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Pistachio consumption is associated with some neurocognitive markers in adults - A cross-sectional study

Kristin Fulgoni* **and Victor L. Fulgoni III**

Abstract

Pistachios are a widely consumed healthy and nutrient rich snack. We hypothesized that pistachio, as a source of important nutrients, would be beneficially associated with neurocognitive health. The objective of the current study was to investigate the cross-sectional association of pistachio consumption with cognitive function in a representative sample of the adult population in the US utilizing various National Health and Nutrition Examination Survey (NHANES) 1988-1994, 1999-2018 cycles for adults age 19+ years (n=64,702). Pistachio consumers were defined as individuals who reported a pistachio food code on either day of dietary recalls. Neurocognitive, depression, and anxiety variables were assessed using questionnaire data. Associations between pistachio consumer status and neurocognition were assessed by regression analysis. Less than 1% of adults were pistachio consumers and usual intake of pistachios was 24.6 g/day among adult consumers. Males and younger adults had higher intakes of pistachios than their respective counterparts. Pistachio consumers age 60+ years had a 16% lower frequency of anxiety than non-consumers. Depression/anxiety also caused 60% less difficulties among adult pistachio consumers age 20-59 years compared to non-consumers. Adult consumers (age 19+ years) of pistachios had 48% lower risk (Odds Ratio 0.52, P=0.0465) of having minor depression (20 events) compared to non-consumers. The results of this cross-sectional regression analysis show that pistachio consumption was associated with lower anxiety frequency, fewer difficulties caused by depression/anxiety and reduced risk of having minor depression. Future research is needed to better understand the relationship of pistachio intake with mental health.

Keywords: Anxiety; Depression; National HANES; Pistachios; Neurocognition

List of Abbreviation: HEI: Healthy Eating Index; NHANES: National Health and Nutrition Examination Survey; OR: odds ratios; US: United States

Introduction

Neurocognitive functions are cognitive skills such as attention, memory, processing speed, executive functions and perceptual-motor skills, and are closely linked to neuronal pathways and specific areas of the brain. Cognitive decline is a major cause of disability among older adults. Approximately 66% of older Americans experience some level of cognitive impairment at age 70 years and lifetime risk for dementia is estimated to be 37% for women and 24% for men [1]. The prevalence of dementia and mild cognitive impairment among older adults in the United States (US) have been estimated to be 10% and 22%, respectively [2]. Diet and nutrition are important determinants of

Affiliation:

Nutrition Impact, LLC, Battle Creek, MI 49014, USA

***Corresponding author:**
Kristin Fulgoni, Nutrition Impact LLC, Battle Creek, MI 49014, USA

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cognitive health and is a modifiable risk factor of cognitive impairment [3-6]. The Mediterranean dietary pattern has been associated with improved cognitive function, lower risk of cognitive impairment, dementia, and Alzheimer's disease [7-10]. Consumption of nuts, especially tree nuts, has also been shown to be associated with improvement of cognitive health and prevention of cognitive decline [11-14].

Pistachios are tree nuts and are consumed universally as healthy snacks. They are important sources of unsaturated fatty acids, proteins, dietary fiber, important vitamins (such as vitamins B_6, E, K) and minerals (such as magnesium, potassium, manganese, calcium) and other bioactive phytochemicals (such as phytosterol, lutein, polyphenols) [15-17]. Regular consumption of pistachios has been associated with improved metabolic conditions such as obesity, type 2 diabetes, cardiovascular disease, and metabolic syndrome [15-17]. In clinical studies, intake of pistachios improved diet quality, satiety, glycemic control and decreased cardiometabolic risk factors [18-21]. However, only limited research is available on the role of pistachios on neurocognitive functions or cognitive decline. A couple of animal studies reported that pistachio extract can improve chemically induced cognitive deficits in mice [22] and regular pistachio supplementation may be useful in preventing neurodegeneration caused by a high fat diet in obese mice [23]. Pistachio supplementation for two weeks has been found effective in increasing macular pigment optical density in healthy adults in a clinical study [24]. In a pilot study, supplementation of pistachios for 4 weeks improved mood state, risk tolerance, decision making strategy, executive function and attention along with lowering waist circumference and cholesterol in overweight young adults [25].

