J Nutr Health Aging
Volume 19, Number 3, 2015

A CROSS SECTIONAL STUDY OF THE ASSOCIATION BETWEEN WALNUT CONSUMPTION AND COGNITIVE FUNCTION AMONG ADULT US POPULATIONS REPRESENTED IN NHANES

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Abstract: *Objective:* To examine the association between walnut consumption and measures of cognitive function in the US population. *Design:* Nationally representative cross sectional study using 24 hour dietary recalls of intakes to assess walnut and other nut consumption as compared to the group reporting no nut consumption. *Setting:* 1988-1994 and 1999-2002 rounds of the National Health and Nutrition Examination Survey (NHANES). *Population:* Representative weighted sample of US adults 20 to 90 years of age. *Main Outcome Measure:* The Neurobehavioral Evaluation System 2 (NES2), consisting of simple reaction time (SRTT), symbol digit substitution (SDST), the single digit learning (SDLT), Story Recall (SRT) and digit-symbol substitution (DSST) tests. *Results:* Adults 20-59 years old reporting walnut consumption of an average of 10.3 g/d required 16.4ms less time to respond on the SRTT, P=0.03, and 0.39s less for the SDST, P=0.01. SDLT scores were also significantly lower by 2.38s (P=0.05). Similar results were obtained when tertiles of walnut consumption were examined in trend analyses. Significantly better outcomes were noted in all cognitive test scores among those with higher walnut consumption (P < 0.01). Among adults 60 years and older, walnut consumers averaged 13.1 g/d, scored 7.1 percentile points higher, P=0.03 on the SRT and 7.3 percentile points higher on the DSST, P=0.05. Here also trend analyses indicate significant improvements in all cognitive test scores (P < 0.01) except for SRTT (P = 0.06) in the fully adjusted models. *Conclusion:* These significant, positive associations between walnut consumption and cognitive functions among all adults, regardless of age, gender or ethnicity suggest that daily walnut intake may be a simple beneficial dietary behavior.

Key words: Cognition, cognitive decline, cognitive function, NHANES, diet, walnut, nuts, epidemiology, nutrition.

Introduction

Despite the evidence that specific macronutrients can affect cognitive performance (1-3), evidence linking consumption of specific foods to cognitive functioning is limited (4). The relationship between Mediterranean diet, defined by high consumption of fruits, vegetables, legumes and nuts, moderate consumption of fish and wine, low consumption of dairy products and meat, and intake of olive oil, and cardiovascular disease risk has recently attracted attention (5). This dietary pattern has also been associated with lower risk of cerebrovascular disease (6) and working memory (7). Mediterranean diets are also associated with lower rates of dementia (8, 9), and other neurodegenerative diseases such as Alzheimer's disease (AD) (10) and Parkinson's disease (11). Basic research suggests that naturally occurring phyto-compounds, such as polyphenolic antioxidants found in fruits, vegetables, herbs and nuts, may potentially inhibit or slow down neurodegeneration, and improve cognitive function (12).

Among the characteristic Mediterranean foods, walnuts have been associated with neuroprotective effect against AD (12). Amyloid beta-protein is the principal component of amyloid plaques in the brains of patients with AD (13). In cell lines, walnut extract reduces amyloid beta protein-induced oxidative stress and cell death (13, 14). These research findings suggest that a diet rich in walnuts may help prevent and delay the onset of AD (12, 14). The aim of this research is to examine the evidence of potential neuroprotective effects of walnut consumption at self-selected levels on cognitive function in a representative sample of the adult population in the United States (US).

Methods

NHANES Study Populations

The National Health and Nutrition Examination Surveys (NHANES) are cross-sectional, probability surveys consisting of the US civilian population ages 1 to 90 years old. In the NHANES III (1988-1994) study, 20,050 individuals were surveyed and provided information on sociodemographic and medical history information. These participants were later invited to participate in part II of the survey at a mobile examination center (MEC) for the collection of biological samples, physical examinations, and physiological tests. There, a random sample of adults 20-59 years old (n =5662) completed central nervous system (CNS) evaluation tests, which included three measures of cognitive function – the simple reaction time test (SRTT), the symbol digit substitution test (SDST), the single digit learning test (SDLT) and a random sample of adults 60 years and older (n=5054) were administered the story recall test (SRT). In a later NHANES conducted between 1999 and 2002, 2,975 adults 60 years and

Received September 4, 2014
Accepted for publication October 17, 2014

older completed the digit-symbol substitution test (DSST). Participants who could not speak either English or Spanish or who were legally blind were not tested. This analysis also excluded participants who had a stroke or a neurological disorder. All individuals that completed a cognitive test and the 24 hour recall data from all survey rounds composed of both tests from NHANES data (1988 to 1994 and 1999-2002) were included in this analysis.

