Association of Body Fat Percentage and Waist-hip Ratio With Brain Cortical Thickness

A Study Among 1777 Cognitively Normal Subjects

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Background: Increasing evidence has emerged that there is a link between body weight and the risk of developing dementia. However, the relationship between adiposity and brain structure has not yet been fully elucidated. We aimed to evaluate the association of body fat composition with cortical thickness in cognitively normal subjects.

Methods: In total, 1777 (887 men and 890 women) cognitively normal subjects, aged 45 years or older, were recruited from the Health Promotion Center in South Korea. Medical records including 3-dimensional magnetic resonance imaging, body fat percentage, waist-hip ratio (WHR), and other factors were reviewed.

Results: In men, the percentage of fat was positively associated with cortical thickness and the highest WHR group showed significantly decreased cortical thickness compared with the reference group. WHR showed an inverted U-shaped association with total cortical thickness and frontal lobe thickness in men. Among women, there was no significant association.

Conclusions: Our findings suggest that in men, body fat is positively associated with cortical thickness, whereas abdominal fat is negatively associated with cortical thickness.

Key Words: cortical thickness, body fat percentage, waist hip ratio, MRI, surface-based morphometric analysis

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Increasing evidence has emerged that there is a link between body weight and the risk of developing dementia.[1–8] Specifically, being underweight or having severe obesity have been associated with greater incidence of cognitive impairment.[4,8] These data have been supported by epidemiological studies, along with neuroimaging studies showing that brain atrophy is associated with underweight patients with Alzheimer's disease (AD) and obese individuals with or without AD.[3,9–15] Therefore, body weight might serve as a possible biomarker for the diagnosis of preclinical AD.[1–5]

The underlying mechanisms of effects of body weight on brain atrophy remain unknown because most studies have used nonspecific measures of body composition such as total body weight or body mass index (BMI). These nonspecific measures are poor at distinguishing between lean body mass and body fat or between central and peripheral adiposity.[16] Furthermore, as normal aging is associated with increase in body fat and decrease in lean mass without overall weight loss, nonspecific adiposity measures such as the BMI have limited value in capturing these changes. To date, only a few studies have investigated the effects of specific body composition on brain atrophy, and these studies had relatively small sample sizes.[3,17]

In the current study, we aimed to explore the association between brain cortical thickness and body fat composition in a large number of subjects. We measured brain cortical thickness as a surrogate marker of neurodegeneration because cortical atrophy reflects the overall neurodegeneration in different types of cognitive impairment.[1–5] Accumulating evidences have shown that there is a general temporal ordering of changes in biomarkers in dementia, in which neurodegeneration precedes clinical symptoms.[18] Thus, cortical atrophy would precede cognitive decline and to detect an early change of degeneration process, we measured brain cortical thickness. Our measures of body fat included body fat amount and waist-hip

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ratio (WHR). We hypothesized that individuals with low or high amounts of fat (or fat percentage) would exhibit cortical atrophy but that the amount of abdominal fat would be negatively associated with cortical thickness as visceral fat is more associated with metabolic syndromes than peripheral fat.[19]

METHODS

Study Participants

Eligible participants in this study were 2310 subjects who visited the Health Promotion Center at Samsung Medical Center. Subjects visited the Center for medical check-ups related to the disease prevention including dementia from September 2008 to December 2012. All participants underwent magnetic resonance imaging (MRI) including 3-dimensional volume images. Twenty-one subjects under age of 45 years were excluded. We also excluded 140 cognitively impaired subjects, as determined by the results of an interview conducted by a qualified neurologist and scores below the 16th percentile for age-matched, sex-matched, and education-matched norms on the Mini-Mental Status Exam (MMSE). In addition, we excluded 216 subjects who had incomplete data including demographics data (152 subjects), anthropometric measurements (7 subjects), history of hypertension (3 subjects), cholesterol or fasting blood sugar levels (50 subjects), and smoking or drinking habits (4 subjects). We also excluded 156 of the remaining 1933 subjects with errors in cortical thickness measurement. After these exclusions, 1777 subjects were analyzed. In men, there were no differences in the demographics between included and excluded subjects, whereas in women, included subjects were younger compared with excluded subjects. Included subjects showed higher cognitive scores for both genders (Supplemental Digital Content 1, Table 1, http://links.lww.com/WAD/A108).

