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Association Between Consumption of Ultraprocessed Foods and Cognitive Decline

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IMPORTANCE Although consumption of ultraprocessed food has been linked to higher risk of cardiovascular disease, metabolic syndrome, and obesity, little is known about the association of consumption of ultraprocessed foods with cognitive decline.

OBJECTIVE To investigate the association between ultraprocessed food consumption and cognitive decline in the Brazilian Longitudinal Study of Adult Health.

DESIGN, SETTING, AND PARTICIPANTS This was a multicenter, prospective cohort study with 3 waves, approximately 4 years apart, from 2008 to 2017. Data were analyzed from December 2021 to May 2022. Participants were public servants aged 35 to 74 years old recruited in 6 Brazilian cities. Participants who, at baseline, had incomplete food frequency questionnaire, cognitive, or covariate data were excluded. Participants who reported extreme calorie intake (<600 kcal/day or >6000 kcal/day) and those taking medication that could negatively interfere with cognitive performance were also excluded.

EXPOSURES Daily ultraprocessed food consumption as a percentage of total energy divided into quartiles.

MAIN OUTCOMES AND MEASURES Changes in cognitive performance over time evaluated by the immediate and delayed word recall, word recognition, phonemic and semantic verbal fluency tests, and Trail-Making Test B version.

RESULTS A total of 15 105 individuals were recruited and 4330 were excluded, leaving 10 775 participants whose data were analyzed. The mean (SD) age at the baseline was 51.6 (8.9) years, 5880 participants (54.6%) were women, 5723 (53.1%) were White, and 6106 (56.6%) had at least a college degree. During a median (range) follow-up of 8 (6-10) years, individuals with ultraprocessed food consumption above the first quartile showed a 28% faster rate of global cognitive decline (β = −0.004; 95% CI, −0.006 to −0.001; *P* = .003) and a 25% faster rate of executive function decline (β = −0.003, 95% CI, −0.005 to 0.000; *P* = .01) compared with those in the first quartile.

CONCLUSIONS AND RELEVANCE A higher percentage of daily energy consumption of ultraprocessed foods was associated with cognitive decline among adults from an ethnically diverse sample. These findings support current public health recommendations on limiting ultraprocessed food consumption because of their potential harm to cognitive function.

Supplemental content

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The prevalence of dementia is estimated to increase from 57 million cases in 2019 to 153 million in 2050 owing to the increase in life expectancy worldwide.[1,2] Dementia is the most important cause of disability in high-income countries, and it is among the 10 most important causes in low-income and middle-income countries.[3] The limited efficacy of available treatments for dementia highlights the importance of identifying interventions that are capable of preventing or delaying dementia onset to decrease the burden caused by this disorder.[4,5] Lifestyle modifications, such as physical activity, healthy dietary habits, and smoking cessation, have been related to dementia prevention.[6] Healthy eating habits, which include a high intake of whole grains, vegetables, fruit, nuts, and fish,[7-11] have been linked to increased brain volume and decreased risk of cognitive decline over time.[8,9,11,12]

In the last 40 years, the food supply industries have increased the commercialization of ultraprocessed foods (UPFs).[13] Such UPFs are formulations of processed food substances (oils, fats, sugars, starch, and protein isolates) that contain little or no whole foods and typically include flavorings, colorings, emulsifiers, and other cosmetic additives.[14] Examples of UPFs are sweet and savory snacks, confectionery, breakfast cereals, ice cream, sugar-sweetened beverages, processed meats, and ready-to-eat frozen meals. Fifty-eight percent of the calories consumed by US citizens, 57% of the calories consumed by British citizens, and 48% of the calories consumed by Canadian citizens come from UPFs.[15-17] In Brazil, this group of foods contributes to 30% of total calorie intake.[18] Consumption of UPFs has been linked to an increased risk of cardiovascular disease, metabolic syndrome, and obesity.[19,20] However, few studies have investigated the association between UPF and cognitive decline in samples from high-income countries.[21-23] Therefore, we aimed to prospectively investigate the association between UPF consumption at baseline and cognitive decline in the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil).

