

Adiposity Estimated Using Dual Energy X-Ray Absorptiometry and Body Mass Index and Its Association with Cognition in Elderly Adults

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OBJECTIVES: To determine whether obesity, estimated according to body mass index (BMI), waist circumference, and body fat and abdominal fat assessed using dual-energy X-ray absorptiometry (DEXA), was associated with cognitive performance.

DESIGN: Cross-sectional.

SETTING: Community based.

PARTICIPANTS: Individuals aged 74–94 (N = 406).

MEASUREMENTS: BMI, waist circumference, body fat, and abdominal fat were assessed using DEXA. Cognitive performance was assessed using a comprehensive neuropsychological battery.

RESULTS: When categorized using BMI, overweight individuals had higher global cognitive function and executive function scores than normal-weight individuals. This relationship did not differ according to sex. When categorized according to DEXA, there were no relationships between body fat and cognitive function in the whole group, but women in the middle and highest tertiles of DEXA body fat had better executive function than those in the lowest tertile. Men in the middle tertile of DEXA body fat had significantly better executive function and memory than those in the lowest tertile. BMI had greater power to pre-

dict executive function than DEXA body fat. No significant associations were found between cognition and estimates of abdominal adiposity.

CONCLUSION: This study found an association between being overweight and better executive function in elderly adults; this association was stronger for the simpler BMI than the more-elaborate DEXA measures. *J Am Geriatr Soc* 62:2311–2318, 2014.

Key words: obesity; body mass index; dual-energy X-ray absorptiometry; fat mass; cognition; elderly

Approximately 1.4 billion adults worldwide are overweight, with a body mass index (BMI) of 25.0–29.9 kg/m²; approximately 500 million of these are obese (BMI ≥ 30.0 kg/m²).¹ Obesity increases the risk of heart disease, hypertension, diabetes mellitus, stroke, dementia, and cancer.² In addition, a systematic review found obesity to be consistently associated with poor cognitive performance, especially in executive function, in children, adolescents, adults, and young-older adults younger than 70,³ but as also noted in the review, in individuals aged 70 and older, being overweight, or even obese, was in some cases associated with better cognitive performance.^{4,5} These conflicting results in two previous studies involving older-old adults did not measure executive function, the most consistent association with obesity in the younger sample. These studies also did not control for important confounding factors such as depression and the apolipoprotein E (APOE) ε4 allele, both known risk factors for cognitive decline and dementia.^{6,7} In addition, previous studies involving older-old adults only measured BMI, a crude estimate of body fat, which is not a good index of body fat in elderly adults because of loss of lean mass.⁸ A more-precise measure of body composition, including percentage of body fat, is dual-energy X-ray absorptiometry (DEXA).⁹

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Although DEXA body fat and BMI correlate positively, as expected because they measure body fat,^{10–12} studies evaluating whether BMI and DEXA measurements correlate similarly with other disease or biological factors have been inconsistent,^{13,14} with BMI being a better predictor of disease in elderly adults. However, because body fat exacerbates inflammation,^{15,16} and inflammation has been found to affect cognitive performance,^{17–21} it is important to measure body fat accurately to better understand the relationship between adiposity and cognitive performance. No study has examined associations between DEXA measurements of body fat and cognitive performance in older people. In addition, abdominal measures, such as waist circumference (WC) and DEXA abdominal fat, have been associated with a higher incidence of diabetes mellitus,²² coronary artery disease,²³ and mortality²⁴ and may also be associated with cognitive dysfunction,¹⁷ although this has not been examined using DEXA.

Thus the current study is the first to investigate the relationship between WC, BMI, and DEXA measurements of body fat and abdominal fat and cognitive function in a large sample of older adults. This study also investigated whether DEXA body fat or BMI was better at predicting cognitive performance. Relationships with an index of global cognitive function, as well as four cognitive domains, were assessed while controlling for a range of potential confounders, including cardiovascular and metabolic factors, symptoms of depression, and APOE.

Although there is a lack of evidence, and the study was exploratory in nature, it was hypothesized that there would be stronger relationships between DEXA body fat and cognition than between BMI and cognition, there would be a negative association between abdominal measures of fat (WC and DEXA abdominal body fat) and cognitive performance, and DEXA measures would provide additional information to BMI in predicting cognitive function.

METHODS

Participants

Participants were drawn from the Sydney Memory and Aging Study (MAS), which has been described in detail elsewhere.²⁵ In brief, MAS is a prospective population-derived cohort comprising community-dwelling adults aged 70–90 at baseline that assesses participants every 2 years. Exclusion criteria at baseline included insufficient English, sensory deficits precluding neuropsychological assessment, psychotic symptoms, schizophrenia, bipolar disorder, multiple sclerosis, motor neuron disease, developmental disability, or progressive malignancy. Individuals were also excluded if they had a prior diagnosis of dementia received after a comprehensive neuropsychiatric assessment or a baseline Mini-Mental State Examination (MMSE) score of less than 24 after adjustment for age, years of education, and non-English-speaking background.^{26,27} Data for this study were from Wave 3, when participants were aged 74–94. Non-English-speaking participants were excluded from the present study because of uncertainty of the validity of their neuropsychological test scores.²⁸

