Role of Educational Status in Explaining the Association between Body Mass Index and Cognitive Function

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Abstract: Preserving physical and cognitive function becomes an important issue as people age. A growing number of studies have found that the correlation between body mass index (BMI) and cognitive function changes in different age groups. It is obvious that higher educational status is linked to higher cognitive function in terms of numerous risk factors that influence cognitive function. This study aimed to investigate the interplay between obesity and cognitive function categorized by different educational status.

This study included 5021 participants aged 20 to 59 years who completed 3 neurocognitive function tests, including a simple reaction time test (SRTT), a symbol digit substitution test (SDST), and a serial digit learning test (SDLT) as reported in the National Health and Nutrition Examination Survey (NHANES) III database. The associations between neurocognitive function and BMI were analyzed using multivariate linear regression while controlling for confounders.

After adjusting for pertinent covariates in mode 3, the β coefficients in the female participants with more than 12 years of education (interpreted as change of 3 neurocognitive function tests for each increment in BMI) comparing obesity groups to those with normal BMI were 16.2 (P < 0.001 for SRTT), 0.14 (P < 0.05 for SDST), and 0.9 (P < 0.05 for SDLT). Male participants with more than 12 years of education and female participants with fewer than 12 years of education demonstrated increased impairment as their BMI increased. However, this association was not significant after adjustments.

Obese individuals had worse neurocognitive function than those of normal weight or overweight, especially in women with a high educational level.

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INTRODUCTION

Recent research suggests that increased adiposity is associated with poor cognitive performance independent of associated medical conditions. A consistent finding across a lifespan has been that obesity is associated with cognitive impairments, especially in executive function, in children, adolescents, and adults. Nevertheless, as evidenced by differing reports, the association between obesity and cognition is inconsistent in the elderly.

Emerging evidence has demonstrated a sex difference in 3 cognitive function tests that had been previously analyzed. Edward et al found that men had a lower average mean reaction time in simple reaction time test (SRTT), a higher average mean total latency in symbol digit substitution test (SDST), and a lower average number of trials to criterion than women in the National Health and Nutrition Examination Survey (NHANES) III study. The interactions among sex, education level, and race-ethnicity were statistically significant. The differences in the hemispheric lateralization of function may explain the differences between men and women.

Level of education is thought to be a protective factor against the decline of cognitive function. Many studies have shown that a low education level is associated with high prevalence of cognitive impairment. In patients with Alzheimer disease, a possible educational reserve in cognitive decline has also been proposed.

Previous studies have attempted to demonstrate the relationship between body mass index (BMI) and decline of cognitive function. However, the effect of educational status on the relationship between BMI and cognitive function has not been determined. In this study, we examined the relationship between BMI, education, and cognitive function in the NHANES program in the United States.

MATERIALS AND METHODS

Study Population

The NHANES was a cross-sectional study conducted with people from different populations since the 1960s in the United States. The NHANES III study included 33,994 persons ages 2 months and older selected from households in 81 counties across the United States. This represented the total civilian noninstitutionalized population from 1988 to 1994. The survey consisted of 2 phases of equal lengths and sample sizes. Both phases comprised random samples of the U.S. population living in households. The protocol included standardized medical examinations, blood samples, and testing. The cognitive function changes were assessed using the NHANES III database.

Abbreviations: BMI = body mass index, NES2 = Neurobehavioral Evaluation System 2, NHANES = National Health and Nutrition Examination Survey, SDLT = serial digit learning test, SDST = symbol digit substitution test, SRTT = simple reaction time test.

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function tests were administered to a random half-sample of all adults 20 to 59 years of age if their identification number ended in an odd digit. All of the protocols and data were published online on the NHANES website. In our study, we enrolled participants who were 20 to 59 years old and had completed 3 cognitive function tests as described later from the NHANES III database. The NHANES study was approval by the National Center for Health Statistics (NCHS) Institutional Review Board, and informed consents were obtained from participants prior to starting the study.

**Definition of Obesity**

Obesity was defined according to the World Health Organization definition, which is a BMI greater than or equal to 30 kg/m². Overweight was defined as a BMI greater than or equal to 25 kg/m². The normal group was defined a BMI range from 18.5 to 25 kg/m². The BMI was calculated as a person’s weight in kilograms divided by the square of height in meters (kg/m²). Participants who were underweight (BMI below 18.5 kg/m²) were excluded due to the possibility of illness-induced weight loss or reverse causation.