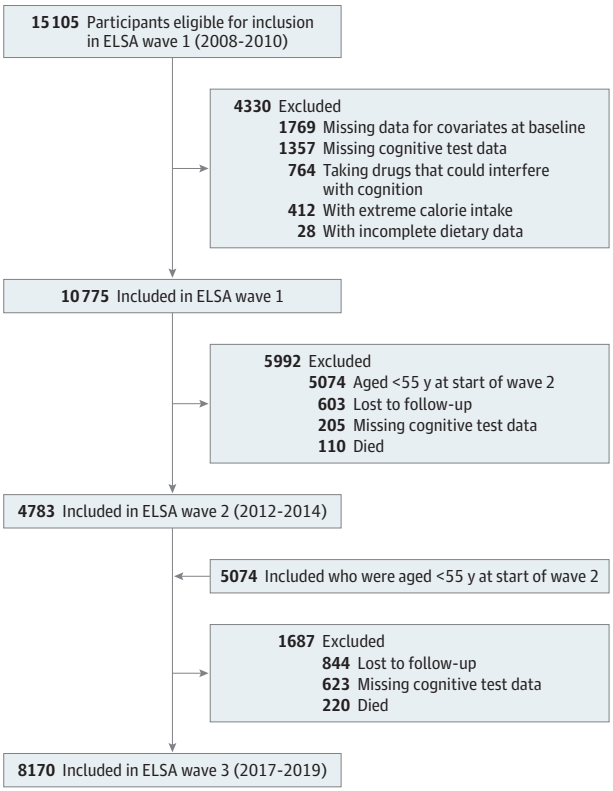
Key Points

Question Is the consumption of ultraprocessed foods associated with cognitive decline?

Findings In a cohort study of 10 775 individuals, higher consumption of ultraprocessed foods was associated with a higher rate of global and executive function decline after a median follow-up of 8 years.

Meaning These findings suggest that limiting consumption of ultraprocessed food could be associated with reduced cognitive decline in middle-aged and older adults.

Figure 1. Flowchart of the Study Sample



ELSA indicates Brazilian Longitudinal Study of Adult Health.

Methods

Participants

The ELSA-Brasil is a multicenter cohort study that comprises public servants aged 35 to 74 years at baseline from 6 Brazilian cities (Belo Horizonte, Porto Alegre, Rio de Janeiro, Salvador, São Paulo, and Vitoria). Data were collected in 3 waves, approximately 4 years apart, starting in 2008 to 2010. The second wave took place in 2012 to 2014, and the third wave was in 2017 to 2019. Inclusion criteria for the ELSA-Brasil study were active or retired employees of the participating institutions. Exclusion criteria were pregnancy, intention to quit working at the institution, cognitive or communication impairment, or, for those retired, residences outside of the study center area. A detailed description of the ELSA-Brasil cohort can be found elsewhere.[24,25]

The current study excluded participants who, at baseline, did not have dietary data, had extreme amounts of energy intake (<600 kcal/day or >6000 kcal/day), had missing data on cognitive tests or covariates, or reported taking medication that could negatively interfere with cognitive performance (**Figure 1**). A comparison between those who were included and excluded from this study analysis can be found in the eAppendix and eTable 1 in the Supplement.

This study was approved by the local ethics committees. The ELSA-Brasil study was conducted according to the guidelines of the Declaration of Helsinki,[26] the procedures were approved by the ethics committees of all study centers, and participants signed an informed consent before participation. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Dietary Assessment

Food and drink consumption in the last 12 months was assessed at baseline using a validated Food Frequency

