Research Article Brain Conflux

Correlation of nighttime fasting duration with cognitive decline in older adults: a cross-sectional study based on NHANES 2011-2014

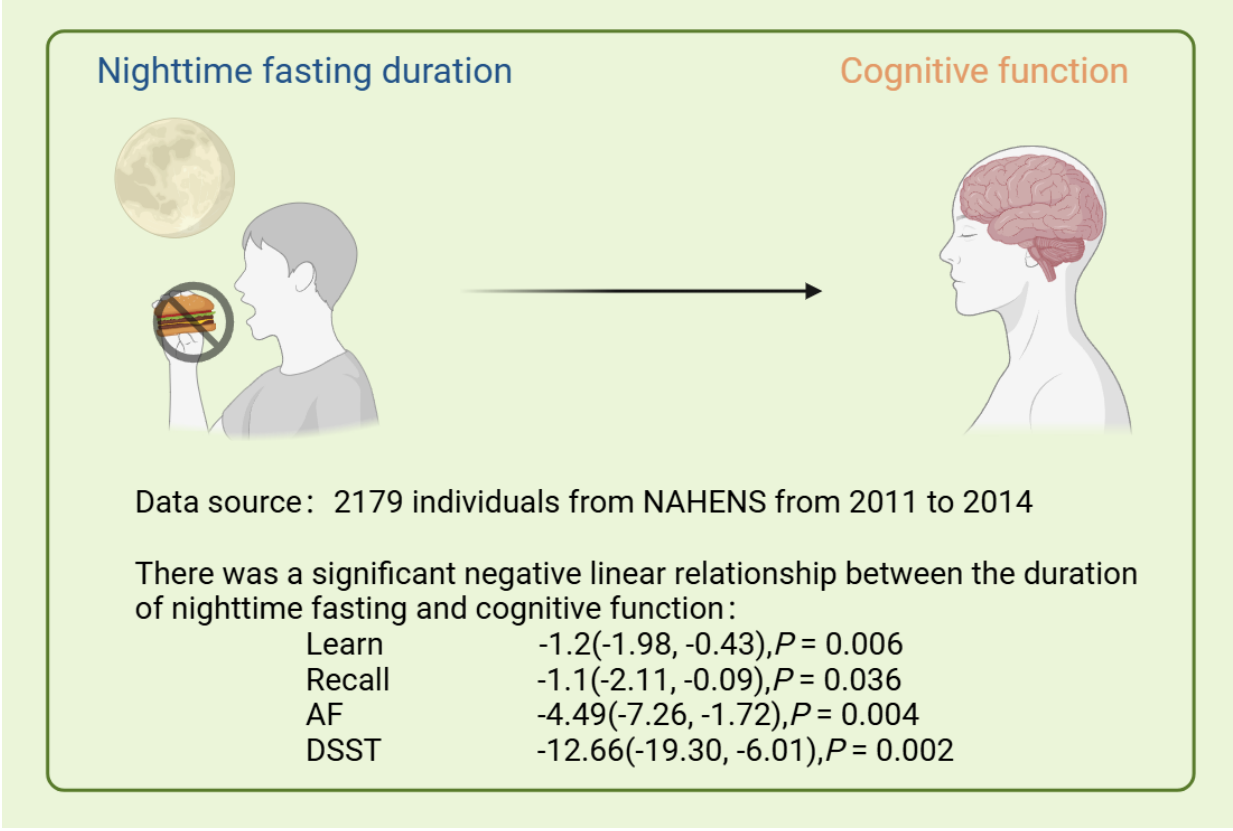
Authors

Zixuan Liu, Tao Yuan, Yuxuan Ma, Ruimin Wang

Correspondence

ruimin-wang@ncst.edu.cn (R. Wang)

Graphical Abstract



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Correlation of nighttime fasting duration with cognitive decline in older adults: a cross-sectional study based on NHANES 2011-2014

Zixuan Liu [1], Tao Yuan [2], Yuxuan Ma [2], Ruimin Wang [1,2*]

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Abstract

Background: Cognitive dysfunction is a significant health challenge in the global elderly population, and its prevalence is associated with multiple factors, including modifiable lifestyle factors. The relationship between nighttime fasting duration, a potential lifestyle factor, and cognitive function has yet to be thoroughly investigated.
Objective: To investigate the association between nighttime fasting duration and cognitive function.
Methods: This cross-sectional study was based on data from the National Health and Nutrition Examination Survey (NHANES) from 2011 to 2014. Weighted multiple linear regression was utilized to examine the relationship between nighttime fasting duration and cognitive function, with additional curve fitting and inflection point analysis conducted to further elucidate this association
Results: There was a significant negative linear relationship between nighttime fasting duration and cognitive function (Learn: β = -1.2, 95% CI: -1.98, -0.43, P = 0.006; Recall: β = -1.1, 95% CI: -2.11, -0.09, P = 0.036; Animal Fluency: β = -4.49, 95% CI: -7.26, -1.72, P = 0.004; Digit Symbol **Substitution Test:** β = -12.66, 95% CI: -19.30, -6.01, P = 0.002). Subgroup analyses showed that this negative correlation was prevalent in most subgroups. Curve fitting revealed a linear relationship between nighttime fasting duration and cognitive function scores, but did not identify a significant inflection point.
Conclusions: Longer nighttime fasting times may be associated with cognitive decline, either as a continuous or categorical variable.
Keywords: Cognitive Function; Nighttime Fasting Duration; US National Health and Nutrition Examination Survey

Introduction

Cognitive dysfunction refers to a range of impairments in cognitive processes, including declines in memory, attention, executive function, language, and visuospatial abilities [1, 2]. As the global population ages, the prevalence of cognitive dysfunction is increasing and has become a significant public health problem. It is estimated that tens of millions of people worldwide are affected by varying degrees of cognitive dysfunction, and this number is expected to grow significantly in the coming decades [3]. Cognitive dysfunction not only has a profound impact on an individual's quality of life but also places a heavy economic burden on families and society [4, 5].

Recent studies have shown that lifestyle, especially dietary habits, may be associated with maintaining and declining cognitive function [6]. The duration of overnight fasting (DNF)—the time interval from the last meal of the day to the first meal of the next—has been proposed as a factor that may affect cognitive function[7, 8]. Prolonged nocturnal fasting duration has been associated with various metabolic and cardiovascular health benefits [9, 10], however, its effect on cognitive function is largely unclear.

