

Original Article

NHANES 2011–2014: Association Between Conicity Index and Cognitive Performance in Older Adults

Fei Chen¹, Ken Chen^{1,*} ¹Department of Geriatric, Chongqing Mental Health Center, 401147 Chongqing, China*Correspondence: 4726905@qq.com (Ken Chen)

Submitted: 1 October 2024 Revised: 7 December 2024 Accepted: 3 January 2025 Published: 25 August 2025

Abstract

Background: The negative impact of obesity on cognitive function (CF) is well-established; nevertheless, no prior studies have explored the link between conicity index and cognitive performance. This research sought to investigate the link between conicity index and cognitive impairment. **Methods:** Data were obtained from a cross-sectional analysis of the National Health and Nutrition Examination Survey 2011–2014 (NHANES), with CF evaluated by the total scores of three cognitive tests (TCT), the delayed recall test (DRT), the immediate recall test (IRT), the animal fluency test (AFT), and the digit symbol substitution test (DSST). The conicity index was derived from waist circumference, height, and weight. Multiple linear regression, smooth curve fitting, and subgroup interaction analyses were utilized to explore the correlation between conicity index and cognitive performance. **Results:** The study included 2752 subjects and the results indicated that increasing conicity index was markedly associated with declining CF. In fully adjusted models, the conicity index was linked to reductions in total cognitive score ($\beta = -16.35$, 95% confidence interval (CI): -26.68 to -6.02 , $p = 0.0019$) and DRT ($\beta = -1.52$, 95% CI: -2.74 to -0.30 , $p = 0.0151$), IRT ($\beta = -2.93$, 95% CI: -5.37 to -0.48 , $p = 0.0190$), AFT ($\beta = -2.03$, 95% CI: -4.88 to 0.82 , $p = 0.1636$), and DSST ($\beta = -9.88$, 95% CI: -17.11 to -2.65 , $p = 0.0075$) scores. However, the negative association between conicity index and AFT score was not statistically significant. **Conclusions:** Lower CF is associated with a higher conicity index. The conicity index is useful for the early detection of cognitive decline.

Keywords: cognitive function; conicity index; cross-sectional survey; older adult; NHANES

Main Points

1. To investigate the link between the conicity index and cognitive function (CF) by cross-sectional study using NHANES data.
2. Lower CF is associated with a higher conicity index.
3. The conicity index proves beneficial for the early detection of cognitive decline.

1. Introduction

In recent decades, the prevalence and fatality rates linked to dementia have shown a consistent upward trend [1]. The World Health Organization estimates that approximately 50 million people worldwide are affected by dementia, with a new diagnosis occurring every three seconds. Projections indicate that by 2050, the number of individuals with dementia is projected to nearly double [2]. Dementia is primarily characterized by cognitive decline and reduced daily functioning, often accompanied by behavioral and psychological symptoms. These symptoms not only diminish the well-being of patients and their families but also impose significant psychological, financial, and caregiving burdens that contribute to an increasing strain on healthcare systems [3]. Cognitive impairment, particularly in the initial phases of dementia and Alzheimer's disease, is a significant clinical manifestation. The progression from cognitive

decline to Alzheimer's disease is irreversible, and current pharmacological interventions remain ineffective in halting or improving its course. Identifying factors that influence cognitive function (CF) is therefore essential to developing preventive strategies.

Globally, obesity has emerged as a serious health concern and a recognized risk factor for various diseases, including metabolic disorders, cardiovascular diseases, osteoarthritis, dementia, depression, and cancer, all of which contribute to reduced life expectancy [4–7]. While numerous investigations have explored the impact of obesity on cognitive impairment in older populations, no definitive conclusions have been reached. Inconsistent findings may be attributed, in part, to differences in the methods used to assess obesity. Among the various metrics, body mass index (BMI) is the most widely used, yet it fails to accurately reflect body composition, particularly in terms of fat and muscle distribution, and is unable to capture the distribution of adiposity [8,9]. The conicity index, a novel anthropometric measure of obesity, takes into account an individual's height, weight and waist circumference and calculates it through specific mathematical formulas, so as to obtain an index reflecting body shape and abdominal obesity. This index aids researchers to evaluate the degree of obesity from the perspective of weight distribution and body size, rather than relying on the traditional BMI. The conicity index is superior to general obesity indicators such as BMI in assess-



ing the risk of diabetes and cardiovascular disease [10,11]. At present, there is no study on the correlation between the conicity index and neurological diseases such as cognitive impairment. However, Diabetes mellitus and cardiovascular disease are also known to increase the risk of cognitive impairment and it is speculated here that the conicity index may have a correlation with CF. Hence, this investigation sought to examine the association between the conicity index and cognitive performance utilizing data from the National Health and Nutrition Examination Survey 2011–2014 (NHANES), and applying a multifactorial analysis of demographic characteristics and medical history.

2. Methods

2.1 Study Population

The data utilized in this research were sourced from the NHANES database (<http://www.cdc.gov/nchs/nhanes/>), a cross-sectional survey aimed at evaluating the health status of the USA population. The survey was executed by the Centers for Disease Control and Prevention, and ethical approval was obtained for all NHANES protocols. Participants provided informed consent before their enrollment in the survey. NHANES is conducted biennially, in each cycle, through a complex multi-stage random sampling design, every year about 5000 people will be included in the survey research. The survey includes face-to-face interviews, physical examinations and laboratory examination. This study is a cross-sectional observational study that collected anonymous demographic and survey data from patients using the NHANES database. The years 2011–2012 and 2013–2014 were the two most recent survey periods with CF test scores, therefore data from these two survey periods was included in this study. A total of 19,931 individuals took part in NHANES from 2011 to 2014, with the current analysis restricted to 3632 participants aged 60 years or older. After excluding individuals with incomplete cognitive test data ($n = 698$) and missing conicity index values ($n = 182$), 2752 eligible subjects were incorporated in the final examination. Inclusion criteria: (1) Database survey data from 2011 to 2012 ($n = 9756$). (2) Database survey data from 2013 to 2014 ($n = 10,175$). Exclusion criteria: (1) Participants were younger than 60 years old ($n = 16,299$). (2) Participants did not have complete data for cognitive function measurements ($n = 698$). (3) Participants had no complete conicity index data (182) (Fig. 1).

2.2 CF Evaluation

CF in individuals aged 60 and above was assessed with three tests: (1) the Center for the Establishment of a Registry for Alzheimer's Disease (CERAD) Word Learning Score Test (CERAD W-L); (2) the Animal Fluency Test (AFT); and (3) the Digit Symbol Substitution Test (DSST). The CERAD W-L test consists of three immediate recall tests (IRT) and one delayed recall test (DRT). In this test, subjects are presented three times with 10 unrelated words,

and instructed to recall as many as possible after each presentation. Recall is delayed by approximately and follows the additional cognitive assessments. In the AFT, participants are allotted one minute to name as many animals as possible, receiving one point for each correct response. The DSST, adapted from the Wechsler Adult Intelligence Scale-III, requires individuals to pair corresponding symbols with numbers in 133 boxes within 120 seconds, with the final score reflecting the number of correct pairings.

In this study, the total scores from the three cognitive tests (TCT), as well as individual scores from the three IRTs, DRT, AFT, and DSST, were used as outcome variables. Since no definitive cut-off values exist for these cognitive measures, the 25th percentile of participants' scores (the lowest 25th percentile) was adopted as the threshold for low CF, consistent with previous research practice [12]. The corresponding cut-off values for cognitive impairment in this cohort were 71, 16, 5, 13, and 34, respectively.

2.3 Conicity Index Assessment

The conicity index represents a novel indicator for assessing obesity, based on the concept that the human body undergoes a transformation from a cylindrical shape to a bi-conical form as abdominal fat accumulates. It is computed utilizing waist circumference, height, and body mass, with the formula:

$$\text{Conicity index} = \text{waist circumference (m)} / (0.109 \times \sqrt{\text{Weight (kg)} / \text{Height (m)}}) [13]$$

In this study, waist circumference, height, and body mass measurements were acquired by qualified health specialists at the Mobile Examination Centers, and the conicity index was used as the primary exposure variable.