Questionnaire (FFQ) with 114 items.[27] The frequency of consumption of each item was transformed into grams per day by multiplying the frequency of consumption by the weight of the portion in grams (further details can be found in the eAppendix in the Supplement). Foods were classified according to the extent of industrial processing using the Nova classification system.[14] Nova includes 4 food groups. Group 1 includes unprocessed or minimally processed foods, such as fresh, dry, or frozen fruits or vegetables, grains, legumes, meat, fish, and milk, which have undergone minimal processing like grinding, roasting, pasteurization, or freezing. Group 2 includes processed culinary ingredients, such as table sugar, oils, salt, and other substances that have been extracted, pressed, or centrifuged from group 1 foods or from nature, and are used to make culinary preparations. Group 3 includes processed foods, which are manufactured using unprocessed or minimally processed foods, and ingredients from group 2 are used to prolong the durability of foods and modify their palatability. Examples of foods in group 3 include canned fruits, artisanal bread and cheese, and salted, smoked, or cured meat or fish. Group 4 includes UPFs, which are formulations of several ingredients from group 2 with food additives not used in home preparations, such as flavors, colors, sweeteners, emulsifiers, and other substances used to disguise undesirable qualities of the final product or imitate the sensorial qualities of culinary preparations from group 1.[14] In the current study, foods were classified in 3 groups (eTable 2 in the Supplement): (1) unprocessed or minimally processed foods and processed culinary ingredients (Nova groups 1 and 2), (2) processed foods (Nova group 3), and (3) UPFs (Nova group 4). We calculated the daily energy consumption of UPF by summing the energy consumption in calories of all the foods in that group. Consumption of UPF was then expressed as a percentage of total daily energy consumption because a relative measure can capture the degree to which UPF composes a participant's diet while accounting for individual differences in caloric intake.

Cognitive Assessment

In this longitudinal study, individuals were tested up to 3 times every 4 years (mean [SD] time between visits, 3.3 [0.5] years). The memory domain included the immediate recall, late recall, and recognition word list tests from the Consortium to Establish a Registry for Alzheimer Disease.[28,29] The executive function domain included the semantic and the phonemic verbal fluency tests,[30] and the Trail-Making Test B version.[31] We calculated *z* scores standardized to wave 1 to compare results from different cognitive tests. A detailed description of each test and the *z* score calculation can be found in the eAppendix in the Supplement.

Covariates

Covariates that might confound the association between UPF consumption and cognitive decline included sociodemographic, clinical, and lifestyle variables. The sociodemographic variables were age, sex, monthly income per capita in US dollars, self-reported race and ethnicity (with categories self-reported by the participants as Black or mixed [ie, mixed Black and White], White, and other races, which include Asian and Indigenous), and education (less than college and college degree or more). Race and ethnicity were assessed in this study because they are important social determinants of health that could influence cognitive performance and UPF consumption. Clinical variables included body mass index (calculated as weight in kilograms divided by height in meters squared) categories (underweight, normal weight, overweight, and obese), diabetes, hypertension, cardiovascular disease, and depression. Lifestyle factors included physical activity (light, moderate, or vigorous), smoking (never, former, or current smoker), alcohol consumption (never, former, or current alcohol use), total energy intake (in kilocalories), and adhesion to a healthy diet. Details about the covariates can be found in the eAppendix in the Supplement.

Statistical Analysis

Data were analyzed from December 2021 to May 2022. Descriptive analyses were presented as mean (SD) for continuous variables and as percentages for categorical variables. We grouped the daily energy percentage contribution of UPF in quartiles (0%-19.9%, 20.0%-26.7%, 26.8%-34.1%, and 34.2%-72.7%). Our initial analysis compared each of the quartiles with the first quartile (reference group). Subsequent analysis grouped the 3 highest quartiles and compared them with the first quartile.[32] We used linear mixed-effects models with random intercepts and slopes to assess the association between quartiles of UPF consumption at baseline and change in cognition over time. The timescale was the participant's age in each wave. The longitudinal association between UPF consumption and cognitive decline was evaluated by the interaction of the UPF and the timescale. The linear mixed models were adjusted for sociodemographic, clinical, and lifestyle variables. To calculate the percentage of cognitive decline rate, we subtracted each quartile slope from the first quartile slope, divided this difference by the slope of the first quartile, and multiplied it by 100. We also investigated the modifying effect of age and healthy diet scores on the association between the percentage of daily energy from UPF and cognitive decline by adding a 3-way interaction among the percentage of daily energy from UPF, the timescale, and each modifier on our main models. The significant interactions were assessed in stratified analyses. Inverse probability weighting (IPW) was used to account for nonresponse across waves.[33,34] Details about the IPW calculation can be found in the eAppendix in the Supplement.

