doi: 10.1002/osp4.145

ORIGINAL ARTICLE

The relationship of waist circumference and body mass index to grey matter volume in community dwelling adults with mild obesity

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Received 20 September 2016; revised 26 November 2017; accepted 27 November 2017

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Summary

Objective

Previous work has shown that high body mass index (BMI) is associated with low grey matter volume. However, evidence on the relationship between waist circumference (WC) and brain volume is relatively scarce. Moreover, the influence of mild obesity (as indexed by WC and BMI) on brain volume remains unclear. This study explored the relationships between WC and BMI and grey matter volume in a large sample of Japanese adults.

Methods

The participants were 792 community-dwelling adults (523 men and 269 women). Brain magnetic resonance images were collected, and the correlation between WC or BMI and global grey matter volume were analysed. The relationships between WC or BMI and regional grey matter volume were also investigated using voxel-based morphometry.

Results

Global grey matter volume was not correlated with WC or BMI. Voxel-based morphometry analysis revealed significant negative correlations between both WC and BMI and regional grey matter volume. The areas correlated with each index were more widespread in men than in women. In women, the total area of the regions significantly correlated with WC was slightly greater than that of the regions significantly correlated with BMI.

Conclusions

Results show that both WC and BMI were inversely related to regional grey matter volume, even in Japanese adults with somewhat mild obesity. Especially in populations with less obesity, such as the female participants in current study, WC may be more sensitive than BMI as a marker of grey matter volume differences associated with obesity.

Keywords: Body fat distribution, body mass index, brain, waist circumference.

Introduction

Obesity is a risk factor for neurodegenerative diseases, such as Alzheimer's disease (1–3), as well as for hypertension (4,5), coronary heart disease (6) and metabolic diseases (7,8). Body mass index (BMI), which has conventionally been used to measure excess body fat, is associated with cerebral atrophy of the temporal region, as evaluated by visual ratings of computed tomography scans (9). Several magnetic resonance imaging studies of healthy participants have revealed specific brain regions in which reduced volume is associated with BMI (10–13). These studies indicate that alterations in specific brain structures associated with obesity may precede clinically significant neurological changes in the brain.

Although widely used, the appropriateness of BMI as a universal indicator of body fatness for all populations

has been questioned (7,14). BMI does not accurately measure fat content, nor does it reflect the proportions of muscle and fat, or account for sex and racial differences in fat content and distribution of intra-abdominal (visceral) and subcutaneous fat (7,15). The risk of high mortality with normal-weight central obesity may be overlooked when only the BMI is used (14). Among the US population, the mortality of metabolically unhealthy people with a normal BMI is higher than that of metabolically healthy people classified as obese by the BMI (7). In Asia in particular, a great concern is that World Health Organization (WHO)-defined BMI cut-offs (16) may underestimate the risk from obesity because Asians tend to have increased body fat at normal BMI values (7,17). Shiwaku *et al*. reported that Japanese with BMIs in the range of 23.0–24.9 are at increased risk for obesity-associated disorders, even though these values are classified as normal according to WHO criteria (17).

Recently, waist circumference (WC), which estimates abdominal fat more directly than does BMI, has been argued to be a better indicator than BMI because WC is more closely correlated with the secondary adverse effects of obesity (18–20). Several previous studies have investigated the relationship between WC and brain structure (10,21,22). Kurth *et al*. demonstrated negative correlations between WC and grey matter volume and between BMI and grey matter volume in several brain regions, including the hypothalamus; the prefrontal, anterior temporal and inferior parietal cortices; and the cerebellum, with women showing more widespread correlations for WC than for BMI (10). Participants in previous studies were Caucasian, although this was not explicitly stated in the study by Debette *et al*. (21). Only the study by Kurth *et al*. (10) showed the actual number of participants with obesity (10% [11/115] with a BMI $\geq$ 30). Indeed, the incidence of obesity, as defined by the WHO criteria of BMI of 30 or greater, is estimated to be 10–20% in Europe and the USA, in contrast to 2–3% in Japan (23). Therefore, evidence on the relationship between WC and brain structure in populations with less obesity, such as the Japanese, remains sparse.