2.4 Covariates

To guarantee the precision of the findings, several covariates related to CF were included based on prior studies. These covariates encompassed age, sex (male or female), race/ethnicity (Mexican American, other Hispanic, non-Hispanic White, non-Hispanic Black, other races), educational attainment (below high school, high school, above high school), marital status (married, widowed, divorced, separated, unmarried, cohabiting), BMI, income-to-poverty ratio (IPR) the ratio of family income to poverty ≤ 1.3 , > 1.3 , ≤ 3.0 , > 3.0), smoking habits (smoked at least 100 cigarettes in life or not), alcohol consumption (had at least 12 alcohol drinks per year or not), diabetes, and hypertension.

2.5 Statistical Analysis

Statistical analyses were performed using EmpowerStats (version 4.2) (<http://www.empowerstats.net/analysis>). In descriptive statistics, continuous variables are given as

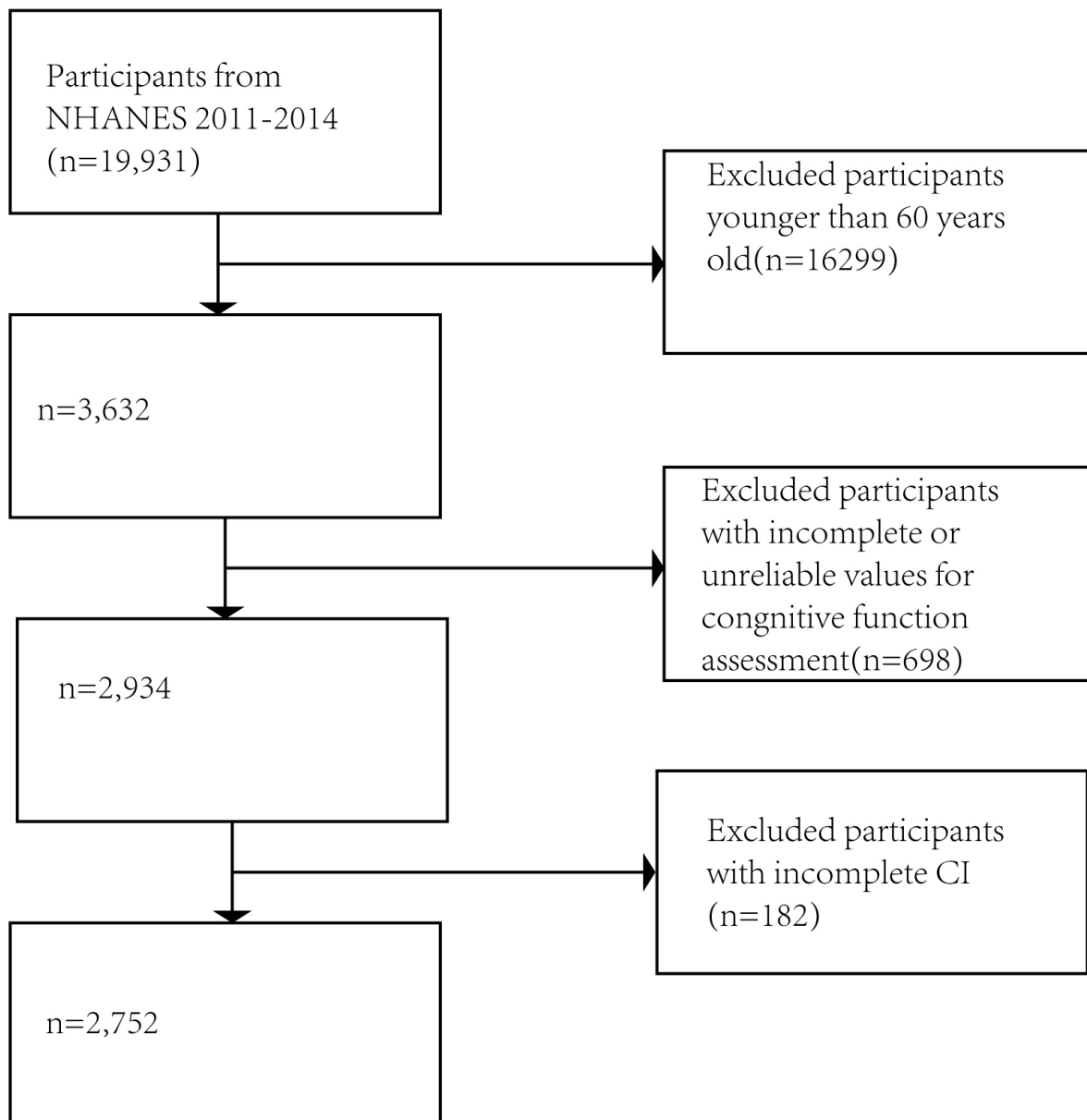


Fig. 1. Flow chart of the screening process for study population.

mean ($\pm$ standard deviations), while categorical variables are given as frequencies and percentages. To assess differences between participants with low and normal CF, the Kruskal-Wallis rank-sum test was used for continuous variables, and Fisher's exact test for categorical variables when the anticipated count was less than 10. Multiple logistic regression models were developed to investigate the link between the conicity index and impaired CF. Three models were tested: Model 1 included no covariate adjustments; Model 2 was adjusted for age, gender, education level, marital status, and race; Model 3 was further adjusted for IPR, BMI, smoking status, alcohol consumption, hypertension, and diabetes.

For missing data, continuous variables were imputed utilizing the mean, while categorical variables were

grouped separately to account for missing values (the missing values of covariates education, marital status, IPR, alcohol consumption, hypertension, diabetes, smoking status were 2, 3, 231, 30, 4, 2 and 2, respectively and other variables had no missing values). And there are few missing values in this study, which is not the key indicator we focus on. The effect of missing values on study outcomes was not significant, so our results can be considered stable and trustworthy. The link between the conicity index and CF was visualized using smooth curve fitting, and interaction tests and subgroup analyses were conducted to verify the consistency of the observed relationship across different population subgroups. Statistical significance was established at $p < 0.05$.

Table 1. Characteristics of the study population, NHANES 2011–2014.