**Assessment of Cognitive Function**

Cognitive function was assessed from a short version of the Neurobehavioral Evaluation System 2 (NES2) developed by Baker and Letz in the 1980s.20 The NES2 is a computerized test designed as a noninvasive tool to evaluate the functional integrity of the nervous system. The short version included 3 central nervous system tests from the NES2: SRTT, SDST, and serial digit learning test (SDLT). All of the test procedures and instructions were published online.18 The SRTT was performed by measuring the motor response time when a visual stimulus appeared. The SDST was performed by scoring the correct digits to the corresponding symbols. The SDLT was performed by recording trials of remembering and matching the digits to the corresponding numbers and scoring the numbers of the wrong digits in each trial. These tests are widely used as a presentation of neurocognitive function, and reflect psychomotor speed and control, learning, and attention.

**Covariables**

Demographic variables such as age, sex, and ethnicity (Mexican-American, non-Hispanic white, and non-Hispanic black) were included. Hypertension, congestive heart failure, diabetes mellitus, and stroke were clinical comorbidities that were related to impaired cognitive function:21–23 these were quantified by systolic blood pressure, fasting serum glucose level, and questions including “Has a doctor ever told you that you had congestive heart failure?” “Have you ever been told you have diabetes?” and “Has a doctor ever told you that you had a stroke?” Smoking was included as a lifestyle variable and was categorized into 2 groups from the question “Have you smoked at least 100 cigarettes during your entire life?” Studies have shown smoking to be a single risk factor for impaired cognitive function.24 In addition, C-reactive protein was also adjusted as a biomarker of inflammation with a positive linear relationship with impaired cognitive function.25 Educational status, which was linked to cognitive function, was recorded by the item “the number of years of education attended and completed” from the household family questionnaire; this was divided dichotomously into those with the equivalent of a high school education (≤12 years) and those with more than a high school education (>12 years) based on the 12-year public education system in the United States. We tested for effect modification by BMI groups and gender by including interaction terms in the models for the NES2. In addition, there was significant interaction between sex and education for SDST (P = 0.002). Based on the significant findings of the interaction testing, we performed further stratified analyses.

**Statistical Analysis**

All statistical analyses were performed using SPSS (statistical package for social science, Version 18.0 for Windows, SPSS, Inc., Chicago, IL) for all analyses. Descriptive results were expressed as the means ± SD for continuous variables and as number and percentage for categorical variables. Analysis of variance (ANOVA) was used to test the difference among 3 BMI groups. We used the Pearson Chi-square test to analyze the differences among the 3 BMI groups in terms of race-ethnicity, education, smoking, and past medical history (diabetes, congestive heart failure, and stroke). The characteristics of the 3 BMI groups (normal BMI, overweight, and obese) were compared. In the regression mode, the subjects with normal weight were regarded as the reference group. The linear regression model was used to find the relationship between different educational status, BMI, and each cognitive test. An extended-model approach was utilized for the adjustment of covariates: Model 1 = unadjusted model; Model 2 = age, gender, race, and educational level; Model 3 = Model 2 + diabetes, congestive heart failure, systolic blood pressure, serum glucose, and serum C-reactive protein. A P-value <0.05 was used to identify statistically significant differences.

**RESULTS**

This study included 5021 participants between 20 and 59 years of age. Of these, 2314 participants were men and 2707 were women. The mean age was 36.7 ± 10.9 years for men and 36.9 ± 10.9 years for women. Most men in this study were normal BMI or overweight (normal BMI 42%, overweight 37.5%, and obese 20%). In women, most of participants were normal BMI or obese (normal BMI 40%, overweight 27.7%, and obese 32.2%). Table 1 shows the characteristics of the 3 BMI groups separated by gender.

The continuous variables of systolic blood pressure, fasting serum glucose, and CRP level increased as the BMI increased, reaching statistical significance (P < 0.001). In men, most overweight and obese participants were Mexican-American. In women, the ethnicity breakdown was different than in men, with more non-Hispanic white individuals in the overweight group and more non-Hispanic black individuals in the obesity group. Most participants had fewer than 12 years of education (men: 66.6%; women: 66.9%). The obese women with fewer than 12 years of education made up the largest proportion (P < 0.001) of all participants. The percentage of diabetes mellitus was 3.6% in men and 5.5% in women, which also increased as the BMI increased (P < 0.001). As the BMI groups increased, the number of participants with congestive heart failure and stroke increased correspondingly.

