Original Research

Effects of Intentional Weight Loss on Physical and Cognitive Function in Middle-Aged and Older Obese Participants: A Pilot Study

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Key words: cognition, obesity, weight loss, physical function, body composition

Objectives: Obesity is a risk factor for cognitive decline and dementia. Whether weight loss improves cognition in older obese adults is not known. The objective was to investigate the effects of intentional weight loss on physical and cognitive function in middle-aged and older obese adults attending a weight loss clinic.

Method: Eleven male and 39 female nonsmoking, adult obese (body mass index 30–50 kg/m^2) participants were recruited. Participants were stratified by age: middle aged (30–59 years) and older aged ($\geq$60 years). The weight loss target for each subject was 8% to 12% of initial body weight. Information on anthropometry, bioelectrical impedance, hand-grip strength, Mini-Mental State Examination (MMSE), Short Portable Mental Status Questionnaire (SPMSQ), and Trail-Making Test (TMT) A and B were collected at baseline and after weight loss.

Results: At baseline, older participants showed a nonsignificant trend for lower global cognitive function (MMSE, SPMSQ) and significantly slower processing speed (TMT-A). Twenty-one participants completed the weight loss study. The average weight loss relative to baseline was 9.7% ± 2.1%. Weight loss was associated with significant improvements in hand-grip strength and cognitive function (MMSE, TMT-A, and TMT-B). MMSE scores improved significantly only in older obese participants ($p < 0.05$).

Conclusions: Weight loss in middle-aged and in older obese participants has a beneficial effect on cognitive and physical function. If confirmed in future trials, weight loss can significantly affect public health strategies for the prevention of dementia as well as on the clinical management of obesity.

INTRODUCTION

Obesity in the aging population is becoming a significant public health problem, with more than 25% of individuals aged 60 years and older in the United States and United Kingdom classified as obese [1,2]. A direct association between obesity and dementia has been reported in cross-sectional and large population-based cohorts [3–7]. Middle-aged obese participants are reported to have a 74% higher risk for dementia in later life compared with normal weight participants [8]. The risk cumulatively increases if obesity is complicated by the presence of metabolic comorbidities such as diabetes, dyslipidemia, or hypertension [9].

Weight loss in older obese adults has beneficial effects on physical and metabolic and cardiovascular functions, but whether the same effects can be observed on cognitive performance and dementia risk is not known [10–12]. However, it is predicted that interventions aimed at improving risk behaviors, including obesity, diabetes, physical inactivity, and poor diet as well as interventions to improve crystallized

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Conflicts of interest: None to declare.

Journal of the American College of Nutrition, Vol. 31, No. 2, 000–000 (2012)
Published by the American College of Nutrition

intelligence could significantly reduce the incidence of dementia [13]. Indeed, a 5% decline in obesity in Australia has been estimated to result in a 6% reduction in dementia prevalence by 2051 [14]. The investment of resources into targeted, multilateral interventions for the primary and secondary prevention of obesity could be an effective and resourceful public health initiative aimed at reducing dementia risk as well as cardiovascular morbidity and mortality.

One possible mechanism by which reducing obesity may decrease an individual's risk of dementia could be through improvements in cognitive function. Higher cognitive reserve, either through increased education or baseline cognitive functioning, has been associated with reduced dementia risk, a result thought to be linked to an increased reliance to neuropathological changes associated with dementia that can occur with aging [15]. Therefore, in this study, we undertook a pilot project to investigate whether a standardized amount of intentional weight loss (~10%) affects cognitive function in middle-aged and older obese participants attending a weight loss clinic. We first tested whether cognitive function was inversely associated with adiposity and then tested whether losing adiposity improved cognitive function. The effect of weight loss on physical (hand-grip strength) functioning was also investigated.

METHODS

The study was conducted at the weight loss clinic of the Department of Nutrition and Dietetic of the University of Naples "Federico II." The study was approved by the Research and Ethics Committee of the Medical School of the University of Naples Federico II.