Four hundred and fifty participants consented to take part in a body composition assessment using DEXA; 28 of these did not complete the test (excess weight for the machine, $n = 2$; equipment or logistical problem, $n = 17$; medical reasons, $n = 6$; unknown, $n = 3$). Seven underweight BMI ($<18.5 \text{ kg/m}^2$) participants were removed from the sample, and nine participants had missing data. Thus, the final sample consisted of 406 individuals. This subsample was similar to the whole sample at baseline ($n = 1,037$) in terms of characteristics and medical health, except that none of the participants in this subsample had ever had a stroke or kidney disease, and their global cognition was slightly higher than that of the baseline sample.²⁹ The University of New South Wales and the South-Eastern Illawarra Area Health Service—Eastern sector granted ethics approval for this study, which was ratified at the University of Western Sydney, and consent was obtained from all participants.

Procedures

The presence of medical conditions was recorded during a face-to-face interview with a trained research assistant. During the same session, participants underwent a series of neuropsychological assessments, and their WC was measured. Information on height and weight was obtained during a second visit 1–2 months after the first visit, and DEXA scans were performed.

Dual Energy X-ray Absorptiometry

DEXA was used to measure body composition. Participants were instructed to take off all jewelry and any clothing containing plastic or metal and were given a gown to wear. A whole-body scan with the participant lying supine on the DEXA bed was then obtained, according to the manufacturer's guidelines. DEXA is able to differentiate bone, muscle, and fat and calculates total body mass (kilograms), fat mass (grams), percentage fat, and lean body mass (grams), as well as the regional distribution of these components (left arm, leg, and trunk; right arm, leg, and trunk; total arm, leg, and trunk). The technique has been used extensively in determination of bone density, has been expanded for use in determination of soft tissue mass, and has been validated as a method of assessing body composition in younger and older persons.³⁰ It has good reported reproducibility and is sensitive to small differences in body composition.³¹

DEXA percentage body fat was determined as total fat mass divided by total body mass. Abdominal fat was determined by delineation of a region of interest from the whole body scan that extended from the inner margin of the ribs between the top of the second and bottom of the fourth lumbar vertebrae, as previously described.³²

Anthropometric Measures

Body Mass Index

Height was measured using a stadiometer, and weight was measured using a scale. BMI was calculated as weight (kilograms) divided by height squared (meters²). BMI

categories were normal weight (18.5–24.9 kg/m²), overweight (25.0–29.9 kg/m²), and obese (≥ 30.0 kg/m²).

Waist Circumference

WC was measured during the medical examination at the midpoint between the lower border of the ribs and the iliac crest using a nonstretch measuring tape. WC was not measured on the same day as the DEXA assessment.

Global Cognition and Cognitive Domains

Trained university graduates in psychology administered a comprehensive neuropsychological test battery. Twelve tests were conducted, measuring four cognitive domains—processing speed, memory, language, executive function. The tests were categorized into domains, based on the principal cognitive function they represented according to convention and psychological theory.³³

The Digit Symbol Coding³⁴ and Trail-Making Test Part (TMT) A³⁵ were used to assess processing speed. Memory was measured using Logical Memory Story A (delayed),³⁶ Rey Auditory Verbal Learning Test (total learning, trials 1–5; short-term recall, trial 6; long-term recall, trial 7),³⁷ and the Benton Visual Retention Test.³⁸ Animal Naming³⁹ and the 30-item Boston Naming Test^{40,41} were used to assess language. Executive function was assessed using Phonemic Fluency (FAS)⁴² to assess fluency, the TMT B³⁵ to assess flexibility, and the Stroop Test⁴³ to measure inhibitory control. Raw scores were converted to quasi Z-scores based on the means and standard deviations of a reference group with normal cognition derived from the cohort. Domain scores were calculated by averaging the Z-score of the component tests. Signs of TMT-A and TMT-B were reversed so that higher scores represented better performances. A composite global cognition score was created by averaging the Z-scores of all the domains.

Covariate Measures

Covariates were selected based on their documented effect on adiposity measures and cognition in elderly adults. The final covariates were age, sex, years of education, symptoms of depression, diagnosed history of angina pectoris, acute myocardial infarction, transient ischemic attack, history of hypertension, diabetes mellitus, high cholesterol, weight change from baseline (4 years), and APOE genotype.

