Observational Study

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Influential factors on cognitive performance in middle-aged cohort

Third National Health and Nutrition Examination Survey-based study

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Abstract

Aging-associated cognitive decline is closely linked to illness, dementia, increased mortality, and is a major health and social issue. The purpose of this study was to determine modifiable factors associated with cognitive performance.

We analyzed data from a random sample of participants of the Third National Health and Nutrition Examination Survey, which is a cross-sectional survey, of the US population, aged 20 to 59 years, who underwent computer-based neurocognitive testing. There were 5 outcome measures in 3 neurocognitive tests: the mean of simple reaction time test, the mean total latency of the symbol digit substitution test (SDST), the average number of errors of the SDST, the average trials to criterion of the serial digit learning test (SDLT), and the average total score of the SDLT.

Socioeconomic status, including older age, black ethnicity, lower income ratio, and lower education level, were associated with poorer neurocognitive function in all analyzed tests. In addition, participants with poor health, nonsmokers, and nondrinkers performed worse in all administered tests compared with individuals with good health, smokers, and participants consuming alcoholic beverages. Dietary and biochemical characteristics of the blood were not consistently associated with neurocognitive performance.

Our results indicate that socioeconomic factors, health-related and dietary habits, biochemical parameters of the blood, and job category were associated with neurocognitive performance in visual attention, learning, and concentration in a large, nationally representative sample of healthy, ethnically diverse 20 to 59-year-olds. Future studies are needed to understand the mechanisms of cognitive aging and the factors that contribute to its individual differences.

Abbreviations: CNS = central nervous system, NCHS = the National Center for Health Statistics, NHANES III = the Third National Health and Nutrition Examination Survey, SDLT = serial digit learning test, SDST = symbol digit substitution test, SRTT = simple reaction time test.

Keywords: neurocognitive function, serial digit learning test, simple reaction time test, symbol digit substitution test, the Third National Health and Nutrition Examination Survey (NHANES III)

1. Introduction

It is projected that by 2050, the number of people aged 60 and over will more than double compared with similar statistics in 2015 (www.un.org). Low birth rates along with improved survival at all ages have contributed to population aging, which has become a growing global socioeconomic concern, as it puts a strain on medical care systems and social services. Cognitive decline, poor memory, and other neurological complications often arise as individuals age. Up to 30% of people aged 85 and over experience mild cognitive impairment,[1] and up to 15% of these patients develop dementia[2]—a condition characterized by severe cognitive decline, disability, and high mortality. Assessment of modifiable factors influencing the neurocognitive outcome is essential for developing of nondrug interventions.

In addition to advanced age, multiple factors might contribute to the development of dementia such as low education level, high blood pressure, diabetes, and smoking.[3] Poor smelling ability, higher homocysteine level,[3] history of depression, low health status, coronary artery disease, stroke, and arthritis were reported as potential risk factors associated with cognitive decline.[4] Interestingly, according to the same study, antidepressant consumption along with kidney disease and married status had inverse correlation with cognitive decline. Several reports supported the idea that exposure to any type of systemic chronic illness over time jeopardizes the integrity of cognitive function.[5] Examples of such chronic illnesses include asthma, chronic obstructive pulmonary disease, liver cirrhosis, renal, autoimmune diseases, sleep disorders, multiple types of cancer, and AIDS.[5]

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Identified risk factors also include neurotoxicity due to environmental or occupational conditions, such as contact with solvents and lead.[6] Genetic factors may also affect cognitive performance. The apolipoprotein E ε4 allele, for instance, is predictive of poorer cognitive function, and the condition could become exacerbated by additional chronic illness.[7] Cognitive function is profoundly affected by unbalanced levels of hormones such as estrogen, thyroid and pituitary hormones, and cortisol.[5] Finally, lifestyle choices and behaviors have a significant impact on health status in general and cognitive performance in particular. Smoking,[8] drug (cocaine, opiates, etc) and alcohol abuse,[9] and physical inactivity[2] along with several dietary insufficiencies such as zinc, thiamine, folate, and vitamins B6 and B12[3] have been associated with compromised cognitive abilities. Neurocognitive performance is affected by nutritional factors obtained through diet: glucose, omega-3 fatty acids, and iron.[10,11] Inconsistent results have been observed when investigating effects of such nutrients as vitamin D,[12] carotenoids, folate, polyunsaturated fatty acids, and curcumin.[1] High calorie diets, and also increased consumption of refined carbohydrates predict poorer cognitive outcome; on the contrary, calorie restriction and adherence to the Mediterranean diet have generated mixed and even conflicting results possibly due to differences in methodology of assessment.[1,13,14] Lack of definitive conclusions on the effects of nutrition on neurocognitive function in aged individuals warrants additional research efforts such as this study to identify modifiable factors linked to cognitive performance.

2. Materials and methods

2.1. Study population

The study analyzed data from the Third National Health and Nutrition Examination Survey (NHANES III)—an assessment by the National Center for Health Statistics (NCHS) of the health and nutrition status of a nationally representative sample of noninstitutionalized US civilians 2 months and older. The goal behind NHANES III was to collect nationally representative data on the nutritional status and health of the US population.[15,16] Cognitive function evaluation was performed on a random half-sample of NHANES III participants 20 to 59 years old (n = 5662). NHANES received approval from the National Center for Health Statistics Research Ethics Review Board, and every participant in the database provided written consent.[17] Also, NHANES III database has been de-identified.

2.2. Testing of cognitive function and definition of outcomes

The primary outcome of the present study was the level of the neurocognitive function, as measured by the following 3 neurobehavioral computerized tests: the simple reaction time test (SRTT), the symbol digit substitution test (SDST), and the serial digit learning test (SDLT).[18,19]

The SRTT is designed to evaluate simple reaction time, general alertness, and motor speed measured in milliseconds. The subjects were instructed to select the button to register their response as soon as they saw the square on the screen. The interval between trials varied randomly according to a uniform distribution ranging from 2.5 to 5.0 seconds to limit anticipatory responses. Participants were given a total of 50 trials. The SRTT was scored as the average reaction time, excluding the first 10 test trials.[18,19]

The SDST is designed to measure coding ability and visual attention. The subject is presented with an array of nine numbers matched with a symbol. Next, a set of symbols is given and the participant must type the correct digit for each symbol as quickly as possible. Four trials are conducted, with a different pairing of digits and symbols on each trial. The SDST was scored as the average total time, in seconds, for completion of the 4 trials.[18,19]

The SDLT evaluates learning and recall. It involves repeated presentation of a sequence of 8 digits displayed 1 at a time on the computer screen. After the sequence of digits is displayed, the subject is required to enter the sequence of numbers in the order in which they were presented. Testing continues until the subject correctly entered 2 consecutive trials or until the subject attempted 8 trials. The total score on the SDLT equals the sum of the errors committed during the trials.[18,19]

There were 5 measures out of 3 neurocognitive tests as dependent variables in this study, including the mean of SRTT, the mean total latency of the SDST, the average number of errors of the SDST, the average trials to criterion of the SDLT, and the average total score of the SDLT.

2.3. Study variables

The variables obtained for each case included patient demographics (age, sex, race/ethnicity, poverty income ratio, education, marital status, occupation), health status/comorbidities (health status, diabetes, hypertension, anemia, major depression, dysthymic disorder, overweight), health behaviors (smoking history, alcohol use, breakfast consumption, walking activity, social support, caring for/living with pets), dietary and nutritional intake (total protein intake, total unsaturated fatty acid intake, total carbohydrate intake, intakes of ascorbic acid, vitamin E, vitamin B12, vitamin B6, riboflavin, thiamin, and folacin), environmental and laboratory variables (room temperature, presence of cigarette smoking, blood lead level, urinary cadmium level, serum C-reactive protein, serum glucose level, glycated hemoglobin level, serum vitamin D level). Marital status was categorized as married, never married, and divorced. Classification of occupations was based on the study by Hnizdo et al,[20] and was re-categorized as office building services, rubber and chemical, transportation and trucking, metal, repair service, construction, and other industries

2.4. Statistical analysis

Data were represented by mean ± standard error for continuous variables, or unweighted counts (weighted %) for categorical variables. Univariate and multivariate linear regression analyses were performed using the Complex Samples General Linear Model (CSGLM) to explore the association of the study variables with the level of central nervous system (CNS) function. Variables that showed a tendency of association with the level of cognitive function ($P < .05$) in univariate analysis were evaluated using a multivariate logistic regression model.