Fifty male and female nonsmoking, adult obese (body mass index [BMI] 30–50 kg/m^2) participants attending the clinic between January and December 2010 were invited to participate and signed a written consent before being enrolled in the study. Age ranged from 30 to 59 years for the middle-aged group and ≥60 years for older participants. Participants were weight stable (weight change <2 kg in the past month) and were excluded if they were diabetic, were pregnant or breastfeeding, had an excessive alcohol intake, had psychiatric or neurological disorders interfering with metabolic and cognitive functions, had a Mini-Mental State Examination (MMSE) score less than 20, or had a history of cancer, anemia, coronary artery disease, kidney failure, or any other medical condition that may have interfered with the primary outcomes. Participants with a diagnosis of hypertension or thyroid disorders were included if pharmacologic doses had remained stable within the past 6 months. Participants working night shifts and taking medications that could interfere with metabolic and cognitive functions (for example, weight loss drugs, insulin, oral hypoglycemic agents, steroids, sedatives, beta-blockers, antidepressants, and drugs with sympathomimetic effects) were also excluded.

Eligible participants were invited to return after 1 week for the baseline assessment of cognitive function and were asked to refrain from any caffeinated drink before the visit. They were reminded to do the same at each monthly follow-up appointment. Participants met with the dietitian to discuss the personalized weight loss plan after the assessment of cognitive function was completed. Participants were asked to return monthly for the measurement of their body weight and review of their dietary plan. Baseline measurements of cognition, psychiatric, and physical functioning were repeated after participants had lost between 8% and 12% of their original baseline body weight. Two participants missed their follow-up appointments when they were close to the 10% loss, and when they returned to the clinic they had lost 13.5% and 16.7% of their body weight. The exclusion of these 2 participants did not change the results, and therefore they were included in the final analysis.

Anthropometry and Body Composition

Body weight and height were measured to the nearest 0.1 kg and 0.1 cm, respectively. Waist and hip circumferences were measured in triplicate according to standardized protocols [16]. Tetrapolar bioelectrical impedance was used to measure fat mass (FM), and fat-free mass (FFM) according to the manufacturer's instructions. FM and FFM were adjusted for height squared [17].

Dietary Intervention

Resting energy expenditure (REE) was calculated using the World Health Organization prediction equation [18], and total energy expenditure was calculated by multiplying the estimated REE for a physical activity level of 1.6, which is representative of the average daily level of activity within the normal population [19]. Energy intake was then reduced by 40% relative to the predicted TEE. The average energy intake (percentage macronutrient composition) was 1616 ± 262 kcal/d (fat = 25% ± 1%; carbohydrate = 535 ± 1%; protein = 22% ± 1%) for middle-aged participants and 1397 ± 124 kcal/d (fat = 25% ± 1%; carbohydrate = 53% ± 1%; protein = 22% ± 1%) for older-aged obese participants. The minimal amount of energy intake was 1200 kcal/d to ensure an adequate daily intake of vitamins and minerals. The dietitian individually met with each patient during the follow-up visits to assess compliance and discuss potential problems. At each follow-up visit, participants were reminded to maintain their habitual physical activity level.

Hand-Grip Strength

Hand-grip strength was measured on the dominant hand to the nearest kilogram using a hand dynamometer (Lafayette

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Instrument 78010) at baseline and after weight loss. During the measurement, the participant was in an upright position and the arm of the measured hand was unsupported and parallel to the body. The width of the dynamometer's handle was adjusted to the participants' hand size, and then participants were instructed to exert maximal force. Three measurements were performed, and the average of recorded measurements was used in the analysis.

Cognitive Function

Evaluation of cognitive abilities was performed in the following domains: global cognition, memory, executive functions, and speed of processing. Global cognitive function was measured using the MMSE [20,21] (validated for use in Italy) and the Short Portable Mental Status Questionnaire (SPMSQ) [22]. The SPMSQ includes 10 items. Wrong answers receive 1 point; possible scores range from 0 to 10. A score of 8–10 indicates severe intellectual impairment, whereas scores of 5–7 and 3–4 show that the examined subject has a moderate or a mild intellectual impairment, respectively. A score of 0–2 indicates intact functioning [22].

The Trail-Making Test (TMT) provides information on visual search, scanning, speed of processing, mental flexibility, and executive functions [23,24]. The TMT consists of 2 parts: A and B. TMT-A requires an individual to draw lines sequentially connecting 25 encircled numbers distributed on a sheet of paper. Task requirements are similar for TMT-B, except the person has to alternate between numbers and letters (e.g., 1, A, 2, B, 3, C, etc.). The score on each part represents the amount of time required to complete the task [23].