Sex was coded 1 for male and 2 for female. Current depression was assessed using the 15-item Geriatric Depression Scale (GDS), which has been shown to be valid and to have excellent test–retest reliability,⁴⁴ higher scores suggested greater depression symptoms. Angina pectoris, acute myocardial infarction, transient ischemic attack, hypertension, diabetes mellitus, and high cholesterol were coded as yes (1) or no (0). Weight change was computed weight at Wave 1 minus weight at Wave 3. The APOE $\epsilon 4$ allele is a risk factor for cognitive decline and dementia.⁶ Genomic deoxyribonucleic acid (DNA) was extracted from peripheral blood leukocytes or saliva samples (Oragene DNA self-collection kit, OG-250; DNA Genotek, Ottawa, ON, Canada) using a fully automated extraction procedure (Autopure LS; Qiagen Inc., Rockville, MD) or the

proteinase K method. APOE genotyping was undertaken by genotyping the two single-nucleotide polymorphisms (rs7412 and rs429358) that distinguish between the three APOE alleles ($\epsilon 2$, $\epsilon 3$, $\epsilon 4$). Genotyping was performed using Taqman assays (Applied Biosystems, Inc., Foster City, CA) and the validity of the APOE genotyping was confirmed in a subsample using an alternate method.⁴⁵ Results were available for more than 99% of the DNA samples, and the allele frequencies in Caucasians for each of the two single-nucleotide polymorphisms were in Hardy-Weinberg equilibrium ($P > .05$). In the analyses, participants were coded according to their APOE allele.

Statistical Analyses

Data analyses were performed using SPSS Statistics version 20 (IBM Corp., Armonk, NY). Bonferroni correction for multiple testing was performed, and the P -value for all of the above analyses was set at .0125.

To examine relationships between continuous measures of obesity (BMI, WC, DEXA body fat, and DEXA abdominal fat) and cognition, scatter plots were first used (suggesting linear and nonlinear associations), and then linear regression analyses, using the enter method, were used, with cognition as the dependent variable, adiposity measures as independent variables, and covariates entered into the second block. These analyses were repeated for each measure of cognition (global, processing speed, memory, language, executive function).

Because the scatter plots suggested nonlinear associations between some of the obesity measures and cognition, and previous studies have suggested that the relationship between adiposity and cognitive performance is not linear,⁵ nonlinear relationships were investigated by entering the squares of adiposity variables as independent variables together with the linear variable within the regression analyses, again with cognition as the dependent variable and covariates as described above.

To further examine relationships between obesity and cognition measures, DEXA body fat was converted to quantiles and used as an independent variable in analysis of covariance (ANCOVA) models to identify differences in cognition. BMI was also categorized according to the usual categories (normal weight, 18.5–24.9 kg/m²; overweight, 25.0–29.9 kg/m²; obese, ≥ 30.0 kg/m²), and DEXA body fat was categorized using tertiles. Covariates were included, and sex differences were also investigated by examining interaction effects.

Hierarchical regression analyses were used to examine whether DEXA body fat provides prediction of cognitive function in addition to that provided by BMI. Cognitive measures that were found to be significant were used as the dependent variables in each model, BMI and DEXA were the independent variables (entered step-wise in that order), and covariates were entered as described above.

RESULTS

Descriptive Statistics

Table 1 presents descriptive statistics of the dependent and independent constructs and covariates of the entire study

Table 1. Descriptive Characteristics and Adiposity Measurements According to Body Mass Index

Characteristic	Total, N = 406	Normal Weight, n = 140	Overweight, n = 178	Obese, n = 88
Female, %	55	55	43	52
Age, mean \pm SD	79.1 \pm 5.5	81.9 \pm 4.5	81.8 \pm 4.4	80.1 \pm 3.8
Education, mean \pm SD	11.4 \pm 3.1	11.9 \pm 3.5	12.3 \pm 3.6	11.8 \pm 3.5
Diabetes mellitus, %	13	8	15	13
Heart attack, %	2.1	1.8	1.0	1.0
Geriatric Depression Scale score, mean \pm SD	2.3 \pm 2.3	2.3 \pm 2.3	2.2 \pm 2.2	2.3 \pm 2.1
Apolipoprotein E4, %	21.3	22.6	21	15.6
Transient ischemic attack, %	3.1	3.6	3.7	5.1
Stroke or kidney disease, %	0	0	0	0
Hypertension, %	62	53	61	68
Cancer, %	14	11	13	12
High cholesterol, %	51	46	57	60
Weight change from baseline, kg (4 years)	1.4 \pm 3.1	0.9 \pm 1.7	1.2 \pm 2.3	1.9 \pm 3.0
Adiposity measurements				
Body mass index, kg/m ² , mean \pm SD	26.9 \pm 4.4	22.9 \pm 1.7	27.4 \pm 1.3	33.0 \pm 3.2
Waist circumference, cm, mean \pm SD	97.0 \pm 8.8	86.8 \pm 8.5	97.6 \pm 7.6	109.5 \pm 10.8
DEXA abdominal fat, kg, mean \pm SD	1.5 \pm 0.44	1.2 \pm 0.43	1.7 \pm 0.44	1.6 \pm 0.44
DEXA fat percentage, mean \pm SD				
Total	33.1 \pm 9.2	27.7 \pm 7.9	34.2 \pm 7.6	41.6 \pm 7.2
Men	28.3 \pm 6.9	22.1 \pm 0.71	28.7 \pm 0.49	35.5 \pm 0.81
Women	37.9 \pm 8.7	30.8 \pm 0.65	40.5 \pm 0.64	46.8 \pm 0.85
Cognitive domains, mean Z-score \pm SD				
Global cognition	-0.37 \pm 1.2	-0.47 \pm 1.3	-0.30 \pm 1.1	-0.34 \pm 1.1
Processing speed	-0.52 \pm 1.4	-0.64 \pm 1.7	-0.47 \pm 1.3	-0.42 \pm 1.3
Language	-0.77 \pm 1.5	-0.89 \pm 1.5	-0.73 \pm 1.6	-0.62 \pm 1.5
Executive function	-0.56 \pm 1.4	-0.72 \pm 1.6	-0.39 \pm 1.1	-0.59 \pm 1.3
Memory	-0.46 \pm 1.3	-0.53 \pm 1.3	-0.42 \pm 1.3	-0.39 \pm 1.3