Measures of Cognitive Function

The cognitive function evaluation component of NHANES III used the NES2, a validated computerized cognitive function test battery. The NES2 consisted of three test components given to individuals 20 to 59 years of age: a) SRTT, b) SDST, and c) SDLT (15).

The SRTT measures visuomotor speed by examining the individual's response time to a random presentation of specific visual symbols over a number of trials. Each selected participant completed 50 consecutive trials of the SRTT. The mean latency (in milliseconds) of these 50 trials was obtained and this mean SRTT score provides one of the outcome measures used in this analysis.

The SDST measures information-processing speed, concentration and motor control by having participants memorize nine symbols matched to integers 1 to 9. The symbols are then shown in a random order and the participant is responsible for providing the corresponding digit as quickly as possible from memory. Four trials of the SDST tests were given to each participant and the number of errors and the corresponding length of time needed for completion for each trial (in seconds) were recorded. The SDST measure, provided by NHANES and used in this analysis, consists of the averages between two of the four trials with the lowest scores.

The third cognitive test in this battery is the SDLT, which measures learning and recall by having participants memorize a predefined sequence of numbers and later tests their ability to repeat the sequence consecutively with as few errors as possible. An overall summary score was calculated based on how many trials needed were completed and how many errors were observed in each trial. The SDLT total score ranged from 0 to 16, with "0" corresponding to fewest and greatest success in the trials and "16" corresponding to the maximum number of trials with the least success in the trials.

Independently, among adults 60 years and older, instead of administering the NMES2 in NHANES III, a story recall (SR) test was used as a test of cognitive attention and delayed verbal memory (16, 17). In the SR tests, participants were informed that a short story would be read to them, and that subsequently they would be asked to repeat the story back to the interviewer. After the participants repeated the details of the story back to the interviewer, the interviewer continued with several other questions unrelated to the story. Participants were then finally asked to repeat the details of the story again for a second time. The SR tests assessed the ability of the participant to remember details from stories narrated to them by the interviewer and were scored according to the number of correct story ideas recalled by the participants.

A different cognitive test, the DSST, was administered to adults 60 years and older in a later NHANES survey; in 1999 to 2002 (17, 18). The DSST assessed response speed, sustained attention, visual spatial skills and associative learning and memory (19). Individuals taking the DSST were given 2 minutes to correctly code a series of symbols. Extensive details on the administration of these tests and performance within

Table 1

Weighted demographic characteristics of NHANES by walnuts, walnuts and other nuts and no nut consumers with cognitive tests and 24H recall data across two surveys for 20-59 and those 60 and older [1]

	Age 20 to 59 y (NHANES III, 1988-94)			Age 60 & up (1988-1994)			Age 60 & up (1999-2002)		
	Walnuts with high certainty (WWHC)	Walnuts with other nuts (WWON)	No nuts (NRNC)	Walnuts with high certainty (WWHC)	Walnuts with other nuts (WWON)	No nuts (NRNC)	Walnuts with high certainty (WWHC)	Walnuts with other nuts (WWON)	No nuts (NRNC)
	(N= 133)	(N=562)	(N=4,661)	(N=58)	(N=120)	(N=4619)	(N= 44)	(N=73)	(N=2,423)
Age, y (SD)	37.6 (10.6)	37.7 (10.9)	36.8 (10.9)	70.9 (8.2)	70.3 (7.8)	70.6 (8.2)	69.2 (8.2)	68.8 (79)	70.8 (7.9)
Gender, %									
Females	53.8%	57.1%	51.6%	57.5%	52.3%	57.8%	67.0%	46.6%	57.4%
Males	46.2%	42.9%	48.4%	42.5%	47.7%	42.2%	33.0%	53.4%	42.6%
Race/Ethnicity%									
White	80.4%	83.6%	75.4%	93.9%	94.5%	83.5%	93.3%	92.1%	82.2%
African-Americans	7.2%	7.6%	11.7%	5.2%	3.0%	8.8%	2.3%	3.0%	7.2%
Hispanics	0.2%	1.7%	6.0%	0.9%	0.9%	2.4%	4.4%	2.1%	8.4%
Others	12.2%	7.1%	6.9%	0.0%	1.6%	5.3%	0.0%	2.8%	2.2%
Education, y (SD)	13.3 (3.7)	13.4 (3.1)	12.7 (3.9)	12.2 (3.9)	12.7 (3.8)	10.9 (4.5)	12.1 (3.9)	12.4 (3.4)	10.8 (4.1)
BMI, kg/m2 (SD)	25.2 (5.9)	26.1 (6.1)	26.6 (5.5)	28.2 (5.8)	26.5 (5.3)	26.9 (5.2)	25.7 (4.7)	26.9 (4.8)	27.2 (5.2)
Smoker, current	37.7%	42.3%	32.3%	7.2%	12.4%	15.6%	1.3%	2.1%	12.9%
Ever drink Alcohol	79.9%	89.3%	88.0%	86.8%	89.8%	77.0%	86.5%	81.9%	77.4%
Number of alcoholic drinks (SD)	1.5 (1.5)	1.5 (2.9)	2.1 (3.2)	1.1 (1.9)	0.9 (1.5)	0.8 (2.4)	1.0 (0.9)	1.0 (1.1)	0.9 (1.7)
Grams Walnuts, g (SD)	10.3 (12.3)	9.03 (11.2)	0	13.1 (19.6)	9.24 (11.9)	0	12.9(17.3)	9.47 (10.3)	0