All analyses included special sample weight (WTPFCNS6, used only in conjunction with the CNS subsample and with items collected as part of the CNS component of the examination); stratum, and primary sampling units (PSU) per recommendations from NCHS; complex sample analysis to address oversampling; nonresponse; and non-coverage to provide nationally representative estimates.

All statistic assessments were 2-sided and were evaluated at the 0.05 level of significance. Statistical analyses were performed by

Table 1

Subject characteristics (unweighted n=5662, weighted n=137,079,473).

Neurocognitive tests	
SRTT/mean reaction time test (ms) (n=5138)	233.76±1.35
SDST/mean total latency (s) (n=5092)	22.78±0.21
SDST/number of errors (n=5092)	1.283±0.06
SDLT/trials to criterion (n=4962)	4.66±0.07
SDLT/total score (n=4962)	4.48±0.15
Demography	
Age	37.10±0.23
Male sex	2594 (49.0)
Race	
White	1924 (74.4)
Black	1791 (11.7)
Mexican-American	1708 (5.9)
Other	239 (8.0)
Income ratio	3.09±0.08
Education (in y)	12.68±0.09
Marital status	
Married	3384 (64.7)
Never married	1310 (21.0)
Divorced	958 (14.4)
Occupation category	
Office building services	805 (19.8)
Rubber and chemical	102 (2.1)
Transportation and trucking	195 (4.7)
Metal	79 (2.3)
Repair service	87 (2.2)
Construction	281 (6.8)
Other industries	2939 (62.1)
Health/comorbidity	
Health status	
Fair	968 (10.1)
Poor	149 (1.7)
Good	4545 (88.2)
Diabetes	266 (3.6)
Hypertension	1093 (17.9)
Anemia	126 (2.1)
Depression	432 (12.7)
BMI	
Normal (<25)	2338 (46.5)
Overweight (≥25)	3324 (53.5)
Health behavior	
Smoking	
Never	2897 (46.6)
Former	1053 (21.4)
Current	1711 (31.9)
Alcohol consumption	
Never	852 (11.3)
Former	1732 (28.5)
Current	2919 (60.2)
Breakfast consumption	
Every day	2495 (42.3)
Some days and weekends only	1972 (33.9)
Rarely and never	1194 (23.7)
Living with pets	
No	3697 (56.0)
Yes	1961 (44.0)
Social support	
Talking on the phone with family or friends (per wk)	
Never	741 (7.4)
Less than median (≤7 times)	3329 (61.2)
More than median (>7 times)	1576 (31.4)
Spending time with friends or relatives (per y)	
Never	338 (3.7)
Less than median (≤52 times)	2946 (50.4)
More than median (>52 times)	2375 45.9)
Visiting neighbors (per y)	
Never	2881 (47.1)
Less than median (≤52 times)	1643 (32.4)
More than median (>52 times)	1135 (20.5)
Walking activity (per mo)	6.28±0.31
Nutrition	
Total protein intake (g)	86.05±0.91
Total unsaturated fatty acid intake (g)	52.66±0.84
Total Carbohydrate intake (g)	283.60±3.50
Ascorbic acid (mg)	106.26±2.33
Vitamin E (mg)	9.77±0.22
Vitamin B12 (mcg)	5.51±0.22
VitaminB6 (mg)	1.93±0.03
Riboflavin (mg)	2.06±0.03
Thiamin (mg)	1.76±0.02
Folacin (mcg)	287.29±5.06
Biochemical parameters	
Blood lead level (μmol/L)	0.16±0.01
Urinary cadmium level (nmol/L)	5.35±0.23
Serum C-reactive protein level (mg/dL)	0.38±0.01
Serum glucose level (mmol/L)	5.20±0.05
Glycated hemoglobin level (%)	5.23±0.03
Vitamin D level (nmol/L)	74.71±1.06

Continuous variables are presented as mean±standard error; categorical variables are presented as unweighted counts (weighted %). Numbers may not add up to full sample due to missing data. BMI=body mass index, SDLT=serial digit learning test, SDST=symbol digit substitution test, SRTT=simple reaction time test.

IBM SPSS statistical software version 22 for Windows (IBM Corp., Armonk, NY).

2.5. Ethics

This study used data from NHANES III database and therefore we did not have to obtain informed consent from the participants or obtain approval from an institutional review board.

3. Results

3.1. Subject characteristics

The NHANES III database (1988–1994) included information on a total of 31,311 participants. Out of 11,306 participants aged between 20 and 59 years, 5662 participants underwent CNS function evaluation. Using NHANES sample weight, the analytic sample size was estimated to be equivalent to a population-based sample size of 137,079,473 participants. The average age of participants was 37 years with 74.4% individuals of white race; the proportion of male subjects was 49%. The subjects' characteristics, and also unadjusted mean cognitive function test scores are summarized in Table 1. The mean of simple reaction time on the SRTT was 233.76 milliseconds, the mean total latency of the SDST was 22.78 seconds, the average number of errors on the SDST was 1.28, the average trials to criterion on the SDLT was 4.66, and the average total score of the SDLT was 4.48 (Table 1).

3.2. Analyses of associated factors on CNS function

3.2.1. SRTT/mean reaction time test. The result of univariate linear regression analysis revealed that demographic and socioeconomic status, including age, sex, race, income ratio, education level, marital status, and occupation category, were associated with changes in the reaction time on the SRTT. In addition, lifestyle factors and health status such as smoking, alcohol consumption, living with pets, talking on the phone with family or friends, spending time with friends or relatives, diabetes diagnosis, hypertension, and body mass index (BMI) also had an effect on the results of the SRTT. And finally, dietary habits, including total protein intake, total unsaturated fatty acid intake, total carbohydrate intake, levels of vitamin E, vitamin B6, riboflavin, thiamin, folacin, urinary cadmium, serum C-reactive protein, serum glucose, glycated hemoglobin, and serum vitamin D affected the reaction time on the SRTT (Table 2).

Multivariate linear regression analysis demonstrated that increased age was associated with increased reaction time on the SRTT (adjusted coefficient 0.362, 95% confidence interval

Table 2

Relationships between subject characteristics and the mean reaction time on the SRTT.

	SRTT/mean reaction time test (ms)			
Characteristics	**Coef. (95% CI)**	***P***	**Adjusted coef. (95% CI)**	***P***
Demography				
Age	**0.327 (0.161, 0.492)**	<.001	**0.362 (0.153, 0.571)**	**.001**
Male sex	**−14.826 (−19.645, −10.008)**	<.001	**−11.353 (−17.238, −5.468)**	<.001
Race				
White	Reference		Reference	
Black	**18.208 (12.927, 23.488)**	<.001	**8.277 (1.646, 14.908)**	**.015**
Mexican-American	**19.071 (13.587, 24.554)**	<.001	2.648 (−4.946, 10.242)	.487
Other	**9.834 (0.054, 19.613)**	**.049**	−2.351 (−12.744, 8.041)	.651
Income ratio	**−3.908 (−4.819, −2.997)**	<.001	**−1.582 (−2.563, −0.600)**	**.002**
Education (in y)	**−3.570 (−4.486, −2.653)**	<.001	**−2.314 (−3.513, −1.114)**	<.001
Marital status				
Married	Reference		Reference	
Never married	3.119 (−2.253, 8.490)	.249	6.350 (−0.041, 12.741)	.051
Divorced	**10.131 (3.051, 17.211)**	**.006**	2.066 (−4.896, 9.027)	.554
Occupation category				
Office building services	Reference		Reference	
Rubber and chemical	−1.980 (−13.697, 9.738)	.736	−0.972 (−13.502, 11.557)	.877
Transportation and trucking	−1.524 (−9.296, 6.248)	.695	−1.410 (−10.010, 7.190)	.743
Metal	10.891 (−1.206, 22.989)	.077	**14.167 (1.980, 26.355)**	**.024**
Repair service	−2.523 (−11.856, 6.810)	.589	−1.986 (−11.869, 7.896)	.688
Construction	2.121 (−4.601, 8.843)	.529	5.996 (−1.591, 13.583)	.119
Other industries	**7.809 (2.637, 12.982)**	**.004**	**5.444 (0.014, 10.874)**	**.049**
Health/comorbidity				
Health status				
Fair	Reference		Reference	
Poor	25.008 (−7.518, 57.533)	.129	19.460 (−19.040, 57.960)	.315
Good	**−23.858 (−32.127, −15.590)**	<.001	**−10.271 (−19.822, −0.721)**	**.036**
Diabetes	**22.468 (3.014, 41.921)**	**.024**	14.147 (−14.586, 42.881)	.327
Hypertension	**10.542 (4.569, 16.515)**	**.001**	2.991 (−2.630, 8.611)	.290
Anemia	5.702 (−4.338, 15.743)	.259		
Depression	3.112 (−4.217, 10.442)	.398		
BMI				
Normal (<25)	Reference		Reference	
Overweight (≥25)	**6.734 (1.835, 11.633)**	**.008**	3.275 (−1.374, 7.923)	.163
Health behavior				
Smoking				
Never	Reference		Reference	
Former	−4.280 (−11.054, 2.493)	.210	0.904 (−6.356, 8.163)	.804
Current	**−4.467 (−8.609, −0.325)**	**.035**	**−5.077 (−9.241, −0.914)**	**.018**
Alcohol consumption				
Never	Reference		Reference	
Former	**−19.995 (−29.519, −10.471)**	<.001	**−15.270 (−25.358, −5.182)**	**.004**
Current	**−31.009 (−41.305, −20.714)**	<.001	**−17.443 (−28.325, −6.561)**	**.002**
Breakfast consumption				
Every day	Reference			
Some days and weekends only	−0.945 (−5.095, 3.204)	.649		
Rarely and never	0.028 (−5.329, 5.386)	.992		
Living with pets				
No	Reference		Reference	
Yes	**−7.073 (−10.402, −3.745)**	<.001	−3.399 (−7.365, 0.567)	.091
Social support				
Talking on the phone with family or friends (per wk)				
Never	Reference		Reference	
Less than median (≤7 times)	**−8.652 (−15.941, −1.364)**	**.021**	4.016 (−3.401, 11.432)	.282
More than median (>7 times)	**−8.523 (−16.724, −0.321)**	**.042**	4.776 (−3.151, 12.703)	.232
Spending time with friends or relatives (per y)				
Never	Reference		Reference	

