Neuroprotective Diets Are Associated with Better Cognitive Function: The Health and Retirement Study

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OBJECTIVES: To evaluate the association between the Mediterranean diet (MedDiet) and the Mediterranean-DASH diet Intervention for Neurodegeneration Delay (MIND diet) and cognition in a nationally representative population of older U.S. adults.

DESIGN: Population-based cross-sectional study.

SETTING: Health and Retirement Study.

PARTICIPANTS: Community-dwelling older adults (N = 5,907; mean age 67.8 ± 10.8).

MEASUREMENTS: Adherence to dietary patterns was determined from food frequency questionnaires using criteria determined *a priori* to generate diet scores for the MedDiet (range 0–55) and MIND diet (range 0–15). Cognitive performance was measured using a composite test score of global cognitive function (range 0–27). Linear regression was used to compare cognitive performance according to tertiles of dietary pattern. Logistic regression was used to examine the association between dietary patterns and clinically significant cognitive impairment. Models were adjusted for age, sex, race, educational attainment, and other health and lifestyle covariates.

RESULTS: Participants with mid (odds ratio (OR) = 0.85, 95% confidence interval (CI) = 0.71–1.02, $P = .08$) and high (OR 0.65, 95% CI = 0.52–0.81, $P < .001$) MedDiet scores were less likely to have poor cognitive performance than those with low scores in fully adjusted models. Results for the MIND diet were similar. Higher scores in each dietary pattern were independently associated with significantly better cognitive function ($P < .001$) in a dose-response manner ($P_{trend} < .001$).

CONCLUSION: In a large nationally representative population of older adults, greater adherence to the MedDiet and MIND diet was independently associated with better cognitive function and lower risk of cognitive impairment. Clinical trials are required to elucidate the role of dietary patterns in cognitive aging. **J Am Geriatr Soc 65:1857–1862, 2017.**

Key words: dietary patterns; cognitive performance

Dementia is a major cause of death and disability in older Americans,[1] and there is considerable interest in identifying lifestyle approaches, such as diet, for prevention of cognitive decline with aging.[2]

The Mediterranean diet (MedDiet), rich in fruit, vegetables, whole grains, nuts, olive oil, and fish, has been proven to have vascular[3] and antiinflammatory[4] benefits and may be neuroprotective. Greater adherence to the MedDiet is associated with slower rate of cognitive decline[5,6] and lower risk of cognitive impairment[7,8] and dementia,[5,8] but findings are conflicting,[9–11] largely owing to significant heterogeneity between studies in terms of populations studied and methods used to assess diet and cognition. Studies from the United States have limited generalizability because of a lack of representative study populations and multiple publications based on the same cohorts. Additionally, most prospective studies have used population-specific median food intake thresholds to measure MedDiet adherence, which further limits the generalizability and comparability of findings, because similar scores reflect different eating patterns in different cohorts.[12] The MedDiet score[13] is a different approach that uses absolute food intake targets derived from a Greek population and allows for more-meaningful comparison of studies. Higher MedDiet score has been associated with slower rate of cognitive decline[14–16] in a small number of studies that have used this dietary assessment method.

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Evidence is suggestive of a neuroprotective role for the MedDiet, but variation between studies makes it difficult to draw firm conclusions. Further investigation is needed to determine whether the MedDiet represents an optimal dietary pattern for protection against neurodegeneration in representative populations.

Another proposed neuroprotective dietary pattern, the Mediterranean-DASH diet Intervention for Neurodegeneration Delay (MIND diet), has been recently described.[16] The MIND diet is a modified version of MedDiet but incorporates additional foods based on current evidence in the study of the effect of diet on dementia.[16] In one population-based study, MIND score was more predictive of cognitive decline than MedDiet score,[16] and higher MIND scores were associated with lower risk of Alzheimer's disease (AD).[17] Although these results in mostly older white women are encouraging, they require confirmation in other populations.

The aim of the current study was to determine the association between proposed neuroprotective dietary patterns characterized by MedDiet and MIND scores and objectively measured cognitive performance in a large sample of older adults from the nationally representative population-based Health and Retirement Study (HRS).