SD = standard deviation; DEXA = dual energy X-ray absorptiometry.

sample and participants categorized according to BMI categories of normal weight, overweight, and obese. These adults with an average age of approximately 80 and evenly split between the sexes were generally healthy, with few major medical events and expected rates of depression, hypertension, and high cholesterol.

Correlations

Table 2 presents the Pearson correlations between the four anthropometric measures: BMI, WC, and DEXA measures of body and abdominal fat. All were significantly positively correlated with each other.

Relationships Between Obesity Measurements and Cognitive Performance

Scatter plots suggested linear and nonlinear relationships for some of these associations, but regression analyses did

not reveal any significant linear effects of any of the four adiposity measures on cognition (results not shown), nor were there any significant interactions with sex. To be consistent it was decided to conduct all analyses again by including the nonlinear relationships. There was a nonlinear relationship between BMI and executive function, as indicated by the statistically significant negative regression coefficient of the BMI squared term ($B = -0.10$; $t_{401} = -2.69$; $P = .01$), showing a relationship with a downward curvature. There was also a statistically significant nonlinear relationship between DEXA body fat and executive function (regression coefficient for DEXA squared, $B = -0.07$; $t_{358} = -2.65$; $P = .008$), also showing a relationship with a downward curvature. No other statistically significant nonlinear effects were found, and the relationships between WC and DEXA abdominal fat and cognition were not investigated further.

Figure 1 shows adjusted mean quantile BMI and DEXA body fat values plotted against executive function (Figure 1). ANCOVA analyses revealed a consistent pattern of best cognitive performance by BMI-determined overweight participants, followed by obese individuals, with worst performances by those of normal weight (Table 3). Statistically significant differences between the BMI normal weight and overweight categories were found for global cognition and the executive function domain ($P < .01$). No sex interactions were found.

ANCOVA showed no significant difference in cognition between DEXA body fat tertiles, although significant sex interactions were found, specifically for processing speed ($F(2, 351) = 5.68$; $P = .004$), executive function

Table 2. Correlations Between Adiposity Measures

Measure	Body Mass Index	DEXA Body Fat	Waist Circumference
Correlation Coefficient (P-Value)			
DEXA body fat	.571 (<.001)		
Waist circumference	.785 (<.001)	.285 (<.001)	
DEXA abdominal fat	.663 (<.001)	.836 (<.001)	.543 (<.001)

DEXA = dual energy X-ray absorptiometry.

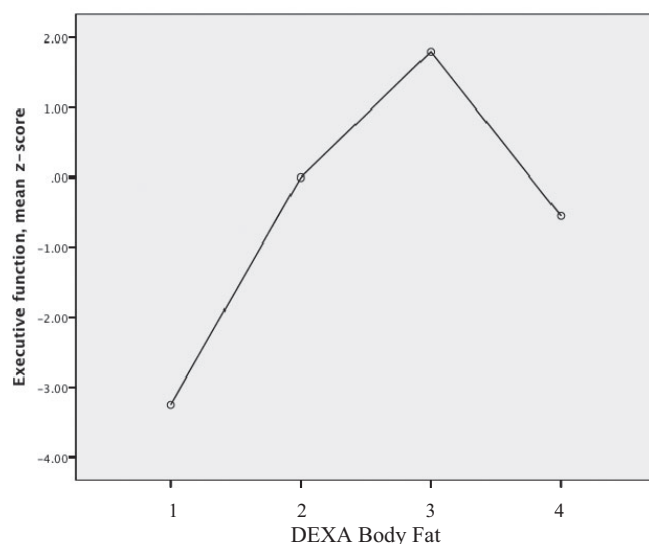
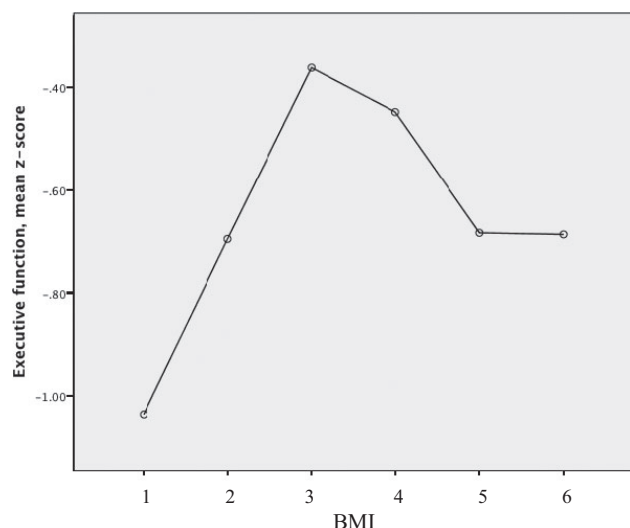


Figure 1. A representation of the shape of the data: mean values of executive function for quantiles of body mass index (BMI) and dual energy X-ray absorptiometry (DEXA) body fat.