This study investigated correlations between brain volumes and obesity in a large Japanese sample, using both WC and BMI. These correlations for the global grey matter volume and for specific grey matter regions were calculated using voxel-based morphometry (VBM). Based on the previous studies mentioned previously, the hypothesis was examined that obesity-related differences in grey matter volume will be seen among individuals of a population with less obesity and that WC may have advantages over BMI in this population. This study also focused on sex-associated differences because sex is a key demographic factor that influences eating behaviour and body-weight regulation (24).

Methods

Participants

The participants were volunteers who had undergone private health screening at the University of Tokyo Hospital between 2008 and 2009. The body weight, height and score on the Mini-Mental State Examination (MMSE) were measured as part of the health screening visit. WC was measured at the umbilicus level, according to the Japanese definition (25). The BMI was calculated as weight divided by height squared (kg m^{-2}). In addition, blood pressure and blood samples, including blood sugar as well as serum levels of lipids, insulin and adiponectin, were evaluated. Patients were defined as having metabolic syndrome when they met the criteria for Japanese metabolic syndrome (25) – central obesity (a WC of 85 cm or more for men and 90 cm or more for women) and any two of the following three risk factors: serum triglycerides $\geq$150 mg dL^{-1}, serum high-density lipoprotein cholesterol $<$40 mg dL^{-1} or both; systolic blood pressure $\geq$130 mmHg, diastolic blood pressure $\geq$85 mmHg or both; and fasting blood glucose levels $\geq$110 mg dL^{-1}. The homeostasis model assessment of insulin resistance (HOMA-IR) index was given as fasting insulin (μIU mL^{-1}) $\times$ fasting glucose (mmol L^{-1}), and the level of insulin resistance was defined as HOMA-IR $>$ 2.5 (26). Although the existence of metabolic syndrome and that of insulin resistance was not considered exclusion criteria here, to include individuals with overweight and obesity in the study, these criteria were used later to divide participants into subgroups to check the potential influence of these parameters on global grey matter volume.

Participants who had a history of neuropsychiatric disorder or central nervous system disease were excluded. Two trained neuroradiologists reviewed all scans (including T2-weighted and fluid-attenuated inversion recovery images), and participants who had old infarcts, haemorrhages or aneurysms were excluded. The inclusion criterion for Fazekas *et al*. visual scale score to assess white matter on magnetic resonance imaging (range, 0 to 3) (27) was restricted to between 0 (absence) and 2 (smooth 'halo'). The institutional ethics committee approved the study. This study complies with the principles of the Declaration of Helsinki. Written informed consent was obtained from each participant after providing a complete explanation of the study. Furthermore, to protect subject confidentiality, patient information was stripped from all data.

Image acquisition

Magnetic resonance imaging data were obtained on two 3T Signa HDx scanners (GE Medical Systems, Milwaukee, Wisconsin, USA) of the exact same model with an 8-channel brain phased-array coil. For the VBM analysis, T1-weighted images were acquired in 124 slices by using three-dimensional spoiled-gradient recalled acquisition in the steady state (repetition time, 6.4 ms; echo time, 2.0 ms; flip angle, 151; field of view, 250 mm; slice thickness, 1 mm with no gap; acquisition matrix, 256 × 256; number of excitations, 0.5). The voxel dimensions were 0.977 × 0.977 × 1.0 mm.

Image analysis

All three-dimensional spoiled-gradient images were processed and examined by using the Statistical Parametric Mapping version 8 (SPM8) software (Wellcome Department of Imaging Neuroscience, London, UK; http://www.fil.ion.ucl.ac.uk/spm), in which VBM implemented in the VBM8 toolbox (http://dbm.neuro.uni-jena.de/vbm.html) with default parameters in MATLAB 7.7.0.471 (The MathWorks, Natick, MA, USA) running on a Windows computer.

A 'nonlinear only' modulation was performed on all images during spatial normalization to express the values in the resultant images as volumes corrected for brain size. The resultant modulated images were smoothed by using a Gaussian kernel of 8 mm (full width at half maximum). In addition, SPM8 default modulation was performed to calculate the total intracranial volume (TIV) as the sum of grey matter, white matter and cerebrospinal fluid volumes. When analysing global grey matter volume, the grey matter fraction (GMF) was defined as the proportion of the TIV occupied by the grey matter volume, to normalize the head size of each subject.

