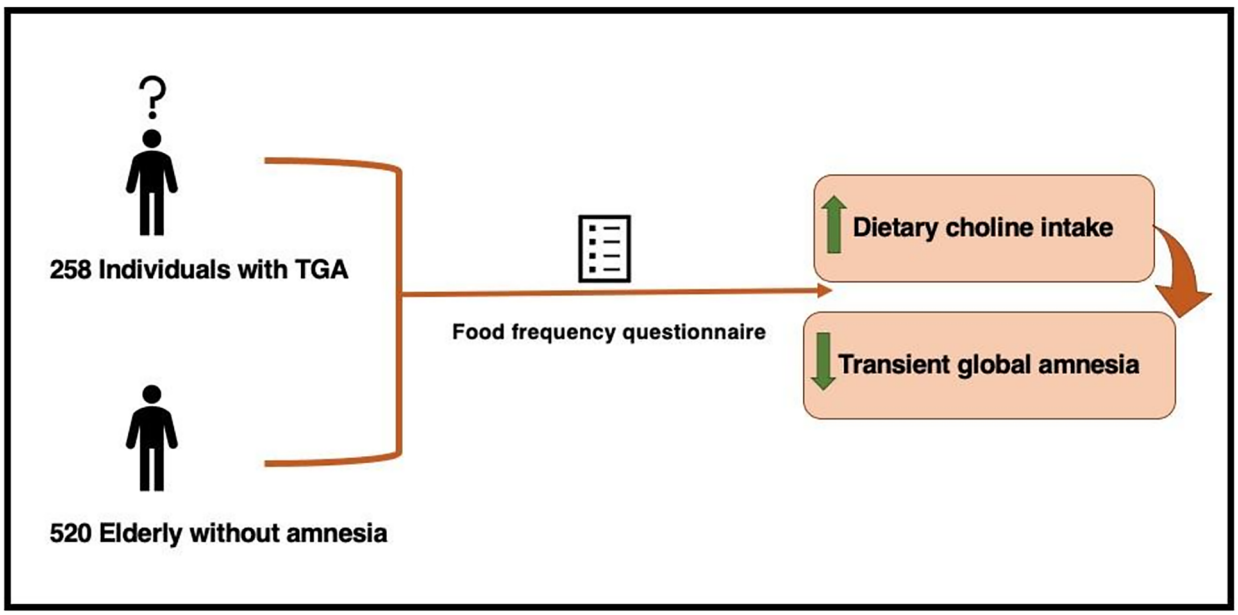
Graphical Abstract



The present study investigated the association between dietary choline intake and Transient Global Amnesia (TGA). A noteworthy inverse association was observed between choline consumption and TGA, even after adjusting for variables including age, gender, BMI, occupation, marital status, and dietary intake.

Introduction

Different types of memory loss including short-term, long-term, transient, or everlasting memory occur in people of nearly any age [1]. The prevalence of memory impairment tends to rise with age, with around forty percent of those aged 60 and above experiencing some level of memory impairment. Amnesia and moderate cognitive impairment are more prevalent among middle-aged and older non-Hispanic blacks and older Latinos compared to non-Hispanic whites. The incidence of amnesia is 1000 to 2600 per 100,000 cases, which corresponds to a prevalence rate of 1.0% to 2.6% in the general population [2].

Amnesia is a type of memory impairment mainly caused by brain damage and disease, and may be caused temporarily by using various sedatives and hypnotics [3]. Depending on the severity of damage, all or some parts of the memory may be lost [4]. Furthermore, memory loss may be caused by a variety of factors including alcoholism, brain injury caused by multiple diseases (e.g., Parkinson's disease, Alzheimer's disease, and vascular dementia), and dietary deficiencies [5]. On the other hand, some activities such as exercise, reading, participating in social interactions, and maintaining a healthy diet are all broad strategies that may be used to protect against memory loss [6, 7]. Dietary factors can significantly influence the risk and management of TGA [8, 9]. Recent studies reported the beneficial effects of certain dietary components such as coffee, tea, eggs, and soya on memory function [10, 11]. For example, an inverse association was found between the risk of TGA and dietary intake of omega-3 fatty acids [8]. Another study found that lycopene may act as a promising cognitive enhancer [12]. On the other hand, a recent study failed to find any connection between dietary intake of caffein and TGA [9].