($F(2, 351) = 8.94$; $P < .001$), and global cognition ($F(2, 351) = 6.00$; $P = .003$), but the number of men and women in each tertile were uneven because tertiles were based on the whole sample (e.g., the third tertile had only 10 men but 121 women). A closer look at the sex differences in DEXA body fat, which have been repeatedly documented in previous studies,^{9,46} revealed sex differences in DEXA body fat to be statistically significant ($F(2, 351) = 148.6$; $P < .001$), so post hoc ANCOVA analyses were performed using tertiles of DEXA body fat based on distributions within each sex separately. It was found that women in the middle tertile of DEXA body fat (Mean (standard error) -0.35 (0.15); $P = .01$) and highest tertile (-0.37 (1.5); $P = .01$) had significantly higher levels of executive function than those in the lowest tertile (-0.90 (0.15)). For men, those in the middle tertile of DEXA body fat had significantly higher levels of executive

Table 3. Cognitive Function According to Body Mass Index (BMI) with Inclusion of Covariates

	Normal Weight, n = 128	Overweight, n = 172	Obese, n = 80
Cognitive Domain	Mean Z-Score (Standard Error)		
Global cognition	-0.42 (0.09) ^a	-0.13 (0.08) ^a	-0.31 (0.12)
Processing speed	-0.58 (0.12)	-0.32 (0.10)	-0.44 (0.16)
Language	-0.83 (0.12)	-0.54 (0.11)	-0.56 (0.16)
Executive function	-0.72 (0.11) ^a	-0.41 (0.10) ^a	-0.57 (0.14)
Memory	-0.52 (0.10)	-0.19 (0.08)	-0.36 (0.13)

Covariates: age, sex, years of education, geriatric depression score, ever had a heart attack, ever diagnosed with cancer, ever had transient ischemic attack, high blood pressure and diabetes mellitus confirmed by doctor, apolipoprotein E, weight change.

^a $P < .01$.

function (-0.42 (0.11)) and memory (-0.18 (0.10)) than men in the lowest tertile (-0.74 (0.11), $P = .046$) and memory (-0.49 (0.10), $P = .03$).

DEXA Fat Versus BMI in Their Incremental Predictive Power on Executive Function

Using hierarchical linear regression analyses (including all covariates), the current study found that the nonlinear effects of DEXA (as defined above) were a statistically significant predictor of executive function (coefficient of determination (R^2) = 0.19, degrees of freedom (df) = 343; $P = .03$). The inclusion of nonlinear effects of BMI in the equation added to the predictive power of the model ($R^2 = 0.21$, R^2 change = 0.018; $df = 341$; $P = .02$), but when the procedure was reversed, DEXA did not have additional predictive power over a model with BMI (R^2 change = 0.009; $df = 341$; $P = .15$).

DISCUSSION

To the best of the knowledge of the authors, this is the first study to investigate the relationship between cognitive performance and BMI, WC, DEXA body fat, and DEXA abdominal fat in a large community-dwelling elderly cohort without dementia. No linear relationships were found between any of the estimates of adiposity and cognition. Contrary to what was hypothesized, BMI and DEXA body fat had a statistically significant nonlinear relationship with executive function, showing a relationship with a downward curvature. When categorized using BMI, results showed that overweight individuals had significantly higher levels of global cognition and executive function than normal-weight individuals. Results for BMI showed a consistent pattern, with best cognitive performance by overweight participants, followed by obese individuals, and worst performance by those of normal weight. When DEXA body fat was categorized according to sex, results showed that women in the middle and highest tertiles had significantly higher levels of executive function than those in the lowest tertile, suggestive of an association between greater adiposity and better cognition.

Executive function and memory were significantly better for men in the middle tertile of DEXA body fat than those in the lowest tertile, suggesting cognitive benefits associated with body fat, but only up to a certain point. DEXA abdominal fat and WC were not associated with cognitive performance.

Contrary to what was hypothesized, DEXA body fat showed no additional benefit over BMI when investigating adiposity and cognitive function during aging, although BMI added to the predictive power of the model using DEXA, specifically when examining executive function. These results indicate that BMI is a better measure for predicting cognitive performance in elderly adults. These results are surprising because the DEXA body fat measure was expected to be the best measure of body fat and thus, based on the hypothesis, to be able to predict cognition more strongly. A previous study suggested a low correlation between cognitive performance and body fat,³¹ which may indicate a confounding effect of sarcopenia, frailty, lean mass, illness, or other conditions having greater influence on cognition than body fat, and perhaps BMI takes these confounding effects into account better than DEXA body fat. The relationship between DEXA and BMI alone in elderly adults needs to be explored further because the correlation was only 0.57, although the direction of association with cognition was similar between the two measures.

