Observational Study

Medicine®

OPEN

Associations between body composition and cognitive function in an elderly Korean population

A cohort-based cross-sectional study

Yun Kyung Seo, MD[a], Chang Won Won, MD, PhD[b], Yunsoo Soh, MD, PhD[a,*]

Abstract

The prevalence of obesity as well as cognitive impairment increases with age. Previous studies showed that obesity is associated with an increased risk of cognitive impairment and dementia. Body composition changes occur as part of the aging process; therefore, the assessment of obesity in elderly populations should include body composition as well as body weight. This study investigated the relationship between body mass index (BMI), body composition, and cognitive function in a community-dwelling elderly Korean population.

This cohort-based cross-sectional analysis included 2386 elderly participants aged between 70 and 84 years from the Korean Frailty and Aging Cohort Study for 2016 to 2017. To investigate the relationship between body composition and cognitive function in community-dwelling individuals, BMI and body composition, including total and trunk fat mass and fat-free mass, were measured by dual-energy X-ray absorptiometry. Fat mass index (FMI), trunk fat mass index (TFMI), and fat-free mass index (FFMI) were used to represent the body composition. A short form of the Korean version of the Consortium to Establish a Registry for Alzheimer disease was used to assess cognitive function. To evaluate the relationship between variables, simple and fully adjusted multivariable analyses were performed using generalized linear regression models.

The mean ages were 76.8 years for males and 76.1 years for females. The BMI of male participants was significantly lower than that of females (23.9 ± 2.89 vs 24.7 ± 3.02 kg/m^2, $P < .001$). Among body composition parameters, the differences in FMI (6.44 ± 1.97 vs 9.29 ± 2.3 kg/m^2), TFMI (3.68 ± 1.33 vs 5.03 ± 1.43 kg/m^2), and FFMI (17.4 ± 1.64 vs 15.3 ± 1.39 kg/m^2) were statistically significant. In linear regression analyses, BMI, FMI, and TFMI showed significant positive correlations with mini-mental state examination in the Korean version of the CERAD assessment packet; wordlist memory, recall, and recognition; and frontal assessment battery only in males. The significant positive correlations persisted even after fully adjusting for age, education periods, location of residence, depression, marriage, annual income, presence of diabetes mellitus, dyslipidemia, and hypertension. However, no significant correlations in either sex were observed between FFMI and cognitive functions in the fully adjusted models.

In this study, BMI, and fat mass-related indexes including FMI and TFMI showed a positive linear correlation with cognitive functions but not FFMI. Moreover, the findings were significant only in men. Besides the difference between sexes, the results of this study showed a more apparent correlation in fat mass than in fat-free mass that comprises body weight.

Abbreviations: AD = Alzheimer disease, BMI = body mass index, CERAD-K = Korean version of the Consortium to Establish a Registry for Alzheimer Disease, FAB = frontal assessment battery, FFMI = fat-free mass index, FMI = fat mass index, KFACS = Korean Frailty and Aging Cohort Study, MMSE-KC = mini-mental state examination in the Korean version of the CERAD assessment packet, TFMI = trunk fat mass index, TMT = trail making test.

Keywords: aged, body composition, body mass index, cognition, obesity

Editor: Manal Kamel Youssef.

This research was supported by a grant from the Korea Health Technology R&D Project through the Korean Health Industry Development Institute, funded by the Ministry of Health and Welfare, Republic of Korea (grant number: HI15C3153).

This manuscript acquired the editorial certificate by "Editage by cactus (https://online.editage.co.kr/)."

The authors have no conflicts of interest to disclose.

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

[a] Department of Physical Medicine & Rehabilitation Medicine, [b] Department of Family Medicine, Kyung Hee University Medical Center, Seoul, Republic of Korea.

[*] Correspondence: Yunsoo Soh, Department of Physical Medicine & Rehabilitation Medicine, Kyung Hee University Medical Center, 23 Kyungheedae-ro, Dongdaemoon-gu, Seoul 02447, Republic of Korea (e-mail: soyuns@gmail.com).

How to cite this article: Seo YK, Won CW, Soh Y. Associations between body composition and cognitive function in an elderly Korean population: a cohort-based cross-sectional study. Medicine 2021;100:9(e25027).

Received: 4 August 2020 / Received in final form: 12 December 2020 / Accepted: 8 February 2021

http://dx.doi.org/10.1097/MD.0000000000025027

1. Introduction

Due to prolonged life expectancy, the elderly population is increasing. In 2017, the proportion of the elderly aged 65 years and over in Korea was 14%, making it an aging society; by 2026, this proportion is expected to increase to 20%, making it an extremely aging society.[1] With an increased elderly population, the prevalence of cognitive impairment also increases[2]; degenerative changes in the brain are part of the aging process that decreases memory and other global cognitive functions in the elderly.[3] This cognitive impairment can lead to dementia and is one of the most critical diseases among elderly health challenges.[4] Therefore, identifying the risk factors for cognitive impairment is necessary in the context of public health.

In the elderly, not only cognitive impairment but also the prevalence of obesity increases.[5] Obesity is a well-known risk factor for cardiovascular diseases, type 2 diabetes, and some cancers and has also been associated as a risk factor for cognitive decline, including dementia and AD.[6] Several pathological changes associated with obesity, such as insulin resistance, chronic inflammation, and mitochondrial dysfunction, are associated with the pathological processes of dementia.[7] As the easiest parameter to measure obesity, body mass index (BMI) is widely used. However, in the aging process, muscle mass decreases and fat mass increases, resulting in body composition changes; thus, BMI is not accurate for evaluating obesity in the elderly population.[8] Increased body fat due to obesity could be a risk factor for metabolic syndrome, including hypertension, diabetes, hypercholesterolemia, which is the major cause of cerebrovascular disease due to intracranial artery-wall thickening, stiffness, and endothelial dysfunction. Furthermore, obesity is also highly associated with vascular dementia.[6,9–11] Recently, interest in obesity as a correctable risk factor for cognitive impairment or dementia has been increasing; however, the association between body fat and incident dementia remains unclear and the results are conflicting depending on the age of study population. Previous studies showed that obesity in midlife is associated with an increased risk of dementia in the elderly, especially Alzheimer disease (AD). In a prospective study over 21 years, Kivipelto et al reported that participants with a BMI over $>30\,kg/m^2$ had a high risk of dementia and AD even after adjusting for sociodemographic variables.[12] In an magnetic resonance imaging study to identify the changes in midlife patients with mild cognitive impairment and dementia, those with higher BMI showed increased frontal, temporal, parietal, and occipital lobe problems with brain volume as well as atrophy findings.[13] In contrast, in the elderly population over 65 years of age, higher BMI in late life was associated with a reduced risk of dementia.[14,15]