In diseases similar to cognitive dysfunction, such as Alzheimer's disease and Parkinson's disease, it has been shown that nocturnal fasting duration, or its associated intermittent fasting pattern, may positively affect the disease process [11, 12]. For instance, in animal models, intermittent fasting enhances the brain's metabolic health, decreases neuroinflammation, and may decelerate cognitive decline. [13, 14]. However, most of these studies have focused on animal experiments, with relatively limited evidence from human studies.

In light of this, this study investigated the relationship between nighttime fasting duration and cognitive dysfunction. We utilized data from the National Health and Nutrition Examination Survey (NHANES) to assess participants' cognitive functioning through objective tests. We examined the possible effects of nighttime fasting duration on it. In addition, we considered a range of potential confounders to

1 School of Basic Medicine, North China University of Science and Technology, Tangshan 063210, China.
2 Key Laboratory of Dementia and Cognitive Dysfunction, School of Public Health, North China University of Science and Technology; International Science & Technology Cooperation Base of Geriatric Medicine; Hebei Province Key Laboratory of Occupational Health and Safety for Coal Industry, North China University of Science and Technology, Tangshan, Hebei, 063210, China
* Corresponding Author.

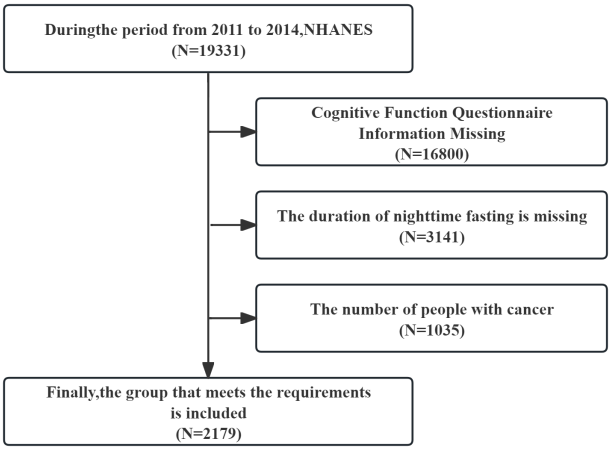
obtain more accurate conclusions. The findings of this study are expected to provide new perspectives on the prevention and intervention of cognitive dysfunction and provide guidance for future research and public health practice.

Materials and Methods

Study sample

NHANES (https://www.cdc.gov/nchs/nhanes/index.htm, accessed on 11 September 2024) was conducted between 2011 and 2014, and 19,331 participants participated. In this study, however, data from 17,152 participants were excluded, mainly due to missing data on the length of nighttime fasting, incomplete data on cognitive functioning scores, or participants being diagnosed with cancer (Fig. 1).

Fig. 1 The flow chart of participant selection.



Cognitive function

In this study, participants' global and domain-specific cognitive functions were assessed by four standardized tests: the immediate recall (CERAD-WL) and delayed recall (CERAD-DR) tests were used to assess immediate and delayed recall of new information [15, 16]; the Animal Fluency test (AF) assessed verbal fluency [17, 18]; and the Digit Symbol Substitution Test (DSST) measures executive function and processing speed [19]. These tests have been validated to effectively differentiate between cognitively impaired and normal individuals [20]. The higher the test score, the better the cognitive function. The results of all tests were standardized to calculate an overall cognitive composite score in a manner consistent with previous studies [21-24].

Duration of nighttime fasting (DNF)

Two 24-hour dietary recalls were used in this study to assess participants' dietary intake. The first dietary recall was completed through a face-to-face interview, and the second was conducted by telephone 3 to 10 days later. Participants were asked to record the duration of each food and beverage intake. Frequency of eating was defined as the point in time at which calorie-containing foods or drinks were ingested, with 50 kCal as the minimum standard for a single eating behavior [25, 26]. DNF was calculated using the following formula: 24 hours - (time of last meal - time of first meal). For example, if a person eats breakfast at 7 a.m. and dinner at 6 p.m., his or her DNF is 13 hours [26, 27].

Assessment of confounders

This study corrected for a range of potential confounders to more accurately assess the relationship between nighttime fasting and cognitive function. These factors included age (years), gender (male/female), race (non-Hispanic white, non-Hispanic black, Mexican American, and other), education level (less than high school, high school, and more than high school), household income-to-poverty ratio (PIR: < 1.5, 1.5-3.5, > 3.5), marital status (partnered/unpartnered), and smoking habits (yes: total cigarettes > 100 cigarettes; No: ≤100 cigarettes), drinking behavior (Yes: alcohol consumption ≥12 drinks per year; No: <12 drinks), body mass index (BMI: <25 kg/m², 25-30 kg/m², >30 kg/m²), sleep duration (hours), systemic immune index (SII) and systemic inflammatory response index (SIRI). Diabetic status (yes/no) was also taken into account [28]. SII was calculated as platelet count x neutrophil count/lymphocyte count [29]. SIRI was calculated as neutrophil count x monocyte count/lymphocyte count [30].

Statistical analysis

In this study, continuous variables were expressed as mean ± standard error, and differences between groups were assessed by weighted t-test; categorical variables were presented as frequency (N) and percentage (%) and analyzed by chi-square test. To improve the reliability of statistical analyses, the study merged the NHANES datasets of the two cycles and applied weighted analyses by applying the mobile check center sample weights (WTINT2YR/2), as described in the CDC's NHANES tutorial.

Weighted multiple linear regression models were used to analyze the linear relationship between nighttime fasting duration and cognitive function scores, and the non-linear relationship was assessed by smoothed curve fitting and threshold effects. Three models were constructed for the study: the uncorrected model was not adjusted for any variables; model 1 was adjusted for age, gender, ethnicity, education level, marital status, and household income-to-poverty ratio; and model 2 was further adjusted for body mass index, cigarette smoking, alcohol consumption, diabetes mellitus, sleep duration, systemic inflammatory response index, and systemic immune-inflammatory index.

Indicators of effect sizes were regression coefficients (Beta) and their 95% confidence intervals (CI), with a statistical significance level of two-sided $P < 0.05$. All statistical analyses were completed using SAS 9.4 and R 4.2.0 software, and records containing missing data were deleted.