1. Data presented as weighted means with standard deviations in parentheses unless reported as percentage of individuals with this characteristic in that survey or age group.

NHANES can be found elsewhere (15-19).

Dietary Intake Assessment

Dietary intake was also assessed in the Mobile Examination Center using an automated 24 hour recall applying the multi-pass approach. The amount of food consumed were recalled by survey participants with the help of portion images, measuring cups and rulers. Survey participants were requested to report all foods and beverages consumed during the past 24 hours from midnight to midnight (20-22). The food codes used for identifying walnut consumption are listed in Table 2. Consumers were characterized based on their consumption of walnuts with high certainty (WWHC) and walnuts with other nuts (WWON). In order not to confound the outcome of the analyses among walnut consumers (WWHC and WWON), participants who consumed other nuts exclusively (i.e., peanuts, almonds, cashews, etc.) and did not consume any walnut in the dietary assessments were excluded from the analyses (N=1496). In the analysis, we calculated the total grams of walnuts consumed for WWHC and WWON. The comparison group in the analyses consisted therefore of all individuals not reporting nut consumption (NRNC) in their 24 hour recalls.

Statistical Analysis

Data from adults ages 20 years and older from NHANES III (1988-1994) were used in the analysis. We also used NHANES 1999-2002 to assess cognitive skills using DSST among adults 60 years of age and older. Sampling weights were used to account for sampling variability and to adjust for differential probability of selection of persons for the complex sampling design. Descriptive statistics were generated to examine how covariate values varied across cognitive test outcomes using weighted means. Separate multiple linear regression analyses with SRTT, SDST, SDLT, SR test and DSST as dependent variables, and WWHC and WWON as independent binary predictor variables were initially performed. SRTT, SDST, and SDLT scores were first analyzed as continuous measures. However, based on an assessment of residuals, the SRTT, SDST and SDLT were log transformed and retransformed to obtain approximate normal distribution for regression analysis. For the SR and DSST tests, the distributions of the scores were also not normally distributed. Log transformation of the variables, however, was not feasible since participants can score 0 in these tests and would drop out of the analysis with log transformation. Rank percentiles of scores for SR and DSST were used in the analysis (23). Instead of using the raw scores, test scores were ranked accordingly in quintiles. Participants who scored in the 1st, 2nd, 3rd, 4th and 5th quintile were scored 90, 70, 50, 30 and 10, respectively. A higher rank percentile score corresponds to better performance in these cognitive tests. No further data transformation was needed for the SR and DSST percentile scores since these measures were normally distributed. The grams of walnuts consumed for WWHC were examined as tertiles ranging from > 0 to 5 g, > 5 g to 11 g, and > 11 g, corresponding to the lowest, middle and highest tertiles. For WWON, the lowest, middle and highest tertiles were > 0 to 4 g,> 4 g to 7.7 g and > 7.7 g, respectively. Trend tests for the tertile groups were examined by obtaining the joint significance of the groups using regression analyses, and the significance of the trend is indicated by P-trend in the tables.

This study also examined a range of covariates in the regression analysis based on their potential associations with the three cognitive measures. The covariates this study selected are thought to be broad representations of the constructs of socioeconomic status, as well as physical activity, fitness and risk behaviors including smoking, and consumption of alcohol. All of these factors have been shown to be associated with cognition in nationally representative data (12, 23). Demographic variables, including gender, age, and reported ethnicity (White, African-American, Hispanic or other race), were also included as additional covariates.