Characteristic changes in body composition differ between men and women as aging progresses.[16] According to a 10-year prospective study in the elderly with an initial age of 60.7 years, the changes in body composition included a 1.2-kg body weight increase in women, mostly body fat and a 1.2-kg gain in body fat with no change in body weight men.[14] The changes in body composition due to aging are characterized by increased fat in the abdominal cavity, muscle, and liver without any change in body weight.[17] Also, as the height decreases and the body composition changes with aging, questions are raised regarding whether BMI should be used as a diagnostic standard for obesity in the elderly.[18] A previous study demonstrated that BMI was not adequate for measuring underlying changes in body fat mass and fat-free mass during aging.[19] BMI is useful for evaluating the body weights of individuals of different heights. Similarly, the fat mass index (FMI), trunk fat mass index (TFMI), and fat-free mass index (FFMI) are useful parameters to evaluate body composition by effectively eliminating differences in height.[20,21] Moreover, there are differences in body composition as a sex hormonal effect between sex, for example, females generally have a higher percentage of total body fat and less lean (muscle and bone) mass than males.[22] Therefore, the assessment of obesity in elderly populations also requires evaluations of body composition depend on sex.

The present cross-sectional study investigated the relationship between BMI, body composition including FMI, TFMI, FFMI, and cognitive impairment in community-dwelling elderly Koreans using baseline data from the Korean Frailty and Aging Cohort Study (KFACS). We hypothesized that there was a correlation between BMI, FMI, TFMI, FFMI, and cognition. Because of the body composition difference between sex, we evaluated these parameters based on sex.

2. Methods

2.1. Data and study population

We performed cohort-based cross-sectional study 2016 to 2017 data from the KFACS to investigate the relationship between body composition and cognitive function in community-dwelling individuals aged between 70 and 84 years. The goal of the KFACS is to identify the risks and preventive measures for side effects in frail community dwellers.[23] Among the 3014 participants, 628 were excluded for dementia, severe cognitive impairment, Parkinson disease, history of cerebrovascular disease, inability to complete the cognitive tests, and without complete dual-energy X-ray absorptiometry (DXA) data. A total of 2386 participants (1131 males and 1255 females) were recruited from 10 centers including 8 medical centers and 2 public health centers across Korea. Trained researchers interviewed the participants individually. The collected data were social-demographic variables including age, education period (less than 6, 7–12, and over 13 years), marriage status, and monthly income (less 1, 1 to 3, and over than 3 million Korean won; 1 million won is approximately 900 US dollars), location of residence, and items related to lifestyles such as drinking habits (drinking alcohol at least once a week) and smoking (smoking more than 1 cigarette per week). Chronic comorbidities such as hypertension, diabetes, hyperlipidemia, osteoarthritis, and depression were also evaluated. During their visit, the participants' body weight and height were measured, and their BMI calculated as body weight in kilograms divided by height squared in meters (total weight [kg]/height $[m]^2$). The KFACS protocol was approved by the Institutional Review Board of the Clinical Research Ethics Committee of Kyung Hee University Medical Center and all participants provided written informed consent (IRB number: 2020-10-012).

2.2. Cognitive function

Cognitive function was evaluated using the Korean version of the Consortium to Establish a Registry for Alzheimer disease (CERAD). The CERAD was originally an English-American version of the clinical and comprehensive neuropsychological assessment batteries for AD. It was initially developed to diagnose AD but was later extended for the diagnosis of other dementia diseases such as vascular dementia, Lewy body dementia, Parkinson disease, and frontotemporal dementia. The CERAD includes 8 tests: verbal fluency, Boston naming, mini-mental state exam (MMSE), word list learning, constructional praxis, word list recall, word list recognition, and constructional praxis recall. This study used the Korean version of the CERAD.[24,25] To reduce time and cost, we applied a short form of the CERAD-K; among the eight tests to evaluate global cognitive function, memory, processing performance, executive function, we used the MMSE in the Korean version of the CERAD assessment packet (MMSE-KC), the Wordlist memory/recall/recognition, digit span (forward, backward), trail making test-A (TMT-A), and frontal assessment battery.

The MMSE-KC, widely used as a screening test for global cognitive function, comprises 5 domains: direction (10 points), memory (6 points), attention (5 points), language ability (6 points), and comprehension and judgment (3 points). The total score is 30 points, with higher scores reflecting better cognitive status.[24] The word list memory test is an immediate memory test for new information. Participants read 10 familiar words and instantly recall as many words as possible in 90 seconds. The total score is 30 points, with higher scores reflecting better immediate memory. The word list recall test evaluates short-term memory. After 15 minutes, participants recall 10 words from the word list memory test in 90 seconds. The total score is 10 points.[26] The Digit Span test is widely used to measure short-term memory, working memory, and attention. Participants hear numbers and then recall the number sequence forward (range 3–9) and backward (range 2–8).[27] The TMT-A is a neuropsychological test that evaluates visual attention, scanning, speed of processing, mental flexibility, and executive functions. Participants draw lines to connect the numbered circles in ascending order from 1 to 25. The maximum time given to complete the test is 300 seconds, with a longer time indicating poor test performance.[26] The FAB is used to assess executive functions such as planning, working memory, mental flexibility, and inhibition. The FAB comprises 6 tasks: similarities (conceptualization), lexical verbal fluency (mental flexibility), motor series (programming), conflicting instructions (sensitivity to interference), Go–Nogo (inhibitory control), and prehension behavior (environmental autonomy). The total score is 18, with higher scores indicating better frontal lobe function.[28]

2.3. Body composition

Body composition including total and trunk fat mass and fat-free mass were measured by DXA (GE Medical Systems Lunar, Madison, WI). FMI and TFMI were used to represent total fat mass and trunk fat mass according to height, total fat, and trunk fat mass in kilograms divided by height meter squared, respectively (fat mass [kg]/height [m]^2).[20,29] FFMI was defined as the total weight minus total fat mass in kilograms divided by height meter squared (fat-free mass [kg]/height [m]^2).[21]

2.4. Statistical analysis

The demographic characteristics were analyzed based on the sex of the participants using Chi-square test and *t*-test for categorical and continuous variables, respectively. The results are presented as means ± standard deviation or numbers (%) according to the characteristics of the variables. Simple and multivariable analyses were performed using generalized linear regression models. These examined the associations between BMI, each body composition as an independent variable, and each cognitive function test as the dependent variable. Multiple linear regression analyses were fully adjusted for multiple correlations between cognitive function and other potential confounders. Potential confounder variables and risk factors for cognitive decline and dementia such as age, education periods, location of residence, depression, marriage, annual income, presence of diabetes mellitus, dyslipidemia, and hypertension were fully adjusted in multiple regression analysis.[30] Body composition parameters showed multicollinearity, with variance inflation factor value over 10. Since there may be mutual interaction among the body composition parameters, the same analyses were repeated using each BMI, FMI, TFMI, and FFMI as independent covariate variables. Coefficients were indicated in 95% confidence intervals.