Results

Baseline characteristics

This study included 2179 subjects with a mean age of 68.52 years, of which 54.15% were female and 45.85% were male. DNF (duration of nightly fasting) quartile subgroups were statistically different from race, education level, marital status, and household income to poverty ratio; however, smoking, alcohol consumption, body mass index, diabetes mellitus,

sleep duration, systemic inflammatory response index (SIRI) and Systemic Immune Inflammatory Index (SII) did not show statistical differences between DNF quartile subgroups. Subjects with longer nighttime fasting duration performed lower on cognitive function scores (Table 1).

Table 1 Characteristics of the study population [M (P25, P75), n(%)]

DNF	Total	Q1[0,0.47)	Q2[0.47,0.53)	Q3[0.53,0.60)	Q4(≥0.60)	F/H/X2	P value
	(n=2179)	(n = 540)	(n = 491)	(n = 601)	(n = 547)		
Weighted	41758460.91	11725810.5	9757617.307	1471117.255	8803915.848		
DNF	0.5 ± 0.1	0.4 ± 0.1	0.5 ± 0.0	0.6 ± 0.0	0.7 ± 0.1	2468.265	< 0.001
Age (years)	68.8 ± 6.6	67.9 ± 6.5	68.9 ± 6.5	69.5 ± 6.8	68.9 ± 6.6	6.083	< 0.001
Gender						9.833	0.02
Male	1069 (49.1)	292 (54.1)	244 (49.7)	270 (44.9)	263 (48.1)		
Female	1110 (50.9)	248 (45.9)	247 (50.3)	331 (55.1)	284 (51.9)		
Race						57.607	< 0.001
Non-Hispanic White	208 (9.5)	44 (8.1)	41 (8.4)	58 (9.7)	65 (11.9)		
Non-Hispanic Black	960 (44.1)	264 (48.9)	234 (47.7)	277 (46.1)	185 (33.8)		
Mexican American	558 (25.6)	115 (21.3)	97 (19.8)	154 (25.6)	192 (35.1)		
Other Race	453 (20.8)	117 (21.7)	119 (24.2)	112 (18.6)	105 (19.2)		
Educational Attainment						43.696	< 0.001
Less than High School	588 (27.0)	114 (21.2)	114 (23.2)	167 (27.8)	193 (35.3)		
High School	521 (23.9)	121 (22.5)	110 (22.4)	156 (26)	134 (24.5)		
High School or above	1068 (49.1)	303 (56.3)	267 (54.4)	278 (46.3)	220 (40.2)		
Marital Status						9.561	0.023
Partner	1239 (56.9)	316 (58.5)	294 (60)	348 (57.9)	281 (51.4)		
Unpartnered	939 (43.1)	224 (41.5)	196 (40)	253 (42.1)	266 (48.6)		
HIPR						46.131	< 0.001
<1.5	726 (36.2)	147 (30.2)	148 (32.2)	206 (36.9)	225 (45)		
1.5-3.5	666 (33.2)	147 (30.2)	170 (37)	183 (32.7)	166 (33.2)		
>3.5	613 (30.6)	192 (39.5)	142 (30.9)	170 (30.4)	109 (21.8)		
Alcohol consumption						5.035	0.169
Yes	1469 (68.0)	378 (70.5)	343 (70.1)	394 (66)	354 (65.7)		
No	692 (32.0)	158 (29.5)	146 (29.9)	203 (34)	185 (34.3)		
Smoking						1.274	0.735
Yes	1088 (50.0)	278 (51.6)	240 (48.9)	293 (48.8)	277 (50.7)		
No	1089 (50.0)	261 (48.4)	251 (51.1)	308 (51.2)	269 (49.3)		
BMI (kg/m2)						5.445	0.488
<25	565 (26.3)	130 (24.3)	139 (28.5)	161 (27.2)	135 (25.1)		

25-30	760 (35.3)	203 (37.9)	160 (32.9)	213 (36)	184 (34.3)		
>30	826 (38.4)	202 (37.8)	188 (38.6)	218 (36.8)	218 (40.6)		
Diabetes						2.517	0.472
Yes	504 (24.3)	136 (26.5)	108 (22.8)	142 (24.8)	118 (22.9)		
No	1571 (75.7)	378 (73.5)	365 (77.2)	430 (75.2)	398 (77.1)		
Sleep duration (h)	7.0(6.0, 8.0)	7.0(6.0, 8.0)	7.0(6.0, 8.0)	7.0(6.0, 8.0)	7.0(6.0, 8.0)	14.414	0.002
SIRI	1.1(0.8, 1.6)	1.1(0.8, 1.7)	1.1(0.8, 1.6)	1.1(0.7, 1.6)	1.1(0.7, 1.6)	6.764	0.08
SII	444.6 (314.7, 637.5)	453.6 (333.4, 642.5)	459.5 (331.3, 663.3)	436.6 (300.2, 623.8)	437.5 (297.5, 628.6)	6.878	0.076
Learn	6.3(5.3, 7.3)	6.7(5.7, 7.7)	6.3(5.3, 7.3)	6.3(5.3, 7.3)	6.3(5.0, 7.3)	26.705	< 0.001
Recall	6.0(4.0, 8.0)	6.0(5.0,8.0)	6.0(5.0, 8.0)	6.0(5.0, 7.0)	6.0(4.0, 7.0)	18.971	< 0.001
Animal fluency	16.0(13.0, 20.0)	17.0(13.0, 21.0)	17.0(13.0, 20.0)	16.0(13.0, 19.0)	15.0(12.0, 19.0)	28.37	< 0.001
Digit Symbol Substitution Test	46.0(33.0, 58.0)	50.0(38.0, 62.0)	47.0(34.5, 59.0)	45.0(33.0, 57.0)	42.0(28.0, 54.0)	59.009	< 0.001
Year of inclusion						6.455	0.091
2011-2012	1045 (48.0)	239 (44.3)	250 (50.9)	302 (50.2)	254 (46.4)		
2013-2014	1134 (52.0)	301 (55.7)	241 (49.1)	299 (49.8)	293 (53.6)		

Further analyses of the correlations between age, DNF, sleep duration, SIRI, SII and cognitive function-related scores (learn, recall, Animal fluency and Digit Symbol Substitution Test) showed that age and DNF were negatively and statistically significant correlations with cognitive function scores, while the correlation between sleep duration and cognitive function scores was not statistically significant. The correlation between SIRI and cognitive function scores was statistically more important compared to SII (Fig. 2).