Variables	TCT			DRT			IRT			DSST			AFT		
	Low cognitive Performance	Normal cognitive performance	<i>p</i> -value	Low cognitive Performance	Normal cognitive performance	<i>p</i> -value	Low cognitive Performance	Normal cognitive performance	<i>p</i> -value	Low cognitive Performance	Normal cognitive performance	<i>p</i> -value	Low cognitive Performance	Normal cognitive performance	<i>p</i> -value
N	718	2034		1091	1661		745	2007		715	2037		992	1760	
Conicity index	1.36 ± 0.08	1.35 ± 0.08	<0.001	1.36 ± 0.08	1.35 ± 0.08	<0.001	1.37 ± 0.08	1.35 ± 0.08	<0.001	1.36 ± 0.08	1.35 ± 0.08	<0.001	1.36 ± 0.08	1.35 ± 0.08	0.210
Age	71.54 ± 6.89	68.44 ± 6.49	<0.001	71.08 ± 6.89	68.06 ± 6.35	<0.001	71.47 ± 6.95	68.43 ± 6.46	<0.001	71.00 ± 6.85	68.64 ± 6.58	<0.001	70.39 ± 6.87	68.61 ± 6.56	<0.001
BMI	28.72 ± 6.06	29.07 ± 6.26	0.235	28.63 ± 5.96	29.21 ± 6.36	0.025	28.42 ± 5.90	29.19 ± 6.31	0.006	28.66 ± 5.96	29.09 ± 6.30	0.204	28.81 ± 6.27	29.08 ± 6.18	0.130
Sex, n (%)			<0.001			<0.001			<0.001			<0.001			0.639
Male	402 (55.99%)	946 (46.51%)		639 (58.57%)	709 (42.69%)		456 (61.21%)	892 (44.44%)		404 (56.50%)	944 (46.34%)		480 (48.39%)	868 (49.32%)	
Female	316 (44.01%)	1088 (53.49%)		452 (41.43%)	952 (57.31%)		289 (38.79%)	1115 (55.56%)		311 (43.50%)	1093 (53.66%)		512 (51.61%)	892 (50.68%)	
Race, n (%)			<0.001			<0.001			<0.001			<0.001			<0.001
Mexican American	93 (12.95%)	156 (7.67%)		113 (10.36%)	136 (8.19%)		83 (11.14%)	166 (8.27%)		97 (13.57%)	152 (7.46%)		83 (8.37%)	166 (9.43%)	
Other Hispanic	134 (18.66%)	153 (7.52%)		131 (12.01%)	156 (9.39%)		103 (13.83%)	184 (9.17%)		140 (19.58%)	147 (7.22%)		121 (12.20%)	166 (9.43%)	
Non-Hispanic White	213 (29.67%)	1084 (53.29%)		497 (45.55%)	800 (48.16%)		320 (42.95%)	977 (48.68%)		191 (26.71%)	1106 (54.30%)		342 (34.48%)	955 (54.26%)	
Non-Hispanic Black	232 (32.31%)	417 (20.50%)		275 (25.21%)	374 (22.52%)		172 (23.09%)	477 (23.77%)		240 (33.57%)	409 (20.08%)		316 (31.85%)	333 (18.92%)	
Other race	46 (6.41%)	224 (11.01%)		75 (6.87%)	195 (11.74%)		67 (8.99%)	203 (10.11%)		47 (6.57%)	223 (10.95%)		130 (13.10%)	140 (7.95%)	
Education, n (%)			<0.001			<0.001			<0.001			<0.001			<0.001
Below high school	394 (54.87%)	296 (14.55%)		383 (35.11%)	307 (18.48%)		310 (41.61%)	380 (18.93%)		409 (57.20%)	281 (13.79%)		370 (37.30%)	320 (18.18%)	
High school	163 (22.70%)	478 (23.50%)		263 (24.11%)	378 (22.76%)		166 (22.28%)	475 (23.67%)		159 (22.24%)	482 (23.66%)		250 (25.20%)	391 (22.22%)	
Above high school	159 (22.14%)	1260 (61.95%)		443 (40.60%)	976 (58.76%)		268 (35.97%)	1151 (57.35%)		145 (20.28%)	1274 (62.54%)		370 (37.30%)	1049 (59.60%)	
Marital Status, n (%)			<0.001			0.004			0.004			<0.001			<0.001
Married	347 (48.33%)	1191 (58.55%)		584 (53.53%)	954 (57.44%)		397 (53.29%)	1141 (56.85%)		347 (48.53%)	1191 (58.47%)		540 (54.44%)	998 (56.70%)	
Widowed	187 (26.04%)	320 (15.73%)		237 (21.72%)	270 (16.26%)		166 (22.28%)	341 (16.99%)		182 (25.45%)	325 (15.95%)		217 (21.88%)	290 (16.48%)	
Divorced	86 (11.98%)	307 (15.09%)		140 (12.83%)	253 (15.23%)		88 (11.81%)	305 (15.20%)		84 (11.75%)	309 (15.17%)		122 (12.30%)	271 (15.40%)	
Separated	39 (5.43%)	39 (1.92%)		34 (3.12%)	44 (2.65%)		27 (3.62%)	51 (2.54%)		42 (5.87%)	36 (1.77%)		37 (3.73%)	41 (2.33%)	
Never married	42 (5.85%)	116 (5.70%)		61 (5.59%)	97 (5.84%)		42 (5.64%)	116 (5.78%)		41 (5.73%)	117 (5.74%)		56 (5.65%)	102 (5.80%)	
Living with partner	17 (2.37%)	58 (2.85%)		35 (3.21%)	40 (2.41%)		25 (3.36%)	50 (2.49%)		19 (2.66%)	56 (2.75%)		19 (1.92%)	56 (3.18%)	
IPR, n (%)			<0.001			<0.001			<0.001			<0.001			<0.001
≤1.3	322 (44.85%)	424 (20.84%)		354 (32.45%)	392 (23.60%)		273 (36.64%)	473 (23.57%)		320 (44.76%)	426 (20.91%)		341 (34.38%)	405 (23.01%)	
>1.3, ≤3	208 (28.97%)	582 (28.61%)		334 (30.61%)	456 (27.45%)		214 (28.72%)	576 (28.70%)		219 (30.63%)	571 (28.03%)		284 (28.63%)	506 (28.75%)	
>3	117 (16.30%)	868 (42.67%)		310 (28.41%)	675 (40.64%)		189 (25.37%)	796 (39.66%)		105 (14.69%)	880 (43.20%)		263 (26.51%)	722 (41.02%)	
Alcohol Consumption, n (%)			<0.001			0.859			0.440			<0.001			<0.001
Yes	438 (61.00%)	1436 (70.60%)		738 (67.64%)	1136 (68.40%)		495 (66.44%)	1379 (68.71%)		439 (61.40%)	1435 (70.45%)		621 (62.60%)	1253 (71.20%)	
No	264 (36.77%)	584 (28.71%)		337 (30.89%)	511 (30.76%)		236 (31.68%)	612 (30.50%)		260 (36.36%)	588 (28.87%)		355 (35.79%)	493 (28.01%)	
Hypertension, n (%)			<0.001			0.160			0.162			<0.001			<0.001
Yes	483 (67.27%)	1213 (59.64%)		689 (63.15%)	1007 (60.63%)		475 (63.76%)	1221 (60.93%)		491 (68.67%)	1205 (59.27%)		660 (66.67%)	1036 (58.93%)	
No	233 (32.45%)	819 (40.27%)		399 (36.57%)	653 (39.31%)		269 (36.16%)	783 (39.07%)		224 (31.33%)	828 (40.73%)		330 (33.33%)	722 (41.07%)	
Diabetes, n (%)			<0.001			0.012			0.055			<0.001			<0.001
Yes	218 (30.36%)	415 (20.40%)		276 (25.30%)	357 (21.49%)		194 (26.04%)	439 (21.87%)		221 (30.91%)	412 (20.23%)		268 (27.02%)	365 (20.74%)	
No	466 (64.90%)	1526 (75.02%)		757 (69.39%)	1235 (74.35%)		515 (69.13%)	1477 (72.10%)		460 (64.34%)	1532 (75.21%)		674 (67.94%)	1318 (74.87%)	
Broadline	33 (4.60%)	92 (4.52%)		58 (5.32%)	67 (4.03%)		36 (4.83%)	89 (4.43%)		33 (4.62%)	92 (4.52%)		49 (4.94%)	76 (4.32%)	
Smoking status, n (%)			0.152			0.022			0.846			0.098			0.892
Yes	381 (53.06%)	1017 (50.00%)		583 (53.44%)	815 (49.07%)		381 (51.14%)	1017 (50.67%)		382 (53.43%)	1016 (49.88%)		506 (51.01%)	892 (50.68%)	
No	336 (46.80%)	1016 (49.95%)		506 (46.38%)	846 (50.93%)		364 (48.86%)	988 (49.23%)		332 (46.43%)	1020 (50.08%)		486 (48.99%)	866 (49.20%)	

Notes: The amount of missing values for the covariates were 2 (0.07%) for education, 3 (0.11%) for marital status, 231 (8.40%) for IPR, 30 (1.10%) for alcohol consumption, 4 (0.15%) for hypertension, 2 (0.07%) for diabetes, 2 (0.07%) for smoking status.

Abbreviations: AFT, animal fluency test; BMI, body mass index; DRT, delayed recall test; DSST, digit symbol substitution test; IPR, income-to-poverty ratio; IRT, immediate recall test; N, number of patients; TCT, three cognitive tests.

Table 2. Link between the conicity index and low cognitive performance.