Although research involving children, adolescents, and adults has repeatedly found adiposity to be associated with poorer cognitive performance, the current findings, together with two other studies involving older-old adults,^{4,5} suggest that this association disappears in those aged 70 and older. Instead, being of normal weight or having a low percentage of body fat could impair cognitive performance. There are compelling potential reasons for this dramatic shift in the association between obesity and cognition throughout the lifespan. For instance, it has been proposed that weight loss in elderly adults contributes to poor cognitive performance and may be a sign of dementia.¹⁵ However, the current study controlled for weight change that might have occurred in the past 4 years, which could be indicative of an underlying medical condition. Some cross-sectional studies have reported that age-related sarcopenia from inactivity or from medical conditions (cachexia) is associated with cognitive deficits. A study found that poor cognitive function assessed using the Short Portable Mental Status Questionnaire was associated with low fat-free mass in a large cross-sectional study of community-dwelling women aged 75 and older ($N = 3,027$).¹⁶ It could therefore be that older adults with higher BMI and higher body fat composition do not suffer as greatly from sarcopenia and its effects on cognition.

Previous studies have found that the relationship between WC and cognition disappears after the age of 70, because this relationship was attenuated with age.¹⁷ It seems that visceral fat, which is relevant in younger samples because of the risk of metabolic syndrome and cognitive impairment,¹⁸ does not affect the brain in elderly adults, and further research is needed to understand the mechanisms.

The current findings appear paradoxical because adiposity induces low-grade elevation in inflammatory

markers,^{19,20} which have repeatedly been shown to be negatively associated with cognitive performance and predict cognitive decline in elderly adults.^{21,47–50} It would be expected that obese individuals would have higher levels of inflammatory markers and consequently lower cognitive performance, but it was found that overweight individuals in the current sample had lower inflammatory markers than those who were normal weight and obese at baseline (unpublished data). This in turn suggests that, although the current findings involving obese individuals and better cognition are contrary to predictions based on low-grade inflammation, less inflammation may explain the association between overweight and better cognition in this sample. Because inflammatory markers were not measured during the same wave as the DEXA measures, this cannot be confirmed in the current sample.

There are other possible biological mechanisms that may explain better cognition in overweight and obese individuals. Overweight individuals retain testosterone or estrogen in the body fat, which in turn could help prevent cognitive impairment.^{51,52} Higher testosterone or estrogen has been linked to higher cognitive function,^{53,54} giving overweight and obese people a cognitive advantage. It is also possible that the findings reflect a “survivor” effect in the sample, which means that overweight and obese individuals are more likely to die at younger ages and that this elderly sample would then include the “survivors,” who are healthier. A study that pooled data from 19 studies and included 1.46 million white men and women aged 19–84 found obese individuals to be 2.5 times as likely to die young.⁵⁵ Together with this “survivor” effect, it is possible that “healthy” obesity, which has been suggested to involve up to 30% of obese people,⁵⁶ explains some of the positive associations.

This study has major strengths, including sample size, use of a comprehensive battery of neuropsychological tests, and incorporation of multiple covariates, including APOE, symptoms of depression, and weight change. The study is limited by its cross-sectional design and a lack of data pertaining to the duration of obesity. The data indicate that the average body weight of the sample increased by 1.4 kg over the 4 years of the study, but body weight and adiposity over the lifespan may influence cognition. Nevertheless, future longitudinal observations in this well-defined population can help delineate whether these relationships are maintained.

In conclusion, this study supports the growing evidence that being overweight, or having extra body fat, in older-old adults (≥ 70) is associated with better cognitive function, and the simpler BMI demonstrated this association better than the more-elaborate DEXA measure. Longitudinal studies are needed to examine the long-term effects of adiposity and changes in adiposity on cognitive performance and change in cognition in individuals aged 70 and older.

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Conflict of Interest: Samaras has received honoraria for seminars and teaching on obesity and type 2 diabetes mellitus and for sitting on an advisory board for Merk Sharpe and Dhome on sitagliptin. Samaras receives royalties on a book on diabetes mellitus she coauthored (*Fast Facts Diabetes*, Health Press Limited, Abingdon, UK). In the past 3 years, Brodaty has been a speaker, consultant, or board member for several pharmaceutical companies—AstraZenica, Eisai, Janssen, Lilly, Lundbeck, Merck, Medivation, Novartis, Nutricia, Pfizer, Sanofi, Servier—none of which have any connection with this paper.

Author Contributions: Smith: concept and design, data analysis and interpretation, writing the manuscript. Crawford: data analysis, manuscript review. Bailey: supervision, manuscript review and editing. Campbell, Baune, Kochan, Samaras, Brodaty, Trollor, Sachdev: concept and design, discussion, manuscript review and editing. Menant, Sturienks: concept and design, data acquisition, manuscript review and editing.