Association between DNF and cognitive functioning

DNF and cognition Specifically, individuals with longer nighttime fasting durations had better performance on learning [learn:β =-1.2, 95% *CI*: -1.98, -0.43, *P* = 0.006] and recall tasks [Recall: β =-1.1,95% *CI*: -2.11, -0.09; *P* = 0.036], Animal fluency [AF: β =-4.49, 95% *CI*: -7.26, -1.72, *P* = 0.004] and poor performance on the Digit Symbol Substitution Test [DSST: β =-12.66, 95% *CI*:-19.30, -6.01, *P*= 0.002]. This association was also present when DNF was converted to quartile categorical variables (Fig. 3). In addition, the results of the primary analysis were further validated by the three-dimensional distribution plots of cognitive function, nighttime fasting duration, and age (Fig. 4).

Uncorrected models did not adjust for any variables; model 1 adjusted for age, sex, race, education level, marital status, and household income to poverty ratio; model 2 further adjusted for body mass index, smoking, alcohol consumption, diabetes, sleep duration, systemic inflammatory response index, and systemic immune inflammation index.

Subgroup analyses

In the subgroup analyses, negative correlations between DNF and cognitive function were significant in most subgroups. There was a significant interaction between smoking status and the effect of DNF on learning ability; ethnicity interacted significantly with the impact of DNF on recall and DSST, and diabetes status interacted considerably with the effects of DNF on AF (Fig. 5).

Red indicates the effect of DNF on learning ability; Green indicates the impact of DNF on recall ability; Blue indicates the influence of DNF on AF; Purple indicates the effects of DNF on DSST.

Curve Fitting of DNF and Cognitive Functioning

After adjusting for the covariates in Model 3, a two-stage linear regression model was used to curve-fit the relationship between DNF and cognitive function. The results showed that DNF was negatively and linearly related to learning ability ($P_{Nonliner}$ = 0.342), recall ability ($P_{Nonliner}$ = 0.479), motor fluency ($P_{Nonliner}$ = 0.601), and Digit Symbol Substitution Test ($P_{Nonliner}$ =0.973) (Fig. 6). The inflection point analysis failed to identify a valid inflection point that would allow the relationship between DNF and cognitive function to be segmented into two statistically significant phases.

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Fig. 2 Correlation and Scatterplot Matrix of Key Variables.