We performed 2 sets of sensitivity analyses. First, we repeated the analysis by excluding participants who reported caloric intakes above the 95th percentile (5831 kcal for men and 4607 kcal for women) and without excluding participants because of caloric intake. Moreover, we verified the robustness of our findings despite the missing cognitive data by design in wave 2 by imputing cognitive data using next observation carried backward using the scores from wave 3 in wave 2 for those who were younger than 55 years in wave 2. We assumed this approach is conservative since cognitive performance is expected to decline over time.[35] The α level was set at the 5% level in 2-sided tests. Statistical analyses were performed using R statistical software version 3.6.3 (R Project for Statistical Computing) using the lme4 package.[36,37]

Table 1. Baseline Characteristics of the Study Sample by Quartiles of the Percentage of Daily Energy From UPFs

Characteristic	Participants, No. (%)					P value
		UPF consumption quartile[a]				
	Total (N = 10 775)	1 (0%-19.9%) (n = 2694)	2 (20.0%-26.7%) (n = 2694)	3 (26.8%-34.1%) (n = 2694)	4 (34.2%-72.7%) (n = 2693)	
Age, mean (SD), y	51.6 (8.9)	54.2 (8.6)	52.0 (9.0)	50.8 (9.0)	49.6 (9.0)	<.001
Sex						
Female	5880 (54.6)	1392 (51.6)	1443 (53.5)	1501 (55.7)	1544 (57.3)	<.001
Male	4895 (45.4)	1302 (48.4)	1251 (46.5)	1193 (44.3)	1149 (42.7)	
Self-reported race						
Black or mixed[b]	4685 (43.5)	1404 (52.1)	1215 (45.3)	1069 (39.7)	1047 (36.9)	<.001
White	5723 (53.1)	1168 (43.3)	1384 (51.4)	1542 (57.2)	1542 (60.5)	
Other[c]	367 (3.4)	122 (4.6)	95 (3.8)	83 (3.1)	67 (2.6)	
Education (less than college degree)	4669 (43.4)	1390 (51.6)	1154 (42.9)	1037 (38.5)	1088 (40.4)	<.001
Monthly income, mean (SD), $US	983.6 (788.1)	953.5 (797.8)	974.3 (785.8)	997.8 (776.5)	1010.4 (791.8)	.004
Body mass index, mean (SD)[d]	26.9 (4.7)	26.9 (4.6)	27.0 (4.6)	27.0 (4.8)	27.0 (4.8)	.25
Total calorie intake, mean (SD), kcal	2855.9 (991.7)	2813.0 (977.0)	2858.0 (999.0)	2860.0 (993.0)	2894.0 (997.0)	.004
Calories from ultraprocessed foods, mean (SD), kcal	785.0 (419.1)	416.0 (185.0)	667.0 (241.0)	865.0 (308.0)	1192.0 (440.0)	<.001
Calories from Nova groups, % of total calories[e]						
Groups 1 and 2	1873.5 (65.6)	2194.1 (78.0)	1986.3 (69.5)	1790.3 (62.6)	1522.2 (52.6)	<.001
Group 3	197.4 (7.0)	202.9 (7.4)	208.7 (7.3)	203.2 (7.3)	179.8 (6.2)	
Group 4	785.0 (27.4)	416.0 (14.8)	663.0 (23.3)	866.5 (30.3)	1192.0 (41.2)	
Physical activity						
None or light	8197 (76.1)	1968 (73.0)	1996 (74.1)	2062 (76.5)	2171 (80.6)	<.001
Moderate	1539 (14.3)	458 (17.0)	406 (15.1)	383 (14.2)	292 (11.0)	
Vigorous	1039 (9.6)	268 (10.0)	292 (10.8)	249 (9.3)	230 (8.4)	
Hypertension, yes	3704 (34.4)	1100 (41.0)	969 (36.0)	813 (30.2)	822 (30.5)	<.001
Diabetes, yes	2016 (18.7)	701 (26.0)	508 (19.0)	424 (15.7)	383 (14.2)	<.001
Cardiovascular disease, yes	578 (5.3)	165 (6.1)	153 (5.7)	139 (5.1)	121 (4.5)	.04
Depressive symptoms, yes	1263 (11.7)	295 (11.0)	306 (11.3)	285 (10.6)	377 (14.0)	<.001
Alcohol consumption						
Never	1061 (9.8)	301 (11.2)	248 (9.2)	259 (9.6)	253 (9.3)	<.001
Former	1967 (18.3)	467 (17.3)	439 (16.3)	475 (17.7)	586 (21.7)	
Current	7747 (71.9)	1926 (71.5)	2007 (74.5)	1960 (72.7)	1854 (69.0)	
Smoking						
Never	6297 (58.4)	1474 (54.7)	1527 (56.7)	1633 (60.6)	1663 (61.7)	<.001
Former	3165 (29.4)	847 (31.4)	851 (31.6)	748 (27.7)	719 (26.7)	
Current	1313 (12.2)	373 (13.9)	316 (11.7)	313 (11.7)	311 (11.6)	

Abbreviation: UPF, ultraprocessed food.