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REFERENCES

- World Health Organization. Obesity and overweight [on-line]. Available at <http://www.who.int/mediacentre/factsheets/fs311/en/> Accessed January 2014.
- Bray GA, Bouchard C, James WPT. Handbook of Obesity. New York: Marcel Dekker, 1998.
- Smith E, Hay P, Campbell L et al. A review of the relationship between obesity and cognition across the lifespan: Implications for novel approaches to prevention and treatment. *Obes Rev* 2011;12:740–755.
- Han C, Jo SA, Seo JA et al. Adiposity parameters and cognitive function in the elderly: Application of the 'Jolly Fat' hypothesis to cognition. *Arch Gerontol Geriatr* 2009;49:e133–e138.
- Nilsson LG, Nilsson E. Overweight and cognition. *Scand J Psychol* 2009;50:660–667.
- Corder EH, Saunders AM, Strittmatter WJ et al. Gene dose of apolipoprotein E type 4 allele and the risk of Alzheimer's disease in late onset families. *Science* 1993;261:921–923.
- Jorm A. Is depression a risk factor for dementia or cognitive decline? A review. *Gerontology* 2000;46:219–227.
- Romero-Corral A, Somers VK, Sierra-Johnson J et al. Accuracy of body mass index in diagnosing obesity in the adult general population. *Int J Obes (Lond)* 2008;32:959–966.
- Kelly TL, Wilson KE, Heymsfield SB. Dual energy x-ray absorptiometry body composition reference values from NHANES. *PLoS One* 2009;4:e7038.
- Flegal KM, Shepherd JA, Looker AC. Comparisons of percentage body fat, body mass index, waist circumference, and waist stature ratio in adults. *Am J Clin Nutr* 2009;89:500–508.
- Evans EM, Rowe DA, Racette SB et al. Is the current BMI obesity classification appropriate for black and white postmenopausal women? *Int J Obes* 2006;30:837–843.
- Gallagher D, Visser M, Sepulveda D et al. How useful is body mass index for comparison of body fatness across age, sex, and ethnic groups? *Am J Epidemiol* 1996;143:228–239.
- De Lorenzo F, Mukherjee M, Kadziola Z et al. Association of overall adiposity rather than body mass index with lipids and procoagulant factors. *Thromb Haemost* 1998;80:603–606.
- Lindsay RL, Tomazic T, Levine MD et al. Attentional function as measured by a continuous performance task in children with dyscalculia. *J Dev Behav Pediatr* 2001;22:287–292.
- Gao S, Nguyen J, Hendrie H et al. Accelerated weight loss and incident dementia in an elderly African-American cohort. *J Am Geriatr Soc* 2011;59:652–665.
- Abellan van Kan G, Cesari M, Gillette-Guyonnet S et al. Sarcopenia and cognitive impairment in elderly women: Results from the EPIDOS cohort. *Age Ageing* 2013;42:196–202.
- Yoon DH, Choi SH, Yu JH et al. The relationship between visceral adiposity and cognitive performance in older adults. *Age Ageing* 2012;41:456–461.
- Taylor VH, MacQueen GM. Cognitive dysfunction associated with metabolic syndrome. *Obes Rev* 2007;8:409–418.
- Yang RZ, Lee MJ, Hu H et al. Acute-phase serum amyloid A: An inflammatory adipokine and potential link between obesity and its metabolic complications. *PLoS Med* 2006;3:e287.
- Yudkin JS, Stehouwer CDA, Emeis JJ et al. C-reactive protein in healthy subjects: Associations with obesity, insulin resistance, and endothelial dysfunction. A potential role for cytokines originating from adipose tissue? *Arterioscler Thromb Vasc Biol* 1999;19:972–997.
- Trollor JN, Smith E, Agars E et al. The association between systemic inflammation and cognitive performance in the elderly: The Sydney Memory and Ageing Study. *Age (Dordr)* 2012;34:1295–1308.
- Janiszewski PM, Janssen I, Ross R. Does waist circumference predict diabetes and cardiovascular disease beyond commonly evaluated cardio metabolic risk factors? *Diabetes Care* 2007;30:3105–3109.
- Wiklund P, Toss F, Weinehall L et al. Abdominal and gynoid fat mass are associated with cardiovascular risk factors in men and women. *J Clin Endocrinol Metab* 2008;93:4360–4366.
- de Hollander EL, Bemelmans WJ, Boshuizen HC et al. The association between waist circumference and risk of mortality considering body mass index in 65- to 74-year-olds: A meta-analysis of 29 cohorts involving more than 58 000 elderly persons. *Int J Epidemiol* 2012;41:805–817.
- Sachdev PS, Brodaty H, Reppermund S et al. The Sydney Memory and Ageing Study (MAS): Methodology and baseline medical and neuropsychiatric characteristics of an elderly epidemiological non-demented cohort of Australians aged 70–90 years. *Int Psychogeriatr* 2010;22:1248–1264.
- Folstein MF, Folstein SE, McHugh PR. 'Mini-mental state'. A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189–198.
- Anderson TM, Sachdev PS, Brodaty H et al. Effects of sociodemographic and health variables on Mini-Mental State Exam scores in older Australians. *Am J Geriatr Psychiatry* 2007;15:467–476.
- Kochan NA, Slavov MJ, Brodaty H et al. Effect of different impairment criteria on prevalence of 'objective' mild cognitive impairment in a community sample. *Am J Geriatr Psychiatry* 2010;18:711–722.
- Fuchs T, Trollor JN, Crawford J et al. Macrophage inhibitory cytokine-1 is associated with cognitive impairment and predicts cognitive decline—the Sydney Memory and Ageing Study. *Aging Cell* 2013;12:882–889.
- Glickman SG, Marn CS, Supiano MA et al. Validity and reliability of dual-energy x-ray absorptiometry for the assessment of abdominal adiposity. *J Appl Physiol* 2004;97:509–514.
- Snijder MB, Visser M, Dekker JM et al. The prediction of visceral fat by dual-energy x-ray absorptiometry in the elderly: A comparison with computed tomography and anthropometry. *Int J Obes Relat Metab Disord* 2002;26:984–993.
- Samaras K, Spector TD, Nguyen TV et al. Independent genetic factors determine the amount and distribution of fat in women after the menopause. *J Clin Endocrinol Metab* 1997;82:781–785.
- Weintraub S, Salmon D, Mercaldo N et al. The Alzheimer's Disease Centers' Uniform Data Set (UDS): The neuropsychologic test battery. *Alzheimer Dis Assoc Disord* 2009;23:91–101.
- Wechsler D. Wechsler Adult Intelligence Scale—III. San Antonio, TX: The Psychological Corporation, 1997.
- Reitan RM, Wolfson D. The Halstead-Reitan Neuro-Psychological Test Battery: Theory and Clinical Interpretation. Tucson, AZ: Neuropsychological Press, 1993.
- Wechsler D. Wechsler Memory Scale, 3rd Ed. San Antonio, TX: Psychological Corporation, 1997.
- Rey A. L'Examen Clinique en Psychologie. Paris: Presses Universitaires de France, 1964.
- Benton Sivan A, Spreen O. Der Benton Test, 7th Ed. Bern, Switzerland: Huber, 1996.
- Spreen O, Benton AL. Neurosensory Center Comprehensive Examination for Aphasia: Manual of Instructions (NCCEA). Victoria, Australia: University of Victoria, 1969.