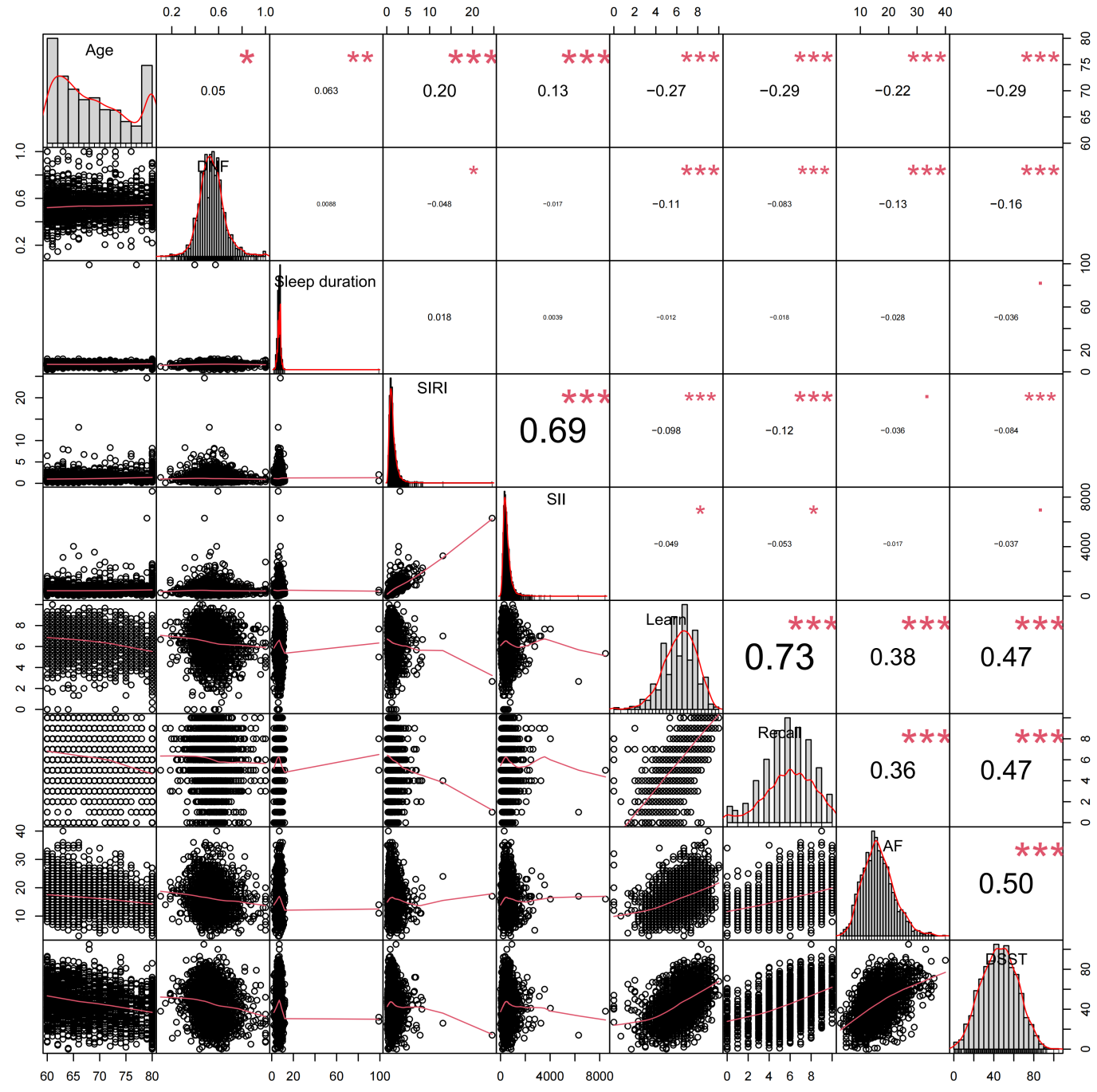

Fig. 3 Primary analysis forest map

group	Characteristics	Beta (95% CI)	P value	Beta (95% CI)	P_value	Beta (95% CI)	P_value
	DNF	-1.84(-2.59, -1.10)	<0.001	-1.25(-2.04, -0.45)	0.004	-1.2(-1.98, -0.43)	0.006
	Q1	Reference		Reference		Reference	
Learn	Q2	-0.15(-0.36, 0.05)	0.133	-0.09(-0.27,0.09)	0.304	-0.13(-0.32, 0.07)	0.17
	Q3	-0.47(-0.73, -0.21)	<0.001	-0.33(-0.58,-0.08)	0.013	-0.36(-0.62, -0.09)	0.014
	Q4	-0.52(-0.76, -0.27)	<0.001	-0.34(-0.59,-0.08)	0.012	-0.33(-0.60, -0.05)	0.025
	Trend test		<0.001		0.005		0.011
	DNF	-1.95(-3.16, -0.73)	0.003	-0.95(-1.88,-0.01)	0.047	-1.1(-2.11, -0.09)	0.036
	Q1	Reference		Reference		Reference	
Recall	Q2	-0.2(-0.57, 0.18)	0.295	-0.08(-0.40,-0.25)	0.623	-0.08(-0.45, 0.30)	0.648
	Q3	-0.68(-1.13, -0.23)	0.004	-0.49(-0.91,-0.08)	0.022	-0.48(-0.93, -0.03)	0.039
	Q4	-0.65(-1.00, -0.30)	<0.001	-0.38(-0.70,-0.05)	0.024	-0.38(-0.75, -0.02)	0.042
	Trend test		<0.001		0.009		0.02
	DNF	-8.83(-11.64, -6.01)	<0.001	-4.66(-7.46,-1.86)	0.002	-4.49(-7.26, -1.72)	0.004
	Q1	Reference		Reference		Reference	
AF	Q2	-1.29(-2.15, -0.43)	0.005	-0.63(-1.40, 0.14)	0.103	-0.7(-1.48, 0.08)	0.073
	Q3	-2.09(-2.94, -1.23)	<0.001	-0.94(-1.76,-0.11)	0.029	-0.98(-1.78, -0.18)	0.022
	Q4	-2.4(-3.24, -1.55)	<0.001	-1.06(-1.86,-0.26)	0.012	-1(-1.83, -0.17)	0.024
	Trend test		<0.001		0.008		0.012
	DNF	-30.89(-37.99, -23.78)	<0.001	-14.4(-21.59,-7.20)	<0.001	-12.66(-19.30, -6.01)	0.002
	Q1	Reference		Reference		Reference	
DSST	Q2	-1.95(-4.65, 0.76)	0.152	-0.19(-2.39, 2.01)	0.859	-0.62(-3.08, 1.84)	0.582
	Q3	-6.05(-8.05, -4.06)	<0.001	-3.14(-4.64,-1.64)	<0.001	-3.13(-5.04, -1.22)	0.005
	Q4	-8.69(-10.79, -6.59)	<0.001	-3.56(-5.65,-1.48)	0.002	-3.14(-5.33, -0.94)	0.01
	Trend test		<0.001		<0.001		0.003

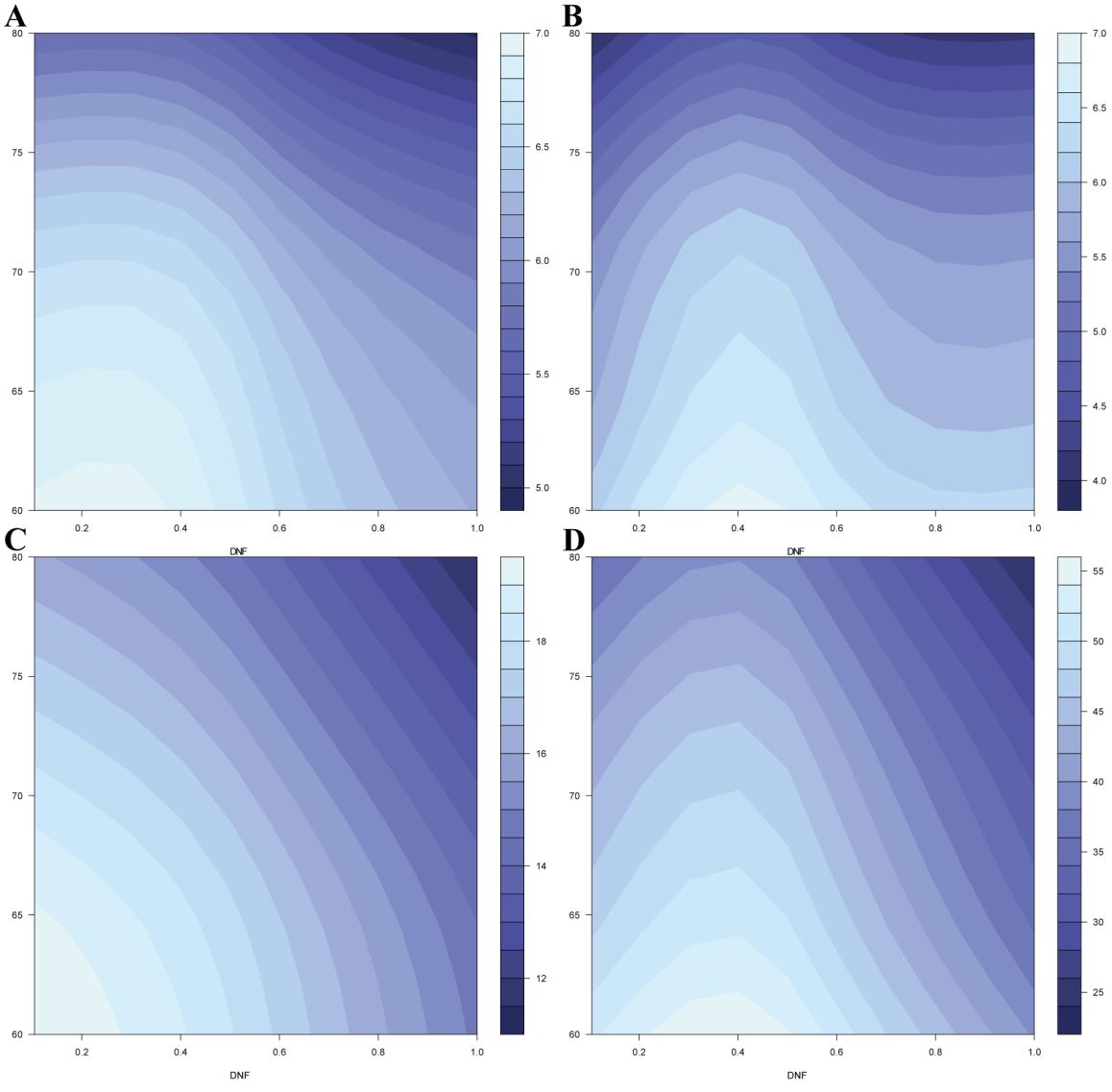

Fig.4 3D distribution diagram (A) Learning scores and DNF 3D distribution maps. (B) Recall scores and DNF 3D distribution maps. (C) Animal fluency and DNF 3D distribution maps. (D) Digit symbol replacement tests and DNF 3D distribution maps.