Results

The demographic characteristics of the walnut consumers are shown in Table 1. Among the 20 to 59 year old participants interviewed in 1988-1994, the weighted average age among WWHC consumers was slightly higher at 37.6 v. 36.8 years for no nut consumers, with 2.2% more females (53.8% v. 51.6%) and 5% more whites (80.4% v. 75.4%) consumed WWHC than those NRNC. WWHC averaged more years of education (13.3 v.12.7), and a 1.4 lower average BMI (25.2 v. 26.6) than the NRNC group. Similarly, among the 60 years and older participants interviewed in 1988-1994, the weighted average age among WWHC consumers was 70.9 years v. 70.6 years for no nut consumers, 57.5% v. 57.8% were females, and 10.4% more were white (93.9% v. 83.5%). They averaged 1.3 more years of education (12.2 v. 10.9) and 1.3 higher BMIs (28.2 v. 26.9). Among the 60 years and older participants interviewed in 1999-2002, the weighted averages were largely similar. The age among WWHC consumers was 69.2 years v. 70.8 years for no nut consumers, 9.6% more were females (67.0% v. 57.4%) and 11.1% more were white (93.3% v. 82.2%). They also averaged 1.3 more years of education (12.1 v. 10.8) but their BMIs were 1.5 lower (25.7 v. 27.2) than those of the group NRNC.

The foods contributing to the categorization of walnut consumption by age and survey are presented in Table 2. The vast majority of walnut consumption in the WWHC group came from plain walnuts (79.7%), followed by walnut cake (33.0%) among those under 60 years old. Fruit, salad or oatmeal mixed in with walnuts composes 15.8% of the total reported walnut food codes. In the older WWHC consumers walnuts also contributed to 59.8% food codes used in identifying WWHC.

In the WWON group, more than 50% of walnut consumption stems from muffins with walnuts. The rest

Table 2
Food Codes Contributing to the classification of Walnuts with high certainty (WWHC) and walnuts with other nuts (WWON)

WWHC			**20 - 59 y**		**60 y+**
Walnuts with high certainty	**Description**	**N**	**Mean weight consumed, g (SD)**	**N**	**Mean weight consumed, g (SD)**
4211600	Walnuts, plain	106	14.3 (23.2)	61	14.4 (20.7)
5311720	Walnut cake with whipped Cream	44	45.1 (38.7)	12	59.8 (59.3)
5722100	Fruit and fiber with walnut	14	57.9 (27.2)	6	46.7 (23.0)
5444	Salad, apple with celery and walnuts	5	68.6 (52.9)	13	96.6 (43.8)
4503	Oatmeal, instant fortified with raisin, date and walnut	2	177 (14.1)	14	191.4 (93.1)
4211610	Honey roasted walnut	1	2	0	---
5730816	Mueslix with walnut	1	59	0	---
	Total	133		102	
WWON		**20 - 59 y**	**60 y+**		
Walnuts with other nuts (includes walnuts with certainty and other nut mixes)	**Description**	**N**	**Mean weight consumed, g (SD)**	**N**	**Mean weight consumed, g (SD)**
5230201	Muffin, fruit and/or nuts	305	66.2 (40.3)	85	58.9 (33.8)
5240510	Bread, fruit, nut	54	57.7 (45.7)	24	61.9 (47.3)
4211010	Mixed nuts, roasted, with peanuts	48	27.2 (33.3)	22	38.0 (38.2)
5116105	Roll, sweet, with nuts, frosted	44	72.6 (68.4)	21	79.2 (83.9)
4250100	Nut mixture with dried fruit and seeds	35	76.6 (59.2)	6	26.3 (15.0)
5116120	Roll, sweet, with nuts, no frosting	22	49.9 (31.3)	5	61.8 (9.31)
4211015	Mixed nuts, roasted, without peanuts	18	54.2 (29.7)	11	53.1 (38.0)
5324160	Cookie, butter or sugar cookie, with fruit and/or nuts	16	21.9 (24.3)	20	20.8 (18.6)
5116115	Roll, sweet, with fruit and nuts, frosted	15	86.7 (74.1)	4	129.0 (115.5)
4211020	Mixed nuts, dry roasted	14	70.9 (73.6)	18	43.6 (34.8)
5321100	Cookie bar, with chocolate, nuts, and graham crackers	9	41.3 (38.2)	3	64.7 (39.1)
5230420	Muffin, oat bran with fruit and/or nuts	9	84.6 (33.9)	5	72.4 (33.3)
9170505	Mixed chocolate candy with fruits and nuts	8	52.5 (39.8)	2	25.3 (10/9)
5130182	Bagel, wheat, with fruit and nuts	8	71.1 (47.3)	3	81.7 (21.7)
4250200	Mut mixture with seeds	5	43.4 (15.9)	2	40.5 (7.8)
5240300	Bread, nut	5	31.4 (17.0)	3	37.3 (16.2)
5230702	Muffin, multigrain, with nuts	3	55.0 (19.1)	0	---
5311531	Cake, nut, without icing	3	19.0 (4.6)	2	21.5 (2.1)
5311532	Cake, nut, with icing	3	226 (218)	0	---
5116110	Roll, sweet, with fruit and nuts, no frosting	3	55.7 (39.8)	2	61.5 (54.4)
5240601	Bread whole wheat with nuts	2	13.0 (5.7)	2	57.5 (57.3)
5320560	Cookie, caramel coated, with nuts	1	28	0	---
5338560	Pie, praline mousse, with nuts	1	77	1	77
5312050	Cake, whole wheat, with fruit and nuts, without icing	1	24	1	79
5116670	Croissant, nut	1	22	0	---
5112190	Bread, NFS, high fiber with fruit and nuts	1	56	0	---
5112191	Bread, NFS, high fiber, w/ fruit and nut, toasted	1	50	0	---
	Total	562		193	