Statistical analysis

Pearson product moment correlations between GMF and WC, BMI, age, MMSE, as well as TIV were calculated separately for each sex to investigate the relationships between global grey matter volume and the other variables. The significance level was set at $P < 0.05$.

Voxel-wise analyses were performed to investigate the correlation between WC or BMI and the regional grey matter volume. Multiple regression was performed in SPM8 separately for each sex. The WC or BMI was treated as a covariate-of-interest. As nuisance variables, individual values for age and MMSE were included in the analysis for each sex. Two linear contrasts (1, −1) were made for positive and negative correlations, respectively. The significance level was set at the family-wise error-corrected P value of less than 0.05.

Results

Characteristics of the study population

Data from 792 participants (523 men and 269 women) were included in the analyses (Table 1). There were no sex differences in age or MMSE. The WC and BMI were significantly different between men and women, with both being greater in men than in women ($P < 0.0001$ for both; Wilcoxon rank-sum test). The TIV was also larger in men than in women ($P < 0.0001$; Student's t-test). In contrast, the GMF was larger in women than in men ($P < 0.0001$; Wilcoxon rank-sum test). There was no sex difference in the prevalence of people who qualified as obese with a BMI ≥ 30. However, the prevalence of participants with each of the following conditions was significantly lower in women than in men: those who (i) qualified as overweight with a BMI between 25 and 30, (ii) met the criteria for metabolic syndrome, (iii) met the criteria for insulin resistance or (iv) had a treatment history of lifestyle-related diseases (all Ps < 0.01; χ^2 test).

Relationships of global grey matter volume to other variables

Table 2 shows Pearson's correlation coefficients between variables for each sex. Neither WC nor BMI was significantly correlated with GMF. This was also the case when the partial correlation coefficients between WC or BMI and GMF adjusted for age, MMSE and TIV were analysed. Age-related increases in WC and BMI were seen only in female participants. The partial correlation coefficient adjusted for MMSE and TIV was also significant between WC and age ($r = 0.28$, $P < 0.01$) and between BMI and age ($r = 0.16$, $P < 0.01$) in female participants. GMF and TIV were negatively correlated with adiponectin in male participants only, although the correlation became non-significant when adjusted for age ($r = -0.08$, $P = 0.09$; $r = -0.04$, $P = 0.34$). The participants were further divided into subgroups with or without metabolic syndrome or insulin resistance to check whether GMF was related to WC or BMI when analysed separately for each subgroup. However, none of the correlations reached statistical significance.

Voxel-wise analysis with voxel-based morphometry

In male participants, widespread regions in which grey matter was negatively correlated with WC or BMI were

Table 1 Characteristics of study participants

	Men (*N* = 523)			Women (*N* = 269)			
	Mean	SD	Range	Mean	SD	Range	*P*
Age	55.3	9.7	23–84	55.2	9.9	24–81	n.s.
MMSE	29.1	1.1	24–30	29.2	1	24–30	n.s.
WC (cm)	88.5	8.1	64–127	81.2	9.8	58–113	<0.0001
BMI (kg m^{-2})	24.7	3.1	15.8–41.2	22	3.3	14.4–34.3	<0.0001
Adiponectin ($\mu g\ mL^{-1}$)	6.9	3.7	0.93–26.8 (*N* = 499)	11.3	5.7	0.83–37.9 (*N* = 258)	<0.0001
TIV (mL)	1477	95	1,233–1,784	1305	92	998–1,578	<0.0001
GMF	0.43	0.021	0.36–0.49	0.447	0.018	0.38–0.49	<0.0001
	N	%		*N*	%		*P*
Prevalence of obesity							
$25 \leq BMI < 30$	203	39		33	12		<0.01
$30 \leq BMI$	21	4		8	3		n.s.
Metabolic syndrome	107	20		6	2		<0.01
Insulin resistance	95	18		4	1		<0.01
Treatment of lifestyle disease	39	7		5	2		<0.01

The sample sizes for adiponectin were smaller due to missing values.
BMI, body mass index; GMF, grey matter fraction; MMSE, Mini-Mental State Examination; n.s., non-significant; SD, standard deviation; TIV, total intracranial volume; WC, waist circumference.

observed: the temporal lobes, thalamus, rectal gyrus, frontal gyrus, precentral gyrus, lingual gyrus, precuneus, posterior cingulate, postcentral gyrus, inferior parietal lobule, cingulate gyrus, insula and superior temporal gyrus (Table 3 and Figure 1, blue). For female participants, significant WC-related or BMI-related decreases in regional grey matter volume were also observed, although the areas were much smaller than in male participants (Table 4 and Figure 1, red). The sum of the significant cluster sizes (number of voxels) for WC was close to that for BMI, although the former was slightly larger than the latter in female participants (WC = 2,358 and BMI = 2,136) and smaller than the latter in male participants (WC = 47,383 and BMI = 53,544).