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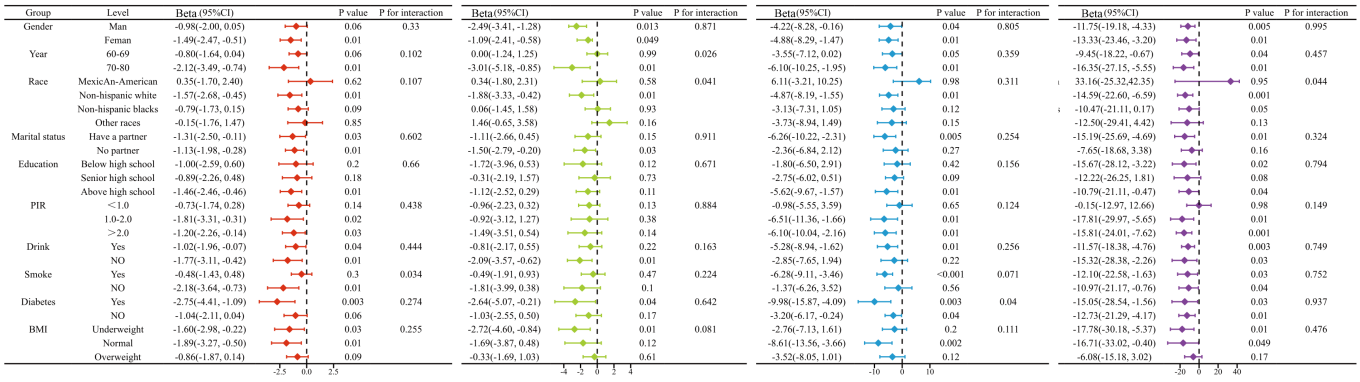
Fig. 5 Subgroup analysis forest plot.



Group	Level	Beta (95%CI)	P value	P for interaction	Beta (95%CI)	P value	P for interaction	Beta (95%CI)	P value	P for interaction	Beta (95%CI)	P value	P for interaction
Gender	Man	-0.98(-2.00, 0.05)	0.06	0.33	-2.49(-3.41, -1.28)	0.013	0.871	-4.22(-8.28, -0.16)	0.04	0.805	-11.75(-19.18, -4.33)	0.005	0.995
	Feman	-1.49(-2.47, -0.51)	0.01		-1.09(-2.41, -0.58)	0.049		-4.88(-8.29, -1.47)	0.01		-13.33(-23.46, -3.20)	0.01	
Year	60-69	-0.80(-1.64, 0.04)	0.06	0.102	0.00(-1.24, 1.25)	0.99	0.026	-3.55(-7.12, 0.02)	0.05	0.359	-9.45(-18.22, -0.67)	0.04	0.457
	70-80	-2.12(-3.49, -0.74)	0.01		-3.01(-5.18, -0.85)	0.01		-6.10(-10.25, -1.95)	0.01		-16.35(-27.15, -5.55)	0.01	
Race	MexicAn-American	0.35(-1.70, 2.40)	0.62	0.107	0.34(-1.80, 2.31)	0.58	0.041	6.11(-3.21, 10.25)	0.98	0.311	33.16(-25.32,42.35)	0.95	0.044
	Non-hispanic white	-1.57(-2.68, -0.45)	0.01		-1.88(-3.33, -0.42)	0.01		-4.87(-8.19, -1.55)	0.01		-14.59(-22.60, -6.59)	0.001	
	Non-hispanic blacks	-0.79(-1.73, 0.15)	0.09		0.06(-1.45, 1.58)	0.93		-3.13(-7.31, 1.05)	0.12		-10.47(-21.11, 0.17)	0.05	
	Other races	-0.15(-1.76, 1.47)	0.85		1.46(-0.65, 3.58)	0.16		-3.73(-8.94, 1.49)	0.15		-12.50(-29.41, 4.42)	0.13	
Marital status	Have a partner	-1.31(-2.50, -0.11)	0.03	0.602	-1.11(-2.66, 0.45)	0.15	0.911	-6.26(-10.22, -2.31)	0.005	0.254	-15.19(-25.69, -4.69)	0.01	0.324
	No partner	-1.13(-1.98, -0.28)	0.01		-1.50(-2.79, -0.20)	0.03		-2.36(-6.84, 2.12)	0.27		-7.65(-18.68, 3.38)	0.16	
Education	Below high school	-1.00(-2.59, 0.60)	0.2	0.66	-1.72(-3.96, 0.53)	0.12	0.671	-1.80(-6.50, 2.91)	0.42	0.156	-15.67(-28.12, -3.22)	0.02	0.794
	Senior high school	-0.89(-2.26, 0.48)	0.18		-0.31(-2.19, 1.57)	0.73		-2.75(-6.02, 0.51)	0.09		-12.22(-26.25, 1.81)	0.08	
	Above high school	-1.46(-2.46, -0.46)	0.01		-1.12(-2.52, 0.29)	0.11		-5.62(-9.67, -1.57)	0.01		-10.79(-21.11, -0.47)	0.04	
PIR	<1.0	-0.73(-1.74, 0.28)	0.14	0.438	-0.96(-2.23, 0.32)	0.13	0.884	-0.98(-5.55, 3.59)	0.65	0.124	-0.15(-12.97, 12.66)	0.98	0.149
	1.0-2.0	-1.81(-3.31, -0.31)	0.02		-0.92(-3.12, 1.27)	0.38		-6.51(-11.36, -1.66)	0.01		-17.81(-29.97, -5.65)	0.01	
	>2.0	-1.20(-2.26, -0.14)	0.03		-1.49(-3.51, 0.54)	0.14		-6.10(-10.04, -2.16)	0.01		-15.81(-24.01, -7.62)	0.001	
Drink	Yes	-1.02(-1.96, -0.07)	0.04	0.444	-0.81(-2.17, 0.55)	0.22	0.163	-5.28(-8.94, -1.62)	0.01	0.256	-11.57(-18.38, -4.76)	0.003	0.749
	NO	-1.77(-3.11, -0.42)	0.01		-2.09(-3.57, -0.62)	0.01		-2.85(-7.65, 1.94)	0.22		-15.32(-28.38, -2.26)	0.03	
Smoke	Yes	-0.48(-1.43, 0.48)	0.3	0.034	-0.49(-1.91, 0.93)	0.47	0.224	-6.28(-9.11, -3.46)	<0.001	0.071	-12.10(-22.58, -1.63)	0.03	0.752
	NO	-2.18(-3.64, -0.73)	0.01		-1.81(-3.99, 0.38)	0.1		-1.37(-6.26, 3.52)	0.56		-10.97(-21.17, -0.76)	0.04	
Diabetes	Yes	-2.75(-4.41, -1.09)	0.003	0.274	-2.64(-5.07, -0.21)	0.04	0.642	-9.98(-15.87, -4.09)	0.003	0.04	-15.05(-28.54, -1.56)	0.03	0.937
	NO	-1.04(-2.11, 0.04)	0.06		-1.03(-2.55, 0.50)	0.17		-3.20(-6.17, -0.24)	0.04		-12.73(-21.29, -4.17)	0.01	
BMI	Underweight	-1.60(-2.98, -0.22)	0.03	0.255	-2.72(-4.60, -0.84)	0.01	0.081	-2.76(-7.13, 1.61)	0.2	0.111	-17.78(-30.18, -5.37)	0.01	0.476
	Normal	-1.89(-3.27, -0.50)	0.01		-1.69(-3.87, 0.48)	0.12		-8.61(-13.56, -3.66)	0.002		-16.71(-33.02, -0.40)	0.049	
	Overweight	-0.86(-1.87, 0.14)	0.09		-0.33(-1.69, 1.03)	0.61		-3.52(-8.05, 1.01)	0.12		-6.08(-15.18, 3.02)	0.17	