The aim of the current research was to examine the cross-sectional association of pistachio consumption at self-selected levels with cognitive function. We hypothesized that pistachio, as a source of important nutrients including bioactive phytonutrients, consumption would be beneficially associated with markers of neurocognitive health. The hypothesis was tested by regression analyses in a representative sample of the adult population in the US using the National Health and Nutrition Examination Survey (NHANES) dataset.

Materials and Methods

Database: NHANES is an ongoing, cross-sectional probability survey of nationally representative US civilian population conducted by the National Center for Health Statistics of the Center for Disease Control and Prevention to monitor nutrition and health status of the US population. Data from eleven NHANES cycles (1988–1994, 1999–2000, 2001–2002, 2003–2004, 2005–2006, 2007–2008, 2009–2010, 2011–2012, 2013–2014, 2015–2016 and 2017–2018) were used for the analysis. NHANES uses a complex stratified multistage cluster sampling probability design and the details of the subject recruitment, survey design, and data collection procedures are available online [26]. All participants provided signed written informed consent forms and NHANES survey protocol was approved by the National Center for Health Statistics Ethics Review Board. This study did not require Institutional Review Board review, as it was a secondary data analysis that lacked personal identifiers. All data obtained from this study are publicly available at: http://www.cdc.gov/nchs/nhanes/ (accessed on 24 October 2024).

Study population: We used the data from free living noninstitutionalized adults age 19+ years participating in NHANES 1988–1994 and NHANES 1999–2018 (n = 76,324). Data from pregnant or lactating females (n = 2,198), those with incomplete dietary data (n = 9,418), and those with zero calorie intake on day 1 (n = 6) were excluded from the analysis and the final sample size was 64,702.

Estimation of dietary intakes: 24 h dietary recall interviews administered using the United States Department of Agriculture's automated, multiple-pass method was used to estimate dietary intakes from foods only (dietary supplement intakes were not included) [27]. Pistachios were defined by using the What We Eat in America food codes for "pistachios": salted pistachios (42114140), lightly salted pistachios (42114142), unsalted pistachios (42114145), pistachios, not further specified (42114130) and food codes for "Other foods" that contain pistachios: mixed nuts, unroasted (42110050), mixed nuts, without peanuts, salted (42110150), mixed nuts, without peanuts, unsalted (42110160). Pistachio consumers were defined as subjects who reported consuming pistachios on either day 1 or day 2 of dietary recalls.

Estimation of Neurocognitive markers: Neurocognition in pistachio consumers and non-consumers was assessed using NHANES questionnaire data [26]. Since the data for different neurocognitive markers were not collected in each NHANES cycle, the analyses for specific neurocognitive markers were limited to the NHANES cycles and age groups in which the markers were available. The following neurocognitive markers were assessed:

A) Neurobehavioral Evaluation System 2 consisting of the Simple Reaction Time Task measuring visuomotor speed, the Symbol Digit Substitution Test measuring information-processing speed and the Single Digit Learning Test measuring learning and recall administered in NHANES III (1988-1994) were used to measure cognitive function in adults age 20-59 years.

B) Data on the Consortium to Establish a Registry for Alzheimer's Disease Word List Learning Test, the Consortium to Establish a Registry for Alzheimer's Disease Word List Recall Test, the Animal Fluency test, and the Digit Symbol Substitution Test (administered

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in 1999-2002 as well) were administered in NHANES 2011-2014 to measure cognitive function in adults age 60+ years.

C) Response to the question "During the past 7 days, how often have you had trouble remembering where you put things like keys or wallet?" was administered in NHANES 2011-2014 to assess memory impairment and its severity as a measure of dementia in adults age 60+ years. This variable is labeled "Trouble remembering score (0-4)".