(*continued*)

Table 2
(continued).

Characteristics	SRTT/mean reaction time test (ms)			
	Coef. (95% CI)	*P*	Adjusted coef. (95% CI)	*P*
Less than median (≤52 times)	**−11.858 (−22.040, −1.677)**	**.023**	−6.521 (−20.817, 7.775)	.364
More than median (>52 times)	**−14.235 (−24.174, −4.295)**	**.006**	−8.046 (−21.248, 5.156)	.227
Visiting neighbors (per y)				
Never	Reference			
Less than median (≤52 times)	−4.581 (−9.823, 0.661)	.085		
More than median (>52 times)	2.577 (−2.648, 7.802)	.327		
Walk activity (per mo)	−0.077 (−0.195, 0.042)	.201		
Diet/nutrition				
Total protein intake (g)	**−0.081 (−0.135, −0.028)**	**.004**	0.009 (−0.062, 0.080)	.792
Total unsaturated fatty acid intake (g)	**−0.139 (−0.200, −0.078)**	**<.001**	−0.070 (−0.162, 0.021)	.129
Total carbohydrate intake (g)	**−0.025 (−0.041, −0.008)**	**.004**	0.008 (−0.012, 0.028)	.424
Ascorbic acid (mg)	−0.015 (−0.034, 0.004)	.113		
Vitamin E (mg)	**−0.387 (−0.594, −0.179)**	**<.001**	0.010 (−0.218, 0.239)	.928
Vitamin B12 (mcg)	−0.121 (−0.257, 0.014)	.079		
VitaminB6 (mg)	**−2.951 (−4.788, −1.114)**	**.002**	0.376 (−2.657, 3.409)	.805
Riboflavin (mg)	**−2.200 (−4.176, −0.223)**	**.030**	**3.927 (0.894, 6.960)**	**.012**
Thiamin (mg)	**−3.309 (−5.337,−1.280)**	**.002**	−1.158 (−4.380, 2.063)	.473
Folacin (mcg)	**−0.014 (−0.024,−0.004)**	**.009**	**−0.019 (−0.033, −0.005)**	**.008**
Biochemical parameters				
Blood lead level (μmol/L)	−7.011 (−21.709, 7.687)	.342		
Urinary cadmium level (nmol/L)	**0.201 (0.008, 0.394)**	**.041**	−0.047 (−0.296, 0.203)	.709
Serum C-reactive protein level (mg/dL)	**6.869 (2.748, 10.989)**	**.002**	0.678 (−4.825, 6.181)	.806
Serum glucose level (mmol/L)	**1.781 (0.808, 2.754)**	**.001**	0.028 (−2.782, 2.839)	.984
Glycated hemoglobin level (%)	**4.351 (2.293, 6.410)**	**<.001**	−1.346 (−6.144, 3.453)	.576
Vitamin D level (nmol/L)	**−0.152 (−0.214, −0.091)**	**<.001**	−0.027 (−0.102,0.049)	.479

Variables with *P* values <.05 in univariate models were included in multivariate analyses.
Bold indicates significance (*P*<.05).
CI = confidence interval, coef. = coefficient, SRTT = simple reaction time test.

[CI] 0.153, 0.571, *P* = .001), whereas higher income ratio and higher education level were associated with decreased reaction time on the SRTT (adjusted coefficient −1.582, 95% CI −2.563, −0.600, *P* = .002; and adjusted coefficient −2.314, 95% CI −3.513, −1.114, *P* < .001, respectively). Males had faster reaction than females (adjusted coefficient −11.353, 95% CI −17.238, −5.468, *P* < 0.001), and black race participants showed increased reaction time compared with white race participants (adjusted coefficient 8.277, 95% CI 1.646, 14.908, *P* = .015). Occupation category was also associated with variation in SRTT reaction time: metal industry workers demonstrated slower reaction compared with office building services employees (adjusted coefficient 14.167, 95% CI 1.980, 26.355, *P* = .024). Participants with good health status had faster reaction than participants in fair health condition (adjusted coefficient −10.271, 95% CI −19.822, −0.721, *P* = .036). Our analysis demonstrated that currently smoking participants had faster reaction compared to participants who never smoked (adjusted coefficient −5.077, 95% CI −9.241, −0.914, *P* = .018); and participants who formerly and currently consumed alcohol had faster reaction than participants who never consumed alcoholic beverages (adjusted coefficient −15.270, 95% CI −25.358, −5.182, *P* = .004; adjusted coefficient −17.443, 95% CI −28.325, −6.561, *P* = .002, respectively). Riboflavin consumption was associated with increased reaction time (adjusted coefficient 3.927, 95% CI 0.894, 6.960, *P* = .012), whereas intake of folacin was associated with faster reaction on the SRTT (adjusted coefficient −0.019, 95% CI −0.033, −0.005, *P* = .008).

3.2.2. SDST/mean total latency. The result of univariate linear regression analysis indicated that demographic and socioeconomic status, including age, sex, race, income ratio, education level, marital status, and occupation category, were associated with changes in the mean total latency in the SDST. In addition, health status and lifestyle habits, such as diagnosed diabetes, hypertension, BMI, smoking, drinking, habits to eat breakfast, living with pets, talking on phone with family or friends, and spending time with friends or relatives, also affected the results for the SDST. Nutrition habits and biochemical parameters, including total protein intake, total unsaturated fatty acid intake, total carbohydrate intake, ascorbic acid, vitamin E, vitamin B6, riboflavin, thiamin, folacin, blood lead levels, urinary cadmium, serum C-reactive protein, serum glucose, glycated hemoglobin, and serum vitamin D levels, were also strongly associated with changes in the mean total latency of SDST (Table 3).

Multivariate linear regression analysis demonstrated that increased age (adjusted coefficient 0.250, 95% CI 0.226, 0.273, *P* < .001) was associated with increased mean total latency in the SDST, whereas higher income ratio and higher education level were associated with decreased mean total latency (adjusted coefficient −0.254, 95% CI −0.374, −0.135, *P* < .001; and adjusted coefficient −0.899, 95% CI −1.021, −0.776, *P* < .001, respectively). Moreover, sex, race, and marital status were associated with variations in the mean total latency. Specifically, males had higher latency time than females (adjusted coefficient 1.862, 95% CI 1.349, 2.374, *P* < .001), Black and Mexican-American participants had higher latency time compared with white participants (adjusted coefficient 2.820, 95% CI 2.269, 3.371, *P* < .001; and adjusted coefficient 2.126, 95% CI 1.179, 3.073, *P* < .001, respectively); and never married participants showed higher latency time compared with married participants (adjusted coefficient 0.762, 95% CI 0.324, 1.200,

Table 3

Relationships between subject characteristics, mean total latency, and the number of errors on the SDST.