This study was approved by the Institutional Review Board of the Samsung Medical Center, and the requirement for patient consent was waived, as only anonymized data that were already collected as part of routine monitoring contributed to the collaborative dataset.

Measurement Variables

All medical examinations were conducted by trained personnel according to standard protocol. The health screening program included a blood test (a complete blood cell count, basic chemistry, serologic test, blood coagulation test, thyroid function test, and assay for tumor markers), stool/urine analysis, abdominal ultrasonography, gastrofiberscopy, chest radiography, pulmonary function test, and electrocardiography.[20] Quality-control procedures were performed in accordance with the Korean Association of Laboratory Quality Control.

A 720 8-polar tactile-electrode impedance-meter body composition analyzer (Biospace, Seoul, Korea) was used to measure body fat percentage, fat mass, regional fat deposits, muscle mass, and fat-free mass (or lean body mass), while whereas the subject stood on a stainless steel scale.[21]

Medical information was gathered through questionnaires, which included questions covering physician-diagnosed diseases, medication history, cigarette smoking, alcohol consumption, and menopausal status. Diabetes was defined by a history of taking diabetes medication or a fasting blood sugar level ≥ 126 mg/dL. Hypertension was defined by a history of taking anti-hypertensive medication, systolic blood pressure (SBP) ≥ 140 mm Hg, or diastolic blood pressure (DBP) ≥ 90 mm Hg measured by a mercury blood pressure device after the subjects had rested for >5 minutes.

All subjects had completed neurological and neuropsychological examinations, the MMSE, the Montreal cognitive assessment (MoCA), and a 3-dimensional (3D) volumetric brain MRI scan. Radiologists inspected all MRI data for evidence of brain tumors of any kind, major infarctions (except lacunar infarction), and hemorrhages (observed as low intensity areas in T2-weighted images).

Image Acquisition

An Achieva 3.0-Tesla MRI scanner (Philips, Best, the Netherlands) was used to acquire 3D T1 turbo field echo (TFE) MRI data from the 1777 subjects with the following imaging parameters: sagittal slice thickness, 1.0 mm; over contiguous slices with 50% overlap; no gap; repetition time, 9.9 ms; echo time, 4.6 ms; flip angle, 8 degrees; and matrix size of 240×240 pixels reconstructed to 480×480 over a field of view of 240 mm.

Image Processing for Cortical Thickness Measurement

Images were processed by the standard Montreal Neurological Institute (MNI) anatomic pipeline. The native MRI images were registered into a standardized stereotaxic space using a linear transformation.[22] Nonuniformity artifacts were corrected, and the images were classified as white matter, gray matter, cerebrospinal fluid, or background using an artificial neural net classifier.[23] The surfaces of the inner and outer cortex were then automatically extracted using the Constrained Laplacian-Based Automated Segmentation with Proximities (CLASP) algorithm.[24]

Cortical thickness was calculated as the Euclidean distance between the linked vertices of the inner and outer surfaces after applying an inverse transformation matrix to the cortical surfaces and reconstructing them in the native space.[24,25] To compare the thicknesses of corresponding regions among the subjects, we employed an improved surface registration algorithm and an unbiased iterative group template, showing enhanced anatomic details.[26] Using the transformation, thickness information on the vertices was then transformed into an unbiased iterative group template.

Statistical Analyses

All analyses were performed separately by sex. Because of a possible nonlinear association between WHR and cortical thickness, WHR was categorized into quartile and then, to examine the effects of extreme groups, we divided the lowest and highest WHR group: ≤ 10, 11 to 25, 25 to 50, 51 to 75, 76 to 90, and >90 percentile. Group 1 corresponds to the lowest WHR group and group 6 corresponds to the highest WHR group. In men, group 4 was used as a reference group because group 4 included the median WHR and showed the thickest cortex. To be consistent with analyses, group 4 was also used as a reference group for women. Smoking status was categorized into nonsmokers, ex-smokers, or current smokers, and alcohol consumption was categorized into nondrinkers or current drinkers.