Statistical Analysis

Nonparametric tests were used to analyze the data. The analysis was conducted on all of the participants recruited at baseline (cross-sectional) and on the completers achieving the target weight loss (longitudinal). The Mann-Whitney *U*-test was used to detect differences between middle-aged and older obese participants. The Spearman-Rank correlation was used to assess the strength of the association between variables. The Wilcoxon signed-rank test was used to assess whether changes in the outcomes of interest were statistically significant after weight loss. In the absence of a control group, we have used age- and education-adjusted normative scores for the MMSE [25], TMT-A [26], and TMT-B [26] to evaluate the relative deviation of the cognitive measures from the normative scores assessed at baseline and after weight loss. The Wilcoxon signed-rank test was used to assess changes in the relative deviations after weight loss in the entire sample and after stratification by age (middle age, older). The significance level (α) was set at 0.05. With an $\alpha = 0.05$ and $1 - \beta = 0.80$, an effect of 0.63 SD from a given mean is detected by a sample size of at least 20 participants, whereas a significant effect of 1 SD from a given mean is detected by a sample size of at least 8 participants. The statistical analyses were carried out using SPSS 16 for Windows (SPSS Inc., Chicago, IL).

Table 1. Differences between Completers and Noncompleters*

		n	Mean	SD
Age (years)	Noncompleters	29	55.5	11.0
	Completers	21	56.9	9.7
Weight (kg)	Noncompleters	29	95.0	18.3
	Completers	21	92.6	16.5
Height (cm)	Noncompleters	29	160.3	8.2
	Completers	21	159.4	10.1
Waist circumference (cm)	Noncompleters	29	113.1	19.5
	Completers	21	111.6	12.6
Hip circumference (cm)	Noncompleters	29	118.3	11.1
	Completers	21	112.6	8.9
Hand-grip strength (kg)	Noncompleters	29	26.0	7.0
	Completers	21	28.2	11.4
Fat mass (kg)	Noncompleters	29	39.9	9.8
	Completers	21	39.0	11.2
Fat-free mass (kg)	Noncompleters	29	55.0	12.6
	Completers	21	55.0	13.9
BMI (kg/m^2)	Noncompleters	29	36.8	5.8
	Completers	21	36.7	5.8
SQSM	Noncompleters	29	.55	.73
	Completers	21	.90	.83
MMSE	Noncompleters	29	27.4	2.6
	Completers	21	28.6	1.4
TRAIL A	Noncompleters	29	50.6	25.0
	Completers	21	55.2	27.5
TRAIL B	Noncompleters	29	103.5	37.4
	Completers	21	114.4	32.5

* All differences were statistically not significant ($p > 0.05$) using the Mann-Whitney *U* test.

RESULTS

Fifty participants were recruited, and of these, 20 achieved the target weight loss and completed set of repeated measurements. Completers were not significantly different from noncompleters for age, education, gender, body composition, hand-grip strength, or measures of cognitive function (Tables 1 and 2).

Cross-Sectional Analysis

The middle-aged (n = 24; M/F = 8/16) and older groups (n = 26; M/F = 3/23) were not different for gender, education, BMI, waist circumference, hip circumference, skinfold thickness, or FM. Older participants had a lower FFM (absolute and height-adjusted) than the younger group did. This difference was reflected in lower hand-grip strength by about 30%, which was still significant when the analysis was adjusted for gender. Older participants showed a nonsignificant trend for lower global cognitive function (MMSE, SPMSQ), and they had a

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Table 2. Differences between Completers and Noncompleters for Gender and Education

	Gender (χ^2 test: $p = 0.66$)				Education (χ^2 test: $p = 0.33$)				
	Female	Male	Total		Degree	High School	Primary	Secondary	Total
Noncompleters	22	7	29	Noncompleters	6	9	4	10	29
Completers	17	4	21	Completers	4	8	3	6	21
Total	39	11	50	Total	10	17	7	16	50

significant slower processing speed on the TMT-A but not on the TMT-B (Table 3).

FFM, waist circumference, and physical function were directly associated with global cognitive function (MMSE). The significant association of waist circumference disappeared when the analysis was adjusted for FFM. Hand-grip strength was significantly associated with better processing speed at the TMT-A (Table 4).

Longitudinal

The average weight loss relative to baseline was 9.7% ± 2.1%, and the average duration to achieve this weight loss was 116.6 ± 27 days. Duration interacted with age as older participants needed on average 20 additional days to lose the same amount of body weight compared with middle-aged obese participants. In the entire sample, weight loss induced significant changes in body composition, and FFM accounted for only 18.2% ± 23% of the total change in body mass, indicating that the vast majority of weight loss was fat loss.