were largely other breads, and grain based desserts including pastries, cakes and cookies. Other mixed nuts contributed 21.4% of food codes in the younger and 30.6% of food codes among those aged 60 or above.

Table 3 displays the weighted mean cognitive test values by WWHC, WWON and no nut consumption. The weighted mean and median scores among those 20 to 59 years old indicate that the WWHC group had the fastest response time, followed by the WWON group. The no nut consumers had the highest mean and median scores which correspond to the slowest response time for SRTT, SDST and SDLT. Among those 60 years and older, WWON group had the highest percentile scores in terms of SR test (55.5) and DSST (59.6), followed by the WWHC group with SR test percentile of 53.1 and DSST percentile score of 59.1. The no nut consumers had the lowest percentile scores in SR test (44.8) and in DSST (47.8).

The predicted difference in cognitive function by walnut consumption after adjusting for the covariates age and gender, race, physical activity, smoking and alcohol intake for SRTT, SDST and SDLT are shown in Table 4. With the exception of SDST, most of the results were consistent with the results from the unadjusted means and medians, WWHC consumers had significantly faster response time compared to no nut consumers. Similarly, the WWON group also had a significantly faster response time compared to no nut consumers. In terms of the magnitude, WWHC had the highest difference. WWHC had the fastest response time relative to no nut consumers for all three cognitive outcome measures. Table 4 also displays the results for the fully adjusted model predicting each cognitive domain score as a function of walnut consumption in terms of WWHC and WWON. In the table, this study shows that even adjusting for potentially confounding covariates, age, gender, race, education, BMI, smoking, alcohol consumption and physical activity, significant differences in cognitive scores for SRTT (-16.4, 95%CI,-21.4, -14.5; P=0.03), SDST (-.39, 95%CI, -.71, -.24; P=0.01), and SDLT (-2.38, 95%CI, -15.11, -.39; P=0.05) scores were found for WWHC and WWON. For those 60 years and older, the fully adjusted

Table 3
Mean, median and percentile scores of cognitive tests by walnuts with high certainty, walnuts and other nuts and no nut consumption

Cognitive Tests (20-59 y)	Walnuts with High Certainty, WWHC* Mean (SD)	Walnuts with Other Nuts, WWON Mean (SD)	No Reported Nut Consumption NRNC Mean (SD)
SRTT, Simple Reaction Time Test , ms	226 (35.6), median = 219	232.9 (40.2), median = 227	243.4 (58.8), median = 229
Lowest tertile	230 (17.6)	232 (39.8)	
Middle tertile	227 (21.2)	233 (40.3)	
Highest tertile	223 (21.0)	230 (40.7)	
SDST, Symbol Digit Substitution Test , s	2.61 (0.53), median = 2.50	2.65 (0.65), median = 2.50	2.96 (1.22), median = 2.70
Lowest tertile	2.65 (0.62)	2.66 (0.74)	
Middle tertile	2.54 (0.51)	2.62 (0.58)	
Highest tertile	2.62 (0.57)	2.65 (0.59)	
SDLT, Serial Digit Learning Test , s	4.66 (4.74), median = 3.0	4.77 (4.67), median = 3.0	6.08 (5.07), median = 4.0
Lowest tertile	4.62 (4.37)	5.19 (4.67)	
Middle tertile	5.11 (4.49)	4.72 (4.08)	
Highest tertile	4.14 (3.98)	4.60 (3.65)	
Cognitive Tests (60 y+)			
SR, Story Recall tests, (NHANES1988-1994)	53.1 (27.5), median = 53	55.5 (27.3), median = 55	44.8 (27.0), median = 45
Lowest tertile	47.6 (25.2)	51.6 (26.5)	
Middle tertile	53.9 (26.2)	55.1 (26.9)	
Highest tertile	56.5 (27.4)	61.2 (28.7)	
DSST, Digit Symbol Substitution Test, (NHANES 1999-2004)	59.1 (30.9), median = 59	59.6 (27.4), median = 59	47.8 (28.0), median = 48
Lowest tertile	57.0 (30.6)	57.6 (26.4)	
Middle tertile	58.9 (31.1)	59.2 (27.1)	
Highest tertile	61.4 (32.4)	61.2 (29.5)	

model also shows significantly higher differences in cognitive percentile scores for SR test (7.09, 95% CI, .62, 13.66; P=0.03) and DSST (7.31, 95% CI, 0.09, 14.6; P = 0.05) for WWHC relative to no nut consumers.