Multiple linear regression analysis was performed to examine the relationship of body fat percentage and/or WHR with cortical thickness ($\times 10^{-1}$ mm); potential confounding factors such as age, education, smoking status, drinking status, systolic blood pressure, diastolic blood

pressure, fasting blood glucose level, cholesterol level, intracranial volume (ICV), and presence of hypertension, diabetes mellitus, hyperlipidemia, previous stroke, or cardiovascular disease were included. Considering that hormonal changes can affect the results, we additionally adjusted the menopausal status for women. Although body fat percentage and WHR were significantly correlated (Pearson's correlation $r = 0.757$, $P < 0.001$), their variance inflation factor (VIF) was 2.774 and 2.717 for body fat percentage and WHR, respectively. During the analysis, violations of statistical assumptions in the linear regression analysis were assessed.

Nonlinear association of body fat percentage and WHR with cortical thickness (mm) was analyzed using a generalized additive model, which included fat percentage, spline of WHR (degrees of freedom = 4), and the potential confounders that were included in the multiple linear regression model. Fat percentage was included as a linear term in the final model because of its linear association with cortical thickness.

In addition, we examined the association of body fat percentage and WHR with MMSE or MoCA scores using a generalized linear model with a negative binomial distribution after controlling for the potential confounders that were included in the multiple linear regression model. Because of the skewed distribution of the MMSE and MoCA, scores subtracted from 30 were included in the analysis. All analyses were conducted with SAS v9.3 (SAS Institute, Cary, NC).

Finally, we entered body fat percentage or WHR as predictors, and vertex-by-vertex cortical thickness as an outcome, to analyze cortical thickness relationship to body fat percentage or WHR on the surface model. A multiple linear regression analysis was then performed after controlling for potential confounding variables. The cortical surface model contained 81,924 vertices; thus, correction for multiple comparisons was performed by a random field theory correction at a probability value of 0.05.

TABLE 1. General Characteristics of Study Participants

	Male (n = 887)	Female (n = 890)	*P*
Age (y)	64.9 ± 7.0	62.6 ± 7.5	< 0.001
Education [n (%)]			
< High school	123 (13.9)	309 (34.7)	< 0.001
High school	206 (23.2)	255 (28.7)	
≥ College	558 (62.9)	326 (36.6)	
Presence of chronic disease [n (%)]			
Hypertension	421 (47.5)	343 (38.5)	< 0.001
Diabetes mellitus	181 (20.4)	95 (10.7)	< 0.001
Hyperlipidemia	252 (28.4)	209 (23.5)	0.020
Stroke	34 (3.8)	23 (2.6)	0.141
Cardiovascular disease	70 (7.9)	42 (4.7)	0.006
Smoking status [n (%)]			
Never smoker	248 (28.0)	851 (95.6)	< 0.001
Ex-smoker	525 (59.2)	29 (3.3)	
Current smoker	114 (12.9)	10 (1.1)	
Drinking status (yes)	703 (79.3)	236 (26.5)	< 0.001
SBP (mm Hg)	123.0 ± 16.7	123.9 ± 19.2	0.301
DBP (mm Hg)	75.5 ± 10.2	73.2 ± 11.1	< 0.001
Fasting blood sugar (mg/dL)	101.3 ± 20.1	96.1 ± 16.9	< 0.001
Total cholesterol (mg/dL)	184.3 ± 34.5	203.2 ± 36.3	< 0.001
Postmenopausal state (n)		738/760 (97.1)	
Body fat percentage (%)	24.0 ± 5.4	32.0 ± 6.0	< 0.001
Waist-hip ratio	0.937 ± 0.036	0.913 ± 0.057	< 0.001
ICV (mL)	1454.8 ± 99.8	1298.6 ± 86.7	< 0.001
Cortical thickness, $\times 10^{-1}$ mm			
Total	30.4 ± 1.1	30.5 ± 1.1	0.009
Frontal lobe	30.8 ± 1.2	31.0 ± 1.1	0.001
Temporal lobe	31.9 ± 1.8	31.9 ± 1.8	0.295
Parietal lobe	29.1 ± 1.6	29.4 ± 1.4	< 0.001
Occipital lobe	27.0 ± 1.3	26.9 ± 1.2	0.310
MMSE	28.2 ± 1.6	27.8 ± 1.9	< 0.001
MoCA	26.0 ± 2.9	25.8 ± 3.3	0.221