	SDST/mean total latency (s)				SDST/Number of errors			
Characteristics	**Coef. (95% CI)**	***P***	**Adj. coef. (95% CI)**	***P***	**Coef. (95% CI)**	***P***	**Adj. coef. (95% CI)**	***P***
Demographics								
Age	**0.242 (0.213, 0.270)**	<.001	**0.250 (0.226, 0.273)**	<.001	**0.034 (0.025, 0.043)**	<.001	**0.038 (0.025, 0.050)**	<.001
Male sex	**1.328 (0.751, 1.905)**	<.001	**1.862 (1.349, 2.374)**	<.001	**−0.378 (−0.531, −0.225)**	<.001	**−0.336 (−0.544, −0.127)**	**.002**
Race								
White	Reference		Reference		Reference		Reference	
Black	**4.098 (3.551, 4.645)**	<.001	**2.820 (2.269, 3.371)**	<.001	**0.810 (0.615, 1.005)**	<.001	**0.618 (0.369, 0.867)**	<.001
Mexican-American	**5.950 (4.929, 6.971)**	<.001	**2.126 (1.179, 3.073)**	<.001	**0.891 (0.645, 1.138)**	<.001	**0.540 (0.210, 0.871)**	**.002**
Other	**4.019 (2.443, 5.595)**	<.001	**1.988 (1.007,2.969)**	<.001	0.425 (-0.062, 0.912)	.086	0.275 (-0.269, 0.818)	.315
Income ratio	**−0.712 (−0.869, −0.554)**	<.001	**−0.254 (−0.374, −0.135)**	<.001	**−0.132 (−0.180, −0.084)**	<.001	**−0.074 (−0.118, −0.030)**	**.001**
Education (in y)	**−1.225 (−1.339, −1.110)**	<.001	**−0.899 (−1.021, −0.776)**	<.001	**−0.136 (−0.170, −0.103)**	<.001	**−0.082 (−0.120, −0.044)**	<.001
Marital status								
Married	Reference		Reference		Reference		Reference	
Never married	**−1.687 (−2.455, −0.920)**	<.001	**0.762 (0.324, 1.200)**	**.001**	**−0.339 (−0.513, −0.164)**	<.001	0.066 (−0.106, 0.238)	.446
Divorced	**1.336 (0.536, 2.135)**	**.002**	−0.088 (−0.755, 0.580)	.793	**0.324 (0.055, 0.594)**	**.019**	0.001 (−0.314, 0.316)	.994
Occupation category								
Office building services	Reference		Reference		Reference			
Rubber and chemical	1.255 (−0.206, 2.716)	.091	−0.092 (−1.068, 0.883)	.850	0.145 (−0.341, 0.631)	.551		
Transportation and trucking	0.631 (−0.472, 1.734)	.256	**−1.027 (−1.960, −0.094)**	**.032**	0.028 (−0.509, 0.564)	.918		
Metal	**3.130 (1.521, 4.739)**	<.001	0.772 (−0.624, 2.168)	.272	−0.011 (-0.726, 0.704)	.976		
Repair service	**3.209 (0.828, 5.590)**	**.009**	0.151 (−1.126, 1.427)	.814	−0.013 (-0.580, 0.555)	.964		
Construction	**2.707 (1.610, 3.804)**	<.001	−0.082 (-0.989, 0.826)	.857	−0.231 (-0.620, 0.158)	.239		
Other industries	**1.861 (1.383, 2.338)**	<.001	0.435 (−0.065, 0.935)	.087	0.125 (−0.090, 0.340)	.248		
Health/comorbidity								
Health status								
Fair	Reference		Reference		Reference		Reference	
Poor	**2.120 (0.179, 4.061)**	**.033**	0.621 (−1.895, 3.136)	.622	−0.319 (−1.033, 0.394)	.373	−0.714 (−1.449, 0.021)	.057
Good	**−5.345 (−6.397, −4.292)**	<.001	**−0.830 (−1.586, −0.073)**	**.032**	**−0.838 (−1.221, −0.456)**	<.001	−0.230 (−0.636, 0.177)	.261
Diabetes	**4.636 (2.114, 7.157)**	**.001**	0.773 (−1.273, 2.820)	.451	0.650 (−0.234, 1.534)	.146		
Hypertension	**2.179 (1.524, 2.835)**	<.001	−0.226 (−0.792, 0.340)	.426	**0.380 (0.149, 0.610)**	**.002**	−0.034 (−0.274, 0.207)	.780
Anemia	−0.890 (−2.503, 0.722)	.273			−0.104 (−0.674, 0.467)	0.717		
Depression	0.230 (−0.388, 0.848)	.459			0.046 (−0.197, 0.288)	0.706		
BMI								
Normal	Reference		Reference		Reference			
Overweight	**1.939 (1.407, 2.472)**	<.001	−0.107 (−0.523, 0.309)	.607	0.095 (−0.031, 0.221)	.135		
Health behavior								
Smoking								
Never	Reference		Reference		Reference			
Former	0.469 (−0.214, 1.153)	.174	−0.503 (−1.006, 0.0001)	.050	−0.041 (−0.247, 0.166)	.695		
Current	**1.462 (0.887, 2.037)**	<.001	−0.037 (−0.538, 0.463)	.881	0.172 (−0.045, 0.390)	.118		
Alcohol consumption								
Never	Reference		Reference		Reference		Reference	
Former	**−2.598 (−3.917, −1.278)**	<.001	**−1.994 (−3.041, −0.947)**	<.001	**−0.336 (−0.661, −0.011)**	**.043**	−0.214 (−0.611, 0.184)	.286
Current	**−4.162 (−5.367, −2.956)**	<.001	**−1.804 (−2.711, −0.897)**	<.001	**−0.643 (−0.968, −0.317)**	<.001	−0.135 (−0.541, 0.270)	.505

(*continued*)

Table 3
(continued).