The 3 BMI groups were further separated by 2 different education levels (more or less than 12 years of education); the relationships between these separated groups are shown in Table 2. In the women with more than 12 years of education, the SRTT and SDST tests showed increased impairment in overweight and obesity groups compared with the normal BMI group. There was statistical significance, especially in the obesity group, for both tests (P < 0.001). After adjusting for...
TABLE 1. Basic Characteristics

| Continuous variables | Male (n = 2314) | Female (n = 2707) | P Value | Male (n = 1087) | Female (n = 749) | P Value | Female (n = 871) | P Value |
|----------------------|----------------|------------------|---------|----------------|------------------|---------|-----------------|---------|
| Age, years, mean (SD) | 34.0 (10.8) | 37.9 (10.6)* | 0.001 | 34.3 (10.6) | 38.1 (11.0)* | 0.001 | 39.0 (10.6) | 0.001 |
| Systolic BP, mmHg, mean (SD) | 118.9 (11.9) | 122.9 (12.7)* | 0.001 | 110.6 (12.7) | 116.6 (14.8)* | 0.001 | 121.7 (16.1) | 0.001 |
| Serum glucose, mg/dL, mean (SD) | 92.0 (21.5) | 97.5 (27.7)* | 0.001 | 87.5 (18.7) | 92.6 (25.0)* | 0.001 | 103.5 (44.1) | 0.001 |
| C-reactive protein, mg/dL, mean (SD) | 0.3 (0.5) | 0.3 (0.4) | 0.001 | 0.4 (0.7) | 0.5 (0.5) | 0.001 | 0.8 (0.8) | 0.001 |
| Cognitive test | | | | | | | | |
| SRTT | 233.4 (53.7) | 228.9 (49.3) | 0.143 | 244.8 (56.4) | 254.0 (59.8) | 0.143 | 258.9 (67.1) | 0.001 |
| SDST | 3.0 (1.1) | 3.0 (1.1) | 0.066 | 2.6 (0.8) | 3.0 (1.6) | 0.001 | 3.1 (1.4) | 0.001 |
| SDLT-trials | 5.2 (2.2) | 5.3 (2.2) | 0.046 | 4.9 (2.2) | 5.6 (2.2)* | 0.001 | 5.7 (2.2) | 0.001 |
| SDLT-score | 5.8 (5.0) | 6.0 (5.0) | 0.064 | 5.1 (4.1) | 6.6 (5.2)* | 0.001 | 7.0 (5.2) | 0.001 |
| Categorical variables | | | | | | | | |
| Race-ethnicity, n, % | | | | | | | | |
| Non-Hispanic white | 344 (35.3) | 308 (35.5) | 0.01 | 489 (45.0) | 248 (33.1) | 0.01 | 216 (24.8) | 0.01 |
| Non-Hispanic black | 317 (32.5) | 225 (25.9) | 0.143 | 299 (27.5) | 240 (32.0) | 0.143 | 355 (40.8) | 0.143 |
| Mexican-American | 276 (28.3) | 305 (40.8) | 0.066 | 255 (23.5) | 233 (31.1) | 0.066 | 272 (31.2) | 0.066 |
| Other | 38 (3.9) | 30 (3.5) | 0.478 | 44 (4.0) | 28 (3.7) | 0.478 | 28 (3.2) | 0.478 |
| Education, n, % | | | | | | | | |
| 0–12 years | 657 (67.9) | 569 (66.1) | 0.478 | 632 (58.6) | 517 (69.3) | 0.478 | 651 (75.2) | 0.478 |
| >12 years | 311 (32.1) | 292 (33.9) | 0.143 | 447 (41.4) | 229 (30.7) | 0.143 | 215 (24.8) | 0.143 |
| Diabetes, n, % | 14 (1.4) | 29 (3.3) | 0.001 | 23 (2.1) | 44 (5.9) | 0.001 | 83 (9.5) | 0.001 |
| Congestive heart failure, n, % | 9 (0.9) | 8 (0.9) | 0.043 | 4 (0.4) | 6 (0.8) | 0.043 | 16 (1.8) | 0.043 |
| Stroke, n, % | 4 (0.4) | 4 (0.5) | 0.11 | 5 (0.5) | 3 (0.4) | 0.11 | 7 (0.8) | 0.11 |
| Smoked (100+ cigarettes in life), n, % | 581 (59.6) | 509 (58.6) | 0.91 | 462 (42.5) | 299 (39.9) | 0.91 | 337 (38.7) | 0.91 |

SDLT = serial digit learning test, SDST = symbol digit substitution test, SRTT = simple reaction time test.