40. Fastenau PS, Denburn NL, Mauer BA. Parallel short forms for the Boston Naming Test: Psychometric properties and norms for older adults. *J Clin Exp Neuropsychol* 1998;20:828–834.
41. Kaplan E, Goodglass H, Weintraub S. *The Boston Naming Test*. Philadelphia: Lippincott Williams and Wilkins, 2001.
42. Benton AL. Problems of test construction in the field of aphasia. *Cortex* 1967;3:32–58.
43. Stroop JR. Studies of interference in serial verbal reactions. *J Exp Psychol* 1935;18:643–662.
44. Sheikh JL, Yesavage JA, Brooks JO et al. Proposed factor structure of the Geriatric Depression Scale. *Int Psychogeriatr* 1991;3:23–28.
45. Hixson JE, Vernier DT. Restriction isotyping of human apolipoprotein E by gene amplification and cleavage with HhaI. *J Lipid Res* 1990;31:545–548.
46. Visser M, Pahor M, Tylavsky F et al. One- and two-year change in body composition as measured by DXA in a population-based cohort of older men and women. *J Appl Physiol* 2003;94:2368–2374.
47. Trollor JN, Smith E, Baune BT et al. Systemic inflammation is associated with MCI and its subtypes: The Sydney Memory and Aging Study. *Dement Geriatr Cogn Disord* 2010;30:569–578.
48. Baune BT, Ponath G, Golledge J et al. Association between IL-8 cytokine and cognitive performance in an elderly general population—the MEMO-Study. *Neurobiol Aging* 2008;29:937–944.
49. Marsland AL, Petersen KL, Sathanoori R et al. Interleukin-6 covaries inversely with cognitive performance among middle-aged community volunteers. *Psychosom Med* 2006;68:895–903.
50. Schram MT, Euser SM, de Craen AJM et al. Systemic markers of inflammation and cognitive decline in old age. *J Am Geriatr Soc* 2007;55:708–716.
51. Gibbs RB. Estrogen therapy and cognition: A review of the cholinergic hypothesis. *Endocr Rev* 2010;31:224–253.
52. Yaffe K, Lui L, Zmuda J et al. Sex hormones and cognitive function in older men. *J Am Geriatr Soc* 2002;50:707–712.
53. Shepherd JE. Effects of estrogen on cognition, mood, and degenerative brain diseases. *J Am Pharm Assoc (Wash)* 2001;41:455–460.
54. Moffat SD, Zonderman AB, Metter EJ et al. Longitudinal assessment of serum free testosterone concentration predicts memory performance and cognitive status in elderly men. *J Clin Endocrinol Metab* 2002;87:5001–5007.
55. Berrington de Gonzalez A, Hartge P, Cerhan JR et al. Body-mass index and mortality among 1.46 million white adults. *N Engl J Med* 2010;363:2211–2219.
56. Pataky Z, Bobbioni-Harsch E, Golay A. Open questions about metabolically normal obesity. *Int J Obes* 2010;34:S18–S23.