METHODS

Data were used from the HRS, a longitudinal, nationally representative survey of 30,000 community-dwelling adults aged 50 and older. The HRS commenced in 1992 to collect data on the antecedents and consequences of retirement in U.S. adults and follows approximately 20,000 participants every two years. A detailed description of HRS has been published elsewhere.[18] The Health Sciences Institutional Review Board at the University of Michigan approved the HRS. All participants provided consent on enrollment.

The present study is a cross-sectional analysis of participants from a core Wave 12 survey (2014) who completed the HRS Health Care and Nutrition (HCNS) substudy (N = 8,035). The HCNS diet assessment was conducted between November 2013 and May 2014, and cognitive, demographic, and covariate data were drawn from the core 2014 survey. Respondents who required a by-proxy core 2014 interview and those with missing or incomplete cognitive data were excluded (n = 981). Those who reported extreme energy intake outside of predefined levels (<800 or >8,000 kcal/d for men and <600 or >6,000 kcal/d for women) (n = 291); those who reported dementia or AD (n = 140) or stroke (n = 430), and those with missing covariates (n = 286) were also excluded. After exclusions, the final analytical sample was 5,907 participants.

Dietary Assessment

Dietary intake was assessed using the validated 163-item semiquantitative Harvard Food Frequency Questionnaire (FFQ).[19,20] Adherence to MedDiet and MIND diet patterns was assessed by calculating summary scores using predefined criteria[13,16] (Tables S1 and S2). First, FFQ food items were selected to create dietary components relevant for each dietary pattern. Next, individual scores were assigned for dietary components based on the frequency of recommended intake servings.

MedDiet Score

The MedDiet score[13] comprises 11 dietary components corresponding to consumption frequency of foods consistent with the traditional MedDiet. Dietary components were scored from 0 to 5 in agreement with predefined frequencies of servings for each point value and then summed, to obtain a total score ranging from 0 to 55. Scores for dietary components consistent with the MedDiet (nonrefined grains, fruits, vegetables, potatoes, legumes, fish, olive oil) increase as consumption frequency increases, and scores for food groups not characteristic of a MedDiet (red meat, poultry, full-fat dairy products) decrease as consumption frequency increases. Alcohol intake was determined according to frequency of alcoholic drinks daily (1 drink equivalent to 150 mL; approximately 12 g ethanol) and scored nonlinearly, with a score of 0 for no consumption or more than 4.5 drinks per day to a maximum score of 5 for up to 2 drinks per day. Overall, higher score indicated better adherence to the traditional Mediterranean diet.

MIND Score

The MIND score[16] consists of 15 dietary components, of which 10 are considered brain-healthy food groups (green leafy vegetables, other vegetables, nuts, berries, beans, whole grains, seafood, poultry, olive oil, wine), and five are considered unhealthy food groups (red meats, butter and stick margarine, cheese, pastries and sweets, fried and fast food). Dietary components were scored 0, 0.5, or 1 depending on level of consumption. Olive oil use was scored 1 if intake was 1 tablespoon or more per day and 0 otherwise. Scores for the 10 healthy components increased monotonically with higher consumption of reported servings, and scores were reversed for the five unhealthy components. Dietary component scores were then summed to obtain an overall score ranging from 0 to 15, with higher scores indicating greater adherence to the MIND diet.

Cognitive Assessment

Cognitive performance was assessed according to a global cognition score comprising three items: immediate and delayed recall of 10 words from a word list randomly assigned for each participant (0–20 points), backward counting (0–2 points), and serial seven subtraction (0–5 points).[21] Possible scores ranged from 0 to 27, with higher scores indicating better overall cognitive function in domains of episodic memory, attention, and working memory.[22] Clinically significantly poor cognitive performance was defined as 1 or more standard deviations (SDs) below the mean global cognition score.

Covariates

Covariates of age, sex, and race (white, black or other) were included. Health and lifestyle covariates previously

identified as potential modifiable risk factors for cognitive decline and dementia were also selected[2] (smoking, hypertension, diabetes mellitus, depression, low educational attainment, physical inactivity, obesity). Depressive symptoms were determined according to Center for Epidemiologic Studies Depression short form (CES-D8) score (range 0–8), with active depressive symptoms defined as a CES-D8 score of 4 or greater.[23] Low educational attainment was classified as have less than a high school education, and physical inactivity was defined as engaging in vigorous activity less than twice weekly, as in a previous HRS analysis.[24] Obesity was defined as a body mass index (BMI) of 30.0 kg/m^2 or greater.