Choline, a vitamin-like substance abundant in fish and dairy products, has been reported to enhance memory function [13, 14]. Choline is responsible for the production of the neurotransmitter acetylcholine (ACh), which plays an essential role in memory function [15]. Some studies reported that endogenous acetylcholine is vital in regulating memory-related procedures such as acquisition [16], encoding [17],

integration [18], reintegration [19], destruction [20], and memory restoration [21]. Choline supplementation may improve cognitive performance [22] and was recently suggested as an efficient treatment for cognitive impairments caused by chemotherapy or radiation therapy [23].

However, contradictory results were reported on the effects of dietary choline on amnesia [24, 25]. For example, the findings of two double-blind, placebo-controlled cross-over experiments investigating the effects of choline bitartrate as a dietary supplement on declarative memory and working memory in young, healthy students suggested that choline probably does not exert any immediate effects on cholinergic memory functions in healthy human subjects. However, few studies focused on dietary choline intake in patients with TGA. So, the aim of this study was evaluating the association between dietary choline consumption and TGA in Iranian adults.

Methods

This was a case–control study performed on 258 people with TGA and 520 adults without amnesia who participated in Sabzevar Persian Cohort, Sabzevar, Iran. The sample size was calculated using OpenEPI online software and the odds ratio obtained in a similar study considering alpha = 0.05, the power = 80%, and the ratio of controls to cases = 2 [26]. Inclusion criteria included obtaining written informed consent, a definitive diagnosis of TGA for the patient, the absence of cognitive disorders in the control group according to the neurologist's approval, non-adherence to specific diets, no food sensitivities, and no prohibition on certain foods. Exclusion criteria included refusal to continue the collaboration, failure to collect the required information, and history of choline supplementation. The Persian cohort questionnaire was used to collect participants' demographic and socio-economic status data including age, gender, having a job (yes/no), and marital status (maried/unmaried). To measure weight and height, the SECA 755 mechanical scale and SECA 204 portable stadiometer were used, respectively, and body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. In this study, alcohol drinking was defined as drinking alcohol at least once per month for six consecutive months and smoking was defined as smoking ≥ 1 cigarette every day or every other day during the previous month. Also, the level of physical activity was assessed using a validated version of international physical activity questionnare (IPAQ) [27]. Initially, screening was performed using International Classification of Diseases (ICD 10:Code G45.4) coding as an initial filter. Subsequently, all identified patients were confirmed by a consultant neurologist using the Caplan and Hodges criteria [28].

A validated food frequency questionnaire (FFQ) includes a list of 168 items of various foods was used to obtain data on dietary intake [29]. Face-to-face interviews were administered by a trained dietitian and the participants were asked to report their consumption frequency. Data on food intake during the last year in the control group and related to food intake in the last year before TGA diagnosis in the case group were collected. All reported consumption frequencies were converted to grams per day by using household measures. Then, these data were used to determine macro and micronutrient intake by the Nutritionist IV software (version 7.0; N-Squared Computing, Salem, OR, USA). The United States Department of Agriculture (USDA) Food Composition Table (FCT), and local food composition tables (for local foods) were used to determine the Choline content of common foods. By multiplying the choline content by the portion size and frequency of consumption for each food item, we were able to sum the total choline intake for each individual.

Statistical analysis

Chi-squared and independent samples t-test methods were used to characterize the for qualitative and quantitative data on participants' anthropometric, social, and demographic factors, respectvely. A variety of logistic regression models were used to ascertain the relationship between choline consumption in the diet and TGA. The confounding factors including age, the level of physical activity, BMI, having a job, marital status, smoking, drinking alcohol, calorie intake, and the consumption of diary products, fuits, vegetables, and fishes were identified based on the previous studies on the factors affecting memory function and TGA [30, 31]. Missing values in the covariates were treated using imputation models. Version 22 of the Statistical Package for the Social Sciences (SPSS) sofware was used to analyze the data, a $P < 0.05$ was regarded as significant in all analyses.