DBP indicates diastolic blood pressure; ICV, intracranial volume; MMSE, mini-mental state examination; MoCA, Montreal cognitive assessment; SBP, systolic blood pressure.

RESULTS

Among the 1777 participants, 887 (49.8%) were men with an average age of 64.9 ± 6.97 years (range, 45 to 91 y) and 890 were women with an average age of 62.6 ± 7.51 years (range, 45 to 85 y). The WHR was lower in women than in men, but the body fat percentage was significantly higher in women (Table 1).

In men, fat percentage was positively associated with cortical thickness in all brain lobes and for the WHR, total cortical thickness and cortical thickness in the frontal lobe were decreased in the lowest WHR group compared with the reference group (Supplemental Digital Content 1, Table 2, http://links.lww.com/WAD/A108). Interestingly, in women, cortical thickness was not significantly associated with fat percentage or WHR.

After including fat percentage and the WHR together in the same multiple linear regression model, we found that fat percentage was positively associated with cortical thickness in all brain lobes in men (Table 2). In addition, individuals with the highest WHR exhibited significantly decreased total cortical thickness and frontal lobe thickness when compared with the reference group. Among women, both fat percentage and WHR were not significantly associated with cortical thickness in all brain lobes. The WHR revealed an inverse U-shaped association with cortical thickness in total and in the frontal lobe among men but not in women (Fig. 1). The results remained the same when we combined variables that are associated with metabolic syndrome (diabetes, hypertension, dyslipidemia, systolic blood pressure, diastolic blood pressure, fasting blood glucose, cholesterol level) into 1 variable "severity of metabolic syndrome" (Supplemental Digital Content 1, Table 3, http://links.lww.com/WAD/A108).

Association direction was evaluated in younger and older adults, stratified by median age (65 y in men and 63 y in women). A positive association between body fat percentage and cortical thickness was still seen in younger and older men but not in women from either age group. Highest WHR group showed significantly decreased frontal cortical thickness compared with the reference group in older, but not in younger men nor women of either age group (Supplemental Digital Content 1, Table 4, http://links.lww.com/WAD/A108).

The imaging analysis revealed a positive association between fat percentage and cortical thickness in the left parietal, left occipital, and right lateral temporal areas in men. In addition, the group with the highest WHR showed significantly

TABLE 2. Association of Body Fat Percentage and Waist-hip Ratio With Cortical Thickness ($\times 10^{-1}$ mm) by Sex