[a] UPFs are represented as a percentage of total daily energy consumption divided in quartiles.

[b] Includes mixed Black and White.

[c] Includes Asian, Indigenous, or other ethnic groups.

[d] Body mass index calculated as weight in kilograms divided by height in meters squared.

[e] Group 1 includes unprocessed or minimally processed foods. Group 2 includes processed culinary ingredients. Group 3 includes processed foods. Group 4 includes UPFs.

Results

Sample Characteristics

A total of 15 105 individuals were recruited and 4330 were excluded, leaving 10 775 participants. The median (range) duration of follow-up was 8 (6-10) years. At baseline, the mean (SD) age of the participants was 51.6 (8.9) years, 5880 participants (54.6%) were women, 5723 (53.1%) were White, and 6106 (56.6%) had at least a college education. The mean (SD) BMI was 26.9 (4.7), and the mean (SD) total daily calorie intake was 2856 (992) kcal, 27% of which came from UPF (mean [SD], 785.0 [419.1] kcal/day). Compared with the lower quartile of the percentage of daily energy from UPF, those in the fourth quartile (ie, highest UPF consumption) were more likely to be younger, women, White, had higher education and income, were more likely to be nonsmokers, and less likely to be current alcohol consumers. The highest quartile also had a higher total energy intake, lower physical activity, and lower frequency of comorbidities, but a higher frequency of depressive symptoms (**Table 1**).

Table 2. Association Between Baseline Quartiles of the Percentage of Daily Energy From Ultraprocessed Foods and Yearly Cognitive Change During the Study Period

Domain	Change in standardized cognitive score per year						
	Model 1[a]		Model 2[b]		Model 3[c]		
	β (95% CI)	*P* value for trend	β (95% CI)	*P* value for trend	β (95% CI)	*P* value for trend	Difference, %[d]
Memory							
All quartiles							
Quartile 1 × time	0 [Reference]	.88	0 [Reference]	.82	0 [Reference]	.80	0 [Reference]
Quartile 2 × time	0.001 (−0.003 to 0.004)		0.001 (−0.004 to 0.006)		0.001 (−0.002 to 0.004)		6
Quartile 3 × time	0.000 (−0.004 to 0.003)		0.000 (−0.005 to 0.004)		0.000 (−0.004 to 0.003)		0
Quartile 4 × time	0.001 (−0.002 to 0.004)		0.002 (−0.003 to 0.006)		0.001 (−0.002 to 0.005)		6
Lowest × highest quartiles							
Quartile 1 (lowest 25%)	0 [Reference]	.86	0 [Reference]	.77	0 [Reference]	.77	0 [Reference]
Quartiles 2-4 (highest 75%)	0.000 (−0.003 to 0.003)		0.000 (−0.002 to 0.003)		0.000 (−0.002 to 0.003)		0
Executive function							
All quartiles							
Quartile 1 × time	0 [Reference]	.23	0 [Reference]	.12	0 [Reference]	.12	0 [Reference]
Quartile 2 × time	−0.003 (−0.006 to 0.000)		−0.003 (−0.006 to 0.000)		−0.003 (−0.006 to 0.000)		25
Quartile 3 × time	−0.002 (−0.005 to 0.001)		−0.003 (−0.006 to 0.000)		−0.003 (−0.005 to 0.000)		25
Quartile 4 × time	−0.002 (−0.005 to 0.001)		−0.002 (−0.005 to 0.001)		−0.002 (−0.005 to 0.001)		16
Lowest × highest quartiles							
Quartile 1 (lowest 25%)	0 [Reference]	.04	0 [Reference]	.01	0 [Reference]	.01	0 [Reference]
Quartiles 2-4 (highest 75%)	−0.002 (−0.005 to 0.000)		−0.003 (−0.005 to 0.000)		−0.003 (−0.005 to 0.000)		25
Global cognition							
All quartiles							
Quartile 1 × time	0 [Reference]	.06	0 [Reference]	.04	0 [Reference]	.04	0 [Reference]
Quartile 2 × time	−0.003 (−0.006 to 0.000)		−0.003 (−0.006 to 0.000)		−0.003 (−0.006 to 0.000)		21
Quartile 3 × time	−0.004 (−0.007 to −0.001)		−0.004 (−0.007 to −0.001)		−0.004 (−0.007 to −0.001)		28
Quartile 4 × time	−0.003 (−0.006 to 0.000)		−0.003 (−0.006 to 0.000)		−0.003 (−0.006 to 0.000)		21
Lowest × highest quartiles							
Quartile 1 (lowest 25%)	0 [Reference]	.004	0 [Reference]	.003	0 [Reference]	.004	0 [Reference]
Quartiles 2-4 (highest 75%)	−0.003 (−0.005 to −0.001)		−0.003 (−0.006 to −0.001)		−0.003 (−0.006 to −0.001)		28