Results

As presented in Table 1, the cases had higher levels of occupation and drinking alcohol and a lower mean of height and weight compared to the control group (All $P < 0.05$). No difference was found between the groups regarding age, gender, smoking, and BMI.

Regarding the participants' dietary intake (Table 2), the controls had a higher intake of choline (252.51 ± 90.05 vs. 233.19 ± 88.5 mg/d, $P = 0.01$) and a higher consumption of dairy products (0.61 ± 0.39 vs. 0.54 ± 0.38, $P < 0.01$), fishes

Table 1 General characteristics of the participants

	Controls (n = 520)	Cases (n = 258)	P*
Age (years)	49.66 ± 9.37	49.86 ± 8.82	0.79
Females n (%)	346 (66.5%)	186 (72.1%)	0.15
Has job n (%)	72 (13.8%)	151 (58.5%)	< 0.01
Married n (%)	261 (50.2%)	128 (49.8%)	0.23
Drinking alcohol n (%)	13 (2.5%)	30 (11.6%)	0.03
Smoking n (%)	11 (2.1%)	21 (8.1%)	0.45
Physical activity as MET (kcal/kg*h)	39.18 ± 9.8	38.04 ± 8.00	0.13
Height (cm)	161.91 ± 9.7	159.28 ± 9.07	< 0.01
Weight (Kg)	74.53 ± 14.6	72.21 ± 12.3	0.04
BMI (kg/m^2)	28.44 ± 5.01	28.49 ± 4.64	0.90

MET metabolic equivalent of task

*Comparing continuous and categorical variables in different outcome groups was performed using independent samples t-test and Chi-squared test, respectively

Table 2 Dietary intake of macronutrients and cholin-rich food groups of the participants

	Controls (n = 520)	Cases (n = 258)	P*
Protein (g/day)	72.94 ± 24.83	70.79 ± 25.27	0.31
Total fat (g/day)	60.13 ± 26.38	59.97 ± 23.79	0.93
Carbohydrate (g/day)	393.1 ± 137.8	376.0 ± 134.0	0.14
Energy (Kcal/day)	2365.5 ± 799.5	2279.5 ± 757.9	0.19
Choline (mg/d)	291.34 ± 117.17	233.19 ± 88.53	< 0.01
Dairy products (serving/d)	0.61 ± 0.39	0.54 ± 0.38	< 0.01
Fishes (serving/week)	2.18 ± 0.56	1.18 ± 0.21	0.01
Fruits (serving/d)	1.12 ± 0.72	1.02 ± 0.58	0.03
Vegetables (serving/d)	1.32 ± 0.63	1.26 ± 0.58	0.16

*All comparisons was performed using independent samples t-test

(2.18 ± 0.56 vs. 1.18 ± 0.21 serving/week, P = 0.01), and fruits (1.12 ± 0.72 vs. 02 ± 0.58 serving/d, P = 0.03) (Fig. 1). No difference was found regarding the intake of dietary calories (2365.5 ± 799.5vs. 2279.5 ± 757.9 kcal/d, P = 0.19), protein (72.94 ± 24.83 vs. 70.79 ± 25.27 g/d, P = 0.31), carbohydrate (393.1 ± 137.8 vs. 376.0 ± 134.0 g/d, P = 0.14), fat (60.13 ± 26.38 vs. 59.97 ± 23.79 g/d, P = 0.93), and the consumption of vegetables (1.32 ± 0.63 vs. 1.26 ± 0.58 serving/d, P = 0.16).

As presented in Table 3, there was an inverse association between TGA and dietary intake of choline after adjusting for age and gender (Model 1) (OR: 0.98, CI 95% 0.96–0.99, P = 0.03). Each 1 mg/d increment of dietary choline intake was related to 3% reduction in the odds of TGA. The association remained significant after