Statistical Analysis

Participant characteristics were compared across tertiles of dietary pattern scores using descriptive statistical tests. Analysis of variance with Bonferroni post hoc comparison was used for continuous variables and chi-square tests for categorical variables, with corresponding tests for linear trend. Pearson correlation coefficients were used to examine correlations for continuous variables. A multivariable general linear model was used to investigate associations between dietary patterns (MedDiet and MIND score modelled in tertiles) and global cognition scores. Participants in tertile 1 (lowest diet adherence) were the reference group for each analysis. Models were adjusted first for classic confounders (age, sex, race, educational attainment (<high school vs ≥high school) and subsequently for potential mediators (total wealth as a measure of socioeconomic status (total assets–total debt), hypertension, diabetes mellitus, current smoking, depression (CES-D8 score ≥4), physical inactivity, obesity (BMI ≥30.0 kg/m^2), and total energy intake (kcal/d)). The risk of poor cognitive performance associated with adherence to each dietary pattern was estimated using binary logistic regression analyses with corresponding odds ratios (ORs) and 95% confidence intervals (CIs), adjusted for covariates using the same approach described above. Sensitivity analyses were conducted after removal of individuals classified as having dementia according to global cognition score. Analyses were repeated after applying *a priori*–defined Greek cutpoints to MedDiet tertiles (0–20, 21–35, 36–55). Analyses were performed using SPSS version 22 (IBM Corp., Armonk, NY).

RESULTS

The mean ± SD age of the 5, 907 participants was 67.8 ± 10.8 at the core 2014 survey. Overall, 60% were women and 78% were white. Mean scores were 27.6 ± 5.4 for MedDiet and 7.3 ± 1.8 for MIND diet, indicating moderate adherence to each dietary pattern. Average MedDiet score was similar to that reported in a Greek population (26.3 ± 3.2).[13] Participants with greatest MedDiet adherence were younger; were more likely to be physically active; were less likely to be hypertensive or obese, to have diabetes mellitus or to report depressive symptoms; and had higher educational attainment than those with the lowest adherence (Table 1). Demographic characteristics were similar for the MIND diet, but there was no observed difference in diabetes mellitus according to tertile of MIND diet score.

Both diet scores were positively correlated (correlation coefficient (r) = 0.68, $P < .001$) and showed a fair level of agreement in the population (Cohen kappa 0.36, $P < .001$).Weekly servings of whole grains, vegetables, fruit, fish, nuts, and olive oil increased linearly with increasing tertile for each dietary pattern ($P_{trend} < .001$), with individuals in the high tertile consuming two to three times as much as those in the low tertile. Conversely, weekly consumption of red meat decreased linearly with increasing tertile of diet score ($P_{trend} < .001$).

Table 2 shows unadjusted and adjusted global cognition score according to tertile of dietary patterns. Participants with high adherence to MedDiet or the MIND diet had significantly better cognitive performance than those with mid or low levels of adherence ($P < .001$ for both dietary patterns). In fully adjusted models, these associations were attenuated, but individuals with the highest diet adherence had significantly better cognitive scores (1.0 for MedDiet, 0.8 points for MIND diet) than those with mid and low adherence, and these associations had a dose-response relationship ($P_{trend} < .001$).

Impaired cognitive performance, defined as more than 1 SD (4.3 points) below the mean global cognitive score, was found in 831 (14%) participants. Figure 1 shows the adjusted likelihood of having poor cognitive performance according to adherence to the dietary patterns. Participants with mid MedDiet scores had 15% lower odds of having poor cognitive performance than those with low scores (OR = 0.85, 95% CI = 0.71–1.02, $P = .08$). The association was significantly stronger for those with the highest MedDiet scores, who had 35% lower odds of having poor cognitive performance than those with the lowest scores (OR = 0.65, 95% CI = 0.52–0.81, $P < .001$). Results were similar for individuals with mid (OR = 0.85, 95% CI = 0.70–1.03, $P = .10$) and high (OR = 0.70, 95% CI = 0.56–0.86, $P = .001$) MIND diet scores. In fully adjusted linear models, each 1 SD increase (5.4 units) in MedDiet was associated with 15% lower odds of poor cognitive performance (OR = 0.85, 95% CI = 0.78–0.93, $P < .001$), and each 1 SD increase (1.8 units) in MIND diet was associated with 14% lower odds of poor cognitive performance (OR = 0.86, 95% CI = 0.79–0.94, $P < .001$).