	Total		Frontal		Temporal		Parietal		Occipital	
	Beta (SE)	***P***	**Beta (SE)**	***P***	**Beta (SE)**	***P***	**Beta (SE)**	***P***	**Beta (SE)**	***P***
Male (n = 887)										
Fat percentage	0.030 (0.010)	0.003	0.028 (0.011)	0.010	0.034 (0.017)	0.046	0.033 (0.015)	0.028	0.041 (0.012)	0.001
Waist-hip ratio										
G1 (≤0.89), n = 93	−0.017 (0.145)	0.907	−0.063 (0.159)	0.692	0.093 (0.242)	0.701	−0.038 (0.212)	0.860	0.129 (0.169)	0.446
G2 (0.90 to 0.91), n = 117	−0.025 (0.125)	0.838	−0.072 (0.136)	0.596	−0.078 (0.208)	0.708	0.090 (0.182)	0.621	−0.017 (0.145)	0.907
G3 (0.92 to 0.93), n = 188	−0.060 (0.100)	0.548	−0.033 (0.109)	0.761	0.038 (0.167)	0.818	−0.126 (0.146)	0.387	0.013 (0.116)	0.910
G4 (0.94–0.96), n = 312	Reference		Reference		Reference		Reference		Reference	
G5 (0.97 to 0.98), n = 109	0.021 (0.120)	0.859	0.012 (0.131)	0.928	−0.077 (0.200)	0.701	0.057 (0.175)	0.743	−0.020 (0.139)	0.888
G6 (≥0.99), n = 68	−0.338 (0.161)	0.036	−0.498 (0.176)	0.005	−0.383 (0.269)	0.154	−0.197 (0.235)	0.404	−0.229 (0.187)	0.222
Female (n = 890)										
Fat percentage	0.016 (0.009)	0.087	0.013 (0.010)	0.167	0.016 (0.016)	0.336	0.018 (0.013)	0.149	0.014 (0.011)	0.194
Waist-hip ratio										
G1 (≤0.84), n = 88	0.025 (0.172)	0.886	0.097 (0.183)	0.599	−0.177 (0.311)	0.570	0.215 (0.239)	0.369	−0.002 (0.205)	0.993
G2 (0.85 to 0.87), n = 137	0.108 (0.137)	0.431	0.178 (0.147)	0.224	0.283 (0.249)	0.256	0.074 (0.191)	0.697	0.126 (0.164)	0.443
G3 (0.88 to 0.91), n = 260	0.118 (0.105)	0.264	0.155 (0.113)	0.170	0.213 (0.192)	0.267	0.089 (0.147)	0.546	0.053 (0.126)	0.676
G4 (0.92 to 0.94), n = 174	Reference		Reference		Reference		Reference		Reference	
G5 (0.95 to 0.98), n = 144	−0.031 (0.119)	0.796	0.002 (0.127)	0.985	0.126 (0.216)	0.560	−0.057 (0.165)	0.730	−0.006 (0.142)	0.969
G6 (≥0.99), n = 87	−0.257 (0.157)	0.101	−0.299 (0.168)	0.075	−0.229 (0.285)	0.421	−0.260 (0.218)	0.234	−0.094 (0.187)	0.615

In the multiple linear regression model, fat percentage, waist-hip ratio, age, education, intracranial volume, smoking status, drinking status, presence of diabetes mellitus, hypertension, dyslipidemia, stroke, and cardiac disease, systolic blood pressure, diastolic blood pressure, fasting blood glucose, cholesterol level, and menopausal status were included.