Fig. 6 Employed weighted multi-model linear regression to analyze the curve fitting between nighttime fasting duration and cognitive function scores. (A) Curve fitting of DNF with learning scores. (B) Curve fitting of DNF with recall scores. (C) Curve fitting of DNF with Animal Fluency. (D) Curve fitting of DNF with Digit Symbol Substitution test.

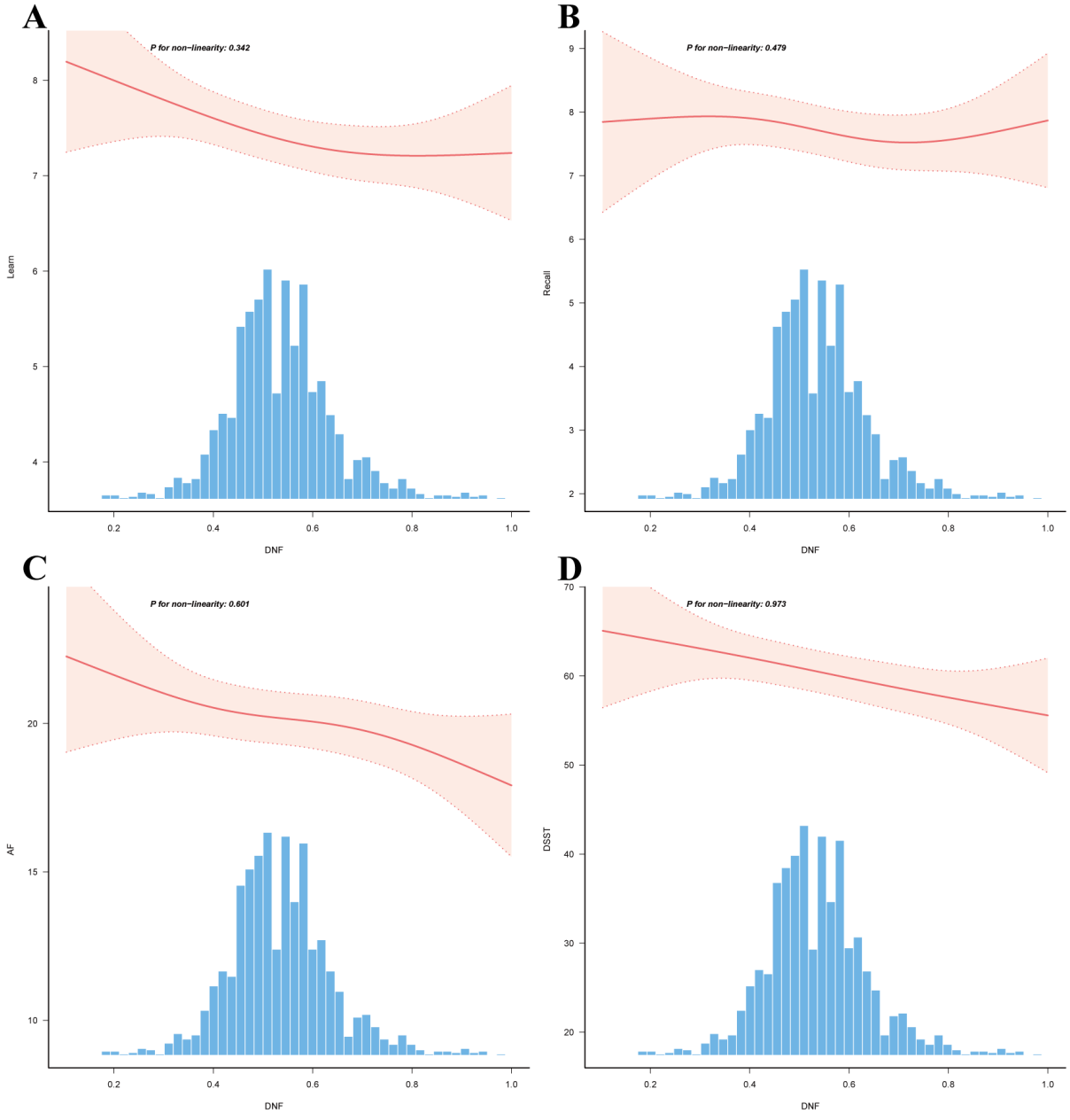


Fig. 7 The inflection point analysis of curve fitting between nocturnal fasting time and cognitive function score was analyzed by weighted multi-model linear regression.