D) The Diagnostic and Statistical Manual of Mental Health 4th edition signs and symptoms of depression [28,29] administered in NHANES 2005-2018 was used to measure depression in adults aged 18-85 years. Severity of depression was judged using Diagnostic and Statistical Manual of Mental Health 4th edition defined cutoffs criteria (≥10 points for minor depression or higher; 10-14 points for minor depression/major depression, mild; 15-19 points for major depression, moderate; >19 points for major depression, severe). Additionally, responses to the question "How difficult have these problems made it for you to do your work, take care of things at home, or get along with people?" administered in NHANES 2005-2018 with respondents 18-85 y was used as a measure of depression level. This variable is labeled "Depression level (1-5)".

E) The level of difficulty depression is causing was determined based on responses to the question "Think about how your life and activities were affected in the past 12 months by your being sad/depressed or empty/losing interest in most things or being irritable and other related problems. Did these problems interfere with your life or activities?" administered in NHANES 2001-2018 in adults age 18-85 years. This variable is labeled "Depression/anxiety causing difficulty".

F) Responses to the questions "How many months out of the last 12 did you feel worried or tense or anxious most days?" (variable label: "Worried or tense months in last 12 (0-12)"), "Have you had an attack like this (panic attack) in the past 12 months?" (variable label: "Panic attack last 12 months (Yes=1; No=0)"), and "Do panic attacks interfere with daily life?" (variable label: "Panic attack effect (0-4)") administered in NHANES 1999-2004 were used to measure anxiety in adults age 20-39 years.

G) Responses to the question "How often do you feel worried, anxious?" (variable label: "Frequency of anxiety") administered in NHANES 2015-2018 in adults 18 years and older was used as an additional measure of anxiety.

Statistical analyses

All analyses were performed using SAS 9.4 (SAS Institute, Cary, NC, USA) software after adjusting the data for the complex sampling design of NHANES using appropriate survey weights, strata, and primary sampling units. Usual intakes of pistachios were determined by the 2-part (amount and frequency) National Cancer Institute method [30]. Least square means +/- standard errors were generated via regression analyses for neurocognitive outcomes in pistachio consumers and non-consumers. Odds ratios (lower confidence level, upper confidence level) for depression severity were calculated based on number of events. Age, gender, ethnicity, physical activity level, poverty income ratio level, weight status, and current smoking status were used as covariates (Model 1). The Healthy Eating Index (HEI) 2015 total score was added as an additional covariate in Model 2; and consumption of "other foods" with pistachios was added as an additional covariate in Model 3. A p-value of <0.05 was used for statistical significance.

Results

Pistachio intake

Less than 1% of adults aged 19+ years were pistachio consumers. Usual intake of pistachios was 24.6 ± 0.7 g/day among adult consumers 19+ years (**Table 1**). Adult male consumers 19+ years consumed 6 g/day more pistachios than adult female consumers and younger adult consumers 20-39 years consumed 8 g/day more pistachios than older adult (60+ years) consumers. The 90th percentile of pistachio usual intake was 41.6 ± 2.3 g/day for adult consumers 19+ years (**Table 1**). Per capita usual intake of pistachios was 0.16 ± 9.3 g/day among adults 19+ years (data not shown).

Associations between Pistachio Consumption and Neurocognitive Variables

Table 2 shows the differences in neurocognitive outcomes among pistachio consumers and non-consumers. In adults 60+ years, consumers of pistachios (n=29) had a 16% lower frequency of anxiety compared to non-consumers after adjusting the data in Model 1 and the differences remained significant after additionally adjusting the data for HEI 2015 scores in Model 2 and for consumption of "other foods" with pistachios in Model 3. Depression/anxiety also caused less difficulties (60% less) among pistachio consumers aged 20-59 years (n=213) as compared to non-consumers. The differences remained significant after additionally adjusting the data for HEI 2015 scores in Model 2 and for consumption of "other foods" with pistachios in Model 3. Results assessing association of pistachio consumption with all other neurocognitive markers were not significant.