Since the body composition differs between men and women and significant differences were observed in the results of cognitive function assessments between the 2 groups, the statistics divided into sex groups.

The collected data were analyzed using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY). *P*-values $<.05$ were considered statistically significant.

3. Results

The baseline characteristics of the participants based on sex are presented in Table 1. The 2386 community-dwelling participants recruited in the current study included 1131 male participants and 1255 female participants. The mean age in the men (76.8 years) was significantly higher than that in women (76.1 years). The BMI of the male participants was significantly lower than that of the females (mean ± standard deviation, 23.9 ± 2.89 vs 24.7 ± 3.02 kg/m^2, $P<.001$). Among body composition parameters in male and female participants, the differences in FMI (6.44 ± 1.97 vs 9.29 ± 2.3 kg/m^2), TFM (I3.68 ± 1.33 vs 5.03 ± 1.43 kg/m^2), and FFMI (17.4 ± 1.64 vs 15.3 ± 1.39 kg/m^2) were statistically significant. The baseline social characteristics differed significantly between the sexes in education years ($P<.001$), marriage ($P<.001$), income per month ($P<.001$), location of residence ($P<.001$), and smoking habit ($P<.001$). The prevalence of comorbidities between sexes differed for hypertension ($P=.013$), dyslipidemia ($P<.001$), depression ($P=.01$), and osteoarthritis ($P<.001$). Due to the demographic difference between sexes, we analyzed the data according to sex.

Table 2 shows the baseline cognitive function test results by sex. The MMSE-KC was significantly higher in males (26.28 ± 2.88) than that in females (25.29 ± 3.33) ($P<.001$). The results of the TMT-A (64.09 ± 41.45 vs 95.056 ± 77.48, $P<.001$), Digit span. (11.88 ± 3.52 vs 10.14 ± 3.69, $P<.001$), and FAB (14.26 ± 2.68 vs 13.12 ± 3.0, $P<.001$) were also significantly better in males, while female participants showed better Wordlist memory results (16.52 ± 4.09 vs 17.26 ± 4.3, $P<.001$).

The results of simple and multiple linear regression analyses of cognitive function scores according to BMI are shown in Table 3. In simple linear regression, significant positive correlations were observed for the MMSE-KC, wordlist memory, recall, recognition, TMT-A, and FAB in males. Even after fully adjusting for age, education periods, location of residence, depression, marriage, annual income, presence of diabetes mellitus, dyslipidemia, and hypertension, MMSE-KC ($P=.016$), wordlist memory ($P=.002$), recall ($P<.001$), recognition ($P=.003$), and FAB ($P=.014$), the significant positive correlations persisted.

Table 1

Baseline demographic characteristics of KFACS participants by sex.

Characteristic	Male (n=1131)	Female (n=1255)	Total (n=2386)	*P*
Age, mean (yr, SD)	76.87 (3.91)	76.12 (3.84)	76.47 (3.8)	**<.001**
BMI (kg/m^2, SD)	23.9 (2.89)	24.7 (3.02)	24.40 (2.99)	**<.001***
Fat mass (kg, SD)	17.54 (5.5)	21.48 (5.56)	19.61 (5.87)	**<.001***
Trunk fat mass (kg, SD)	10.01 (3.64)	11.62 (3.37)	10.86 (3.59)	**<.001***
FMI (kg/m^2, SD)	6.44 (1.97)	9.29 (2.30)	7.94 (2.58)	**<.001***
TFMI (kg/m^2, SD)	3.68 (1.33)	5.03 (1.43)	4.39 (1.54)	**<.001***
FFMI (kg/m^2, SD)	17.4 (1.64)	15.37 (1.39)	16.33 (1.82)	**<.001***
PBF (%. SD)	26.56 (6.04)	37.22 (5.86)	32.1 (7.9)	**<.001***
SBP (mm Hg, SD)	132.25 (16.55)	133.34 (17.13)	132.8 (16.8)	.113
DBP (mm Hg, SD)	78.93 (9.79)	78.19 (9.89)	78.54 (9.85)	.65
Education years (n, %)				**<.001***
Less than 6	294 (26.0)	718 (57.2)	1,012 (42.4)	
7–12	484 (42.8)	413 (32.9)	897 (37.6)	
Over than 13	353 (31.2)	124 (9.9)	477 (20.0)	
Marriage (n, %)				**<.001***
Married	1038 (91.8)	814 (64.9)	534 (22.4)	
Bereavement, separation, divorced, single	93 (8.2)	441 (35.1)	1,852 (77.6)	
Income per month (n, %)				**<.001***
More than 3 million won	218 (19.3)	230 (18.3)	448 (18.8)	
1–3 million won	564 (49.9)	460 (36.7)	1,024 (42.9)	
Less than 1 million won	349 (30.9)	565 (45.0)	914 (38.3)	
Residency (n, %)				**<.001***
Urban	884 (78.2)	1059 (84.4)	1,943 (81.4)	
Rural	247 (21.8)	196 (15.6)	443 (18.6)	
Current smoker (n, %)	741 (65.5)	23 (1.8)	764 (32.0)	**<.001***
Alcohol use (n, %)	674 (59.6)	730 (58.2)	1404 (58.8)	.480
HTN (n, %)	607 (53.7)	744 (59.3)	1,351 (56.6)	**.013**
Dyslipidemia (n, %)	278 (24.6)	510 (40.6)	788 (33.0)	**<.001***
DM (n, %)	275 (24.3)	255 (20.3)	530 (22.2)	.062
Depression (n, %)	21 (1.9)	44 (3.5)	65 (2.7)	.01
OA (n, %)	124 (11)	404 (32.2)	528 (22.1)	**<.001***
WBC ($10^3/\mu L$, SD)	5.89 (1.55)	5.77 (1.63)	5.83 (1.5)	**.058**
Hb (gm/dL, SD)	14.12 (1.38)	12.86 (1.15)	13.4 (1.4)	**<.001**

BMI=body mass index, DBP=diastolic blood pressure, DM=diabetes mellitus, FFMI=fat-free mass index, FMI=fat mass index, Hb=hemoglobin, HTN=hypertension, KFACS=Korean Frailty, and Aging Cohort Study, OA=osteoarthritis, PBF=percent of body fat, SBP=systolic blood pressure, TFMI=trunk fat mass index, WBC=white blood cell.
1 million won = approximately 900 USD.
* $P<.05$.

However, the positive correlation in TMT-A was attenuated in the adjusted model ($P=.053$). The cognitive function scores according to BMI showed no significant correlations in the female participants (Table 3).