Group	Item	Breakpoint.Beta	lower95ci	upper95ci	*P* value
Learn	E_BK1	0.6	0.592	0.609	
	slope1	-1.637	-2.73	-0.544	0.003
	slope2	-0.627	-2.329	1.075	0.469
	Likelihood Ratio test				0.251
Recall	E_BK1	0.784	0.758	0.81	
	slope1	-1.316	-2.411	-0.222	0.018
	slope2	3.56	-6.939	14.059	0.494
	Likelihood Ratio test				0.624
AF	E_BK1	0.823	0.777	0.869	
	slope1	-2.53	-4.908	-0.153	0.037
	slope2	-0.476	-48.853	47.902	0.982
	Likelihood Ratio test				0.591
DSST	E_BK1	0.828	0.78	0.876	
	slope1	-9.805	-16.148	-3.463	0.002
	slope2	-21.513	-173.563	130.536	0.741
	Likelihood Ratio test				0.95

Discussion

This study aimed to assess the effect of duration of night fasting (DNF) on cognitive functions, including learning, recall, motor fluency, and Wechsler Adult Intelligence Scale scores in older adults. The study was based on the National Health and Nutrition Examination Survey (NHANES) data from 2011 to 2014 and analyzed 2179 subjects. The length of nighttime fasting was recorded through two 24-hour dietary recall interviews, and cognitive function was assessed using standardized neuropsychological tests. After adjusting for confounders, the results showed that DNF was significantly negatively correlated with cognitive function scores, and this relationship was prevalent in most subgroups.

Intermittent fasting (IF) consists of a variety of fasting patterns, including alternate-day fasting, time-limited fasting, 5:2 intermittent fasting, 16+8 hour fasting, and caloric restriction, which focuses on controlling daily calorie intake. Previous studies have shown that fasting can optimize metabolic efficiency by activating autophagy and ketone body metabolism, especially in individuals with impaired glucose metabolism has a neuroprotective effect [31]. IF can regulate the structure of intestinal flora through the gut-brain axis, increase the abundance of probiotics (such as lactobacillus), promote the production of short-chain fatty acids (SCFAs) and neuroactive metabolites (such as 5-HT and TUDCA), and thus improve synaptic plasticity and inhibit neuroinflammation[32]. IF can significantly alleviate cognitive impairment in diabetic mice by improving insulin sensitivity and activating neuroprotective pathways (such as ERK/BDNF) by inhibiting inflammatory signaling (such as NF-κB/JNK) [33, 34]. IF can also reduce the neuroinflammation induced by postoperative cognitive dysfunction (POCD) in elderly mice, thereby improving the pathological injury of hippocampus and enhancing cognitive performance[35].

However, intermittent fasting is a double-edged sword, and functional magnetic resonance imaging (fMRI) studies have found that 14 hours of night fasting leads to physiological hypoglycemia, causing decreased activation of the bilateral dorsal midline thalamus and basal ganglia, suggesting that these brain regions are sensitive to blood sugar fluctuations[36]. Prolonged nighttime fasting (e.g., >12 hours) increases the risk of metabolic syndrome, and metabolic abnormalities (e.g., high triglycerides, insulin resistance) have been shown to be independent risk factors for cognitive decline[37]. This suggests that fasting may indirectly affect cognitive function through metabolic pathways. Studies in humans have shown that prolonged fasting (for example, more than 14 hours) can lead to a decline in short-term memory and vocabulary production, hinting at a potential effect of species differences or fasting patterns. Sustained calorie restriction will reduce processing speed and working memory, may lead to impaired cognitive flexibility, and may have serious, irreversible consequences for individuals who continue to practice calorie restriction[38].

At present, there is still a lack of clinical studies on IF in the population, so this study from the night fasting duration as a starting point, revealed the negative correlation between night fasting duration and cognitive function in the elderly. From a physiological perspective, prolonged nighttime fasting duration may affect cognitive function through multiple mechanisms. Previous studies have shown that intermittent fasting improves insulin sensitivity and lowers blood glucose levels [39, 40], which is essential for maintaining brain health and preventing neurodegenerative diseases associated with cognitive decline [41, 42]. In addition, prolonged nighttime fasting duration is associated with lower levels of inflammation and reduced circulating concentrations of inflammatory mediators such as C-reactive protein (CRP) and interleukin-6 (IL-6) [43], which may help to reduce neuroinflammation and protect neuronal cells from damage [44, 45]. Based on the fact that sex hormones such as estrogen have a modulatory role in neuroprotective and inflammatory responses, it can be explained that differences in the strength of associations observed in specific gender and age groups may be related to changes in hormone levels [46, 47]. In addition, differences between ethnic groups may be related to differences in genetic background, cultural practices, or environmental factors, all of which may influence an individual's perception of the effects of nighttime fasting duration on cognitive function [48].

The strengths of this study are the use of representative NHANES data and the use of rigorous statistical methods to control for confounders. However, there were limitations to the study: the cross-sectional design did not allow for the identification of causality, the DNF measure may have been influenced by recall bias, and other potential influences (e.g., genetic predisposition or chronic stress) were not considered. Future research incorporating prospective or longitudinal analyses is anticipated to provide further in-depth insights.

The findings support the association between DNF and cognitive decline in older adults and emphasize the potential for improving cognitive health through lifestyle interventions. Future studies must explore the mechanisms of action and differences in different populations further.

Conclusion

This study investigated the relationship between nighttime fasting duration and cognitive function in older adults using data from the National Health and Nutrition Examination Survey (NHANES) from 2011 to 2014. The results demonstrated a significant negative correlation between longer nighttime fasting duration and cognitive function scores, particularly in learning, recall, attention, and the Digit

Symbol Replacement Test. Subgroup analyses revealed that this negative correlation was prevalent across most demographic and health-related subgroups. Curve fitting further confirmed a linear relationship between nighttime fasting duration and cognitive function scores. These findings suggest that nighttime fasting duration may be a modifiable lifestyle factor influencing cognitive health in older adults. Future research should explore the underlying mechanisms and consider longitudinal studies to establish causality.

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Conflict of Interest Statement

There are no conflicts of interest in this study.

Competing Interests

The authors declare that they have no existing or potential commercial or financial relationships that could create a conflict of interest at the time of conducting this study.

Data Availability

All data needed to evaluate the conclusions in the paper are present in the paper or the Supplementary Materials. Additional data related to this paper may be requested from the authors.

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