Analyses were repeated after removing participants with global cognition scores of 6 or less (n = 143), but no notable changes were found in observed results. The analyses were also repeated using *a priori*–defined cutpoints for MedDiet tertiles derived from a Greek population,[13] and similar results were observed. In fully adjusted models, individuals in the highest Greek MedDiet tertile had 35% lower odds of cognitive impairment (OR 0.65, 95% CI = 0.44–0.98, $P = .04$) than those in the lowest Greek tertile.

DISCUSSION

In this large general population of community-dwelling older adults, neuroprotective dietary patterns characterized according to MedDiet and MIND scores were significantly associated with moderately better cognitive performance in

Table 1. Participant Characteristics According to Tertiles of Mediterranean Diet (MedDiet) and Mediterranean-DASH diet Intervention for Neurodegeneration Delay (MIND Diet) Scores (n = 5,907)

	MedDiet Score[a]				MIND Diet Score[b]			
Characteristic	Tertile 1 (Low; ≤25), n = 2,110	Tertile 2 (Mid; 26–30), n = 2,064	Tertile 3 (High; 31–55), n = 1,733	*P* for Trend	Tertile 1 (Low; ≤6.5), n = 2,219	Tertile 2 (Mid; 6.4–8.0), n = 1,825	Tertile 3 (High; 8.1–15.0), n = 1,863	*P* for Trend
Age, mean ± SD	68.2 ± 10.6	67.8 ± 10.4	67.1 ± 10.7	.001	68.5 ± 10.6	68.2 ± 10.6	66.5 ± 10.4	<.001
Female, n (%)	1,261 (60)	1,215 (59)	1,072 (62)	.22	1,235 (56)	1,067 (59)	1,246 (67)	<.001
Race, n (%)								
White	1,636 (78)	1,627 (79)	1,326 (77)	<.001	1,790 (80)	1,406 (77)	1,393 (75)	<.001
Black	360 (17)	301 (15)	233 (13)		299 (14)	298 (16)	297 (16)	
Other	114 (5)	136 (7)	174 (10)		130 (6)	121 (7)	173 (9)	
Energy intake, kcal, mean ± SD								
Male	1,940 ± 862	1,899 ± 826	2,167 ± 881	<.001	1,883 ± 801	2,008 ± 889	2,131 ± 899	<.001
Female	1,641 ± 731	1,693 ± 762	2,040 ± 815	<.001	1,617 ± 708	1,784 ± 821	1,935 ± 798	<.001
Education less than high school, n (%)	397 (19)	243 (12)	195 (11)	<.001	369 (17)	270 (15)	196 (11)	<.001
Current smoker, n (%)	332 (16)	207 (10)	93 (5)	<.001	355 (16)	172 (9)	105 (6)	<.001
Clinically obese, n (%)	1,029 (49)	959 (47)	673 (39)	<.001	1,034 (47)	845 (46)	782 (42)	.004
Hypertension, n (%)	1,359 (64)	1,212 (59)	933 (54)	<.001	1,384 (62)	1,103 (60)	1,017 (55)	<.001
Diabetes mellitus, n (%)	538 (26)	421 (20)	332 (19)	<.001	498 (22)	413 (23)	380 (20)	.13
Center for Epidemiologic Studies Depression short form depression score <4, n (%)	598 (28)	424 (21)	312 (18)	<.001	592 (27)	392 (22)	350 (19)	<.001
Physically inactive, n (%)	1,732 (82)	1,517 (74)	1,058 (61)	<.001	1,724 (80)	1,349 (74)	1,184 (64)	<.001
Diet components, servings per week, mean ± SD								
Whole grains	4.9 ± 6.1	6.9 ± 6.6	9.0 ± 7.9	<.001	4.9 ± 5.8	6.5 ± 6.5	9.7 ± 8.1	<.001
Vegetables	9.8 ± 7.1	17.2 ± 10.4	26.8 ± 14.2	<.001	11.3 ± 8.5	16.1 ± 10.7	26.6 ± 14.5	<.001
Fruit	6.8 ± 6.1	10.3 ± 7.8	15.4 ± 10.8	<.001	6.6 ± 6.3	10.1 (8.1)	16.1 (10.3)	<.001
Red meat	5.8 ± 4.2	5.4 ± 4.0	4.2 ± 3.4	<.001	6.2 ± 4.4	5.0 ± 3.8	4.0 ± 3.2	<.001
Fish	0.5 ± 0.6	0.9 ± 0.9	1.4 ± 1.3	<.001	0.5 ± 0.6	0.8 ± 0.9	1.4 ± 1.4	<.001
Nuts	1.3 ± 2.5	2.1 ± 3.3	3.8 ± 4.9	<.001	1.1 ± 2.2	2.0 ± 3.3	4.2 ± 5.0	<.001