[a] Model 1 includes linear mixed models adjusted for age, sex, race and ethnicity, education, and income.

[b] Model 2 includes linear mixed models additionally adjusted for physical activity, body mass index, hypertension, diabetes, cardiovascular disease, depressive symptoms, alcohol consumption, and smoking.

[c] Model 3 includes linear mixed models additionally adjusted for total calories and healthy eating score.

[d] Difference is between each quartile and the first quartile in model 3.

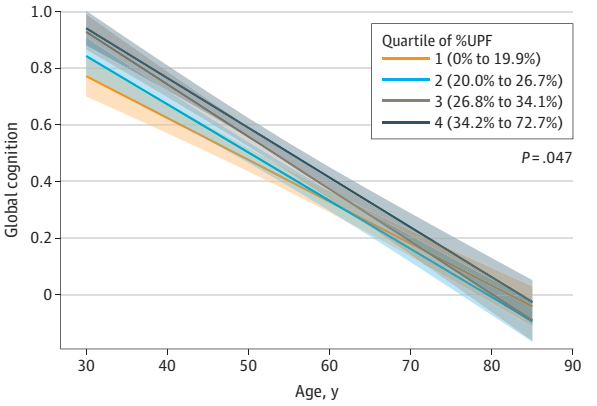
Cognitive Performance and Consumption of UPFs

After a median follow-up of 8 years, participants who reported consumption of UPF of more than 19.9% of daily calories had a 28% faster rate of global cognitive decline compared with those who reported consumption of UPF up to 19.9% of daily calories (β = −0.004; 95% CI, −0.006 to −0.001; *P* = .003) (**Table 2** and **Figure 2**). Moreover, participants who reported consumption of UPF more than 19.9% of daily calories had a 25% faster rate of executive function decline compared with those who reported consumption of UPF less than or equal to 19.9% of daily calories (β = −0.003, 95% CI, −0.005 to 0.000; *P* = .01) (Table 2). We found no association between the percentage of daily energy from UPF and the memory score. Age was an effect modifier in the association of the percentage of daily energy from UPF and cognitive function (*P* for interaction < .001). Participants younger than 60

years with UPF consumption greater than 19.9% showed a faster global cognition decline compared with those with UPF consumption less than 19.9% (β = −0.006; 95% CI, −0.009 to −0.003; *P* < .001) (eTable 3 in the Supplement), whereas there was no association of the percentage of daily energy from UPF and global cognition decline for those aged 60 years or older (eTable 3 in the Supplement). Adhesion to a healthy diet was also an effect modifier on the association of UPF and global cognitive function (*P* for interaction = .04). Participants with low healthy diet scores who consumed more than 19.9% of calories from UPF showed a faster global cognition decline compared with those who consumed less than 19.9% (β = −0.005; 95% CI, −0.009 to −0.002; *P* = .004) (eTable 4 in the Supplement and **Figure 3**A). We found no association between the percentage of daily energy from UPF and global cognition for participants with high healthy diet scores (eTable 4 in the Supplement and Figure 3B).