Table 3 provides odds ratios (OR) of severity of depression among adult pistachio consumers aged 19+ years (n=269). OR were calculated based on the proportional number of "events". Adult consumers of pistachios had about 50% lower risk (OR 0.52, P=0.0465) of having minor depression (20 events) compared to non-consumers after adjusting the data in Model 1. Odds of having minor depression also remained

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Table 1: Usual intake (g/day) of pistachios among adult consumers by age and gender.

Age		N	Mean	33rd Percentile	67th Percentile	90th Percentile
19+ years	All	337	24.6 ± 0.7	18.2 ± 1.3	30.0 ± 1.2	41.6 ± 2.3
	Male	175	27.5 ± 0.8	20.9 ± 0.9	30.1 ± 0.8	41.5 ± 2.7
	Female	162	21.5 ± 0.9	12.3 ± 1.4	25.5 ± 1.9	40.2 ± 0.8
20-39 years	All	102	28.2 ± 1.7	20.2 ± 2.6	36.1 ± 3.0	46.5 ± 4.5
	Male	46	33.2 ± 0.4	28.8 ± 0.5	36.7 ± 0.9	48.0 ± 0.3
	Female	56	23.6 ± 0.9	13.0 ± 1.2	30.3 ± 1.2	41.7 ± 3.1
20-59 years	All	220	26.1 ± 0.8	18.5 ± 1.3	31.7 ± 1.2	43.1 ± 1.9
	Male	109	30.0 ± 0.9	23.3 ± 1.4	34.6 ± 1.4	43.7 ± 2.2
	Female	111	22.1 ± 1.1	12.4 ± 1.4	27.6 ± 1.8	41.7 ± 1.4
60+ years	All	111	20.2 ± 0.7	14.2 ± 1.4	24.1 ± 1.2	32.7 ± 1.6
	Male	61	20.6 ± 0.5	18.7 ± 1.1	24.1 ± 1.3	26.8 ± 0.5
	Female	50	19.7 ± 0.1	8.2 ± 0.2	23.0 ± 0.1	37.6 ± 0.03

NHANES 1988-1994, 1999-2018. Data presented as Mean ± Standard Error.

Table 2: Associations between Pistachio Intake and Neurocognitive Variables in adults (male and female combined).

Neurocognitive Variable	NHANES Cycles	Age (years)	Non-consumers		Consumers		Consumers Vs Non-consumers		
			N	LSM ± SE	N	LSM ± SE	$P_{Model\ 1}$	$P_{Model\ 2}$	P_{Model3}
Measures of Cognitive Function									
Simple Reaction Time Task (msec)	1988-1994	20-59	4,463	233 ± 1	0	NA	NA	NA	NA
Symbol Digit Substitution Test (sec/digit)	1988-1994	20-59	4,414	2.66 ± 0.02	0	NA	NA	NA	NA
Single Digit Learning Test score	1988-1994	20-59	4,326	4.38 ± 0.11	0	NA	NA	NA	NA
Word list learning score (0-30)	2011-2014	60+	2,573	19.6 ± 0.2	24	21.0 ± 1.0	0.1768	0.2356	0.1768
Word list recall score (0-10)	2011-2014	60+	2,571	6.21 ± 0.09	24	6.71 ± 0.56	0.3782	0.4203	0.3782
Animal fluency score (0-40)	2011-2014	60+	2,574	18.1 ± 0.2	23	17.9 ± 1.3	0.8828	0.6561	0.8828
Digital symbol subst. score (0-133)	1999-2002	60+	4,691	50.3 ± 0.3	30	53.8 ± 2.4	0.1461	0.2555	0.1476
Trouble remembering score (0-4)	2011-2014	60+	2,748	0.72 ± 0.02	25	0.50 ± 0.15	0.1850	0.2121	0.1850
Depression Measures									
Depression screening score (0-27)	2005-2018	19+	29,793	3.08 ± 0.04	255	3.50 ± 0.44	0.3273	0.2285	0.3277
		20-59	19,155	3.22 ± 0.05	163	3.34 ± 0.33	0.7134	0.4916	0.7120
		60+	9,775	2.68 ± 0.06	89	3.78 ± 1.26	0.3837	0.3419	0.3850
Depression level (1-5)	2005-2018	19+	9,793	1.35 ± 0.01	255	1.45 ± 0.09	0.2449	0.1776	0.2453
		20-59	19,155	1.37 ± 0.01	163	1.42 ± 0.08	0.5779	0.4351	0.5773
		60+	9,775	1.29 ± 0.01	89	1.51 ± 0.22	0.3106	0.2750	0.3124
Depression/anxiety causing difficulty (Yes=1; No=0)	2001-2018	19+	43,497	0.04 ± 0.001	320	0.04 ± 0.02	0.8232	0.9368	0.8223
		20-59	27,625	0.05 ± 0.002	213	0.02 ± 0.01	**0.0001**	**0.0005**	**0.0001**
		60+	14,365	0.04 ± 0.003	102	0.11 ± 0.07	0.3111	0.3023	0.3127