For both male and female participants, neither the correlation between regional grey matter volume and WC nor that between regional grey matter volume and BMI was positive.

Table 2 Pearson product moment correlations between variables for each sex

	WC	BMI	Age	MMSE	TIV	Adiponectin
Women						
BMI	0.87**					
Age	0.28**	0.16**				
MMSE	−0.03	−0.05	−0.31**			
TIV	0.02	−0.01	−0.12*	0.17**		
Adiponectin	−0.26**	−0.27**	0.16*	−0.10	−0.03	
GMF	−0.07	0.01	−0.50**	0.17**	−0.16**	−0.10
Men						
BMI	0.87**					
Age	0.05	−0.07				
MMSE	−0.07	−0.06	−0.26**			
TIV	0.04	0.07	−0.22**	0.13**		
Adiponectin	−0.24**	−0.28**	0.27**	−0.08	−0.10*	
GMF	−0.05	0.01	−0.61**	0.21**	−0.05	−0.22**

**$P < 0.01$,
*$P < 0.05$.
BMI, body mass index; GMF, grey matter fraction; MMSE, Mini-Mental State Examination; TIV, total intracranial volume; WC, waist circumference.

Discussion

The relationships of grey matter volume to WC and BMI in a large number of Japanese adults were evaluated. As for global grey matter volume, neither the relationship between GMF and WC nor that between GMF and BMI was significant. However, both WC and BMI were negatively correlated with regional grey matter volume in several structures. These regions were more widespread in men than in women.

As hypothesized, the participants in this study were classified as less obese than in previous studies: compared with the mean BMI reported in previous studies (25.02 ± 4.13 (10), 28 ± 5 (21) and 27.4 ± 4.5 or 27.2 ± 4.4 (22)), the mean BMI in this study was relatively low (24.7 ± 3.1 or 22.0 ± 3.3 for men or women, respectively, shown in Table 1) and classified as normal by WHO criteria (16). The percentage of participants with obesity with BMI of at least 30 was 4% for men and 3%

Table 3 MNI coordinates and grey matter regions negatively correlated with WC or BMI in male participants