Table 4 shows the results of simple and multiple linear regression analyses of cognitive function scores according to FMI based on sex. Similar to the results in BMI, the unadjusted models showed significant positive correlations for MMSE-KC, wordlist memory, recall, recognition, TMT-A, and FAB in males. The fully adjusted models also showed persisting significant positive correlations for MMSE-KC ($P=.016$), wordlist memory ($P<.001$), recall ($P<.001$), recognition ($P=.003$), TMT-A

Table 2

Baseline cognitive function in KFACS participants by sex.

Cognitive function	Male (n=1131)	Female (n=1255)	Total (n=2386)	*P*
MMSE-KC (SD)	26.28 (2.88)	25.29 (3.33)	25.76 (3.1)	**.042***
Wordlist: memory (SD)	16.52 (4.09)	17.26 (4.30)	16.91 (4.2)	**<.001***
Wordlist: recall (SD)	5.55 (2.04)	5.60 (2.12)	5.57 (2.0)	.612
Wordlist: recognition (SD)	8.61 (1.83)	8.60 (1.84)	8.60 (1.8)	.894
TMT-A (SD)	64.09 (41.45)	95.05 (77.48)	80.37 (64.8)	**<.001***
Digit span (SD)	11.88 (3.52)	10.14 (3.69)	10.97 (3.7)	**<.001***
FAB (SD)	14.29 (2.68)	13.12 (3.00)	13.67 (2.9)	**<.001***

TMT-A showed time second, the longer number indicates poor test performance.
FAB=frontal assessment battery, KFACS=Korean Frailty and Aging Cohort Study, MMSE-KC=MMSE in the Korean version of the Consortium to Establish a Registry for Alzheimer disease (CERAD) assessment packet, TMT=trail making test.
* $P<.05$.

Table 3

Simple and multiple linear regression analyses between cognitive functions and BMI based on sex.

	Male			Female		
	Coefficient (SE)	95% CI	*P*	Coefficient (SE)	95% CI	*P*
MMSE KC						
Unadjusted	+0.096 (0.026)	0.038–0.154	.001*	+0.011 (0.031)	−0.05 to 0.073	.713
Fully adjusted	+0.07 (0.029)	0.013–0.126	.016*	+0.012 (0.028)	−0.044 to 0.067	.684
Wordlist: memory						
Unadjusted	+0.164 (0.042)	0.082–0.246	.000*	+0.036 (0.04)	−0.043 to 0.115	.376
Fully adjusted	+0.123 (0.04)	0.044–0.202	.002*	+0.039 (0.038)	−0.035 to 0.113	.300
Wordlist: recall						
Unadjusted	+0.092 (0.21)	0.052–0.133	.000*	−0.003 (0.02)	−0.042 to 0.036	.888
Fully adjusted	+0.082 (0.02)	0.041–0.122	.000*	+0.005 (0.019)	−0.033 to 0.042	.798
Wordlist: recognition						
Unadjusted	+0.062 (0.019)	0.025–0.099	.001*	−0.003 (0.017)	−0.037 to 0.031	.876
Fully adjusted	+0.058 (0.019)	0.02–0.095	.003*	+0.005 (0.017)	−0.029 to 0.039	.792
TMT-A						
Unadjusted	−0.999 (0.425)	−1.832 to −0.167	.019*	−0.588 (0.724)	−2.008 to 0.831	.416
Fully adjusted	−0.785 (0.404)	−1.578 to 0.009	.053	−0.514 (0.646)	−1.782 to 0.753	.426
Digit span						
Unadjusted	−0.021 (0.036)	−0.92 to 0.05	.569	0.021 (0.034)	−0.047 to 0.089	.540
Fully adjusted	−0.038 (0.035)	−0.107 to 0.031	.285	0.016 (0.031)	−0.045 to 0.077	.603
FAB						
Unadjusted	+0.075 (0.028)	0.021–0.129	.007*	0.018 (0.019)	−0.037 to 0.074	.511
Fully adjusted	+0.064 (0.026)	0.013–0.114	.014*	0.025 (0.025)	−0.024 to 0.075	.315

Unless otherwise indicated, data are reported as relative risk (95% confidence interval). Fully adjusted analyses were adjusted for age, education, alcohol use, current smoker, depression, marriage, annual income, residence location, presence of osteoarthritis diabetes mellitus, dyslipidemia, and hypertension.

TMT-A showed time second, the longer number indicates poor test performance.

BMI = body mass index, CI = confidence interval, FAB = frontal assessment battery, MMSE-KC = MMSE in the Korean version of the Consortium to Establish a Registry for Alzheimer disease (CERAD) assessment packet, TMT = trail making test.

* $P < .05$.

Table 4

Simple and multiple linear regression analyses between cognitive functions and FMI based on sex.

	Male			Female		
	Coefficient (SE)	95% CI	*P*	Coefficient (SE)	95% CI	*P*
MMSE KC						
Unadjusted	+0.143 (0.043)	0.058–0.228	***.001****	+0.119 (0.041)	0.039–0.199	***.004****
Fully adjusted	+0.105 (0.043)	0.020–0.189	***.016****	+0.041 (0.038)	−0.033 to 0.115	.277
Wordlist: memory						
Unadjusted	+0.258 (0.061)	0.137–0.378	***.000****	+0.122 (0.053)	0.019–0.226	***.021****
Fully adjusted	+0.238 (0.06)	0.12–0.355	<***.001****	+0.033 (0.05)	−0.065 to 0.131	.508
Wordlist: recall						
Unadjusted	+0.116 (0.031)	0.056–0.176	***.000****	+0.026 (0.026)	−0.025 to 0.078	.312
Fully adjusted	+0.122 (0.03)	0.062–0.182	<***.001****	−0.002 (0.025)	−0.052 to 0.047	.922
Wordlist: recognition						
Unadjusted	+0.08 (0.028)	0.026–0.134	***.004****	+0.017 (0.023)	−0.028 to 0.061	.464
Fully adjusted	+0.085 (0.029)	0.029–0.141	***.003****	+0.001 (0.023)	−0.045 to 0.046	.981
TMT-A						
Unadjusted	−1.581 (0.624)	−2.805 to −0.357	***.011****	−4.33 (0.943)	−6.179 to −2.48	***.000****
Fully adjusted	−1.277 (0.603)	−2.461 to −0.093	***.034****	−2.152 (0.855)	−3.83 to −0.474	***.012****
Digit span						
Unadjusted	−0.014 (0.053)	−0.118 to 0.09	.794	+0.101 (0.045)	0.012–0.19	.026
Fully adjusted	−0.040 (0.053)	−0.143 to −0.063	.447	−0.012 (0.041)	−0.092 to 0.069	.780
FAB						
Unadjusted	+0.141 (0.04)	0.061–0.22	***.001****	+0.152 (0.037)	0.05–0.224	***.000****
Fully adjusted	+0.109 (0.038)	0.034–0.185	***.005****	+0.079 (0.034)	0.014–0.145	***.018****

Unless otherwise indicated, data are reported as relative risk (95% confidence interval). Fully adjusted analyses have been adjusted for age, education, alcohol use, current smoker, depression, marriage, annual income, residence location, presence of osteoarthritis diabetes mellitus, dyslipidemia, and hypertension.