Characteristics	SDST/mean total latency (s)				SDST/Number of errors			
	Coef. (95% CI)	P	Adj. coef. (95% CI)	P	Coef. (95% CI)	P	Adj. coef. (95% CI)	P
Breakfast consumption								
Every day	Reference		Reference		Reference		Reference	
Some days and weekends only	**−0.784 (−1.397, −0.171)**	**.013**	**−0.738 (−1.198, −0.278)**	**.002**	0.021 (−0.178, 0.220)	.832	0.075 (−0.145, 0.296)	.496
Rarely and never	−0.650 (−1.417, 0.117)	.095	**−0.856 (−1.303, −0.409)**	**<.001**	**−0.292 (−0.505, −0.079)**	**.008**	**−0.303 (−0.552, −0.054)**	**.018**
Living with pets								
No	Reference		Reference		Reference		Reference	
Yes	**−1.282 (−1.824, −0.741)**	**<.001**	**−0.621 (−1.053, −0.188)**	**.006**	**−0.178 (−0.348, −0.009)**	**.040**	−0.072 (−0.246, 0.103)	.414
Social support								
Talking on the phone with family or friends (per wk)								
Never	Reference		Reference		Reference		Reference	
Less than median (≤7 times)	**−4.100 (−5.295, −2.904)**	**<.001**	−0.272 (−1.134, 0.590)	.529	**−0.857 (−1.389, −0.325)**	**.002**	−0.634 (−1.281, 0.013)	.055
More than median (>7 times)	**−5.458 (−6.700, −4.216)**	**<.001**	−0.594 (−1.499, 0.312)	.194	**−0.987 (−1.559, −0.414)**	**.001**	−0.702 (−1.423, 0.018)	.056
Spending time with friends or relatives (per y)								
Never	Reference		Reference		Reference		Reference	
Less than median (≤52 times)	**−4.063 (−6.258, −1.869)**	**.001**	−0.474 (−1.525, 0.577)	.369	−0.235 (−0.650, 0.180)	.261	0.370 (−0.086, 0.825)	.110
More than median (>52 times)	**−5.234 (−7.361, −3.107)**	**<.001**	−0.525 (−1.649, 0.599)	.352	**−0.454 (−0.844, −0.063)**	**.024**	0.313 (−0.154, 0.780)	.184
Visiting neighbors (per y)								
Never	Reference				Reference			
Less than median (≤52 times)	−0.331 (−0.989, 0.326)	.316			0.065 (−0.087, 0.217)	.393		
More than median (>52 times)	0.433 (−0.217, 1.083)	.187			0.101 (−0.115, 0.316)	.353		
Walking activity (per mo)	0.010 (−0.011, 0.032)	.337			−0.003 (−0.009, 0.004)	.402		
Diet/nutrition								
Total protein intake (g)	**−0.006 (−0.011, −0.001)**	**.015**	0.002 (−0.006, 0.010)	.579	**−0.003 (−0.005, −0.001)**	**.003**	−0.001 (−0.004, 0.003)	.682
Total unsaturated fatty acid intake (g)	**−0.017 (−0.024, −0.009)**	**<.001**	−0.010 (−0.023, 0.002)	.093	**−0.004 (−0.006, −0.001)**	**.006**	0.001 (−0.003, 0.005)	.622
Total Carbohydrate intake (g)	**−0.005 (−0.007, −0.003)**	**<.001**	−0.002 (−0.004, 0.001)	.118	**−0.002 (−0.002, −0.001)**	**<.001**	−0.001 (−0.002, 0.0002)	.150
Ascorbic acid (mg)	**−0.003 (−0.005, −0.001)**	**.015**	−0.00003 (−0.002, 0.002)	.977	**−0.001 (−0.002,−0.0002)**	**.010**	−0.0003 (−0.001, 0.001)	.564
Vitamin E (mg)	**−0.060 (−0.087, −0.033)**	**<.001**	0.004 (−0.028, 0.035)	.822	**−0.010 (−0.019,−0.0004)**	**.042**	0.003 (−0.007, 0.012)	.581
Vitamin B12 (mcg)	−0.003 (−0.028, 0.023)	–	–		−0.005 (−0.010, 0.001)	.096		
VitaminB6 (mg)	**−0.301 (−0.418, −0.184)**	–	–	.469	**−0.127 (−0.191, −0.062)**	**<.001**	−0.080 (−0.218, 0.058)	.249
Riboflavin (mg)	**−0.400 (−0.578, −0.222)**	**<.001**	−0.016 (−0.347, 0.315)	.925	**−0.099 (−0.165, −0.033)**	**.004**	0.110 (−0.018, 0.237)	.090
Thiamin (mg)	**−0.448 (−0.674, −0.222)**	**<.001**	0.019 (−0.358, 0.395)	.921	**−0.150 (−0.224, −0.076)**	**<.001**	−0.005 (−0.146, 0.136)	.941
Folacin (mcg)	**−0.001 (−0.002, −0.001)**	**.001**	−0.001 (−0.002, 0.001)	.206	**−0.0004 (−0.001, −0.0001)**	**.022**	−0.0001 (−0.001, 0.001)	.738
Biochemical parameters								
Blood lead level (μmol/L)	**11.274 (8.356, 14.192)**	**<.001**	**2.640 (0.618, 4.663)**	**.012**	**0.903 (0.337, 1.468)**	**.002**	0.209 (−0.495, 0.912)	.554
Urinary cadmium level (nmol/L)	**0.129 (0.026, 0.232)**	**.015**	0.006(−0.017, 0.028)	.616	0.025 (−0.006, 0.056)	.116		
Serum C-reactive protein level (mg/dL)	**1.613 (0.823, 2.403)**	**<.001**	0.483(−0.192, 1.158)	.157	**0.442 (0.149, −0.735)**	**.004**	**0.393 (0.075, 0.710)**	**.016**
Serum glucose level (mmol/L)	**0.832 (0.451, 1.214)**	**<.001**	0.009(−0.316, 0.334)	.957	0.101 (−0.008, 0.210)	.068		
Glycated hemoglobin level (%)	**2.162 (1.675, 2.649)**	**<.001**	0.257(−0.311, 0.825)	.367	**0.259 (0.101, 0.418)**	**.002**	0.010 (−0.157, 0.177)	.907
Vitamin D level (nmol/L)	**−0.027 (−0.037, −0.017)**	**<.001**	0.005(−0.002, 0.012)	.176	**−0.005 (−0.007, −0.002)**	**<.001**	0.001 (−0.002, 0.004)	.577

Variables with P values <.05 in univariate models were included in multivariate analyses.
Bold indicates significance ($P<.05$).
Adj. coef. = adjusted coefficient, CI = confidence interval, coef. = coefficient, SDST = symbol digit substitution test.

$P<.001$). Participants with good health status had lower latency time than participants with fair health status (adjusted coefficient −0.830, 95% CI −1.586, −0.073, $P=.032$). Health-related behaviors, including drinking, habit to eat breakfast, and living with pets, were also associated with the changes in the mean total latency in the SDST. Specifically, former and current alcohol consumers had lower latency time than participants who never consumed alcoholic beverages (adjusted coefficient −1.994, 95% CI −3.041, −0.947, $P<.001$; adjusted coefficient −1.804, 95% CI −2.711, −0.897, $P<.001$, respectively); participants who ate breakfast occasionally or rarely had lower latency time than those who regularly ate breakfast (adjusted coefficient −0.738, 95% CI −1.198, −0.278, $P=.002$; adjusted coefficient −0.856, 95% CI −1.303, −0.409, $P<.001$); participants who lived with pets also had lower latency time than those who did not live with pets (adjusted coefficient −0.621, 95% CI −1.053, −0.188, $P=.006$). Higher levels of lead in the blood were associated with increase in the mean total latency of SDST (adjusted coefficient 2.640, 95% CI 0.618, 4.663, $P=.012$).

3.2.3. SDST/number of errors. The result of univariate linear regression analysis indicated that demographic and socioeconomic status, including age, sex, race, income ratio, education level, and marital status, was significantly associated with number of errors in the SDST. In addition, health status and lifestyle habits, such as hypertension, drinking, habit to eat breakfast, living with pets, habit to talk on the phone with family or friends, and spending time with friends or relatives, had an effect on the errors in the SDST. Dietary habits and blood biochemical parameters, including total protein intake, total unsaturated fatty acid intake, total carbohydrate intake, ascorbic acid, levels of vitamin E, vitamin B6, riboflavin, thiamin, folacin, blood lead, serum C-reactive protein, glycated hemoglobin, and serum vitamin D, were also associated with the number of errors in the SDST (Table 3).

Multivariate linear regression analysis demonstrated that increased age was associated with increased number of errors on the SDST (adjusted coefficient 0.038, 95% CI 0.025, 0.050, $P<.001$), whereas higher income ratio and higher education level were associated with decreased number of errors on the SDST (adjusted coefficient −0.074, 95% CI −0.118, −0.030, $P=.001$; and adjusted coefficient −0.082, 95% CI −0.120, −0.044, $P<.001$, respectively). We found that sex and race had a strong association with the number of errors of SDST, with males having a lower number of errors than females (adjusted coefficient −0.336, 95% CI −0.544, −0.127, $P=.002$), and black and Mexican-American participants having a higher number of errors than white participants (adjusted coefficient 0.618, 95% CI 0.369, 0.867, $P<.001$; adjusted coefficient 0.540, 95% CI 0.210, 0.871, $P=.002$, respectively). A habit to eat breakfast was associated with the number of errors on the SDST, with participants who rarely eat breakfast having a lower number of errors than participants who eat breakfast every day (adjusted coefficient −0.303, 95% CI −0.552, −0.054, $P=.018$). Higher levels of serum C-reactive protein was associated with increased number of errors on the SDST (coefficient 0.393, 95% CI 0.075, 0.710, $P=.016$).

3.2.4. SDLT/trials to criterion. The result of univariate linear regression analysis revealed that demographic and socioeconomic status, including age, race, income ratio, education level, marital status, and occupation category, was significantly associated with the number of trials to reach criterion in the SDLT. Health status and lifestyle habits, such as diabetes, hypertension, BMI, smoking, drinking, living with pets, talking on the phone with family or friends, and spending time with friends or relatives, also effected the number of trials to reach criterion in the SDLT. In addition, dietary habits and blood biochemical parameters, including total protein intake, total unsaturated fatty acid intake, total carbohydrate intake, ascorbic acid, vitamin E, vitamin B12, vitamin B6, riboflavin, thiamin, folacin, blood lead, urinary cadmium, serum C-reactive protein, serum glucose, glycated hemoglobin, and serum vitamin D, were significantly associated with the number of trials needed to reach criterion in the SDLT (Table 4).