Cluster size (voxels)	MNI coordinates			peakT	*P*	R/L	Region
	x	*y*	*z*				
WC							
6,588	66	−28.5	−25.5	9.554	<0.001	R	Inferior temporal gyrus
	69	−34.5	−16.5	8.280	<0.001	R	Middle temporal gyrus
	60	−13.5	−36	7.582	<0.001	R	Inferior temporal gyrus
3,124	−61.5	−22.5	−30	9.284	<0.001	L	Fusiform gyrus
	−67.5	−21	−19.5	8.385	<0.001	L	Inferior temporal gyrus
	−55.5	−9	−39	8.204	<0.001	L	Inferior temporal gyrus
5,448	−1.5	−19.5	−6	9.277	<0.001	L	Red nucleus
	−3	−27	9	6.323	<0.001	L	Thalamus
	−12	−13.5	16.5	5.705	<0.001	L	Thalamus
5,983	−3	49.5	−25.5	8.049	<0.001	L	Medial frontal gyrus
	−12	45	−22.5	7.584	<0.001	L	Medial frontal gyrus
	30	48	−7.5	6.423	<0.001	R	Superior frontal gyrus
10,027	−3	−69	−46.5	7.808	<0.001	L	Inferior semi–lunar lobule
	13.5	−69	−49.5	7.299	<0.001	R	Inferior semi-lunar lobule
	13.5	−60	−51	6.858	<0.001	R	Cerebellar tonsil
6,016	58.5	−1.5	33	7.412	<0.001	R	Precentral gyrus
	54	13.5	27	7.047	<0.001	R	Inferior frontal gyrus
	60	−9	12	6.997	<0.001	R	Postcentral gyrus
4,837	−4.5	−84	−4.5	6.649	<0.001	L	Lingual gyrus
	−3	−70.5	18	6.006	<0.001	L	Cuneus
	−4.5	−63	21	5.997	<0.001	L	Posterior cingulate
571	−13.5	49.5	15	6.398	<0.001	L	Medial frontal gyrus
	−22.5	39	25.5	5.029	0.007	L	Medial frontal gyrus
2,671	−61.5	−22.5	15	6.326	<0.001	L	Postcentral gyrus
	−63	−34.5	36	6.080	<0.001	L	Inferior parietal lobule
	−48	−19.5	36	6.038	<0.001	L	Postcentral gyrus
77	33	40.5	13.5	6.050	<0.001	R	Medial frontal gyrus
861	−4.5	−31.5	39	6.041	<0.001	L	Cingulate gyrus
	−9	−16.5	33	5.731	<0.001	L	Cingulate gyrus
	9	−12	36	5.486	0.001	R	Cingulate gyrus
498	21	−72	−12	5.749	<0.001	R	Posterior lobe
	30	−78	−13.5	5.452	0.001	R	Posterior lobe
113	−19.5	−24	−19.5	5.363	0.001	L	Parahippocampal gyrus
55	4.5	−12	25.5	5.300	0.002	R	Cingulate gyrus
90	−48	−37.5	39	5.087	0.005	L	Supramarginal gyrus
89	10.5	−51	−24	5.053	0.006	R	Anterior lobe
	4.5	−45	−27	4.648	0.033	R	Anterior lobe
122	−13.5	−51	−25.5	5.012	0.007	L	Anterior lobe
151	31.5	24	3	4.925	0.010	R	Claustrum
62	−58.5	−58.5	18	4.841	0.015	L	Superior temporal gyrus
BMI							
34,647	−3	−19.5	−6	9.593	<0.001	L	Red nucleus
	−63	−22.5	−28.5	8.979	<0.001	L	Fusiform gyrus
	−67.5	−21	−19.5	8.735	<0.001	L	Inferior temporal gyrus
11,421	66	−31.5	−24	9.036	<0.001	R	Inferior temporal gyrus
	69	−39	−13.5	8.388	<0.001	R	Middle temporal gyrus
	31.5	15	−42	8.060	<0.001	R	Superior temporal gyrus
2,130	−12	46.5	−24	7.230	<0.001	L	Medial frontal gyrus
	−3	48	−25.5	7.179	<0.001	L	Medial frontal gyrus
	−30	45	−19.5	5.905	<0.001	L	Middle frontal gyrus
668	−13.5	49.5	15	6.572	<0.001	L	Medial frontal gyrus
	−7.5	52.5	22.5	5.853	<0.001	L	Medial frontal gyrus

Continues

Table 3. *Continued*

Cluster size (voxels)	MNI coordinates			peakT	*P*	R/L	Region
	x	*y*	*z*				
3,055	43.5	37.5	−15	6.194	<0.001	R	Inferior frontal gyrus
	19.5	52.5	0	6.094	<0.001	R	Medial frontal gyrus
	12	58.5	7.5	5.945	<0.001	R	Medial frontal gyrus
931	−4.5	−31.5	39	6.036	<0.001	L	Cingulate gyrus
	−9	−18	33	5.541	0.001	L	Cingulate gyrus
	6	−34.5	39	5.430	0.001	R	Cingulate gyrus
78	21	46.5	19.5	5.635	<0.001	R	Medial frontal gyrus
34	39	−73.5	4.5	5.545	0.001	R	Inferior occipital gyrus
61	−52.5	19.5	0	5.532	0.001	L	Precentral gyrus
109	16.5	42	19.5	5.524	0.001	R	Anterior cingulate
	10.5	33	28.5	4.896	0.012	R	Cingulate gyrus
39	31.5	42	12	5.488	0.001	R	Middle frontal gyrus
79	−30	−85.5	10.5	5.379	0.001	L	Middle occipital gyrus
71	−48	−37.5	39	5.173	0.003	L	Supramarginal gyrus
	−49.5	−45	43.5	4.821	0.016	L	Inferior parietal lobule
70	−28.5	3	−48	5.120	0.004	L	Superior temporal gyrus
	−28.5	10.5	−45	4.789	0.018	L	Superior temporal gyrus
76	60	−58.5	25.5	5.085	0.005	R	Superior temporal gyrus
40	36	−79.5	13.5	5.016	0.007	R	Middle occipital gyrus
35	−22.5	40.5	25.5	4.961	0.009	L	Medial frontal gyrus