SD = standard deviation.
[a]Possible range 0–55.
[b]Possible range 0–15.

a dose-response relationship. Individuals with the highest adherence to neuroprotective diets had a 30% to 35% lower risk of cognitive impairment defined as more than 1 SD (4.3 points) below the population mean global cognition score. Although the incidence of clinical cognitive impairment according to the global cognition score was low (14%) in this healthy population, these findings lend support to the hypothesis that diet modification may be an important public health strategy to protect against neurodegeneration during aging.

This study adds to the limited work performed to investigate relations between dietary patterns and brain health. Although previous prospective studies examining associations between MedDiet and cognitive outcomes have reported contradictory findings, recent results from the Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Trial substudy, which demonstrated small but significantly better cognitive function in response to greater MedDiet adherence,[25] support the findings of the current study. The effects of the MIND diet on cognitive health have not been evaluated, but greater adherence to the MIND diet is linked to slower rates of cognitive decline[16] and lower risk of AD.[17] These studies were conducted exclusively in one older, largely female, population from the Rush Memory and Aging Project and require replication in other cohorts. The current findings support a protective association of the MIND diet on cognitive performance in a general population.

The MedDiet and MIND diet have similar dietary profiles and involve high intakes of plant foods, limited meat consumption, moderate intake of alcohol (wine in particular), and use of olive oil as a primary fat source. Unique to the MIND diet are green vegetables and berries, which are independently reported to protect against neurodegeneration.[12] In contrast, the MedDiet places greater emphasis on potatoes, fish, and overall fruit and vegetable intake. Both dietary patterns are rich in antioxidants and monounsaturated and omega-3 fatty acids and low in saturated fat. These individual nutrients have also been independently related to cognitive performance; for example, observational evidence has shown an association between greater intake of monounsaturated fat and omega-3 fatty acids and lower risk of cognitive decline and dementia,[5] whereas greater saturated fat intake is shown to increase the risk of cognitive decline and dementia.[26] The biological mechanisms for how dietary patterns exert neuroprotective

Table 2. Global Cognition Scores[a] According to Mediterranean Diet (MedDiet) and Mediterranean-DASH diet Intervention for Neurodegeneration Delay (MIND Diet) Score Tertiles (N = 5,907)

	MedDiet Score				MIND Diet Score			
	Low, n = 2,110	Mid, n = 2,064	High, n = 1,733		Low, n = 2,219	Mid, n = 1,825	High, n = 1,863	
Model	Mean (SE)			*P* for Trend	Mean (SE)			*P* for Trend
Unadjusted	14.5 (0.09)	15.3 (0.09)	16.0 (0.10)	<.001	14.6 (0.09)	15.2 (0.10)	16.0 (0.10)	<.001
Model 1[b]	14.7 (0.09)	15.2 (0.09)	15.9 (0.09)	<.001	14.8 (0.08)	15.2 (0.09)	15.8 (0.09)	<.001
Model 2[c]	14.8 (0.09)	15.2 (0.08)	15.7 (0.10)	<.001	14.9 (0.10)	15.2 (0.09)	15.6 (0.09)	<.001

SE = standard error.