Multivariate linear regression analysis demonstrated that increased age was associated with increased number of trials needed to reach criterion in the SDLT (adjusted coefficient 0.044, 95% CI 0.032, 0.055, $P<.001$), whereas higher income ratio and higher education level were associated with reduced number of trials needed to reach criterion in the SDLT (adjusted coefficient −0.126, 95% CI −0.174, −0.078, $P<.001$; and adjusted coefficient −0.209, 95% CI −0.244, −0.175, $P<.001$, respectively). In addition, we found that race, marital status, and occupation category were associated with the number of trials needed to reach criterion in the SDLT. Specifically, black and Mexican-American participants needed more trials compared with white participants (adjusted coefficient 0.654, 95% CI 0.418, 0.890, $P<.001$; adjusted coefficient 0.882, 95% CI 0.594, 1.170, $P<.001$, respectively); divorced participants needed fewer trials than married participants (adjusted coefficient −0.303, 95% CI −0.524, −0.083, $P=.008$); participants working in the transportation and trucking needed more trials than office building services workers (adjusted coefficient 0.632, 95% CI 0.163, 1.100, $P=.009$). Health-related behaviors, such as smoking and alcohol consumption, were also associated with the variations in the number of trials needed to reach criterion in the SDLT. Participants who used to smoke and former and current drinkers required fewer trials compared with participants who never smoked and never consumed alcoholic beverages (adjusted coefficient −0.263, 95% CI −0.453, −0.074, $P=.007$; and adjusted coefficient −0.332, 95% CI −0.609, −0.056, $P=.020$ and coefficient −0.424, 95% CI −0.739, −0.109, $P=.009$, respectively).

3.2.5. SDLT/total score. The result of univariate linear regression analysis indicated that demographic and socioeconomic status, including age, race, income ratio, education level, marital status, and occupation category, were significantly associated with the total score on the SDLT. In addition, health status and lifestyle habits, such as diabetes diagnosis, hypertension, BMI, smoking, drinking, living with pets, talking on phone with family or friends, and spending time with friends or relatives, affected the total score on the SDLT. Dietary habits and biochemical parameters, including total protein intake, total unsaturated fatty acid intake, total carbohydrate intake, ascorbic acid, levels of vitamin E, vitamin B12, vitamin B6, riboflavin, thiamin, folacin, blood lead, urinary cadmium, serum C-reactive protein, serum glucose, glycated hemoglobin, and serum vitamin D, were also significantly associated with the total score on the SDLT (Table 4).

Multivariate linear regression analysis demonstrated that increased age was associated with higher total score on the SDLT (adjusted coefficient 0.088, 95% CI 0.067, 0.108, $P<.001$), whereas higher income ratio and higher education level were associated with lower score on the SDLT (adjusted

Table 4

Relationships between subject characteristics, number of trials needed to reach criterion, and the total score on the SDLT.

	SDLT/trials to criterion				SDLT/Total score			
	Coef. (95% CI)	*P*	Adj. coef. (95% CI)	*P*	Coef. (95% CI)	*P*	Adj. coef. (95% CI)	*P*
Demographics								
Age	**0.037 (0.029, 0.045)**	<.001	**0.044 (0.032, 0.055)**	<.001	**0.079 (0.062, 0.096)**	<.001	**0.088 (0.067, 0.108)**	<.001
Male sex	−0.101 (−0.274, 0.072)	.247			−0.086 (−0.437, 0.264)	.624		
Race								
White	Reference		Reference		Reference		Reference	
Black	**1.024 (0.844, 1.204)**	<.001	**0.654 (0.418, 0.890)**	<.001	**2.343 (1.954, 2.732)**	<.001	**1.384 (0.882, 1.886)**	<.001
Mexican-American	**1.791 (1.532, 2.051)**	<.001	**0.882 (0.594, 1.170)**	<.001	**4.181 (3.502, 4.861)**	<.001	**1.990 (1.391, 2.589)**	<.001
Other	**1.250 (0.834, 1.666)**	<.001	**0.897 (0.531, 1.263)**	<.001	**2.988 (1.901, 4.075)**	<.001	**2.059 (1.076, 3.042)**	<.001
Income ratio	**−0.253 (−0.309, −0.197)**	<.001	**−0.126 (−0.174, −0.078)**	<.001	**−0.564 (−0.674, −0.455)**	<.001	**−0.242 (−0.341, −0.142)**	<.001
Education (in y)	**−0.301 (−0.328, −0.274)**	<.001	**−0.209 (−0.244, −0.175)**	<.001	**−0.685 (−0.743, −0.626)**	<.001	**−0.476 (−0.551, −0.401)**	<0.001
Marital status								
Married	Reference		Reference		Reference		Reference	
Never married	**−0.391 (−0.651, −0.131)**	**.004**	−0.044 (−0.319, 0.231)	.749	**−0.661 (−1.178, −0.145)**	**.013**	0.104 (−0.368, 0.575)	.661
Divorced	0.144 (−0.127, 0.415)	.290	**−0.303 (−0.524, −0.083)**	**.008**	**0.545 (0.014, 1.076)**	**.045**	−0.310 (−0.744, 0.124)	.158
Occupation category								
Office building services	Reference		Reference		Reference		Reference	
Rubber and chemical	0.680 (−0.043, 1.403)	.065	0.314 (−0.240, 0.868)	.260	**1.261 (0.052, 2.470)**	**.041**	0.480 (−0.361, 1.321)	.257
Transportation and trucking	**0.895 (0.383, 1.407)**	**.001**	**0.632 (0.163, 1.100)**	**.009**	**1.474 (0.563, 2.385)**	**.002**	**0.946 (0.056, 1.835)**	**.038**
Metal	0.148 (−0.464, 0.760)	0.630	−0.145 (−0.660, 0.370)	0.574	0.478 (−0.628, 1.584)	.389	−0.305 (−1.149, 0.539)	.471
Repair service	0.367 (−0.367, 1.101)	0.320	−0.221 (−0.803, 0.360)	0.448	1.003 (−0.513, 2.519)	.190	−0.436 (−1.556, 0.683)	.437
Construction	**0.530 (0.076, 0.984)**	**0.023**	0.109 (−0.348, 0.567)	0.633	**1.251 (0.352, 2.150)**	**.007**	0.429 (−0.382, 1.241)	.293
Other industries	**0.492 (0.182, 0.802)**	**0.002**	0.173 (−0.084, 0.431)	0.182	**1.112 (0.483, 1.740)**	**.001**	0.406 (−0.082, 0.894)	.101
Health/comorbidity								
Health status								
Fair	Reference		Reference		Reference		Reference	
Poor	0.456 (−0.241, 1.152)	.195	−0.036 (−0.564, 0.491)	.890	1.182 (−0.579, 2.943)	.184	0.161 (−1.301, 1.622)	.826
Good	**−1.244 (−1.512, −0.975)**	<.001	−0.276 (−0.582, 0.031)	.077	**−3.071 (−3.725, −2.416)**	<.001	**−0.805 (−1.489, −0.121)**	**.022**
Diabetes	**1.020 (0.489, 1.551)**	<.001	0.408 (−0.080, 0.896)	.099	**2.052 (0.934, 3.170)**	**.001**	0.527 (−0.399, 1.453)	.258
Hypertension	**0.396 (0.205, 0.588)**	<.001	−0.087 (−0.307, 0.134)	.434	**0.961 (0.545, 1.378)**	<.001	−0.137 (−0.580, 0.306)	.538
Anemia	0.019 (−0.472, 0.510)	.938			0.180 (−1.053, 1.412)	.771		
Depression	0.112 (−0.268, 0.492)	.557			0.107 (−0.592, 0.807)	.759		
BMI								
Normal	Reference		Reference		Reference		Reference	
Overweight	**0.437 (0.257, 0.618)**	<.001	−0.031 (−0.225, 0.163)	.748	**1.020 (0.637, 1.403)**	<.001	0.055 (−0.320, 0.429)	.770
Health behavior								
Smoking								
Never	Reference		Reference		Reference		Reference	
Former	−0.189 (−0.441, 0.063)	.139	**−0.263 (−0.453, −0.074)**	**.007**	**−0.520 (−1.013, −0.027)**	**.039**	**−0.603 (−0.995, −0.211)**	**.003**
Current	**0.183 (0.003, 0.362)**	**.047**	−0.183 (−0.377, 0.011)	.064	0.361 (−0.024, 0.746)	.065	**−0.400 (−0.747, −0.052)**	**.025**
Alcohol consumption								
Never	Reference		Reference		Reference		Reference	
Former	**−0.573 (−0.895, −0.251)**	**.001**	**−0.332 (−0.609, −0.056)**	**.020**	**−1.597 (−2.383, −0.810)**	<.001	**−1.021 (−1.657, −0.385)**	**.002**
Current	**−1.196 (−1.536, −0.856)**	<.001	**−0.424 (−0.739, −0.109)**	**.009**	**−2.912 (−3.755, −2.070)**	<.001	**−1.177 (−1.874, −0.480)**	**.001**

(*continued*)

Table 4
(continued).