CI = confidence interval, FAB = frontal assessment battery, FMI = fat mass index, MMSE-KC = MMSE in the Korean version of the CERAD assessment packet, TMT = trail making test.

* $P < .05$.

Table 5

Simple and multiple linear regression analyses between cognitive functions and TFMI based on sex.

	Male			Female		
	Coefficient (SE)	95% CI	P	Coefficient (SE)	95% CI	P
MMSE KC						
Unadjusted	+0.184 (0.064)	0.059–0.31	***.004****	+0.108 (0.065)	−0.02 to 0.236	.099
Fully adjusted	+0.130 (0.063)	0.006–0.254	***.040****	+0.041 (0.060)	−0.076 to 0.158	.495
Wordlist: memory						
Unadjusted	+0.339 (0.091)	0.161–0.517	***.000****	+0.099 (0.085)	−0.067 to 0.265	.243
Fully adjusted	+0.310 (0.087)	0.138–0.481	***<.001****	+0.026 (0.079)	−0.130 to 0.181	.747
Wordlist: recall						
Unadjusted	+0.17 (0.045)	0.081–0.259	***.000****	−0.004 (0.042)	−0.086 to 0.077	.914
Fully adjusted	+0.177 (0.045)	0.089–0.264	***<.001****	−0.023 (0.040)	−0.102 to 0.056	.565
Wordlist: recognition						
Unadjusted	+0.100 (0.041)	0.021–0.018	***.014****	+0.015 (0.036)	−0.056 to 0.086	.677
Fully adjusted	+0.100 (0.042)	0.019–0.182	***.016****	+0.010 (0.036)	−0.062 to 0.081	.790
TMT-A						
Unadjusted	−2.077 (0.921)	−3.883 to −0.271	***.024****	−5.654 (1.514)	−8.624 to −2.685	***.000****
Fully adjusted	−1.726 (0.882)	−3.456 to 0.004	.051	−3.674 (1.354)	−6.331 to −1.017	***.007****
Digit span						
Unadjusted	−0.001 (0.078)	−0.155 to 0.153	.989	+0.098 (0.072)	−0.044 to 0.241	.175
Fully adjusted	−0.025 (0.077)	0.175 to −0.126	.747	−0.008 (0.065)	−0.137 to 0.120	.898
FAB						
Unadjusted	+0.209 (0.06)	0.093–0.326	***.000****	+0.178 (0.059)	0.063–0.294	***.003****
Fully adjusted	+0.179 (0.056)	0.069–0.289	***.001****	+0.118 (0.053)	0.014–0.222	***.026****

Unless otherwise indicated, data were reported as relative risk (95% confidence interval). Fully adjusted analyses were adjusted for age, education, alcohol use, current smoker, depression, marriage, annual income, residence location, presence of osteoarthritis diabetes mellitus, dyslipidemia, and hypertension.

CI = confidence interval, FAB = frontal assessment battery, MMSE-KC = MMSE in the Korean version of the CERAD assessment packet, TFMI = trunk fat mass index, TMT = trail making test.

* $P < .05$.

($P = .034$), and FAB ($P = .005$). The female participants showed significant positive correlations for TMT-A ($P = .012$) and FAB ($P = .018$) in the fully adjusted models.

The results of the analysis of TFMI and cognitive functions based on sex are shown in Table 5. In males, both unadjusted and fully adjusted models showed that TFMI was significantly correlated with MMSE-KC ($P = .04$), wordlist memory ($P < .001$), recall ($P < .001$), recognition ($P = .016$), and FAB ($P = .001$). Like the correlations in FMI, the female participants showed significant positive correlations for TMT-A ($P = .007$) and FAB ($P = .026$) in fully adjusted models.

Table 6 shows the results of simple and multiple linear model analyses of cognitive function scores according to FFMI based on sex. Unlike fat-related mass indexes such as FMI and TFMI, multiple linear regression correlations in Wordlist recall and recognition attenuated the positive correlations in the male participants and MMSE-KC, TMT-A, digit span, and FAB in the female participants. No significant correlations were observed between FFMI and cognitive functions in the fully adjusted models.

4. Discussion

The present study assessed the cognitive functions and body composition by measuring total fat mass and trunk fat mass using DXA. Using DXA, we evaluated body composition over two thousand participants aged 70 to 84. The correlations between cognitive functions and body composition showed positive in some parameters. These results also showed a difference depending on sex and body composition parameters. In previous studies evaluating BMI and cognitive functions in old age, the relationship was unclear and mixed results were reported.[31–33] A meta-analysis of epidemiological studies reported that obesity with high BMI in old age was associated with an increased risk of dementia, especially AD.[34] In an 18-year prospective study of 392 Swedish participants aged 70 to 88 years, Gustafson et al reported that 93 participants were diagnosed with AD during the follow-up period and a higher BMI at 70 years was associated with an increased risk of AD, especially in older women.[35] While the study was meaningful as a prospective study with an extended follow-up period, other studies showed that high BMI lowered the risk of dementia or cognitive decline.

Among studies reporting the association between higher BMI and lower risk of cognitive decline, Dahl et al reported that participants with higher BMI scores showed less dementia risk after adjusting for age, sex, education, diabetes, hypertension, dyslipidemia, cardiovascular disease, and smoking during an 8-year follow-up of 605 participants aged between 65 and 92 years.[32] Luchsinger et al reported that higher BMI decreased the risk of dementia in subjects over 76 years of age.[33] Large cohort studies in Korea have reported that obese participants with a BMI of 25 kg/m^2 or more showed less cognitive decline than those with normal weight. This relationship also persisted after adjusting for confounding factors such as socioeconomic factors or comorbidity.[36]

With the aging, body composition changes as muscle mass decreases, and fat mass increases, BMI is not accurate for evaluating obesity in the elderly population.[8] The present study evaluated body composition, including fat mass, as well as BMI reflecting total body weight. A population-based study conducted in Italy assessed body fat mass and cognitive functions including MMSE, reporting that subjects with higher BMI (over 29.4 kg/m^2) and particularly higher body fat mass (BFM) (over 34.6 kg) showed better cognitive function.[37] However, in that study, BFM was calculated from skinfold thickness, according to Pineau

Table 6

Simple and multiple linear regression analyses between cognitive functions and FFMI based on sex.