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Anxiety Measures									
Panic attack last 12 months (Yes=1; No=0)	1994-2004	20-39	1,638	0.15 ± 0.01	11	0.32 ± 0.21	0.4324	0.4027	0.4328
Panic attack effect (0-4)	1994-2004	20-39	1,533	0.22 ± 0.03	11	0.91 ± 0.62	0.2701	0.2496	0.2703
Worried or tense months in last 12 (0-12)	1994-2004	20-39	1,638	0.79 ± 0.09	11	2.08 ± 1.07	0.2411	0.2253	0.2414
Frequency of anxiety	2015-2018	19+	8,466	2.81 ± 0.02	93	2.64 ± 0.21	0.4605	0.5322	0.4578
		20-59	5,359	2.92 ± 0.03	63	2.83 ± 0.28	0.7717	0.9034	0.7717
		60+	2,917	2.51 ±0.03	29	2.11 ± 0.11	**0.0027**	**0.0025**	**0.0027**

Data presented as Least Square Mean (LSM) ± SE (standard error) after adjusting for age, gender, ethnicity, physical activity level, poverty income ratio, weight status, current smoking status (Model 1). The Healthy Eating Index 2015 score was added as an additional covariate in Model 2; and consumption of "other foods" with pistachios was added as an additional covariate in Model 3. NA, Data not available as zero consumers. A p-value of <0.05 was considered significant.

Table 3: Odds ratios (OR) of severity of depression among adult pistachio consumers age 19+ years.

Depression Severity	Non-consumers (n=32,787)		Consumers (n=269)		Consumers Vs Non-consumers		
	Events	OR	Events	OR (95th CI)	$P_{Model\ 1}$	$P_{Model\ 2}$	P_{Model3}
Minor Depression	2,885	1.00	20	0.52 (0.28, 0.99)	**0.0465**	**0.0255**	**0.0472**
Mild Depression	1,793	1.00	15	0.55 (0.25, 1.22)	0.1399	0.0893	0.1414
Moderate Depression	783	1.00	4	0.42 (0.10, 1.77)	0.2363	0.2177	0.2372
Severe Depression	309	1.00	1	1.82 (0.25, 13.35)	0.5534	0.6899	0.5516

NHANES 1988-1994, 1999-2018. Depression severity was defined using the DSM-IV defined cutoffs for depression severity (≥10 pts for minor depression; 10-14 pts. mild depression, 15-19 moderate depression, >19 severe depression). Odds ratios (OR) were calculated based on number of events. Data were adjusted for age, gender, ethnicity, physical activity level, poverty income ratio, weight status, current smoking status (Model 1). The Healthy Eating Index 2015 score was added an additional covariate in Model 2; and consumption of "other foods" with pistachios was added as an additional covariate in Model 3. A p-value of <0.05 was considered significant.

significantly less than 1.00 after additionally adjusting the data for HEI 2015 scores in Model 2 and for consumption of "other foods" with pistachios in Model 3. There were no significant differences in OR for the risk of developing mild, moderate or severe depression between pistachio consumers and non-consumers.