	SDLT/trials to criterion				SDLT/Total score			
	Coef. (95% CI)	***P***	**Adj. coef. (95% CI)**	***P***	**Coef. (95% CI)**	***P***	**Adj. coef. (95% CI)**	***P***
Breakfast consumption								
Every day	Reference				Reference			
Some days and weekends only	0.020 (−0.170, 0.210)	.836			0.092 (−0.322, 0.505)	.659		
Rarely and never	−0.102 (−0.332, 0.129)	.379			−0.207 (−0.679, 0.264)	.381		
Living with pets								
No	Reference		Reference		Reference		Reference	
Yes	**−0.334 (−0.549, −0.120)**	**0.003**	−0.144 (−0.336, 0.048)	.137	**−0.622 (−1.017, −0.228)**	**.003**	−0.174 (−0.509, 0.161)	.303
Social support								
Talking on the phone with family or friends (per wk)								
Never	Reference		Reference		Reference		Reference	
Less than median (≤7 times)	**−0.824 (−1.263, −0.386)**	**<.001**	0.141 (−0.247, 0.529)	.469	**−2.189 (−3.234, −1.144)**	**<.001**	0.036 (−0.942, 1.013)	.942
More than median (>7 times)	**−1.149 (−1.593, −0.704)**	**<.001**	−0.035 (−0.445, 0.375)	.864	**−2.894 (−3.911, −1.877)**	**<.001**	−0.367 (−1.366, 0.631)	.463
Spending time with friends or relatives (per y)								
Never	Reference		Reference		Reference		Reference	
Less than median (≤52 times)	**−0.809 (−1.345, −0.273)**	**.004**	−0.056 (−0.630, 0.517)	.844	**−1.927 (−2.973, −0.881)**	**.001**	−0.075 (−1.076, 0.927)	.881
More than median (>52 times)	**−1.196 (−1.766, −0.626)**	**<.001**	−0.210 (−0.812, 0.392)	.487	**−2.748 (−3.844, −1.652)**	**<.001**	−0.416 (−1.462, 0.630)	.428
Visiting neighbors (per y)								
Never	Reference				Reference			
Less than median (≤52 times)	−0.064 (−0.265, 0.136)	.521			−0.237 (−0.621, 0.146)	.220		
More than median (>52 times)	0.139 (−0.121, 0.398)	.289			0.246 (−0.268, 0.761)	.340		
Walking activity (per mo)	0.001 (−0.008, 0.010)	.790			0.007 (−0.012, 0.025)	.475		
Diet/nutrition								
Total protein intake (g)	**−0.004 (−0.005, −0.002)**	**<.001**	−0.0002 (−0.004, 0.004)	.939	**−0.009 (−0.013, −0.005)**	**<.001**	−0.001 (−0.009, 0.007)	.812
Total unsaturated fatty acid intake (g)	**−0.005 (−0.008, −0.003)**	**<.001**	−0.001 (−0.005, 0.003)	.676	**−0.014 (−0.019, −0.009)**	**<.001**	−0.003 (−0.010, 0.004)	.357
Total carbohydrate intake (g)	**−0.002 (−0.002, −0.001)**	**<.001**	−0.001 (−0.002, 0.0001)	.073	**−0.004 (−0.006,−0.002)**	**<.001**	**−0.002 (−0.004, −0.0005)**	**.013**
Ascorbic acid (mg)	**−0.001 (−0.002, −0.001)**	**.001**	−0.0001 (−0.001, 0.001)	.783	**−0.002 (−0.004, −0.001)**	**.003**	0.000 (−0.002, 0.002)	.898
Vitamin E (mg)	**−0.021 (−0.030, −0.011)**	**<.001**	−0.001 (−0.013, 0.012)	.893	**−0.048 (−0.066, −0.030)**	**<.001**	−0.002 (−0.024, 0.019)	.821
Vitamin B12 (mcg)	**−0.010 (−0.015, −0.005)**	**<.001**	−0.004 (−0.009, 0.002)	.172	**−0.022 (−0.030, −0.013)**	**<.001**	−0.008 (−0.016, 0.001)	.092
VitaminB6 (mg)	**−0.162 (−0.233, −0.090)**	**<.001**	0.016 (−0.107, 0.139)	.795	**−0.324 (−0.465, −0.184)**	**<.001**	0.103 (−0.128, 0.335)	0.374
Riboflavin (mg)	**−0.201 (−0.260, −0.141)**	**<.001**	−0.072 (−0.231, 0.087)	.367	**−0.435 (−0.560, −0.310)**	**<.001**	−0.120 (−0.464, 0.225)	.488
Thiamin (mg)	**−0.176 (−0.266, −0.085)**	**<.001**	0.158 (−0.001, 0.317)	.051	**−0.386 (−0.585, −0.187)**	**<.001**	0.325 (−0.021, 0.671)	.065
Folacin (mcg)	**−0.001 (−0.001, −0.0005)**	**<.001**	−0.0005 (−0.001, 0.0003)	.220	**−0.002 (−0.002, −0.001)**	**<.001**	−0.001 (−0.002, 0.001)	.200
Biochemical parameters								
Blood lead level (μmol/L)	**1.494 (0.638, 2.351)**	**.001**	0.401 (−0.425, 1.228)	.334	**3.561 (1.601, 5.520)**	**.001**	1.039 (−0.746, 2.824)	.248
Urinary cadmium level (nmol/L)	**0.024 (0.007, 0.041)**	**.006**	−0.003 (−0.012, 0.006)	.491	**0.057 (0.013, 0.100)**	**.011**	−0.002 (−0.019, 0.015)	.839
Serum C-reactive protein level (mg/dL)	**0.354 (0.162, 0.546)**	**.001**	0.065 (−0.093, 0.223)	.410	**0.852 (0.373, 1.330)**	**.001**	0.269 (−0.093, 0.630)	.142
Serum glucose level (mmol/L)	**0.133 (0.046, 0.220)**	**.003**	−0.012 (−0.120, 0.096)	.819	**0.282 (0.104, 0.460)**	**.003**	−0.031 (−0.204, 0.142)	.722
Glycated hemoglobin level (%)	**0.366 (0.237, 0.496)**	**<.001**	−0.0001 (−0.135, 0.135)	.999	**0.803 (0.534, 1.071)**	**<.001**	−0.002 (−0.273, 0.269)	.989
Vitamin D level (nmol/L)	**−0.007 (−0.010, −0.004)**	**<.001**	0.001 (−0.002, 0.004)	.693	**−0.017 (−0.024, −0.010)**	**<.001**	0.001 (−0.006, 0.007)	.817

Variables with *P* values <.05 in univariate models were included in multivariate analyses.
Bold indicates significance ($P<.05$).
Adj. coef. = adjusted coefficient, CI = confidence interval, coef. = coefficient, SDLT = serial digit learning test.

coefficient −0.242, 95% CI −0.341, −0.142, $P<.001$; and adjusted coefficient −0.476, 95% CI −0.551, −0.401, $P<.001$, respectively). Race and occupation category were significantly associated with the total score on the SDLT, with black and Mexican-American participants having higher total scores than white participants (adjusted coefficient 1.384, 95% CI 0.882, 1.886, $P<.001$; adjusted coefficient 1.990, 95% CI 1.391, 2.589, $P<.001$, respectively); and transportation and trucking industry workers having higher total scores than office building services workers (adjusted coefficient 0.946, 95% CI 0.056, 1.835, $P=.038$). Good health status was associated with lower total scores than fair health status (adjusted coefficient −0.805, 95% CI −1.489, −0.121, $P=.022$). Smoking and drinking were also significantly associated with the total score on the SDLT. Current and former smokers was lower total score than never smoking participants (adjusted coefficient −0.400, 95% CI −0.747, −0.052, $P=.025$; adjusted coefficient −0.603, 95% CI −0.995, −0.211, $P=.003$, respectively); and former and current drinkers also had lower total score compared with never drinking individuals (adjusted coefficient −1.021, 95% CI −1.657, −0.385, $P=.002$; adjusted coefficient −1.177, 95% CI −1.874, −0.480, $P=.001$, respectively). Increased total carbohydrate intake was significantly associated with lower total score on the SDLT (adjusted coefficient −0.002, 95% CI −0.004, −0.0005, $P=.013$).