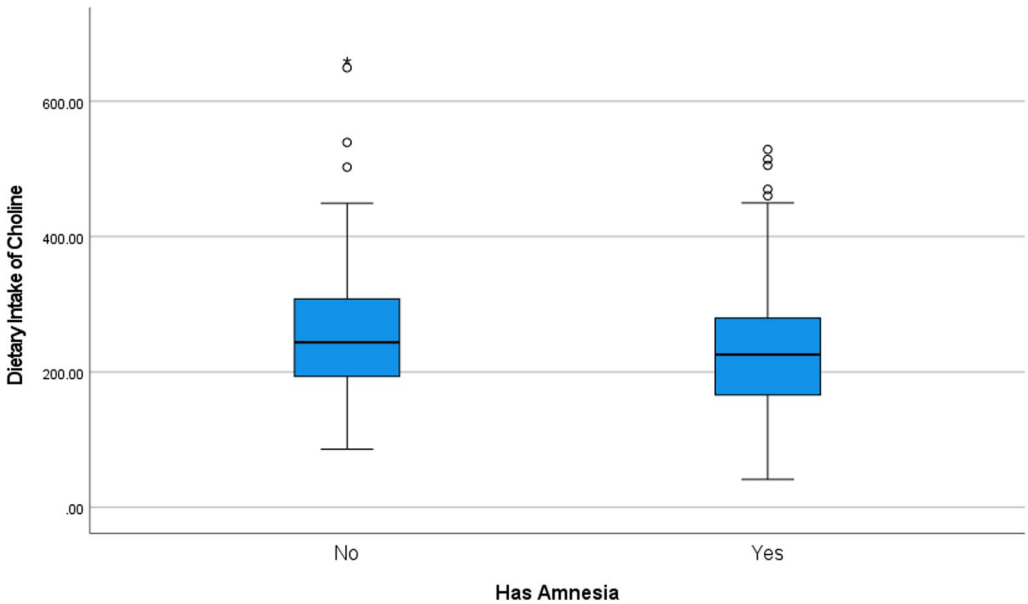


Fig. 1 The amount of dietary intake of choline among patients with amnesia and the controls

Table 3 The association between transient global amnesia (TGA) and dietary intake of choline

	Quantitative		Categorical							
			Quartile 1 < 181.31 mg/d		Quartile 2 181.31–236.25 mg/d		Quartile 3 236.25–293.11 mg/d		Quartile 4 293.11 < mg/d	
	OR (CI 95%)	P	OR (CI 95%)	P	OR (CI 95%)	P	OR (CI 95%)	P	OR (CI 95%)	P
Model 1	0.98 (0.96–0.99)	0.03	1.00	1.00	0.74 (0.45–1.21)	0.23	0.93 (0.56–1.53)	0.77	0.49 (0.3–0.81)	0.01
Model 2	0.98 (0.96–0.99)	0.04	1.00	1.00	0.74(0.45–1.22)	0.24	0.93(0.56–1.53)	0.77	0.49 (0.3–0.82)	0.01
Model 3	0.98 (0.96–0.99)	0.03	1.00	1.00	0.63 (0.38–1.06)	0.08	0.67 (0.39–1.16)	0.15	0.28 (0.15–0.53)	< 0.01

Model 1: adjusted for age and gender, Model 2: additional adjusted for physical activity, BMI, job, marital status, smoking, and drinking alcohol, Model 3: additional adjusted for calorie intake, and consumption of fruits, vegetables, and fishes

additional adjusting for physical activity, BMI, occupation, and marital status (Model 2) (OR: 0.98, CI 95% 0.96–0.99, P = 0.04), and after further adjustment for calorie intake, and the consumption of dairy products, fruits, vegetables, and fishes (Model 3) (OR: 0.98, CI 95% 0.96–0.99, P = 0.01).

In the categorical analysis, choline intake was divided into quartiles. Compared to the lowest quartile (Q1), the highest quartile (Q4) in model 1 had 51% lower odds of TGA (OR: 0.49, CI 95% 0.3–0.81, P = 0.01). Similar results were observed in Model 2 (OR: 0.49, CI 95% 0.3–0.82, P = 0.01). Model 3, with the most comprehensive adjustments, showed that Q4 has 72% lower odds of TGA compared to Q1 (OR: 0.28, CI 95% 0.15–0.53, P < 0.01). This analysis suggests a strong inverse relationship between higher dietary choline intake and the risk of TGA, especially evident in the fully adjusted Model 3. The results of logistic regression indicated that both of dose–response and linear inverse associations exist between dietary intake of choline and TGA.