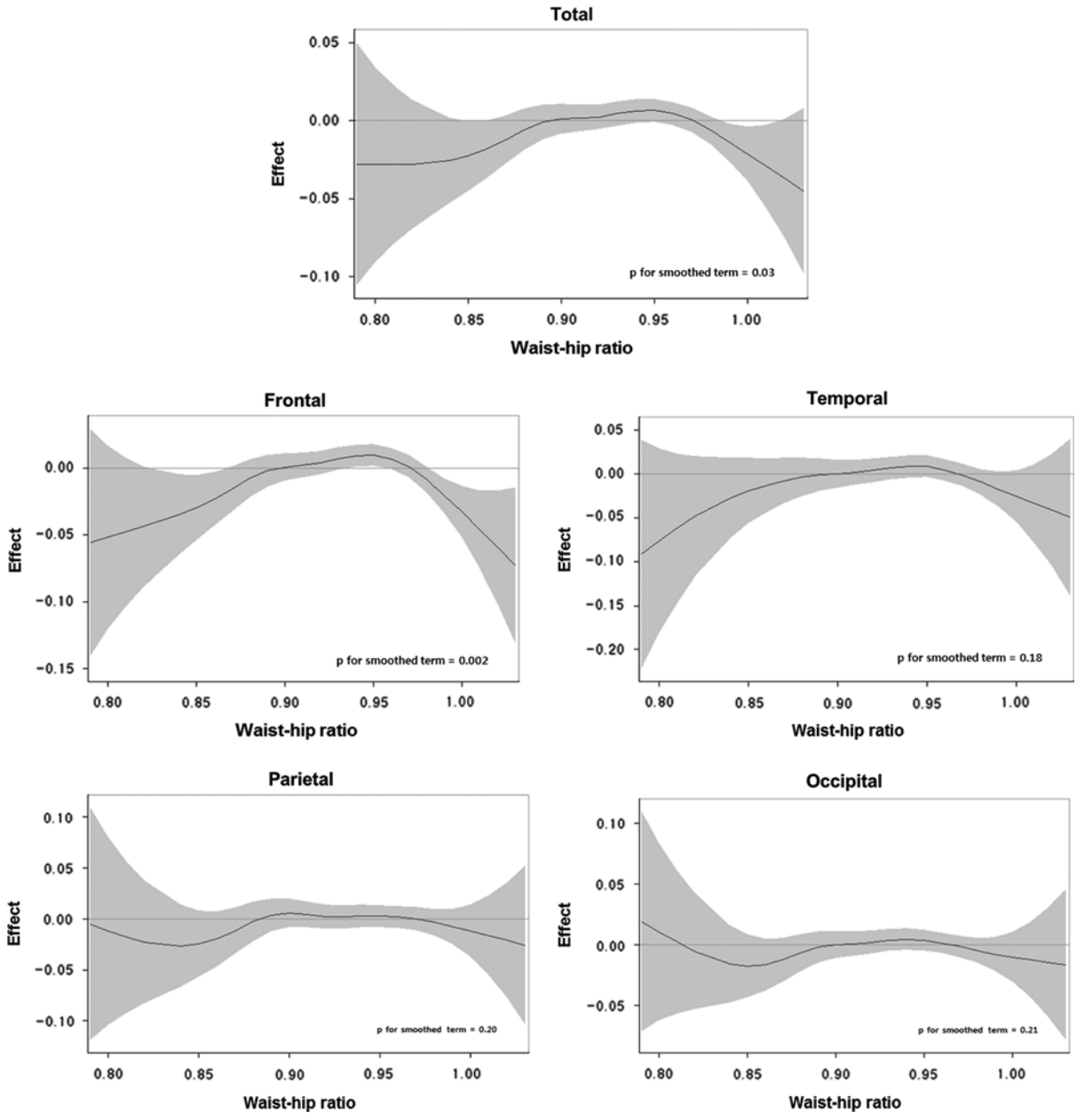

FIGURE 1. The nonlinear association of waist-hip ratio with cortical thickness in total and frontal brain regions among men. In the generalized additive model, we included spline of waist-hip ratio (degrees of freedom = 4), fat percentage, age, education, smoking status, drinking status, systolic blood pressure, diastolic blood pressure, fasting blood glucose, cholesterol level, intracranial volume, presence of diabetes mellitus, hypertension, dyslipidemia, stroke, or cardiac disease. Because the *P* value for the smoothed term was not statistically significant, a linear term of fat percentage was included in the final model. The fitted line and a 95% confidence interval (shaded area) are shown. The *y*-axis (mm) delineates decreases or increases in cortical thickness (cortical thickness was centered in the analysis).

decreased cortical thickness in the left paracentral lobule, right posterior cingulate gyrus, and left medial frontal areas compared with the reference group in men (Fig. 2, Supplemental Digital Content 1, Table 5, http://links.lww.com/WAD/A108). Among women, statistically significant differences were not observed.

There was also no statistically significant association between MMSE or MoCA scores and body fat percentage or WHR in either men or women (Supplemental Digital Content 1, Table 6, http://links.lww.com/WAD/A108).

DISCUSSION

In the present study, we analyzed the association of body fat percentage and WHR with cortical thickness using brain imaging data for a large sample size. We found that in men, body fat percentage was positively associated with brain cortical thickness in contrast to a high WHR being negatively associated with cortical thickness. However, we did not find significant associations between these variables in women.