The predicted difference in cognitive function by grams of walnut consumption expressed as tertiles after adjusting for the covariates age and gender, race, physical activity, smoking and alcohol intake for SRTT, SDST and SDLT are shown in Table 5. With the exception of SDST, most of the results show that higher consumption of walnuts had significantly faster response time compared to no nut consumers. For SDST in the fully adjusted model for WWHC, the middle tertile (> 5 to 11 g) had a slightly faster response time of -0.40 vs -0.39 for the highest tertile (> 11 g) but this difference was minimal. For SDST in the fully adjusted model for WWON, both the middle and highest tertile groups have the same response time of -0.33 relative to the no reported nut consumption group. In terms of the magnitude, WWHC had the highest difference, therefore the fastest response time relative to no nut consumers for SRTT and SDLT cognitive outcomes and show an increasing trend from the lowest to the highest tertile of walnut consumption. The fully adjusted model controls for the covariates age, gender, race, education, BMI, smoking, alcohol consumption and physical activity. In table 5, we show that even adjusting for potentially confounding covariates, significant differences in cognitive scores for SRTT (-17.1, 95%CI,-43.9, -8.13; P=0.01) , SDST (-.39, 95%CI, -.90, -.04; P=0.03) , and SDLT (-2.59, 95%CI, -4.15, -1.04; P=0.001) scores were found for the highest tertile for WWHC. Similar results were also found for WWON. For those 60 years and older, the fully adjusted model also shows significantly higher differences in cognitive percentile scores for SR test (18.1, 95% CI, 12.6, 23.6; P<0.001) and DSST (8.20, 95% CI, 2.42, 16.9; P < 0.001) for the highest tertile of WWHC relative to no nut consumers.

Discussion

Results from this study showed that walnut consumption, defined by either WWHC or WWON, had significant and positive associations with cognitive functions as measured by the three cognitive domains for 20 to 59 years old participants (SRTT, SDST and SDLT) as well as cognitive scores in SR test and DSST among 60 years and older participants in the NHANES survey. These results are supported by other cross sectional findings in the literature on walnuts and nut consumption in general. In one study on consumption of fruit and vegetable, including nuts, cognitive function was measured by various cognition tests and dietary intake of the subject was assessed through FFQ, and nut intake was categorized by quintiles of absolute amounts consumed (24). The global cognition function and cognitive function specifically on memory, speed and flexibility was measured using the World Verbal Learning Test (VLT) score to measure memory, the Stroop Colour World Test (SCWT) and the Letter Digit Substitution Test (LDST) to measure cognitive speed. The summation of all three tests represented the Global cognition function which was better among those in quintile 5 for nut consumption (i.e. highest nuts consumption) as compared with those in the four other quintiles. The cognitive tests showed that nuts consumers had better memory and cognition speed at the baseline. They reported the difference in cognitive function

Table 4
Differences in Cognitive Function: Test scores as a function of walnut consumption (β coefficients)

	Data source	Model adjusted by age and gender Walnut with High Certainty, WWHC	Walnut with Other nuts, WWON	Fully adjusted model** Walnut with High Certainty, WWHC	Walnut with Other nuts, WWON
Cognitive tests, 20 -59 y					
SRTT, ms*	NHANES III	-15.6 (-17.1, -14.4), P = 0.03	-11.1 (-2.1, -10.2), P = 0.03	-16.4 (-21.4, -14.5), P = 0.03	-10.5 (-13.7, -9.3), P = 0.02
SDST, s*	NHANES III	-0.30 (-0.49,-0.21), P= 0.01	-0.31 (-0.60, -0.21), P < 0.001	-0.39 (-0.71,-0.24), P = 0.01	-0.30 (-0.70, -0.31), P = .001
SDLT, s*	NHANES III	-2.11 (-5.62, -0.79), P = 0.04	-2.04 (-5.43, -0.81), P = 0.001	-2.38 (-15.11,-0.39), P = 0.05	-2.21 (-14.47 -0.51), P = 0.001
Cognitive tests, 60+ y					
SR Test total, percentile scores	NHANES III	8.38 (1.46, 15.23), P = 0.02	10.41 (5.62, 15.24), P = 0.01	7.09 (0.62, 13.66), P= 0.03	8.11 (3.53, 12.68), P = 0.001
DSST, percentile scores	NHANES, 1999-2002	10.67 (1.88, 19.41), P = 0.02	9.81 (5.62, 13.87), P = 0.01	7.31 (0.09, 14.6), P = 0.05	4.82 (0.89, 8.72), P = 0.02