Discussion

Results of the present analysis of NHANES (1988–1994, and 1999–2018) covering over three decades indicates that less than 1% of US adults consume pistachios and their intake was about 25 g/day. The regression analysis indicated that after adjusting the data for various demographic, lifestyle, dietary, and health-related factors, pistachio intake was inversely associated with frequency of anxiety, pistachio consumers experience less difficulties due to depression/ anxiety and possibly had a lower risk of minor depression. To the best of our knowledge, this is the first large representative study of pistachio intake at self-selected levels and cognitive functions using all available cognitive data across multiple NHANES surveys.

Anxiety is defined as an unpleasant state of inner turmoil, anticipation of a future threat or a feeling of fear or uneasiness. Anxiety disorders include generalized anxiety disorder, panic disorder, social anxiety disorder and various phobia-related disorders and are the most common mental health disorders [31]. A recent analysis of 2019 US National Health and Wellness Survey database estimated that 44% of US adults experience anxiety symptoms [32]. Anxiety disorders can impact brain structure and function, affect daily activities such as job performance, schoolwork, and relationships and may lead to decreased quality of life [31,33]. There is growing scientific evidence that anxiety may also increase the risk of chronic general medical conditions such as digestive issues, heart disease, stroke, hypertension, chronic pain and obesity [34-36] and the risk of dementia [37]. The present regression analysis of cross-sectional data from NHANES shows that the adults who consume pistachios had a lower frequency of anxiety, experience less difficulties due to depression/ anxiety and possibly had a lower risk for minor depression compared to adults who do not consume pistachios. Diet has been reported to be a critical factor for anxiety and depression [38-40]. Healthy dietary patterns such as Mediterranean diet containing nuts and seeds along with fruit and vegetables have been associated with a lower risk of anxiety disorders [41,42]. Consumption of nuts and legumes were also independently associated with improved mood and lowered

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risk of anxiety and depression in some studies [43-45]. A pilot uncontrolled human feeding study with 30 young adults reported that intake of 30 g pistachios per day for 4 weeks was associated with improved mood with decreased anxiety, anger-hostility and sadness-depression [25]. The present study is the first analysis of a large nationally representative population of over 64,000 adults achieved and demonstrated that consumption of pistachios at self-selected levels is associated with decreased anxiety. However, we did not find any significant effects of pistachio intake on other measures of cognitive function in our regression analysis.

A major strength of this study includes the fact that the evidence of the effect of pistachios intake on anxiety was obtained using a nationally representative population-based sample of adults achieved through combining several sets of NHANES across over three decades of survey cycles. Additionally, we used several covariates to adjust data to remove potential confounding factors; however, even with these covariates, some residual confounding may still exist. A major limitation of this study is the use of cross-sectional study design, which might be biased by underlying differences between the groups and cannot be used to determine cause and effect. The use of self-reported 24 h dietary recalls relying on memory is prone to a potential source of bias for reporting of intake. While the 24-hour dietary recall data in NHANES was collected using one of the best available and validated methodology, the automated, multiple-pass method, there are still limitations with it [46]. Additionally, while the total sample size was very large, the number of pistachio consumers was a small fraction of the total sample size. As such, these results are likely best used for hypothesis generation for future research, to inform analyses of other large health and nutrition databases that have mental health variables, and to inform design of future clinical trials which are required before firm conclusions regarding the impact pistachio consumption on neurocognition can be made.

Conclusion

In conclusion, the results of this cross-sectional regression analysis show that while pistachio consumption was not associated with many of the neurocognitive measures, it was inversely associated with anxiety among adults. Future research is needed to better understand the relationship of pistachio intake with mental health.

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Conflicts of interest

KF and VLF at Nutrition Impact LLC perform consulting and database analyses for various food and beverage companies and related entities.

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