Although until now, no study has evaluated the relationship between body fat composition and cortical thickness,

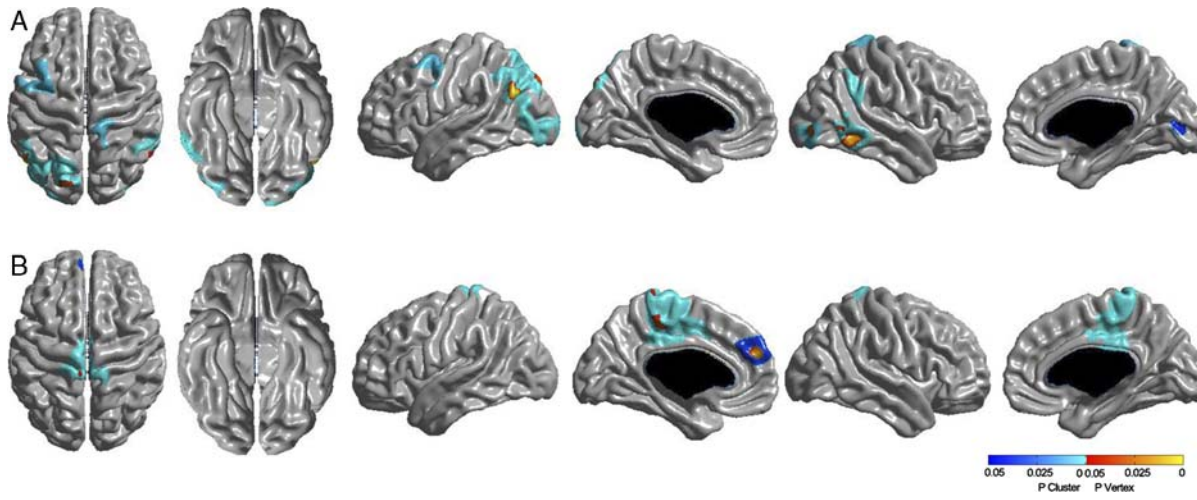

FIGURE 2. The topography of decreased cortical thickness as it relates to body fat percentage (A) and waist-hip ratio (B) in cognitively normal men. Fat percentage was included as a continuous variable (A). The areas of decreased cortical thickness in the highest WHR group compared with those in the reference group (B). RFT corrected ($P < 0.05$). Results were adjusted for age, education, hypertension, diabetes mellitus, hyperlipidemia, previous stroke, cardiovascular disease, smoking status, alcohol drinking status, systolic blood pressure, diastolic blood pressure, fasting blood sugar level, cholesterol level, intracranial volume, and body fat percentage (or waist-hip ratio).

previous studies have reported an association between a lower BMI and an increased risk of dementia.[2,8,17,27,28] In addition, the BMI has been reported to be negatively associated with AD pathologies, such as cerebral amyloid and tau, even in cognitively normal or MCI individuals.[28–30] Furthermore, a few neuroimaging studies, which investigated the association between brain atrophy and low body weight/lean body mass in AD, reported that weight loss might be a marker of preclinical AD.[31,32] However, because of the lack of information on body fat composition, these studies did not explore the relationship between the amount of body fat or the WHR and brain atrophy. Thus, the results of these prior studies might be confounded by body fat composition.

Positive association of fat with brain cortical thickness might be related to the presence of adipocytokines (adipose releasing factors) such as adiponectin and leptin secreted from the fat tissue.[33] Previous studies have shown that adiponectin has anti-inflammatory, insulin-sensitizing, and antiatherogenic effects,[34] and leptin has neuroprotective effects against brain atrophy and dementia.[35–37] Therefore, further study is necessary to check adipocytokine levels and evaluate whether they mediate the effect of low fat percentage on brain atrophy.

Alternatively, decreased cortical thickness in individuals with a low fat percentage might be an initial manifestation of the dementia process. AD pathology usually begins in the medial temporal regions, resulting in reductions in food intake and body weight as a consequence.[28,38] However, a reverse association is an unlikely explanation of our results as decreased cortical thickness associated with body fat percentage did not occur in the medial temporal area and because all our subjects were cognitively normal.