* Post-hoc analysis by Scheffe method, compared to the normal BMI group if P < 0.05.
| TABLE 2. Association Between Neurocognitive Function and Body Mass Index According to Education Level |
|--------------------------------------------------------------------------------------------------|
| **Below 12 years of Education** | **Above 12 years of Education** |
| Male | Female | Male | Female | Male | Female | Male | Female | Male | Female | Male | Female |
|-------|--------|-------|--------|-------|--------|-------|--------|-------|--------|-------|--------|
| SRTT  |        |       |        |       |       |       |       |       |       |       |       |
| Model 1 | 0 (Ref) | −7.2 (3.2)* | −0.02 (3.9) | 0 (Ref) | 2.0 (2.9) | 0.1 (3.5) | 0 (Ref) | 7.8 (4.0) | 8.2 (3.8)* | 0 (Ref) | 4.6 (3.4) | 16.5 (3.5)** |
| Model 2 | 0 (Ref) | −10.4 (3.3)* | −3.9 (4.0) | 0 (Ref) | 2.0 (1.0) | 0.09 (3.5) | 0 (Ref) | 4.1 (4.1) | 3.4 (3.9) | 0 (Ref) | 4.0 (3.6) | 16.8 (3.7)** |
| Model 3 | 0 (Ref) | −10.1 (3.3)* | −3.6 (4.1) | 0 (Ref) | 2.0 (3.0) | −0.9 (3.7) | 0 (Ref) | 3.5 (4.1) | 1.7 (4.1) | 0 (Ref) | 3.9 (3.6) | 16.2 (4.0)** |

SDST |
| Model 1 | 0 (Ref) | 0.1 (0.1) | 0.2 (0.1) | 0 (Ref) | 0.1 (0.05) | 0.2 (0.1)* | 0 (Ref) | 0.4 (0.1)** | 0.4 (0.1)** | 0 (Ref) | 0.1 (0.04)* | 0.3 (0.05)** |
| Model 2 | 0 (Ref) | −0.1 (0.1)* | −0.2 (0.1) | 0 (Ref) | −0.1 (0.1) | 0.02 (0.1) | 0 (Ref) | 0.2 (0.1) | 0.1 (0.1) | 0 (Ref) | 0.05 (0.04) | 0.2 (0.04)** |
| Model 3 | 0 (Ref) | −0.1 (0.1)* | −0.2 (0.1)* | 0 (Ref) | −0.001 (0.1) | 0.02 (0.1) | 0 (Ref) | 0.1 (0.1) | 0.03 (0.1) | 0 (Ref) | 0.04 (0.04) | 0.14 (0.05)* |

SDLT-trials |
| Model 1 | 0 (Ref) | 0.1 (0.1) | 0.2 (0.2) | 0 (Ref) | 0.4 (0.2)* | 0.6 (0.2)* | 0 (Ref) | 0.6 (0.1)** | 0.5 (0.1)** | 0 (Ref) | 0.2 (0.2) | 0.7 (0.2)** |
| Model 2 | 0 (Ref) | −0.2 (0.1) | −0.03 (0.2) | 0 (Ref) | 0.3 (0.2) | 0.4 (0.2) | 0 (Ref) | 0.3 (0.1)* | 0.1 (0.1) | 0 (Ref) | −0.1 (0.2) | 0.4 (0.2)* |
| Model 3 | 0 (Ref) | −0.2 (0.1) | −0.1 (0.2) | 0 (Ref) | 0.2 (0.2) | 0.3 (0.2) | 0 (Ref) | 0.3 (0.1)* | 0.05 (0.1) | 0 (Ref) | −0.1 (0.2) | 0.3 (0.2) |

SDLT-score |
| Model 1 | 0 (Ref) | −0.03 (0.3) | 0.7 (0.4) | 0 (Ref) | 0.9 (0.3)* | 1.2 (0.4)* | 0 (Ref) | 1.6 (0.3)** | 1.4 (0.3)** | 0 (Ref) | 0.4 (0.3) | 1.5 (0.3)** |
| Model 2 | 0 (Ref) | −0.7 (0.3)* | −0.2 (0.4) | 0 (Ref) | 0.7 (0.3)* | 0.6 (0.4) | 0 (Ref) | 0.7 (0.3)* | 0.3 (0.3) | 0 (Ref) | −0.02 (0.3) | 1.0 (0.3)* |
| Model 3 | 0 (Ref) | −0.8 (0.3)* | −0.4 (0.4) | 0 (Ref) | 0.7 (0.3)* | 0.6 (0.4) | 0 (Ref) | 0.7 (0.3)* | 0.06 (0.3) | 0 (Ref) | 0.03 (0.3) | 0.9 (0.3)* |