To assess the robustness of our findings, we performed sensitivity analyses excluding participants who reported caloric intakes above the 95th percentile by sex and without excluding participants because of caloric intake. We also imputed data for cognitive performance for participants younger than 55 years in wave 2. The results of the sensitivity analyses were similar to those found in the main analysis (eTable 5 and eTable 6 in the Supplement).

Figure 2. Trajectories of Global Cognitive Performance Over Time According to Quartiles of the Percentage of Daily Energy From Ultraprocessed Foods (%UPF)



Mixed linear regression models with random intercepts and slopes were adjusted for age, sex, race and ethnicity, education, income, physical activity, body mass index, hypertension, diabetes, cardiovascular disease, depressive symptoms, alcohol consumption, smoking, total calories, and healthy eating score. *P* values were calculated for the interaction between UPF quartiles (ordinal continuous variable) and age as the timescale. Shaded areas indicate 95% CIs.

Discussion

In this cohort study of 10 775 individuals followed for a median of 8 years, we found that consumption of UPF greater than 19.9% of total daily calories was associated with a faster decline in global cognitive performance and executive function compared with consumption less than 19.9% of total daily calories. We also found that the percentage of daily energy from UPF was associated with cognitive decline in participants younger than 60 years, which suggests the importance of preventive interventions in middle-aged adults. Additionally, the percentage of daily energy from UPF was associated with cognitive decline in participants with a low healthy diet score, whereas there was no association in those with a high healthy diet score. Our findings are in line with previous studies linking consumption of UPF and adverse health outcomes, such as the increased risk of overweight and obesity,[38,39] metabolic syndrome,[40] cancer,[41] cardiovascular diseases,[42] and all-cause mortality.[43,44]

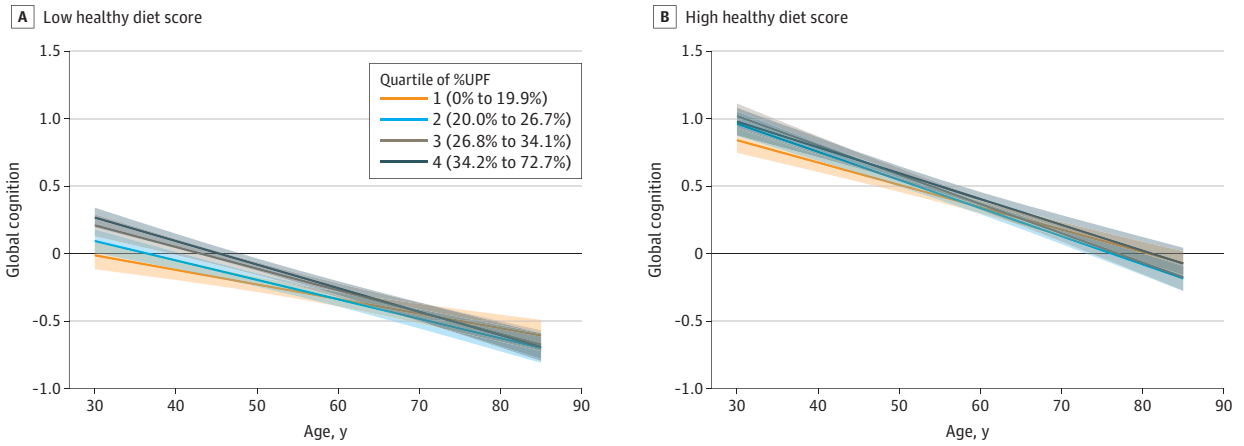
A prior study[21] that investigated the association of UPF and cognition in 568 individuals with type 2 diabetes found no association between total calorie consumption of UPF and cognitive decline, likely because of the small sample size or reverse causation, since individuals who develop diabetes could have reduced their UPF consumption after diagnosis. Our findings are in line with 2 recent studies[22,23] that investigated the association between UPF consumption and cognition. A cross-sectional study[22] of older US adults found an association between UPF consumption and worse verbal fluency performance in participants without preexisting chronic health conditions. Another study[23] investigated the association between consumption of UPF and dementia in 72 083 adults aged 55 years or older from the UK Biobank. Consumption of UPF was associated with a higher risk of all-cause dementia, vascular dementia, and Alzheimer disease after 10 years of follow-up.[23] The association between UPF and cognitive decline found in our study, particularly the decline in executive function, could be secondary to cerebrovascular lesions resulting from UPF consumption, because these functions are particularly sensitive to microvascular lesions.[42,45]