* Estimates are based on a linear regression with log transformation and appropriate retransformation algorithm; ** Fully adjusted models adjust for age, gender, race, physical activity, and past/current smoking, number of alcoholic drinks consumed

Table 5
Differences in Cognitive Function: Test scores as a function of grams of walnut consumption (β coefficients)

	Data source	Gram tertiles1	Model adjusted by age and gender Walnut with High , Certainty WWHC	Walnut with Other , nuts WWON	Fully adjusted model** Walnut with High Certainty, WWHC	Walnut with Other nuts, WWON
Cognitive tests, 20 - 59 yrs						
SRTT, msecs*	NHANES III	Lowest tertile	-12.2 (-33.6, -0.78) P = 0.04	-11.4 (-27.3, 4.94) P = 0.16	-12.3 (-23.4, -1.19) P = 0.04	-10.1 (-25.9, 5.73) P = 0.21
		Middle tertile	-14.7 (-35.1, -4.42) P = 0.02	-10.7 (-24.8, 3.42) P = 0.14	-15.1 (-30.2, 0.02) P = 0.05	-8.21 (-22.3, 5.87) P = 0.25
		Highest tertile	-19.5 (-37.6, -11.3) P =.001	-13.3 (-28.7, -1.97) P = 0.04	-17.1 (-43.9, -8.13) P = 0.01	-13.8 (-29.0, -1.49) P = 0.05
			P-trend < 0.001	P-trend = 0.06	P-trend < 0.001	P-trend = 0.06
SDST, secs*	NHANES III	Lowest tertile	-0.27 (-0.81, -0.03) P = 0.04	-0.23 (-0.51, -0.07) P = 0.02	-0.28 (-0.89, -0.05) P = 0.03	-0.26 (-0.58, -0.05) P = 0.02
		Middle tertile	-0.38 (-0.83, -0.10) P = 0.01	0.34 (-0.78, -0.21) P = 0.001	-0.40 (-0.91, -0.03) P = 0.02	-0.33 (-0.68, -0.09) P = 0.01
		Highest tertile	-0.30 (-1.01, -0.17) P = 0.01	-0.29 (-0.74, -0.15) P = 0.01	-0.39 (-0.90, -0.04) P = 0.03	-0.33 (-0.67, -0.07) P = 0.02
			P-trend = 0.02	P-trend = 0.01	P-trend = 0.003	P-trend < 0.001
SDLT, secs*	NHANES III	Lowest tertile	-2.52 (-4.43, -0.60) P = 0.01	-1.59 (-2.97, -0.20) P = 0.03	-2.04 (-4.07, -0.68) P = 0.01	-1.47 (-2.83, -0.11) P = 0.03
		Middle tertile	-2.03 (-4.71, -1.14) P = 0.001	-2.06 (-3.36, -0.95) P = 0.001	-2.13 (-4.17, -0.59) P = 0.01	-2.18 (-2.89, -0.49) P = 0.01
		Highest tertile	-3.00 (-4.59, 1.41) P < 0.001	-2.18 (-3.51, - 0.85) P < 0.001	-2.59 (-4.15, -1.04) P = 0.001	-2.51 (-3.91, -0.59) P = 0.004
			P-trend = 0.03	P-trend < 0.001	P-trend = 0.004	P-trend < 0.001
Cognitive tests, 60+ yrs						
SR Test total	NHANES III	Lowest tertile	4.08 (-6.44, 10.59) P = 0.63	5.43 (-9.53, 6.68) P = 0.73	3.85 (-4.54, 12.2) P = 0.37	3.02 (-2.83, 8.83) P = 0.31
		Middle tertile	10.6 (-4.04, 29.3) P = 0.14	8.92 (-9.34, 23.4) P = 0.40	7.69 (0.18, 15.2) P = 0.04	7.91 (1.58, 14.3) P = 0.01
		Highest tertile	12.9 (5.42, 24.5) P = 0.002	15.0 (5.66, 24.4) P = 0.002	18.1 (12.6, 23.6) P < 0.001	12.6 (6.10, 19.1) P < 0.001
			P-trend < 0.001	P-trend < 0.001	P-trend < 0.001	P-trend < 0.001
DSST	NHANES, 1999-2002	Lowest tertile	8.2 (-4.29, 21.7) P = 0.13	8.17 (3.46, 18.9) P = 0.01	6.6 (-7.48, 30.6) P = 0.22	3.89 (-0.08, 10.9) P = 0.06
		Middle tertile	10.1 (6.41, 26.8) P = 0.01	9.79 (4.40, 20.8) P = 0.004	7.35 (0.33, 15.8) P = 0.04	4.65 (1.87, 13.0) P = 0.01
		Highest tertile	12.6 (2.95, 29.4) P = 0.02	11.8 (3.02, 19.6) P < 0.001	8.20 (2.42, 16.9) P < 0.001	5.71 (2.43, 14.9) P = 0.008
			P-trend < 0.001	P-trend < 0.001	P-trend < 0.001	P-trend < 0.001