BMI, body mass index; L, left; MNI, Montreal Neurological Institute; R, right; WC, waist circumference.

for women, which are lower than the general prevalence of obesity in Europe and the USA (10–20%) (23). This may be one of the reasons why an association between global grey matter volume and WC or BMI was not seen in the present study. The participants in the report by Taki *et al*. (12) were Japanese, and their BMI was as low as that in this study (23.41 ± 3.00 for men and 22.23 ± 2.97 for women): they reported negative correlations between BMI and global grey matter volume in male but not female subjects among 1,428 participants. Their larger number of participants may account for this difference. Another explanation could be the use of self-report data instead

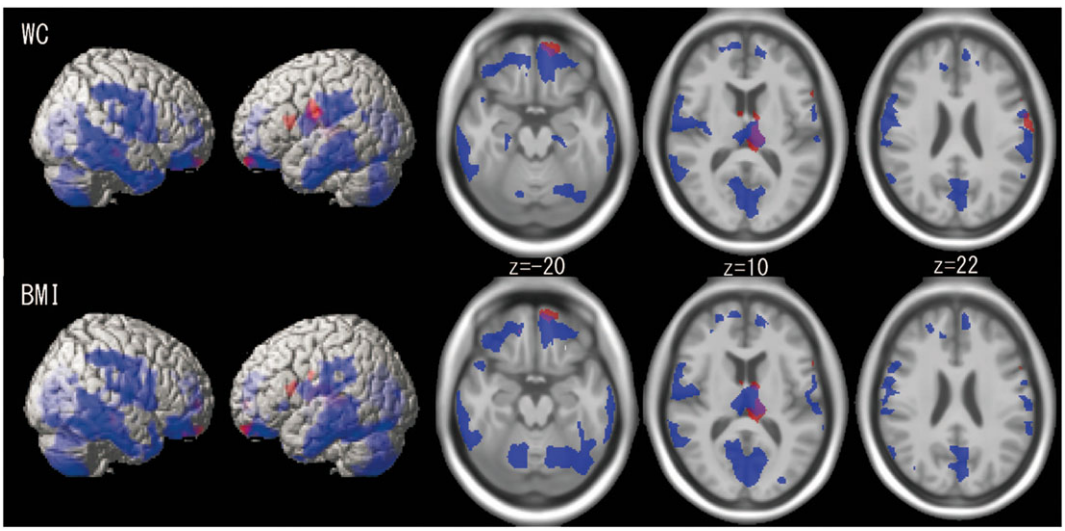

Figure 1 Lateral and axial images of the extent of grey matter regions that show negative correlations with waist circumference (WC) or body mass index (BMI) in male (blue) and female (red) participants. Overlapping areas are indicated in purple. The regions are almost identical for WC and BMI and are more widespread in male than in female participants.

Table 4 MNI coordinates and grey matter regions negatively correlated with WC or BMI in female participants

Cluster size (voxels)	MNI coordinates			peakT	*P*	R/L	Region
	x	*y*	*z*				
WC							
1,380	−10.5	−12	18	6.317	<0.001	L	Thalamus
	3	−15	−7.5	6.032	<0.001	R	Red nucleus
	−4.5	−33	10.5	5.897	<0.001	L	Thalamus
349	−60	−4.5	28.5	5.890	<0.001	L	Precentral gyrus
111	−57	12	19.5	5.739	<0.001	L	Inferior frontal gyrus
253	−7.5	58.5	−22.5	5.595	0.001	L	Medial frontal gyrus
	−16.5	55.5	−21	5.490	0.001	L	Medial frontal gyrus
124	40.5	−22.5	−12	5.380	0.002	R	Hippocampus
87	7.5	37.5	−30	5.166	0.006	R	Rectal gyrus
54	6	0	10.5	5.165	0.006	R	Thalamus
BMI							
1,601	−12	−13.5	16.5	6.377	<0.001	L	Thalamus
	4.5	−16.5	−7.5	6.350	<0.001	R	Red nucleus
	−4.5	−18	−4.5	6.299	<0.001	L	Thalamus
79	−57	12	19.5	5.877	<0.001	L	Inferior frontal gyrus
238	−7.5	58.5	−22.5	5.633	0.001	L	Medial frontal gyrus
	−13.5	48	−24	4.807	0.025	L	Superior frontal gyrus
84	10.5	57	1.5	5.204	0.005	R	Medial frontal gyrus
48	15	43.5	−22.5	5.177	0.005	R	Medial frontal gyrus
32	−60	−4.5	28.5	5.045	0.009	L	Precentral gyrus
54	33	−22.5	−10.5	4.844	0.021	R	Hippocampus