	Male			Female		
	Coefficient (SE)	95% CI	*P*	Coefficient (SE)	95% CI	*P*
MMSE KC						
Unadjusted	+0.077 (0.052)	−0.025 to 0.179	.141	−0.21 (0.067)	−0.342 to −0.078	***.002****
Fully adjusted	+0.052 (0.051)	−0.048 to 0.152	.305	+0.013 (0.062)	−0.109 to 0.136	.830
Wordlist: memory						
Unadjusted	+0.119 (0.074)	−0.027 to 0.264	.109	−0.155 (0.087)	−0.326 to 0.016	.075
Fully adjusted	+0.028 (0.071)	−0.111 to 0.167	.696	+0.113 (0.083)	−0.050 to 0.275	.175
Wordlist: recall						
Unadjusted	+0.108 (0.037)	0.036–0.18	***.003****	−0.087 (0.043)	−0.172 to −0.003	.043
Fully adjusted	+0.070 (0.036)	0.000–0.141	.052	+0.030 (0.042)	−0.053 to 0.112	.481
Wordlist: recognition						
Unadjusted	+0.078 (0.033)	0.013–0.142	***.019****	−0.045 (0.037)	−0.118 to 0.029	.234
Fully adjusted	+0.060 (0.034)	−0.006 to 0.126	.076	+0.032 (0.038)	−0.043 to 0.0106	.402
TMT-A						
Unadjusted	−0.673 (0.75)	−2.144 to 0.798	.369	+8.424 (1.551)	5.382–11.466	***.000****
Fully adjusted	−0.479 (0.712)	−1.876 to 0.917	.501	+2.678 (1.417)	−0.103 to 5.458	.059
Digit span						
Unadjusted	−0.029 (0.064)	−0.154 to 0.096	.653	−0.205 (0.075)	−0.351 to −0.059	***.006****
Fully adjusted	−0.046 (0.062)	−0.167 to 0.076	.462	+0.082 (0.068)	−0.052 to 0.216	.228
FAB						
Unadjusted	+0.007 (0.049)	−0.088 to 0.103	.881	−0.321 (0.06)	−0.439 to −0.203	***.000****
Fully adjusted	+0.022 (0.045)	−0.067 to 0.111	.630	−0.088 (0.055)	−0.197 to 0.021	.114

Unless otherwise indicated, data are reported as relative risk (95% confidence interval). Fully adjusted analyses were adjusted for age, education, alcohol use, current smoker, depression, marriage, annual income, residence location, presence of osteoarthritis diabetes mellitus, dyslipidemia, and hypertension.

CI = confidence interval, FAB = frontal assessment battery, FFMI = fat-free mass index, MMSE-KC = MMSE in the Korean version of the Consortium to Establish a Registry for Alzheimer disease (CERAD) assessment packet, TMT = trail making test.

* $P < .05$.

and Frey, which may be less accurate than DXA.[38] Noh et al evaluated the correlation between MMSE and body composition in 320 Koreans aged 65 years and older, reporting that, in females, the highest tertile fat mass group had a lower risk of cognitive impairment compared to that in the lowest tertile groups.[39] However, no correlation between cognitive impairment and fat mass was observed in men. These findings were not consistent with those of the present study, possibly due to differences in statistical or evaluation methods. The previous study calculated the relative risk of cognitive impairment, which was different from our linear regression analysis, and the sample size was relatively small.[39] Another population study including 5607 postmenopausal women with a mean age of 63.8 years evaluated the relationship between total and trunk fat mass, and cognitive functions by DXA. In the multivariate logistic model, the risk of cognitive impairment was lower in women in the higher quartile of the fat mass group compared to those in the first quartile (second quartile, 18%; third quartile, 32%; fourth quartile, 48%).[40] That study also measured estradiol level, which was positively correlated with fat mass, suggesting the possible protective effects of increased fat mass and estradiol on cognitive impairment.

In the present study, only males showed significant positive correlations between cognitive function and BMI, FMI, and TFMI. Since there was also no association with FFMI, this correlation could explain these results due to fat mass. We propose the following hypothesis to explain the sex differences and fat mass correlations. The relationship between fat mass and cognitive function can be explained by increased aromatase activity due to increased fat mass. The level of estradiol, the major biologically active formula of estrogen, is increased in older men due to increased aromatase activity and an age-related testosterone level decrease, which plays an important role in the regulation of gonadotropin feedback, bone maturation, lipid metabolism, regulation of bone resorption, and even brain functions.[41] The aromatase activity increases with age and obesity, mainly in fat and muscle tissue, although its increase in other tissues including those in the brain, liver, reproductive organs has also been reported.[42] Previous studies showed positive correlations between endogenous estrogen and testosterone levels, and cognition in older men. Older men with high serum estradiol levels performed better performance in working memory,[43] visual memory,[44] verbal memory,[45] spatial scan,[46] and global cognitive function.[47] Obesity and cognitive function based on sex have been studied before, with other studies also reporting differences between sexes. Previous 2 years of community-dwelling elderly study in Korea, when obese in the baseline, males showed a positive change in cognitive function when increased obesity over time. In contrast, increased obesity has also been reported to cause a cognitive decline in women with normal weight at baseline.[48] These results suggest that the "obesity paradox" hypothesis in the elderly regarding cognitive function may only apply to men. The results of this study are consistent with those of our study. Besides, in women, changes in estrogen hormones have not shown to affect cognitive function. In a large randomized controlled clinical trial of 4381 community-dwelling women aged 65 years and older who received postmenopausal hormone treatment, estrogen plus progestin did not show correlation with cognitive function when compared to that with placebo.[49] This result indicates that obesity and estradiol have different effects on cognitive function among elderly men and women, which supports our hypothesis.

Unfortunately, our study does not include the levels of estradiol and testosterone; therefore, further studies are needed.

This study measured not only MMSE but also memory, recall, recognition, performance speed, and executive functions to evaluate the overall cognitive function, with meaningful results obtained in various domains. To our knowledge, this study is the first to evaluate memory, attention, and executive functions as well as MMSE. Kuo et al studied the correlation between BMI and global cognition, memory, reasoning, and speed of processing in elderly aged over 65 years, reporting that overweight participants showed better reasoning and visuospatial speed of processing results than those of normal-weight participants.[50] In multiple regression analyses after adjusting for confounders, Tikhonoff et al reported that higher body fat mass was directly associated with better performance in clock drawing test and TMT-A, representing executive and selective functions.[37] The results of these studies are consistent with our findings. However, other studies reported negative associations between obesity and measures of memory and executive functions, which were attributed to brain pathologies caused by increased blood pressure facilitated by fat tissue.[51] Further study is necessary to clarify the association between body fat mass and memory, executive function, and attention function association.