*P < 0.05, **P < 0.001. BMI = body mass index, SE = standard error, SDLT = serial digit learning test, SDST = symbol digit substitution test, SRTT = simple reaction time test. Model 1 = unadjusted; Model 2 = Model 1 + age, race-ethnicity; Model 3 = Model 2 + diabetes, congestive heart failure, systolic blood pressure, serum glucose, serum c-reactive protein. SRTT: simple reaction time test, mean reaction time, SDST: symbol digit substitution test, mean of two lowest corrected latencies, SDLT-trials: serial digit learning test, trials to criterion, SDLT-scores: serial digit learning test, total score.
variables, there was still a statistically significant difference in the obesity group (SRTT Model 2: 16.5 ± 3.7, P < 0.001; Model 3: 17.4 ± 4.1, P < 0.001; SDST Model 2: 0.2 ± 0.4, P < 0.001; and Model 3: 0.2 ± 0.1, P < 0.05). The SDLT test also showed significant impact in the obesity group compared with the normal BMI group. The significance of the SDLT-score persisted after adjustment.

Among women with fewer than 12 years of education, the trend of the 3 BMI groups and the SRTT and SDST tests was not seen after adjusting for age and race-ethnicity. Neither SDLT-trials nor SDLT-score showed significance after adjustment in the obesity group. Nevertheless, in the overweight group, statistical significance was found in the SDLT-score test after all adjustments (P < 0.05).

In men with more than 12 years of education, compared to the normal BMI group, there was increased impairment in the 3 cognitive tests as the 3 BMI groups increased. However, some of these lacked statistical significance; moreover, the statistical significance disappeared after adjustment in Model 2 and Model 3.

**DISCUSSION**

In this study, we examined the relationship between increased BMI groups and different educational status and decline of cognitive function in the NHANES study from the United States. Consistent with previous studies, a strong association between cognitive function and BMI was observed among obese women with more than 12 years of education. In women with fewer than 12 years of education and men with more than 12 years of education, there was a trend of increased BMI groups with impaired cognitive function. However, the trend lacked statistical significance after adjustment for all covariates.

An influence of early life educational level on the neurocognitive function test has been found in previous studies. In a study conducted by Sheridan and his colleagues, it was shown that the relationship between women’s education and written SDMT score reached significance only when individuals had 13 or more years of education. Emerging evidence demonstrates that the protective effect of early life educational status is linked to cognitive function in later life. Older individuals with high educational attainment exhibit better cognitive functioning and may tolerate higher levels of brain pathology before clinical manifestations.

In the Victoria Longitudinal Study of 1023 participants to examine the effects of education on cognitive function, education was related to cognitive performance but unrelated to cognitive decline, thus supporting the hypothesis of passive cognitive reserve with aging. In our studies, obese women with more than 12 years of education had poorer neurocognitive function compared with normal-weight women with more than 12 years of education. BMI is still an important impediment in adult women’s cognitive performance.

The natural history of dynamic factors in relationship to dementia, the disease of latest life, has been difficult to understand because epidemiologic studies of adequate duration and frequency are challenging and relatively rare. BMI is a common measure of overweight and obesity and has been related to dementia, including Alzheimer disease (AD). Throughout the lifespan, BMI is dynamic and evolves in relation to physical growth, puberty and reproductive status, nutritional health and adequacy, and aging. Because BMI reflects, in a gross way, body adiposity, the evolution of BMI represents an evolutionary metabolism, and as such, the potential relationships between BMI and corresponding metabolic factors with cognition and thus, cognitive impairments and dementia, change overtime.

Obesity is an abnormal accumulation of body fat over an individual’s body. It has become a critical issue worldwide due to its association with increased risks of disease, disability, and death. Diseases such as coronary heart disease, hypertension, diabetes, stroke, and cancer are associated with obesity; some comorbidities directly induce cognitive impairment. Although these diseases have complex impacts on cognitive impairment, obesity itself may have some specific associations with cognitive function. In an animal study, obese rats were significantly and selectively impaired at performing long-interval episodic memory. Memory impairments were substantially enhanced in groups fed high-fat diets. The potential relationships between BMI and corresponding metabolic factors with cognition and thus, cognitive impairments and dementia, change overtime.

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obese women with a high educational level. Previous studies support a hypothesis of early life obesity and its relationship with poor cognitive performance. Although more research is needed to understand the mechanisms and relationship between obesity and cognition, treatments aimed at correcting possible deficits could be undertaken as a test of this hypothesis. Furthermore, studies investigating possible mediators such as inflammatory markers, insulin resistance, glucose, and lipid profiles will help us to clarify the mechanisms between obesity and cognitive deficits.

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