BMI, body mass index; L, left; MNI, Montreal Neurological Institute; R, right; WC, waist circumference.

of measured data. As they have discussed, Taki *et al*. obtained data on height and weight by self-questionnaire, and their study population might contain more people with overweight or obesity because subjects with higher BMIs significantly underestimated their weights, compared with those with smaller BMIs (12). Regarding this reporting bias, data of this study obtained by actually measuring height and weight may have estimated more precisely the correlations between BMI and global grey matter volume. The results of this study suggest that mild obesity in individuals with slightly high values of WC and BMI may influence regional grey matter volumes, even when these influences were not reflected in global grey matter volume.

The candidate mechanisms for obesity-related differences in brain volume are excess body fat-induced vascular abnormalities (28) and metabolic disorders (such as diabetes mellitus) (19,20), both of which cause brain ischaemia, which in turn lead to brain atrophy. Together with previous studies (10,12,22), the present study suggests that several brain regions are affected by obesity: the bilateral frontal cortex, temporal cortex, inferior parietal cortex and medial occipital cortex, as well as bilateral cerebellar and midbrain thalamic regions. In female participants, the regions were more restricted to the frontal and left thalamic regions. Importantly, the regions that were affected in both male and female participants may be involved in obesity. Several investigators have proposed that the frontal regions are key to the regulation of taste, reward and behavioural control (11,29). The thalamic region is one of the areas thought to be involved in motivational processes, along with the anterior cingulate cortex, caudate nucleus, putamen, hippocampus, hypothalamus, insula and medial prefrontal cortex (30).

Waist circumference and BMI were highly correlated, and the regional grey matter areas associated with each overlapped. However, in female participants, the total area of the regions correlated with WC was slightly greater than that of regions correlated with BMI. Some studies have reported that WC is a more sensitive than BMI as an indicator of differences in brain structure (10,31). As in this study, Kurth *et al*. (10) found that the area of grey matter reduction associated with increases in WC was greater than that associated with increases in BMI when examined in female participants separately. Consistent with previous work, findings of this study suggest that WC is an effective index of risk for neurodegenerative disorders related to obesity, especially in populations with less obesity, such as the female participants of this study.

A sex-associated difference exists in body fat deposition (32,33). Indeed, sex-dependent influences of obesity

on brain volume have been reported in several studies (10,12,34). The present study suggests that sex influences the pattern of structure in the brain associated with body fat and that men are more susceptible to obesity-related differences in brain volume. Both WC and BMI in the current study were larger in men than in women. Therefore, female participants with WC or BMI levels comparable with those in men may show patterns of regional grey matter volume difference similar to those in men: a future study in a more homogeneous group is needed to examine this possibility.

In summary, this finding of low regional grey matter volume associated with high WC and BMI in community-dwelling adults suggests that even mild obesity can affect regional brain structures. Although future studies will be needed to confirm whether the relationship between mild obesity and brain volume is quantitative or qualitative (i.e. ethnicity-specific), this finding suggests that interventions to people with mild obesity should be offered because, like people with obesity, they too may potentially be at risk for future declines in brain function.

Conflict of Interest Statement

The authors declare no conflicts of interest.

Acknowledgements

This work was funded by the ImPACT Program of Council for Science, Technology and Innovation (Cabinet Office, Government of Japan) and was supported in part by a High Technology Research Center Grant from the Ministry of Education, Culture, Sports, Science, and Technology of Japan (MEXT) and MEXT-Supported Program for the Strategic Research Foundation at Private Universities, 2014–2018.

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