4. Discussion

Our results indicate that in 20 to 59-year-old NHANES III participants who underwent 3 computerized tests to evaluate cognitive functioning demographic and socioeconomic status, including older age, black ethnicity, lower income ratio, and lower education level, were associated with poorer neurocognitive function in all analyzed tests. In addition, participants with poor health, nonsmokers, and nondrinkers performed worse in all administered tests compared with individuals with good health, smokers, and participants consuming alcoholic beverages. Dietary and biochemical characteristics of the blood were not consistently associated with neurocognitive performance. Folacin intake was associated with faster reaction in SRTT, carbohydrate intake was associated with lower total score on the SDLT, while riboflavin consumption was associated with increased reaction time in SRTT. In addition, higher blood lead level was associated with increase in the mean total latency in the SDST. Overall, office building workers performed better in the administered neurocognitive tests. Specifically, office building services employees demonstrated faster reaction compared with metal industry workers in SRTT, and needed less trials to reach criterion and obtained lower total scores in SDLT than participants working in the transportation and trucking industry.

Advanced age was identified as a potential risk factor for neurocognitive decline in our study. Because population aging is taking place in nearly all countries of the world, considerable cognitive decline in a wide spectrum of cognitive abilities seen in older individuals is a major health and social issue.[21] Cognitive decline is closely linked to dementia and illness, and associated with increased mortality.[22] Therefore, further research is needed to understand the mechanisms of cognitive aging and the factors that contribute to its individual differences.

According to recent studies, differences seen in cognitive functioning of older individuals of different races could be attributed to social and cultural factors.[8–11] In general, the findings from previous research and our results indicate that older adults of African-American and Hispanic descent demonstrate lower performance on cognitive tests compared with whites.[23,24] The observed results can be due to substantial differences in the attainment of education, as it was shown before and further supported by our results that higher level of education is associated with better cognition and a decreased risk for dementia during old age.[25–27]

Similarly, evidence suggests that lower occupational status (eg, manual labor, trade, farmer) may be associated with poorer cognitive function,[28] and increased risk of dementia and Alzheimer's disease (AD), while occupations with higher mental or intellectual demands are associated with better cognitive performance and reduced risk of dementia.[22] Occupational exposures also contribute to cognitive performance in later life. Low-status employees are generally at higher risk for occupational exposures, and therefore more likely to suffer a nervous system damage.[22,29] Our results showed that office building service workers performed better in the administered neurocognitive tests compared with metal industry workers, and transportation and trucking industry workers.

Diet and lifestyle habits as modifiable factors that can play a role in cognitive aging have received a lot of interest in the scientific community and general public. It is reasonable to hypothesize that improving the diet of older people might help to delay the onset, or slow the progression of age-associated cognitive decline. However, despite widespread advertising of benefits associated with various vitamins and supplements, the solid scientific data supporting their use for cognitive health are limited. Goodwin et al[30] were among the first to show a role of folate, vitamin B12, vitamin B6, and omega-3s in cognitive function. The authors showed that healthy older subjects who had low blood levels of vitamins C, B12, riboflavin, and folic acid scored poorly on tests of memory and nonverbal abstract thinking.[3,30] Interestingly, it was demonstrated that supplementation of cobalamin-deficient patients with vitamin B12 lead to significant improvements in neuropsychiatric functions and cognitive recovery, suggesting that poor vitamin intake is at least partially responsible for the cognitive decline seen in some older persons.[3,31,32] B vitamins participate in regulating homocysteine levels, which is an independent risk factor for cognitive decline[3] and a stronger predictor of cognitive performance than either vitamin B12 or folate.[33] Homocysteine levels can be lowered by supplementation with B vitamins; however, it was shown that decrease of homocysteine levels does not improve cognitive function.[34] Moreover, a recent evidence-based review concluded that B12 supplementation did not improve cognitive function in patients with cognitive decline.[35] In addition, Malouf et al[36] showed that folic acid supplementation did not have any beneficial effect on measures of cognition or mood in older healthy women, and patients with mild to moderate cognitive decline and different forms of dementia. Altogether, experimental evidence supporting a beneficial effect of the micronutrient supplementation on cognitive health in older age is inconclusive. Possible reasons for inconsistent findings include different study designs, especially differences in the doses of the supplements and timing of interventions. It is also possible that some supplements may produce varying effect if received from food or obtained via supplementation. In addition, other active ingredients in the food or supplement itself may be responsible for the observed effects. It is possible that more complex interaction between dietary habits, that is, amounts of consumed proteins, fats, and carbohydrates, and also vitamins and minerals can influence the individual's response to aging. It was shown, for example, that dietary pattern with high caloric intake in the form of carbohydrates and low caloric intake in the form of fat and proteins may increase the risk of mild cognitive impairment or dementia in older persons.[37] Moreover, genetic background, especially metabolism-related polymorphisms, can also play a role.

In our study, we found that folacin intake was associated with faster reaction on the SRTT, while riboflavin consumption was associated with increased reaction time on the SRTT. In addition, we found that increased carbohydrate intake was associated with lower total score on the SDLT. Clearly, more controlled further studies focusing on individual response are needed to establish a more definitive role of vitamin supplementation and dietary habits in cognitive aging.

In conjunction with diet, other lifestyle factors such as smoking and drinking influence cognitive aging. While excessive alcohol consumption can cause long-term cognitive damage, evidence suggests that moderate levels of alcohol consumption in older people can be beneficial, possibly due to protective effects of ethanol on cardiovascular and cerebrovascular health.[38–41] Ganguli et al[42] showed that compared to no drinking, both minimal and moderate drinking were associated with better performance on cognitive tests. Interestingly, these associations were more pronounced when comparing current drinkers to former drinkers than to lifelong abstainers.[42] In agreement, our study showed that drinking was associated with better performance on all cognitive tests.

While smoking is a significant risk factor for heart disease, stroke, cancer, and other conditions, its effect on the cognitive function is controversial. Smoking increases the risk of stroke and therefore is expected to increase the risk of vascular dementia and cognitive decline. On the contrary, nicotine increases the release of acetylcholine, which can increase attention and information processing.[22] A recent systematic review showed that 16 out of the 29 selected cohort studies found the relationship between smoking and various cognitive outcomes, 4 found this relationship for some outcomes or certain subgroups, while the remaining 9 studies did not find an association or found an inverse association.[22] Only 2 out of 7 cross-sectional studies found an association between smoking and poor cognitive function. Our data demonstrate that smoking is associated with improved cognitive function.[22] Although further studies are needed to dissect the effect of smoking on cognition, its effect on other health aspects provides enough reasons to quit.

This study has several limitations. Because our study was a cross-sectional analysis by design, inferences regarding causality cannot be made. Moreover, because NHANES III is a US-based survey, the results need to be validated in other countries. Because only 3 cognitive function tests were administered as part of NHANES III, this study cannot provide a comprehensive cognitive assessment. In addition, there was an overall test nonresponse rate of 9%. Nonresponse rates increased with age, decreased with educational level, were higher for men, and were lower for non-Hispanic white individual than other ethnic groups, potentially introducing some bias into the study.[18]

Despite the limitations, our study has several strengths. NHANES III is a population-based survey that included validated examination measures, biological specimen collection, and limited measures of health status. Rigorous training in recruitment and data collection ensures high response rates, national representativeness, and high quality of collected data. The sample size is sufficient for precise prevalence measures at the national level. A large multiethnic population sample allowed us to explore the racial/ethnic heterogeneity in the association with neurocognitive function. This analysis was conducted in a nationally representative sample; therefore, our results may be generalized to the entire US adult population.

5. Conclusions

Our results indicate that age, ethnicity, income, education level, overall health, smoking status, drinking status, and dietary and biochemical characteristics of the blood, and job category were associated with neurocognitive performance in visual attention, learning, and concentration in a large, nationally representative sample of healthy, ethnically diverse 20 to 59-year-olds. Future studies are needed to understand the mechanisms of cognitive aging and the factors that contribute to its individual differences.

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