This study has several limitations. First, while this study is cross-sectional, the results of the analysis of this large cohort with over 1000 participants of each sex are still meaningful. Furthermore, previous studies measured fat mass by skinfold thickness and body impedance, which are less accurate than our DXA results. Further prospective or randomized control studies are warranted to strengthen our findings. Second, previous studies reported a significant correlation between fat mass and estradiol in both sexes; however, we did not measure estradiol levels.[52–54] This factor may link the correlation between fat mass and cognitive function; therefore, further research needs to study biochemical markers including estradiol and testosterone levels. Third, this study did not distinguish between visceral and subcutaneous fats. These 2 fats secrete different adipocytokines, such as adiponectin and leptin, which secreted from more in subcutaneous than in visceral adipose tissue, which may affect cognitive function.[55,56] Differences in cognitive function according to these fats warrant further study. Fourth, this study did not evaluate the nutrition status including diet and polypharmacy; both of these factors could affect cognition.[57,58] In other studies, consumption of a high fat diet induces hippocampal and hypothalamic neuronal apoptosis and a reduction in hippocampal weight. So, dietary could affect both cognition and body composition.[59,60] Fifth, there is some evidence that visceral fat related to cognition including executive function.[61,62] Further studies will need to study these correlations. Despite several limitations, our study is still meaningful to assess executive functions, memory, attention, processing speed, mental flexibility, and body composition simultaneously in 1 large cohort population.

5. Conclusions

This study investigated the association between BMI, body composition, and cognitive functions in a community-dwelling elderly population over 70 years of age. Due to the difference in body composition between the sexes, our study analyzed the 2 groups separately and obtained meaningful results. To our knowledge, this is the first large-scale cohort study in Asia including over 1000 participants of each sex. This study measured not only BMI but also fat mass by DXA to study the correlations between body composition based on FMI, TFMI, and FFMI and various cognitive functions. These results were more correlated with cognitive function in males than in females and fat mass was more correlated with cognitive function than fat-free mass constituting body weight. Additional studies are needed to clarify the differences between sexes and hormonal effects due to fat mass.

Author contributions

Conceptualization: Yun kyung Seo, Chang Won Won, Yunsoo Soh.
Data curation: Yun kyung Seo, Yunsoo Soh.
Formal analysis: Yun kyung Seo.
Investigation: Yunsoo Soh.
Methodology: Yunsoo Soh.
Project administration: Yunsoo Soh.
Software: Yunsoo Soh.
Supervision: Chang Won Won.
Validation: Yunsoo Soh.
Writing – original draft: Chang Won Won.
Writing – review & editing: Chang Won Won, Yunsoo Soh.

References

[1] Lowe-Lee F. Is Korea ready for the demographic revolution? The KEI Exchange. 2009.
[2] Petersen RC, Smith GE, Waring SC, et al. Aging, memory, and mild cognitive impairment. Int Psychogeriatr 1997;9(S1):65–9.
[3] Murman DL. The impact of age on cognition. Seminars in Hearing 2015;36:111–21.
[4] DeCarli C. Mild cognitive impairment: prevalence, prognosis, aetiology, and treatment. Lancet Neurol 2003;2:15–21.
[5] Inelmen EM, Sergi G, Coin A, et al. Can obesity be a risk factor in elderly people? Obes Rev 2003;4:147–55.
[6] Pi-Sunyer X. The medical risks of obesity. Postgrad Med 2009;121:21–33.
[7] De Felice FG, Ferreira ST. Inflammation, defective insulin signaling, and mitochondrial dysfunction as common molecular denominators connecting type 2 diabetes to Alzheimer disease. Diabetes 2014;63:2262–72.
[8] Zamboni M, Zoico E, Scartezzini T, et al. Body composition changes in stable-weight elderly subjects: the effect of sex. Aging Clin Exp Res 2003;15:321–7.
[9] Gustafson D. A life course of adiposity and dementia. Eur J Pharmacol 2008;585:163–75.
[10] Deckers K, Schievink SH, Rodriquez MM, et al. Coronary heart disease and risk for cognitive impairment or dementia: systematic review and meta-analysis. PLoS One 2017;12:e0184244.
[11] Koliaki C, Liatis S, Kokkinos A. Obesity and cardiovascular disease: revisiting an old relationship. Metabolism 2019;92:98–107.
[12] Kivipelto M, Ngandu T, Fratiglioni L, et al. Obesity and vascular risk factors at midlife and the risk of dementia and Alzheimer disease. Arch Neurol 2005;62:1556–60.
[13] Gazdzinski S, Kornak J, Weiner MW, et al. Body mass index and magnetic resonance markers of brain integrity in adults. Ann Neurol 2008;63:652–7.
[14] Hughes T, Borenstein A, Schofield E, et al. Association between late-life body mass index and dementia: the Kame Project. Neurology 2009;72:1741–6.
[15] Fitzpatrick AL, Kuller LH, Lopez OL, et al. Midlife and late-life obesity and the risk of dementia: cardiovascular health study. Arch Neurol 2009;66:336–42.
[16] St-Onge M-P, Gallagher D. Body composition changes with aging: the cause or the result of alterations in metabolic rate and macronutrient oxidation? Nutrition 2010;26:152–5.
[17] Ponti F, Santoro A, Mercatelli D, et al. Aging and imaging assessment of body composition: from fat to facts. Front Endocrinol 2019;10:861.