Cognitive function	Model 1 β (95% CI)	<i>p</i> value	Model 2 β (95% CI)	<i>p</i> value	Model 3 β (95% CI)	<i>p</i> value
TCT						
Conicity index	−35.18 (−46.54, −23.81)	<0.0001	−16.84 (−25.77, −7.92)	0.0002	−16.35 (−26.68, −6.02)	0.0019
DRT						
Conicity index	−2.93 (−4.00, −1.86)	<0.0001	−0.72 (−1.75, 0.31)	0.1695	−1.52 (−2.74, −0.30)	0.0151
IRT						
Conicity index	−6.26 (−8.41, −4.12)	<0.0001	−2.14 (−4.19, −0.08)	0.0415	−2.93 (−5.37, −0.48)	0.0190
AFT						
Conicity index	−1.44 (−4.01, 1.13)	0.2712	−1.61 (−4.00, 0.77)	0.1853	−2.03 (−4.88, 0.82)	0.1636
DSST						
Conicity index	−24.54 (−32.51, −16.57)	<0.0001	−12.37 (−18.65, −6.09)	0.0001	−9.88 (−17.11, −2.65)	0.0075

Model 1, did not adjust for any confounders.

Model 2, adjusted for age, gender, race, education level and, marital status.

Model 3, adjusted for age, gender, race, education level, marital status, IPR, BMI, smoking status, alcohol consumption, hypertension, and diabetes. CI, confidence interval.

3. Results

3.1 Baseline Characteristics

This investigation analyzed 1348 males and 1404 females from the 2011–2014 NHANES cohort, with an average age of 69.25 ± 6.73 years and a mean conicity index of 1.35 ± 0.08 . The CF tests—TCT, DRT, IRT, DSST, and AFT—revealed that 26.09%, 39.64%, 27.07%, 25.98%, and 36.05% of participants, respectively, exhibited low cognitive performance. Significant differences in age, race, education level, IPR, and marital status were observed between individuals with low and normal CF across all five tests ($p < 0.01$). Participants with lower CF tended to be older, less educated, financially disadvantaged, widowed, and of non-Hispanic black ethnicity. In the low cognitive cohort, TCT, DRT, IRT, and DSST scores were markedly correlated with higher conicity index values ($p < 0.01$), while AFT scores were not correlated with the conicity index. Cognitive decline measured by TCT, DSST, and AFT was positively associated with the presence of diabetes and hypertension. According to DRT, individuals with poor cognitive performance were more likely to have diabetes compared to those with normal cognition. DRT revealed a higher prevalence of smokers in the low cognitive cohort (Table 1).

3.2 Association Between Conicity Index and Cognitive Performance

An increasing conicity index was associated with declining CF. In the comprehensive adjusted model (Model 3), a one-unit rise in conicity index corresponded to a 16.35-point reduction in TCT scores [$\beta = -16.35$, 95% confidence interval (CI): (−26.68, −6.02), $p = 0.0019$], a 1.52-point decrease in DRT scores [$\beta = -1.52$, 95% CI: (−2.74, −0.30), $p = 0.0151$], a 2.93-point decrease in IRT scores [$\beta = -2.93$, 95% CI: (−5.37, −0.48), $p = 0.0190$], a 2.03-point decrease in AFT scores [$\beta = -2.03$, 95% CI: (−4.88, 0.82), $p = 0.1636$], and a 9.88-point decrease in DSST scores [β

$= -9.88$, 95% CI: (−17.11, −2.65), $p = 0.0075$]. However, no significant negative correlation was found between the conicity index and AFT scores (Table 2). The smooth curve fitting further confirmed the negative association between the conicity index and CF (Fig. 2).

To evaluate the consistency of a link between the conicity index and cognitive decline, subgroup analyses and interaction tests were executed, categorized by gender, age, education level, race, marital status, IPR, BMI, smoking status, alcohol consumption, hypertension, and diabetes. As shown in Table 3, non-Hispanic whites and Mexican American displayed a more pronounced inverse correlation between the conicity index and TCT, AFT, and DSST scores relative to other ethnic cohorts ($p < 0.05$). No other stratifications demonstrated significant effects on the link between the conicity index and CF.

4. Discussion

Research indicates that by addressing risk factors for cognitive impairment, the likelihood of developing cognitive decline can be reduced by up to 35% [14]. Thus, identifying modifiable risk factors is a crucial strategy for preventing cognitive deterioration. This study conducted a cross-sectional analysis of 2752 older individuals aged 60 and above in the United States to elucidate the link between cognitive impairment and the conicity index. Findings demonstrated that, in the completely adjusted model (Model 3), the conicity index was markedly negatively correlated with TCT, DRT, IRT, and DSST scores. This correlation persisted independently of age, gender, race, education level, IPR, BMI, smoking status, alcohol consumption, hypertension, or diabetes. However, no notable inverse link was found between conicity index and AFT scores, which may be attributed to AFT primarily assessing semantic long-term memory, whereas early cognitive decline in dementia typically manifests as episodic memory impairment [15]. Further subgroup analyses and interaction tests

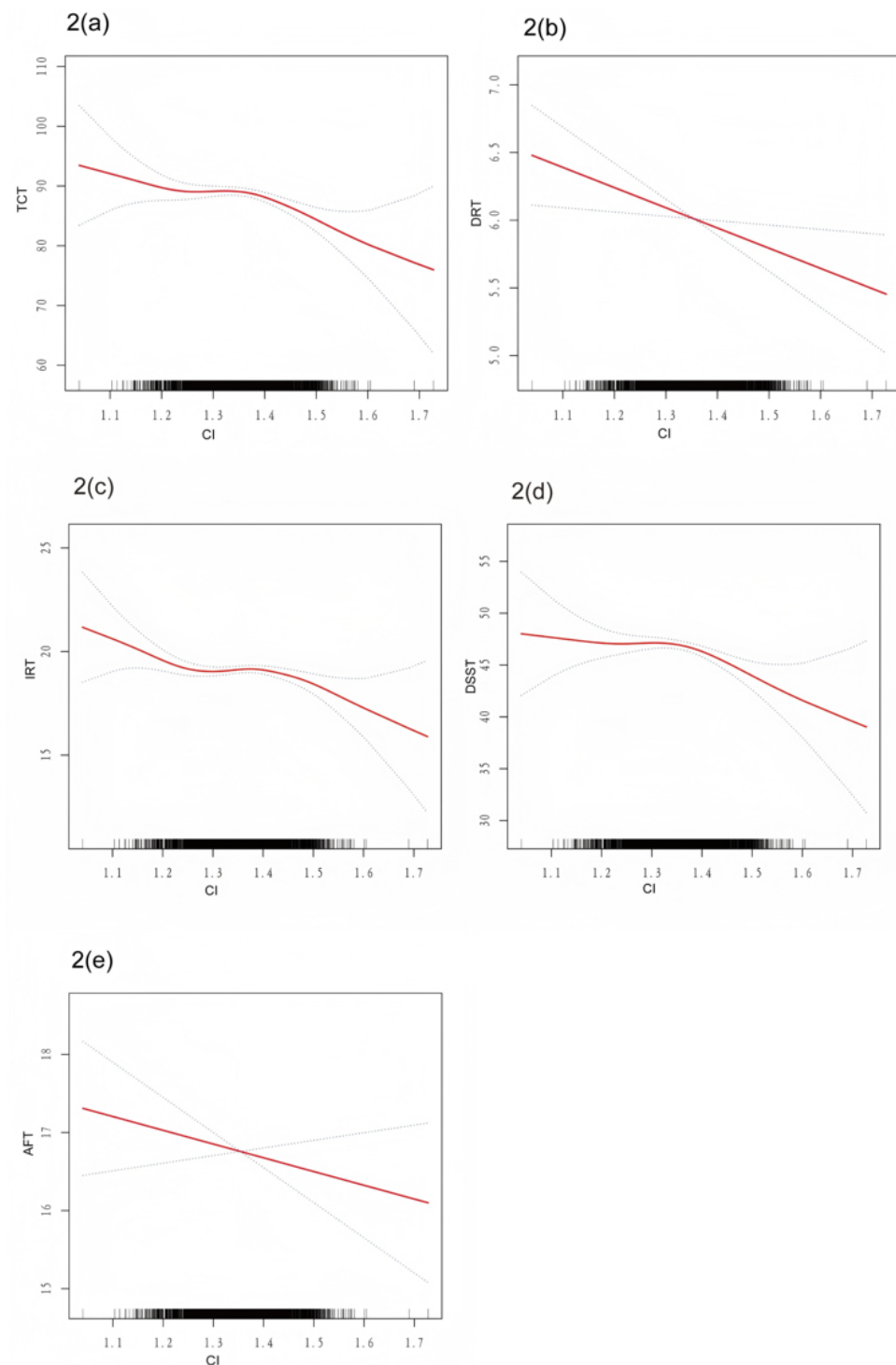


Fig. 2. Smooth curve fitting for conicity index and low cognitive performance. (a) Related to TCT. (b) Related to DRT. (c) Related to IRT. (d) Related to DSST. (e) Related to AFT. Legend: Solid red lines represent the smooth curve fit between the variables, while blue bands indicate the 95% CI derived from this fit.