1. WWHC grams are > 0 to 5 g, > 5 g to 11 g, and > 11 g for the lowest, middle the highest tertiles respectively; WWON grams are >0 to 4 g, > 4 g to 7.7 g and > 7.7 g for the lowest, middle the highest tertiles respectively; * Estimates are based on a linear regression with log transformation and appropriate retransformation algorithm; ** Fully adjusted models adjust for age, gender, race, physical activity, and past/current smoking, number of alcoholic drinks consumed

between the lowest and the highest quintile of nut consumption as equivalent to 5-8 years difference in age (24).

Another cross-sectional study on food intake and cognition among elders found that nut consumption was significantly associated with cognitive functioning as measured using six different cognition tests, which included Kendrick Object Learning Test (KOLT), Trail Making Test A (TMT-A), modified version of Digital Symbol Test (m-DST), short form of Block Design (m-BD), modified Mini –Mental State Examination (m-MMSE) and abridged version of Controlled Oral Word Association Test (S-Task) (25). However, the results were not statistically significant after adjusting for sex, education and vitamin supplement use.

One randomized control study had reported on college students with the age of 18-25 to examine the effect of walnut consumption on cognitive function during a cross over design involving consumption of 60g of walnuts per day for 8 weeks. In this study, there was no improvement in the Weschler Memory Scale-Third Edition (WMS-III), Raven's Advanced Progress Matrices (AMP) or Walson-Glser Critical Thinking Appraisal (WGCTA) among these healthy adults (26).

Similar to other cross sectional study findings, the results of the NHANES cross-sectional analysis indicated that there was a significant association between walnut consumption and cognitive function. However, the cross sectional nature of this study is a weakness and might be biased by underlying differences between the groups. A randomized design would be preferable in controlling for such imbalances between the groups. Another weakness is that the presented analyses are based on single 24 hour recalls, which reflect only one day of intake. This limitation is likely to contribute to the inclusion of infrequent consumers in NRNC categories, which would dilute any effect of walnut consumption. However, despite this compelling and statistically significant effect, there seems to be an underestimation of a true effect. In addition, using doubly labeled water, this study and others have found that a single recall can outperform the validity noted when a food frequency questionnaire (FFQ) is used. The strengths of these findings include the fact that evidence of an effect in a nationally representative sample and effects seen independently across survey years and age groups speak to a greater external generalizability and consistency of effect.

The presence of an effect in studies of older individuals, but not among young college students, might reflect a greater vulnerability in older subjects (24) and therefore a greater potential benefit. Our study spanned all adults but was much more heavily geared to older adults.

This is the first large representative study of walnut intake and cognitive function and the only study to include all available cognitive data across multiple NHANES surveys. In the exclusion of peanut consumers and other nuts, the effect of walnuts is more closely isolated. The consistency and magnitude of these findings across tests of cognitive function and the strengthening of effect after adjustment for confounders lend encouragement to the value of future research in a carefully controlled study to better evaluate walnut-specific cognition interactions. The hope is to identify healthful actionable approaches to slow cognitive decline across the population and through minor changes in dietary intake to lessen the social and economic burden of cognitive impairment.

Acknowledgements: We are indebted to Robin Faria for her multi-talented support in many facets of the work and thank Maria-Kassandra Coronel and Phoebe Long for their assistance in the preparation of this manuscript and the literature review.

Statement of author's contributions to manuscript: Both authors, Lenore Arab and Alfonso Ang, were responsible for design, writing, statistical analysis, and final content of this manuscript. Both authors have read and approved the final manuscript.

Ethical standards: This experiment complies with current laws of the country in which they were performed.

Sources of Financial Support: The analyses were funded by the California Walnut Council.

Author disclosures: L. Arab, A. Ang, no conflicts of interest.

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