[18] Ritz P. Obesity in the elderly: should we be using new diagnostic criteria? J Nutr Health Aging 2009;13:168.
[19] Thibault R, Pichard C. The evaluation of body composition: a useful tool for clinical practice. Ann Nutr Metab 2012;60:6–16.
[20] Schutz Y, Kyle U, Pichard C. Fat-free mass index and fat mass index percentiles in Caucasians aged 18-98 y. Int J Obes 2002;26:953–60.
[21] Kyle UG, Schutz Y, Dupertuis YM, et al. Body composition interpretation: contributions of the fat-free mass index and the body fat mass index. Nutrition 2003;19:597–604.
[22] Bredella MA. Sex differences in body composition, sex and gender factors affecting metabolic homeostasis, diabetes and obesity. Advances in experimental medicine and biology, vol 1043. Springer 2017;9–27.
[23] Won CW, Lee Y, Choi J, et al. Starting construction of frailty cohort for elderly and intervention study. Ann Geriatr Med Res 2016;20:114–7.
[24] Lee JH, Lee KU, Lee DY, et al. Development of the Korean Version of the Consortium to Establish a Registry for Alzheimer's Disease Assessment Packet (CERAD-K) clinical and neuropsychological assessment batteries. J Gerontol Series B Psychol Sci Soc Sci 2002;57:47–53.
[25] Chandler MJ, Lacritz LH, Hynan LS, et al. A total score for the CERAD neuropsychological battery. Neurology 2005;65:102–6.
[26] Beeri M, Schmeidler J, Sano M, et al. Age, gender, and education norms on the CERAD neuropsychological battery in the oldest old. Neurology 2006;67:1006–10.
[27] Baddeley A. Working memory. Science 1992;255:556–9.
[28] Dubois B, Slachevsky A, Litvan I, et al. The FAB: a frontal assessment battery at bedside. Neurology 2000;55:1621–6.
[29] Kim JH, Chon J, Soh Y, et al. Trunk fat mass correlates with balance and physical performance in a community-dwelling elderly population: results from the Korean Frailty and aging cohort study. Medicine 2020;99:e19245.
[30] Livingston G, Sommerlad A, Orgeta V, et al. Dementia prevention, intervention, and care. Lancet 2017;390:2673–734.
[31] Stewart R, Masaki K, Xue Q-L, et al. A 32-year prospective study of change in body weight and incident dementia: the Honolulu-Asia Aging Study. Arch Neurol 2005;62:55–60.
[32] Dahl AK, Löppönen M, Isoaho R, et al. Overweight and obesity in old age are not associated with greater dementia risk: (see editorial comments by Dr. David S. Knodman. pp 2349–2350). J Am Geriatr Soc 2008;56:2261–6.
[33] Luchsinger JA, Patel B, Tang M-X, et al. Measures of adiposity and dementia risk in elderly persons. Arch Neurol 2007;64:392–8.
[34] Anstey K, Cherbuin N, Budge M, et al. Body mass index in midlife and late-life as a risk factor for dementia: a meta-analysis of prospective studies. Obes Rev 2011;12:e426–37.
[35] Gustafson D, Rothenberg E, Blennow K, et al. An 18-year follow-up of overweight and risk of Alzheimer disease. Arch Intern Med 2003;163: 1524–8.
[36] Kim S, Kim Y, Park SM. Body mass index and decline of cognitive function. PLOS One 2016;11:e0148908.
[37] Tikhonoff V, Casiglia E, Guidotti F, et al. Body fat and the cognitive pattern: a population-based study. Obesity 2015;23:1502–10.
[38] Pineau JC, Frey A. Comparison of skinfold thickness models with DEXA: impact of visceral adipose tissue. J Sports Med Phys Fitness 2016;56: 541–5.
[39] Noh H-M, Oh S, Song HJ, et al. Relationships between cognitive function and body composition among community-dwelling older adults: a cross-sectional study. BMC Geriatr 2017;17:259.
[40] Bagger YZ, Tankó LB, Alexandersen P, et al. The implications of body fat mass and fat distribution for cognitive function in elderly women. Obes Res 2004;12:1519–26.
[41] Vermeulen A, Kaufman J, Goemaere S, et al. Estradiol in elderly men. Aging Male 2002;5:98–102.
[42] Stocco C. Tissue physiology and pathology of aromatase. Steroids 2012;77:27–35.
[43] Carlson LE, Sherwin BB. Higher levels of plasma estradiol and testosterone in healthy elderly men compared with age-matched women may protect aspects of explicit memory. Menopause 2000;7:168–77.
[44] Wibowo E. Cognitive impacts of estrogen treatment in androgen-deprived males: what needs to be resolved. Curr Neuropharmacol 2017;15:1043–55.
[45] Yaffe K, Barnes D, Lindquist K, et al. Endogenous sex hormone levels and risk of cognitive decline in an older biracial cohort. Neurobiol Aging 2007;28:171–8.
[46] Hogervorst E, De Jager C, Budge M, et al. Serum levels of estradiol and testosterone and performance in different cognitive domains in healthy elderly men and women. Psychoneuroendocrinology 2004;29:405–21.
[47] Senanarong V, Vannasaeng S, Poungvarin N, et al. Endogenous estradiol in elderly individuals: cognitive and noncognitive associations. Arch Neurol 2002;59:385–9.
[48] Han C, Jo SA, Seo JA, et al. Adiposity parameters and cognitive function in the elderly: application of "Jolly Fat" hypothesis to cognition. Arch Gerontol Geriatr 2009;49:e133–8.
[49] Rapp SR, Espeland MA, Shumaker SA, et al. Effect of estrogen plus progestin on global cognitive function in postmenopausal women: the Women's Health Initiative Memory Study: a randomized controlled trial. JAMA 2003;289:2663–72.
[50] Kuo HK, Jones RN, Milberg WP, et al. Cognitive function in normal-weight, overweight, and obese older adults: an analysis of the advanced cognitive training for independent and vital elderly cohort. J Am Geriatr Soc 2006;54:97–103.
[51] Elias M, Elias P, Sullivan L, et al. Lower cognitive function in the presence of obesity and hypertension: the Framingham heart study. Int J Obes 2003;27:260–8.
[52] Colleluori G, Chen R, Napoli N, et al. Fat mass follows a U-shaped distribution based on estradiol levels in postmenopausal women. Front Endocrinol 2018;9:315.
[53] Marchand GB, Carreau A-M, Weisnagel SJ, et al. Increased body fat mass explains the positive association between circulating estradiol and insulin resistance in postmenopausal women. Am J Physiol Endocrinol Metab 2018;314:E448–56.
[54] Gates MA, Mekary RA, Chiu GR, et al. Sex steroid hormone levels and body composition in men. J Clin Endocrinol Metab 2013;98:2442–50.
[55] Forny-Germano L, De Felice FG, Vieira MNdN. The role of leptin and adiponectin in obesity-associated cognitive decline and Alzheimer's disease. Front Neurosci 2019;12:1027.
[56] Farr OM, Tsoukas MA, Mantzoros CS. Leptin and the brain: influences on brain development, cognitive functioning and psychiatric disorders. Metabolism 2015;64:114–30.
[57] Scarmeas N, Anastasiou CA, Yannakoulia M. Nutrition and prevention of cognitive impairment. Lancet Neurol 2018;17:1006–15.
[58] Rawle MJ, Cooper R, Kuh D, et al. Associations between polypharmacy and cognitive and physical capability: a British birth cohort study. J Am Geriatr Soc 2018;66:916–23.
[59] Magierski R, Kłoszewska I, Sobow T. Evaluation of the influence of metabolic processes and body composition on cognitive functions: nutrition and dementia project (NutrDem Project). Eur J Clin Nutr 2014;68:1200–3.
[60] Nguyen JC, Killcross AS, Jenkins TA. Obesity and cognitive decline: role of inflammation and vascular changes. Front Neurosci 2014;8:375.
[61] Isaac V, Sim S, Zheng H, et al. Adverse associations between visceral adiposity, brain structure, and cognitive performance in healthy elderly. Front Aging Neurosci 2011;3:12.
[62] Schwartz DH, Leonard G, Perron M, et al. Visceral fat is associated with lower executive functioning in adolescents. Int J Obes 2013;37:1336–43.