Neuroimaging studies[46,47] have found that high consumption of a Western dietary pattern was related to a reduction in the left hippocampus and gray matter volume in cognitively healthy individuals. Another possible biological mechanism for the decline in executive function and global cognition seen in our study may be related to systemic inflammation caused by the consumption of UPF, because increased levels of circulating proinflammatory cytokines have been associated with cognitive decline.[48-52] On the other hand, healthy dietary patterns were associated with higher gray and white matter volume, total brain volume, and Aβ42/40 ratio, as well as lower oxidative stress and inflammation,[53,54] which could explain our findings that the percentage of daily energy from UPF was associated with cognitive decline in participants with a low healthy diet score, but not in those with a high healthy diet score.

Strengths and Limitations

This study has some strengths. First, this is a large ethnically diverse cohort study from a low- and middle-income country with up to 10 years of follow-up. Second, the diet assessment was conducted using a validated questionnaire.[27] Moreover, we found that UPF consumption was associated with cognitive decline in middle-aged participants. The inclusion of

Figure 3. Trajectories of Global Cognitive Performances Over Time in Participants With Low Healthy Diet Scores and High Healthy Diet Scores



Graphs show trajectories of global cognitive performances over time according to quartiles of the percentage of daily energy from ultraprocessed foods (%UPF). Mixed linear regression models with random intercepts and slopes were adjusted for age, sex, race and ethnicity, education, income, physical activity, body mass index, hypertension, diabetes, cardiovascular disease, depressive symptoms, alcohol consumption, smoking, total calories, and healthy eating score. Shaded areas indicate 95% CIs.

middle-aged participants in studies about risk factors for cognitive decline is particularly important to understand potential preventive targets early in the life course.[55,56]

However, our findings should be considered in light of study limitations. Attrition is a concern for a long-term study, and participants younger than 55 years were not submitted to cognitive assessment during the second visit, because of the study design. Nevertheless, the use of IPW provided some correction for selection bias. Moreover, the imputation of missing cognitive data by design in wave 2 did not change the main study findings. In addition, diet was assessed only at baseline, which may not reflect longitudinal diet changes and may lead to an underestimation of the associations between UPF and cognition.[57] A few food items may have been misclassified because the FFQ was not specifically designed to assess the degree of processing. Because the FFQ was self-reported, the UPF consumption could be underreported owing to social desirability bias, which could have biased associations toward the null. Using the same calorie cutoff interval for men and women may introduce bias due to different caloric intake needs. However, the use of a relative measure as the exposure variable (percentage of the daily energy from UPF) minimizes the effect of extreme total energy intakes on the studied association.[58] Additionally, a sensitivity analysis using different cutoffs for calorie intake in men and women showed similar results to our main analysis. Although the use of software based on North American foods to estimate calorie content may be a limitation, it is unlikely to bias the UPF consumption estimations, because the UPF classification used the composition of products commonly consumed in Brazil and did not consider the nutritional composition from the software. Additionally, our findings may be subjected to selection bias, because the characteristics of those included and those excluded in the study at baseline differed. Although we adjusted the analyses for several sociodemographic and clinical confounders, we cannot exclude the possibility of residual confounding. Furthermore, since neuroimaging is not available in the ELSA-Brasil study, we were not able to investigate possible mechanisms that could explain the association between UPF consumption and cognitive decline in our study.

Conclusions

In this large cohort study, a higher percentage of daily energy from UPF was associated with cognitive decline during 8 years of follow-up. Intact cognitive function is key to successful aging. Therefore, despite the small effect size of the association between UPF consumption and cognitive decline, our findings are meaningful to cognitive health. Limiting UPF consumption, particularly in middle-aged adults, may be an efficient form to prevent cognitive decline. Future studies investigating the mechanism by which UPF may lead to cognitive decline are needed, as well as confirmation of our findings in other longitudinal studies and randomized clinical trials.

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