Table 3. Subgroup analysis of the associations between conicity index and cognitive performance.

Subgroup	TCT		DRT		IRT		AFT		DSST	
	β (95% CI) <i>p</i> value	<i>p</i> interaction	β (95% CI) <i>p</i> value	<i>p</i> interaction	β (95% CI) <i>p</i> value	<i>p</i> interaction	β (95% CI) <i>p</i> value	<i>p</i> interaction	β (95% CI) <i>p</i> value	<i>p</i> interaction
Gender		0.1413		0.5059		0.5978		0.0709		0.2004
Male	−19.2 (−35.8, −2.6) 0.0236		−1.8 (−3.4, −0.2) 0.0244		−4.0 (−7.1, −0.8) 0.0131		0.8 (−3.0, 4.6) 0.6702		−14.3 (−25.9, −2.6) 0.0164	
Female	−36.4 (−52.1, −20.60) <0.0001		−2.5 (−4.0, −1.1) 0.0008		−5.1 (−8.1, −2.2) 0.0007		−4.0 (−7.6, −0.4) 0.0296		−24.8 (−35.8, −13.7) <0.0001	
Age		0.6835		0.6232		0.2737		0.8146		0.6751
60–69	−21.5 (−36.4, −6.6) 0.0047		−1.6 (−3.0, −0.2) 0.0228		−4.1 (−7.0, −1.3) 0.0044		0.3 (−3.2, 3.7) 0.8830		−16.0 (−26.5, −5.5) 0.0030	
70–79	−31.5 (−52.5, −10.6) 0.0032		−2.8 (−4.8, −0.8) 0.0052		−7.0 (−11.0, −3.0) 0.0007		1.5 (−3.4, 6.3) 0.5510		−23.2 (−38.1, −8.4) 0.0022	
≥80	−18.4 (−46.1, 9.2) 0.1911		−1.8 (−4.5, 0.8) 0.1666		−1.7 (−7.0, 3.5) 0.5206		−1.1 (−7.4, 5.2) 0.7339		−13.8 (−33.3, 5.8) 0.1681	
BMI		0.5091		0.3751		0.2975		0.7199		0.3216
<25	−52.2 (−72.0, −32.5) <0.0001		−4.9 (−6.8, −3.0) <0.0001		−10.6 (−14.3, −6.9) <0.0001		−1.3 (−5.8, 3.2) 0.5657		−35.4 (−49.2, −21.5) <0.0001	
≥25, <30	−43.0 (−64.4, −21.6) <0.0001		−3.0 (−5.0, −1.0) 0.0038		−6.3 (−10.4, −2.3) 0.0022		−3.7 (−8.6, 1.1) 0.1316		−30.0 (−45.0, −14.9) <0.0001	
≥30	−34.2 (−57.5, −10.9) 0.0041		−3.7 (−5.9, −1.5) 0.0009		−7.9 (−12.3, −3.5) 0.0004		−3.6 (−8.9, 1.7) 0.1816		−19.0 (−35.4, −2.6) 0.0229	
Race		0.0010		0.4668		0.0993		0.0049		0.0008
Mexican American	−61.8 (−97.4, −26.2) 0.0007		−3.4 (−7.0, 0.1) 0.0560		−8.1 (−15.2, −1.1) 0.0243		−11.3 (−19.5, −3.1) 0.0069		−38.9 (−63.6, −14.3) 0.0020	
Other Hispanic	−30.7 (−71.8, 10.5) 0.1445		−2.1 (−6.2, 2.0) 0.3081		−3.3 (−11.5, 4.9) 0.4276		−5.2 (−14.7, 4.4) 0.2881		−20.1 (−48.6, 8.5) 0.1682	
Non-Hispanic White	−66.8 (−82.2, −51.4) <0.0001		−3.8 (−5.4, −2.3) <0.0001		−9.6 (−12.7, −6.6) <0.0001		−7.5 (−11.1, −3.9) <0.0001		−45.8 (−56.5, −35.1) <0.0001	
Non-Hispanic Black	−11.1 (−33.1, 11.0) 0.3239		−1.4 (−3.5, 0.8) 0.2227		−3.2 (−7.6, 1.2) 0.1518		−1.0 (−6.1, 4.1) 0.7027		−5.5 (−20.8, 9.7) 0.4776	
Other race	−31.9 (−68.5, 4.7) 0.0880		−3.1 (−6.7, 0.5) 0.0949		−2.9 (−10.2, 4.4) 0.4337		7.5 (−1.0, 15.9) 0.0838		−33.3 (−58.7, −7.9) 0.0101	

Table 3. Continued.

Subgroup	TCT		DRT		IRT		AFT		DSST	
	β (95% CI) <i>p</i> value	<i>p</i> interaction	β (95% CI) <i>p</i> value	<i>p</i> interaction	β (95% CI) <i>p</i> value	<i>p</i> interaction	β (95% CI) <i>p</i> value	<i>p</i> interaction	β (95% CI) <i>p</i> value	<i>p</i> interaction
Education		0.2329		0.2418		0.9588		0.8505		0.0658
Below high school	-12.1 (-32.2, 8.0) 0.2367		-1.3 (-3.5, 0.8) 0.2158		-5.0 (-9.3, -0.8) 0.0196		-0.7 (-5.7, 4.3) 0.7853		-5.1 (-19.0, 8.9) 0.4792	
High school	-30.6 (-51.0, -10.2) 0.0033		-3.9 (-6.1, -1.8) 0.0003		-5.9 (-10.2, -1.6) 0.0068		-1.2 (-6.3, 3.8) 0.6375		-19.5 (-33.7, -5.3) 0.0071	
Above high school	-32.7 (-46.3, -19.2) <0.0001		-2.5 (-3.9, -1.1) 0.0006		-5.5 (-8.4, -2.7) 0.0002		0.4 (-2.9, 3.8) 0.8062		-25.1 (-34.5, -15.7) <0.0001	
Marital Status		0.6074		0.3103		0.9335		0.7392		0.4240
Married	-44.1 (-59.6, -28.7) <0.0001		-4.1 (-5.5, -2.6) <0.0001		-6.7 (-9.7, -3.8) <0.0001		-1.4 (-4.9, 2.2) 0.4500		-32.0 (-42.8, -21.1) <0.0001	
Widowed	-30.6 (-56.2, -5.0) 0.0193		-1.6 (-4.0, 0.9) 0.2081		-4.5 (-9.4, 0.4) 0.0713		-2.7 (-8.5, 3.1) 0.3613		-21.8 (-39.8, -3.8) 0.0174	
Divorced	-19.9 (-48.5, 8.7) 0.1728		-1.7 (-4.5, 1.0) 0.2129		-6.2 (-11.7, -0.7) 0.0263		3.3 (-3.2, 9.8) 0.3161		-15.3 (-35.4, 4.8) 0.1351	
Separated	-30.3 (-95.9, 35.4) 0.3667		-0.6 (-6.9, 5.6) 0.8451		-3.2 (-15.7, 9.4) 0.6212		-5.1 (-20.0, 9.8) 0.5033		-21.4 (-67.4, 24.7) 0.3634	
Never married	-13.8 (-55.4, 27.8) 0.5164		-1.8 (-5.7, 2.2) 0.3795		-4.7 (-12.6, 3.3) 0.2517		-3.7 (-13.2, 5.7) 0.4411		-3.6 (-32.8, 25.6) 0.8075	
Living with partner	-26.4 (-95.3, 42.4) 0.4520		0.2 (-6.4, 6.7) 0.9540		-10.3 (-23.5, 2.8) 0.1246		-3.4 (-19.0, 12.3) 0.6747		-12.9 (-61.2, 35.3) 0.5993	
IPR, n (%)		0.2493		0.1257		0.8079		0.5858		0.1794
≤1.3	-15.2 (-35.5, 5.1) 0.1414		-3.2 (-5.3, -1.2) 0.0020		-4.6 (-8.7, -0.6) 0.0260		1.5 (-3.3, 6.3) 0.5404		-8.9 (-23.0, 5.2) 0.2159	
>1.3, ≤3	-24.5 (-43.8, -5.3) 0.0126		-1.0 (-2.9, 0.9) 0.3138		-6.4 (-10.3, -2.6) 0.0011		0.1 (-4.5, 4.6) 0.9791		-17.2 (-30.6, -3.8) 0.0120	
>3	-37.9 (-55.8, -20.0) <0.0001		-3.6 (-5.4, -1.8) <0.0001		-5.9 (-9.5, -2.3) 0.0013		-1.8 (-6.1, 2.4) 0.3954		-26.6 (-39.0, -14.1) <0.0001	

Table 3. Continued.