Discussion

The present study investigated the association between dietary choline intake and TGA. A noteworthy inverse association was observed between choline consumption and TGA, even after adjusting for variables including age, gender, BMI, occupation, marital status, and dietary intake. Few studies have been conducted on dietary choline and TGA, but positive benefits of dietary choline on memory function have been observed in a number of human and animal studies [32, 33]. As an example, one study found that in 14.5-month-old mice were more susceptible to amnesia from anisomycin (ANI) and a choline-enriched diet reduced this susceptibility and prevented ANI-induced amnesia [34]. Also, it has been established that high choline intake throughout pregnancy and the early postnatal period may improve cognitive function in children [35]. During pregnancy, maternal choline level may influence the methylation of fetal DNA and histones [36], suggesting that an epigenomic mechanism is responsible for the long-lasting effects of choline. Moreover, choline intake in adulthood was reported to be neuroprotective in various experimental models of neuronal damage and may be critical for normal cognitive function [37].

Some evidence is now available to support the belief that proper choline consumption is critical for brain development, adult cognitive function, and resistance to the cognitive decline associated with aging and neurodegenerative diseases. Poly et al. in a cohort study found that better verbal memory (VM) and visual memory (VsM) are related to a higher choline intake. In line with our study, a study conducted by Lu Liu et al. found that higher consumption of choline (187.06–399.50 mg/day) was associated with a reduction in the risk of impaired cognitive function by approximately 50% compared to intake at < 187.6 mg/day in people aged > 60 years [38].

Consistent with our results, MPT Ylilauri et al. discovered that in middle-aged and older men in eastern Finland, increased phosphatidylcholine consumption was associated with a decreased risk of dementia and improved cognitive function [39]. A 12-week randomized, double-blind, placebo-controlled study involving Japanese adults aged 60–80 conducted by Soyogu Yamashita et al. demonstrated that daily intake of 300 mg of choline improved verbal memory [40].

The specific mechanism by which choline exerts its influence on TGA is not entirely understood. Dietary choline may have significant effects on brain development and adult brain function through its influence on the peripheral and central metabolism of polyunsaturated species of phosphatidylcholine [41]. Brown et al. [42] suggested that increasing dietary choline intake may potentially decrease brain inflammation caused by both neurodegenerative diseases and the aging. Another study indicated that the combination of choline alphoscerate with a ChE-I (Cholinesterase inhibitors) may enhance the effectiveness of cholinergic therapies in Alzheimer's disease when there is also concurrent ischemic cerebrovascular injury [43]. In another study, Carotenuto et al.

found that patients who received donepezil combined with choline alphoscerate had fewer behavioral problems than those who received donepezil alone [44].

One of the strengths of this study was that it examined dietary choline intake specifically in people with TGA. However, the present study had some limitations regarding measurement bias in diagnosing TGA and recall bias in assessing dietary intake of choline. Further, it is necessary to do a longitudinal study in order to validate these results and uncover the underlying processes that are responsible for the effects of choline on TGA.

Conclusion

In summary, this research provides the first evidence, to our knowledge, for a link between TGA and dietary intake of choline. Our study suggests a potential advantage of choline intake against the risk of TGA. Larger, more definitive studies and randomized controlled trials may bring us closer to a practical dietary approach for prevention of TGA, a primary cause of functional impairment in the adult population.

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Author contributions
SD, MR, MSh, MKM, ZM, ZS and MGH designed the study, and were involved in the data collection, analysis, and drafting of the manuscript. KHAM, MGH, SSH, AR, SKH and AK, AP were involved in the design of the study, analysis of the data, and critically reviewed the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets in the present study are available upon reasonable request from the corresponding author. No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The investigation received approval from the ethics committee of Sabzevar University of Medical Sciences, Sabzevar, Iran (Code 403024). A statement attesting to the adherence of all procedures to the applicable regulations and guidelines. A written informed consent form was completed by every participant at each cohort center. In order to gain access to the study's data, authorization was obtained from the PERSIAN central office, as the information is not available to the public.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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