[a]Possible range 0–27.

[b]Adjusted for sex, age, race (white, black, other), low education attainment (less than high school completed).

[c]Model 1 adjusted for current smoking, total wealth (assets–debt), obesity (body mass index ≥30 kg/m^2), hypertension, diabetes mellitus, physical inactivity; depression (Center for Epidemiologic Studies Depression Scale 8 score ≥4), and total energy intake (kcal/d).

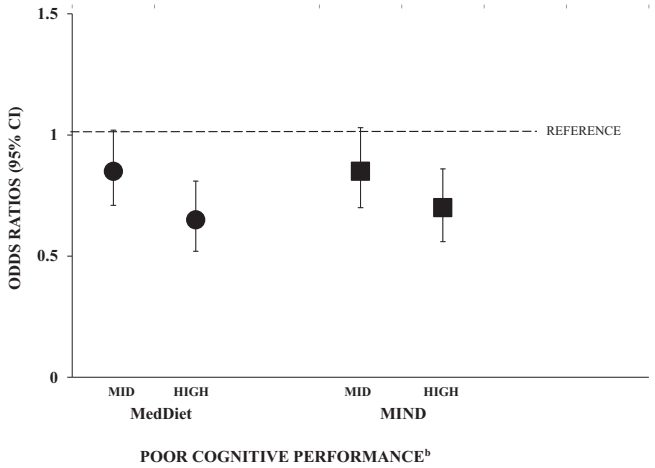

Figure 1. Adjusted[a] odds ratios (95% confidence intervals (CIs)) for poor cognitive performance according to tertiles of Mediterranean diet (MedDiet) and Mediterranean-DASH diet Intervention for Neurodegeneration Delay (MIND diet) scores. [a]Adjusted for sex, age, race (white, black, other), low education attainment (<high school completed), current smoking, obesity (body mass index ≥30.0 kg/m^2), total wealth, hypertension, diabetes mellitus, physical inactivity, depression (Center for Epidemiologic Studies Depression Scale 8 score ≥4), and total energy intake (kcal/d). [b]Poor cognitive performance defined as more than 1 SD below the mean cognitive score (n = 831, 14% of population).

effects are not clear. Several putative mechanisms for the MedDiet have been proposed,[27] including beneficial effects on neuronal cell signalling, vascular health, and antioxidant and antiinflammatory biological pathways, but more-comprehensive investigation is required. Furthermore, although the MedDiet and the new MIND diet have attracted attention in the literature, they may not reflect an optimal dietary pattern for protection against neurodegeneration during aging.

Strengths of this study include its large sample size and community-based population of older adults, which increase the external validity of findings. In addition, an extensively validated semiquantitative FFQ was used to assess dietary exposure. Furthermore, dietary scores were generated based on predefined absolute food intake thresholds, which increases the ability to compare the findings with those of studies that have used a similar standardized dietary pattern methodology. A major limitation is the cross-sectional study design, meaning that it was not possible to establish a causal relationship between dietary patterns and cognitive outcomes. In addition, dietary misclassification is possible because individuals may have changed their eating behavior as a result of cognitive impairment or other disease, although in the sensitivity models, removal of participants with low cognitive scores did not alter the findings. As with all observational studies, residual confounding is a possibility even though the analyses were adjusted for known confounders of the association between diet and dementia. Finally, the use of a summary cognition score allowed global cognitive function to be examined but not individual cognitive domains, which age and lifestyle factors may differentially influence.

In conclusion, this study shows that greater adherence to MedDiet and MIND diet patterns are associated with better overall cognitive function in older adults and lower odds of cognitive impairment, which could have important public health implications for preservation of cognition during aging. Given the limited evidence base and lack of clear dietary recommendations for cognitive health, further prospective population-based studies and clinical trials are required to elucidate the role of dietary patterns in cognitive aging and brain health.

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Author Contributions: CTM, KY: study design. CTM, KY, HG: analysis and data interpretation. CTM, KY, HG, KML: preparation of manuscript.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Table S1. Dietary component servings and maximum scores for MedDiet pattern (range 0–55)

Table S2. Dietary component servings and maximum scores for MIND dietary pattern (range 0–15)

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