Subgroup	TCT		DRT		IRT		AFT		DSST	
	β (95% CI) <i>p</i> value	<i>p</i> interaction	β (95% CI) <i>p</i> value	<i>p</i> interaction	β (95% CI) <i>p</i> value	<i>p</i> interaction	β (95% CI) <i>p</i> value	<i>p</i> interaction	β (95% CI) <i>p</i> value	<i>p</i> interaction
Alcohol consumption, n (%)		0.2092		0.8644		0.4890		0.8816		0.0943
Yes	−42.5 (−56.4, −28.7) <0.0001		−3.0 (−4.3, −1.7) <0.0001		−7.1 (−9.7, −4.4) <0.0001		−1.9 (−5.1, 1.2) 0.2260		−30.6 (−40.3, −20.9) <0.0001	
No	−27.1 (−46.9, −7.2) 0.0075		−3.2 (−5.1, −1.3) 0.0009		−5.4 (−9.2, −1.7) 0.0047		−2.4 (−6.8, 2.1) 0.3051		−16.1 (−30.0, −2.2) 0.0235	
Hypertension, n (%)		0.0945		0.1024		0.2789		0.1874		0.1480
Yes	−23.0 (−37.6, −8.4) 0.0021		−2.0 (−3.4, −0.6) 0.0042		−5.0 (−7.8, −2.2) 0.0004		1.0 (−2.3, 4.3) 0.5359		−17.0 (−27.2, −6.7) 0.0012	
No	−43.0 (−61.3, −24.6) <0.0001		−3.9 (−5.6, −2.1) <0.0001		−7.5 (−11.0, −4.0) <0.0001		−2.5 (−6.6, 1.6) 0.2336		−29.1 (−42.0, −16.2) <0.0001	
Diabetes, n (%)		0.1498		0.4280		0.3450		0.4016		0.1352
Yes	−8.1 (−33.4, 17.2) 0.5291		−1.4 (−3.8, 1.0) 0.2668		−4.5 (−9.4, 0.3) 0.0650		0.8 (−4.9, 6.6) 0.7734		−3.1 (−20.8, 14.7) 0.7343	
No	−32.9 (−46.3, −19.5) <0.0001		−3.0 (−4.3, −1.8) <0.0001		−6.5 (−9.1, −4.0) <0.0001		−0.6 (−3.6, 2.4) 0.7002		−22.8 (−32.2, −13.4) <0.0001	
Broadline	−1.3 (−53.7, 51.1) 0.9619		−1.4 (−6.4, 3.5) 0.5693		0.6 (−9.4, 10.5) 0.9104		7.6 (−4.2, 19.5) 0.2066		−8.1 (−44.8, 28.6) 0.6672	
Smoking status, n (%)		0.6968		0.2621		0.2641		0.4565		0.8919
Yes	−31.6 (−48.0, −15.1) 0.0002		−2.3 (−3.8, −0.7) 0.0039		−4.8 (−7.9, −1.7) 0.0025		−0.5 (−4.2, 3.2) 0.8001		−24.0 (−35.5, −12.5) <0.0001	
No	−36.1 (−52.0, −20.2) <0.0001		−3.5 (−5.0, −2.0) <0.0001		−7.3 (−10.3, −4.3) <0.0001		−2.4 (−6.0, 1.2) 0.1829		−22.9 (−34.1, −11.8) <0.0001	

Notes: Age, gender, race, education level, marital status, IPR, BMI, smoking status, alcohol consumption, hypertension, and diabetes are adjusted.

revealed a relatively stable negative association between the conicity index and cognitive decline across various population subgroups. Notably, non-Hispanic whites exhibited a more substantial inverse link between the conicity index and TCT, AFT, and DSST scores relative to other ethnic cohorts, suggesting that obesity may exert a greater influence on CF in non-Hispanic whites than in other racial or ethnic cohorts.

Obesity is an increasingly problematic global health issue with a rising prevalence. Previous research has identified obesity as a potential risk factor for cognitive decline. Clinical studies have shown that obese individuals tend to have reduced brain volumes, particularly in the hippocampus, which is essential for CF. Additionally, decreased levels of gray matter have been observed in brain regions such as the hippocampus, prefrontal cortex, and other subcortical areas [16]. Cheke *et al.* [17] found that obesity diminished functional activity in cortical areas related to episodic memory, including the hippocampus, angular gyrus, and dorsolateral prefrontal cortex. This may explain the lack of a significant correlation between conicity index and AFT, which primarily assesses semantic long-term memory in this study.

The mechanisms by which obesity may lead to cognitive impairment largely involve neuroinflammation, insulin resistance (IR) and gut microbiota dysregulation. First, excessive adipose tissue in obese subjects results in chronic low-grade peripheral inflammation. Inflammatory markers like tumor necrosis factor- α (TNF- α) and interleukin-6 (IL-6), secreted by adipocytes, can infiltrate the brain through various pathways, triggering neuroinflammatory responses, particularly in the hypothalamus. This may lead to synaptic remodeling, neurodegeneration, and impaired neuronal connectivity, ultimately affecting CF [18–20]. Second, obesity is frequently associated with varying degrees of insulin resistance, which leads to elevated insulin levels. Insulin plays a critical role in regulating neuro-metabolism and glucose uptake in the hippocampus and temporal lobes, influencing neurotransmitter release and re-uptake (e.g., dopamine, acetylcholine), thereby enhancing cognition. However, when insulin levels become excessive in the brain, insulin-degrading enzymes prioritize insulin removal over amyloid- β clearance, allowing amyloid accumulation, which can impair CF [21–23]. Third, the composition of gut microbiota and the metabolism of aromatic amino acids can also be influenced by obesity, potentially impairing memory [24]. A animal study has shown that diet-induced obese mice exhibit increased intestinal permeability, and alterations in gut flora may impact CF through the gut-brain axis [25]. Epidemiological studies and meta-analyses have further revealed a significant link between obesity and an elevated likelihood of dementia. A meta-analysis of 19 longitudinal investigations, encompassing 58,964 individuals aged 35 to 65 years with up to 42 years of follow-up, found that obesity marked increases the risk

of dementia [26]. Central obesity, in particular, has shown a strong association with poor cognitive performance [27].

Given these findings, the use of simple anthropometric measures to assess obesity could be an effective means of identifying individuals at risk for cognitive impairment. Monitoring and maintaining these measurements within normal ranges may improve screening and intervention strategies aimed at preventing cognitive decline. Currently, BMI is the most widely used indicator of obesity in epidemiological research. A study involving 6582 British individuals aged 50 and older, with a mean follow-up period of 11 years, revealed that a BMI ≥ 30 kg/m² was linked to an elevated likelihood of dementia [28].