In contrast to previous studies in which obesity or high BMIs exhibited negative effects on brain structures in cognitively normal individuals,[9–13] we found that body fat percentage in men was linearly associated with cortical thickness. In other words, a nonlinear association between body fat percentage and cortical thickness was not observed. Furthermore, abdominal obesity, as measured by the WHR, was significantly related to decreased cortical thickness in men. The prevailing concept is that obesity in mid-life increases risk for developing dementia,[4,6] whereas obesity in late-life decreases the risk.[2,17,39] Our results suggest that these associations might be confounded by body fat composition. Specifically, our results suggest that the association between obesity and brain atrophy might be caused by body fat distribution rather than fat amount. Our findings are consistent with previous studies suggesting that central obesity increases risk of dementia development.[19,40,41] Previous studies have also revealed that a greater WHR is negatively related to hippocampal volume[42] and that computed tomography-based measurements of abdominal fat exhibit an inverse association with total brain volume.[40]

The idea that visceral fat is more harmful to brain structures than overall body fat percentage could be explained in several ways. First, visceral fat has a stronger influence over insulin resistance than subcutaneous fat,[18] and an increase in insulin resistance could lead to more brain atrophy.[7] Second, visceral fat has a specific pattern of adipose tissue-derived hormone secretion. Levels of adipose-derived hormones, such as leptin, have been shown to be lower in visceral adipose tissue compared with subcutaneous adipose tissue.[43] In addition, compared with subcutaneous adipose tissue, visceral adipose tissue has a larger pattern of proatherogenic gene expression.[44] Unfortunately, plasma levels of adipocytokines were not available in our current study; therefore, we were unable to determine their relationship with neurodegeneration.

Compared with individuals who fell into the 50 to 75 percentile group of the WHR, individuals who fell into the highest WHR (>90 percentile) group showed decreased cortical thickness in the paracentral lobule, which contributes to the control of movement, the posterior cingulate gyrus, which is related to memory function, and the medial frontal area, which is responsible for motivation. However, the relationship between each cognitive function and the WHR is not yet understood and will therefore need to be studied further.

This study did not show any significant relationship between cortical thickness, fat percentage, and WHR in women. Sex differences in the relationship between obesity and decreased cortical thickness might be related to normal sexual dimorphism effects on body fat composition[45,46] or to hormonal change differences by sex during aging.[47] A majority of women in our study (738/760) were in postmenopausal state, and we may assume that there might have been redistribution of body fat composition. Again, further studies on this issue will be necessary to completely understand this difference between women and men.

It is clinically important to note that low fat percentage and central obesity were associated with decreased cortical thickness but not cognitive score. As mentioned earlier, according to temporal ordering of changes in biomarkers in dementia, cortical atrophy, a surrogate marker of neurodegeneration, precedes clinical symptoms. Our results suggest that low body fat percentage and central obesity impact the cortex before disease is clinically evident. Indeed, cortical atrophy preceeding cognitive decline has been shown in cognitively normal elderlies.[18,48] Alternatively, fat/WHR and cognition may not have been correlated because there was low cognitive score variability for our cognitively normal subjects. Further longitudinal study is necessary to tract whether individuals with low body fat percentage and central obesity show faster cognitive decline.

Because of the observational and cross-sectional nature of our study, several limitations should be considered. First, although prior history of chronic diseases was accounted for in our analyses and all study subjects were cognitively normal, early stages of dementia might cause a change in body fat percentage or the WHR. Therefore, further longitudinal studies will be necessary to confirm the findings of our study. Second, our measurement of bioelectrical impedance is a double indirect method.[49] However, we applied the same device throughout the study period in an attempt to reduce measurement error. Thus, relative differences in measured values among subjects might not be affected by measurement error or validity of measured values, and results might not be biased. Third, because the body fat data in our study was shifted to the left in comparison with western studies, it is possible that we could have missed an association between extremely high body fat percentage and decreased cortical thickness. Fourth, relatively highly educated and unhealthy subjects were recruited for this study compared with the Korea National Health and Nutrition Examination Survey (KNHANES), a nation-wide cross-sectional data set (Supplemental Digital Content 1, Table 7, http://links.lww.com/WAD/A108). This might limit the generalizability of our results.

In conclusion, the results of the current study suggest that low amounts of body fat and central obesity are negatively associated with brain cortical thickness.

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