A large cross-sectional investigation conducted in Western China similarly found that elevated BMI increased the likelihood of cognitive decline in middle-aged men aged 50–59 [29]. However, a study has yielded opposite findings. For example, a baseline survey in 2014, followed by a 2018 reassessment of 5156 participants aged ≥ 65 years in China, suggested that the incidence of cognitive impairment in the obesity cohort (as defined by BMI) was lower than in the normal-weight cohort [30]. Additionally, in a study of older Indonesian individuals aged 60–65, it was found that the probability of cognitive impairment in the obese cohort (BMI ≥ 27.5 kg/m²) was reduced by 95.7% compared to the normal BMI cohort (18.5–22.9 kg/m²) [31]. These contradictory results may stem from differences in follow-up periods, comorbidities, or reverse causality. Moreover, BMI is calculated using only height and weight, in fails to capture fat distribution, which might contribute to inconsistent conclusions. In contrast, the conicity index, based on a two-cone principle, more accurately reflects abdominal fat deposition and increases with the proportion of abdominal adipose tissue [32,33]. The conicity index is considered a reliable alternative indicator of obesity and has been used to predict visceral (abdominal) fat [34]. Abdominal obesity, compared to peripheral fat deposits in the thighs, buttocks, and limbs, is more strongly associated with an increased risk of cognitive impairment [35,36]. Therefore, it is speculated that the conicity index may demonstrate a stronger correlation with CF than traditional indicators such as BMI. The study also confirmed lower cognitive function is associated with a higher conicity index. Intervention study results demonstrated the impact of weight loss on cognitive function. In animal model research, high-fat diet-induced obese mice that underwent exercise training exhibited improvements in CF, synaptic plasticity, and reduced neuroinflammation as body mass decreased [37]. Similarly, a clinical study shows the same findings, Alosco *et al.*'s [38] research found that the cognitive function of 78 bariatric surgery patients improved after surgery. In 2023, the Johns Hopkins University School of Medicine conducted a study on 35 women with a BMI ≥ 35 kg/m² before and after weight loss surgery, who showed improvements in auditory attention and executive function and all tests of processing

speed [39]. The study by Hathaway *et al.* [40] also demonstrated that cognition appears generally likely to improve following bariatric surgery. Therefore, for the older population, screening for the conicity index and cognitive function should be strengthened to improve cognitive function through targeted weight management in the early stages of cognitive decline. This is of great significance for improving the quality of life of older adults, promoting healthy aging and reducing the burden on families and society.

This study is cross-sectional and therefore is neither able to demonstrate a causal relationship between the temporal progression of cognitive impairment and the conicity index with these data, nor draw the conclusion that body surface measurement indicators change with time, there is also a lack of research on the possible influencing factors, including environment, region, diet, climate and drugs, which may limit the applicability of the results to people in different regions.

5. Conclusions

This study demonstrated that a higher conicity index is correlated with an elevated risk of cognitive dysfunction. The conicity index is helpful for the early detection of cognitive decline.

Availability of Data and Materials

The data utilized for this research is openly accessible and obtainable from the website <http://www.cdc.gov/nchs/nhanes/>.

Author Contributions

FC: conception, design, supervision, data collection and processing, analysis and interpretation, literature review, writing, critical review; KC: conception, design, supervision, fundings, materials, data collection and processing, analysis and interpretation, literature review, writing, critical review. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

Not applicable.

Funding

This research was funded by the Chongqing Medical Scientific Research Project (Joint Project of Chongqing Health Commission and Science and Technology Bureau), Grant 2021MSXM252.

Conflict of Interest

The authors declare no conflict of interest.

References

- [1] Ren R, Qi J, Lin S, Liu X, Yin P, Wang Z, *et al.* The China Alzheimer Report 2022. *General Psychiatry*. 2022; 35: e100751. <https://doi.org/10.1136/gpsych-2022-100751>.
- [2] GBD 2019 Dementia Forecasting Collaborators. Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: an analysis for the Global Burden of Disease Study 2019. *The Lancet. Public Health*. 2022; 7: e105–e125. [https://doi.org/10.1016/S2468-2667\(21\)00249-8](https://doi.org/10.1016/S2468-2667(21)00249-8).
- [3] Bartley MM, Suarez L, Shafi RMA, Baruth JM, Benarroch AJM, Lapid MI. Dementia Care at End of Life: Current Approaches. *Current Psychiatry Reports*. 2018; 20: 50. <https://doi.org/10.1007/s11920-018-0915-x>.
- [4] Chobot A, Górowska-Kowolik K, Sokołowska M, Jarosz-Chobot P. Obesity and diabetes-Not only a simple link between two epidemics. *Diabetes/metabolism Research and Reviews*. 2018; 34: e3042. <https://doi.org/10.1002/dmrr.3042>.
- [5] Koliaki C, Liatis S, Kokkinos A. Obesity and cardiovascular disease: revisiting an old relationship. *Metabolism: Clinical and Experimental*. 2019; 92: 98–107. <https://doi.org/10.1016/j.metabol.2018.10.011>.
- [6] Avgerinos KI, Spyrou N, Mantzoros CS, Dalamaga M. Obesity and cancer risk: Emerging biological mechanisms and perspectives. *Metabolism: Clinical and Experimental*. 2019; 92: 121–135. <https://doi.org/10.1016/j.metabol.2018.11.001>.
- [7] Bhaskaran K, Dos-Santos-Silva I, Leon DA, Douglas IJ, Smeeth L. Association of BMI with overall and cause-specific mortality: a population-based cohort study of 3·6 million adults in the UK. *The Lancet. Diabetes & Endocrinology*. 2018; 6: 944–953. [http://doi.org/10.1016/S2213-8587\(18\)30288-2](http://doi.org/10.1016/S2213-8587(18)30288-2).
- [8] Rico-Martín S, Calderón-García JF, Sánchez-Rey P, Franco-Antonio C, Martínez Álvarez M, Sánchez Muñoz-Torrero JF. Effectiveness of body roundness index in predicting metabolic syndrome: A systematic review and meta-analysis. *Obesity Reviews: an Official Journal of the International Association for the Study of Obesity*. 2020; 21: e13023. <https://doi.org/10.1111/obr.13023>.
- [9] Nkwana MR, Monyeke KD, Lebelo SL. Body Roundness Index, A Body Shape Index, Conicity Index, and Their Association with Nutritional Status and Cardiovascular Risk Factors in South African Rural Young Adults. *International Journal of Environmental Research and Public Health*. 2021; 18: 281. <https://doi.org/10.3390/ijerph18010281>.
- [10] Motamed N, Perumal D, Zamani F, Ashrafi H, Haghjoo M, Saeedian FS, *et al.* Conicity Index and Waist-to-Hip Ratio Are Superior Obesity Indices in Predicting 10-Year Cardiovascular Risk Among Men and Women. *Clinical Cardiology*. 2015; 38: 527–534. <https://doi.org/10.1002/clc.22437>.
- [11] Liu XC, Liu YS, Guan HX, Feng YQ, Kuang J. Comparison of six anthropometric measures in discriminating diabetes: A cross-sectional study from the National Health and Nutrition Examination Survey. *Journal of Diabetes*. 2022; 14: 465–475. <https://doi.org/10.1111/1753-0407.13295>.
- [12] Chen SP, Bhattacharya J, Pershing S. Association of Vision Loss With Cognition in Older Adults. *JAMA Ophthalmology*. 2017; 135: 963–970. <https://doi.org/10.1001/jamaophthalmol.2017.2838>.
- [13] Ruperto M, Barril G, Sánchez-Muniz FJ. Usefulness of the conicity index together with the conjoint use of adipocytokines and nutritional-inflammatory markers in hemodialysis patients. *Journal of Physiology and Biochemistry*. 2017; 73: 67–75. <https://doi.org/10.1007/s13105-016-0525-1>.

- [14] Livingston G, Sommerlad A, Orgeta V, Costafreda SG, Huntley J, Ames D, *et al.* Dementia prevention, intervention, and care. *Lancet* (London, England). 2017; 390: 2673–2734. [https://doi.org/10.1016/S0140-6736\(17\)31363-6](https://doi.org/10.1016/S0140-6736(17)31363-6).
- [15] Henry JD, Crawford JR, Phillips LH. Verbal fluency performance in dementia of the Alzheimer's type: a meta-analysis. *Neuropsychologia*. 2004; 42: 1212–1222. <https://doi.org/10.1016/j.neuropsychologia.2004.02.001>.
- [16] Uraga RM, Keller JN. The Complex Interactions Between Obesity, Metabolism and the Brain. *Frontiers in Neuroscience*. 2019; 13: 513. <https://doi.org/10.3389/fnins.2019.00513>.
- [17] Cheke LG, Bonnici HM, Clayton NS, Simons JS. Obesity and insulin resistance are associated with reduced activity in core memory regions of the brain. *Neuropsychologia*. 2017; 96: 137–149. <https://doi.org/10.1016/j.neuropsychologia.2017.01.013>.
- [18] Huang X, Hussain B, Chang J. Peripheral inflammation and blood-brain barrier disruption: effects and mechanisms. *CNS Neuroscience & Therapeutics*. 2021; 27: 36–47. <https://doi.org/10.1111/cns.13569>.
- [19] Chen X, Huang Q, Feng J, Xiao Z, Zhang X, Zhao L. GLP-1 alleviates NLRP3 inflammasome-dependent inflammation in perivascular adipose tissue by inhibiting the NF- κ B signalling pathway. *The Journal of International Medical Research*. 2021; 49: 300060521992981. <https://doi.org/10.1177/0300060521992981>.
- [20] Gómez-Apo E, Mondragón-Maya A, Ferrari-Díaz M, Silva-Pereyra J. Structural Brain Changes Associated with Overweight and Obesity. *Journal of Obesity*. 2021; 2021: 6613385. <https://doi.org/10.1155/2021/6613385>.
- [21] Barber TM, Kyrou I, Randeve HS, Weickert MO. Mechanisms of Insulin Resistance at the Crossroad of Obesity with Associated Metabolic Abnormalities and Cognitive Dysfunction. *International Journal of Molecular Sciences*. 2021; 22: 546. <https://doi.org/10.3390/ijms22020546>.
- [22] Wang J, Li L, Zhang Z, Zhang X, Zhu Y, Zhang C, *et al.* Extracellular vesicles mediate the communication of adipose tissue with brain and promote cognitive impairment associated with insulin resistance. *Cell Metabolism*. 2022; 34: 1264–1279.e8. <https://doi.org/10.1016/j.cmet.2022.08.004>.
- [23] Cholerton B, Baker LD, Craft S. Insulin, cognition, and dementia. *European Journal of Pharmacology*. 2013; 719: 170–179. <https://doi.org/10.1016/j.ejphar.2013.08.008>.
- [24] Arnoriaga-Rodríguez M, Mayneris-Perxachs J, Burokas A, Contreras-Rodríguez O, Blasco G, Coll C, *et al.* Obesity Impairs Short-Term and Working Memory through Gut Microbial Metabolism of Aromatic Amino Acids. *Cell Metabolism*. 2020; 32: 548–560.e7. <https://doi.org/10.1016/j.cmet.2020.09.002>.
- [25] Lam YY, Ha CWY, Campbell CR, Mitchell AJ, Dinudom A, Oscarsson J, *et al.* Increased gut permeability and microbiota change associate with mesenteric fat inflammation and metabolic dysfunction in diet-induced obese mice. *PloS One*. 2012; 7: e34233. <https://doi.org/10.1371/journal.pone.0034233>.
- [26] Albanese E, Launer LJ, Egger M, Prince MJ, Giannakopoulos P, Wolters FJ, *et al.* Body mass index in midlife and dementia: Systematic review and meta-regression analysis of 589,649 men and women followed in longitudinal studies. *Alzheimer's & Dementia* (Amsterdam, Netherlands). 2017; 8: 165–178. <https://doi.org/10.1016/j.dadm.2017.05.007>.
- [27] West NA, Lorette ST, Cannon VA, Turner ST, Mosley TH, Jr, Windham BG. Adiposity, Change in Adiposity, and Cognitive Decline in Mid- and Late Life. *Journal of the American Geriatrics Society*. 2017; 65: 1282–1288. <https://doi.org/10.1111/jgs.14786>.
- [28] Ma Y, Ajnakina O, Steptoe A, Cadar D. Higher risk of dementia in English older individuals who are overweight or obese. *International Journal of Epidemiology*. 2020; 49: 1353–1365. <https://doi.org/10.1093/ije/dyaa099>.
- [29] Liu X, Chen X, Hou L, Xia X, Hu F, Luo S, *et al.* Associations of Body Mass Index, Visceral Fat Area, Waist Circumference, and Waist-to-Hip Ratio with Cognitive Function in Western China: Results from WCHAT Study. *The Journal of Nutrition, Health & Aging*. 2021; 25: 903–908. <https://doi.org/10.1007/s12603-021-1642-2>.
- [30] Ren Z, Li Y, Li X, Shi H, Zhao H, He M, *et al.* Associations of body mass index, waist circumference and waist-to-height ratio with cognitive impairment among Chinese older adults: Based on the CLHLS. *Journal of Affective Disorders*. 2021; 295: 463–470. <https://doi.org/10.1016/j.jad.2021.08.093>.
- [31] Vidyanti AN, Hardhantyo M, Wiratama BS, Prodjohardjono A, Hu CJ. Obesity Is Less Frequently Associated with Cognitive Impairment in Elderly Individuals: A Cross-Sectional Study in Yogyakarta, Indonesia. *Nutrients*. 2020; 12: 367. <https://doi.org/10.3390/nu12020367>.
- [32] Valdez R, Seidell JC, Ahn YI, Weiss KM. A new index of abdominal adiposity as an indicator of risk for cardiovascular disease. A cross-population study. *International Journal of Obesity and Related Metabolic Disorders: Journal of the International Association for the Study of Obesity*. 1993; 17: 77–82.
- [33] Bozorgmanesh M, Sardarinia M, Hajsheikholeslami F, Azizi F, Hadaegh F. CVD-predictive performances of “a body shape index” versus simple anthropometric measures: Tehran lipid and glucose study. *European Journal of Nutrition*. 2016; 55: 147–157. <https://doi.org/10.1007/s00394-015-0833-1>.
- [34] Peterson CM, Su H, Thomas DM, Heo M, Golnabi AH, Pietrobelli A, *et al.* Tri-Ponderal Mass Index vs Body Mass Index in Estimating Body Fat During Adolescence. *JAMA Pediatrics*. 2017; 171: 629–636. <https://doi.org/10.1001/jamapediatrics.2017.0460>.
- [35] Kanaya AM, Lindquist K, Harris TB, Launer L, Rosano C, Satterfield S, *et al.* Total and regional adiposity and cognitive change in older adults: The Health, Aging and Body Composition (ABC) study. *Archives of Neurology*. 2009; 66: 329–335. <https://doi.org/10.1001/archneurol.2008.570>.
- [36] Yoon DH, Choi SH, Yu JH, Ha JH, Ryu SH, Park DH. The relationship between visceral adiposity and cognitive performance in older adults. *Age and Ageing*. 2012; 41: 456–461. <https://doi.org/10.1093/ageing/afs018>.
- [37] Kim TW, Choi HH, Chung YR. Treadmill exercise alleviates impairment of cognitive function by enhancing hippocampal neuroplasticity in the high-fat diet-induced obese mice. *Journal of Exercise Rehabilitation*. 2016; 12: 156–162. <https://doi.org/10.12965/jer.1632644.322>.
- [38] Alosco ML, Spitznagel MB, Strain G, Devlin M, Cohen R, Crosby RD, *et al.* The effects of cystatin C and alkaline phosphatase changes on cognitive function 12-months after bariatric surgery. *Journal of the Neurological Sciences*. 2014; 345: 176–180. <https://doi.org/10.1016/j.jns.2014.07.037>.
- [39] Smith KR, Steele KE, Papantoni A, Harris C, Speck CL, Bakker A, *et al.* The relationship between weight loss and cognitive function in bariatric surgery. *Surgical Endoscopy*. 2023; 37: 1976–1984. <https://doi.org/10.1007/s00464-022-09581-4>.
- [40] Hathaway I, Momodu OE, Williams DM, Beamish AJ, Barry J, Stephens JW. Changes in Cognitive Function Following Bariatric Surgery: An Updated Systematic Review. *Obesity Surgery*. 2024; 34: 2216–2226. <https://doi.org/10.1007/s11695-024-07235-z>.