Middle-aged and older obese participants showed similar changes in body composition after weight loss. However, FFM loss was marginally greater in older participants as FFM contributed to 20% ± 21% and 16% ± 23% of total body mass change in older and middle-aged participants, respectively. However, this greater loss did not affect the efficiency of muscular function, as a greater (+2.2 ± 3.5 kg, $p = 0.05$) increase in hand-grip strength was observed in the older participants compared with middle-aged participants (+0.7 ± 2.8 kg, $p = 0.52$; Table 5).

Global cognitive performance on the MMSE improved significantly only in older obese participants, whereas both groups showed a significant improvement of speed processing, as assessed by the TMT-B (Table 5).

The MMSE, TMT-A, and TMT-B cognitive scores measured at baseline and after weight loss were compared with age- and education-adjusted normative scores. MMSE and TMT-B scores improved significantly after weight loss in older obese participants, whereas the middle-aged group showed a generalized improvement in speed processing (TMT-A and B; Fig. 1).

Table 3. Baseline Characteristics of Middle-Aged and Older Obese Participants Enrolled in the Study*

	Middle-Aged	Older Aged	*p* Value
N	24	26	
M/F	8/16	3/23	NS
Age (years)	47.1 (6.9)	64.5 (4.1)	<0.001
Education			
Primary	2	5	NS
Secondary	7	10	
High school	10	7	
Degree	5	4	
Weight (kg)	100.0 (17.9)	88.4 (15.3)	<0.05
Height (cm)	163.8 (8.3)	156.4 (8.2)	<0.01
BMI (kg/m^2)	37.0 (5.7)	36.1 (5.4)	NS
Waist circumference (cm)	111.0 (14.7)	113.9 (18.7)	NS
Hip circumference (cm)	118.0 (12.0)	114.1 (8.7)	NS
Skinfold triceps (mm)	29.4 (10.6)	29.7 (8.6)	NS
Fat mass (kg)	38.1 (9.1)	40.1 (10.3)	NS
Fat mass index (kg/m^2)	14.3 (3.8)	16.4 (4.2)	NS
Fat-free mass (kg)	61.8 (13.8)	48.3 (8.0)	<0.001
Fat-free mass index (kg/m^2)	22.8 (4.0)	19.6 (2.1)	<0.001
Total body weight (kg)	45.2 (10.1)	38.0 (6.4)	<0.01
Hand-grip strength (kg)	31.4 (9.7)	21.4 (5.4)	<0.001
SPMSQ	0.67 (0.70)	0.54 (0.70)	NS
MMSE	28.33 (2.0)	27.5 (2.4)	NS
TMT-A	44.0 (21.3)	59.2 (28.1)	<0.05
TMT-B	104.1 (34.0)	110.3 (38.4)	NS

* Data are shown as mean (SD). M = male, F = female, BMI = body mass index, SPMSQ = Short Portable Mental Status Questionnaire, MMSE = Mini Mental State Examination, TMT = Trail-Making Test, NS = not significant. The Mann-Whitney *U* test was used to detect differences between the 2 groups.

Table 4. Correlation between Measures of Cognition with Body Composition and Hand-Grip Strength in the Entire Sample (n = 50)*

	SPMSQ	MMSE	TMT-A	TMT-B
Age (years)	−0.12	−0.10	0.34[a]	0.13
BMI (kg/m^2)	0.02	0.22	−0.01	−0.12
Waist circumference (cm)	0.04	0.28[a]	0.03	−0.20
Hip circumference (cm)	−0.21	0.11	−0.03	−0.19
Skinfold triceps (mm)	−0.11	−0.09	0.06	0.009
Fat mass index (kg/m^2)	−0.02	0.07	0.13	−0.01
Fat-free mass index (kg/m^2)	−0.06	0.36[b]	−0.22	−0.21
Hand-grip strength (kg)	0.11	0.31[a]	−0.32[a]	−0.13

* Significant results are shown in bold. BMI = body mass index, SPMSQ = Short Portable Mental Status Questionnaire, MMSE = Mini Mental State Examination, TMT = Trail-Making Test. Spearman-rank correlation was used to assess the strength of the association between variables.
[a] $p < 0.05$; [b] $p < 0.01$; [c] $p < 0.001$.

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Table 5. Effects of Weight Loss on Body Composition and Physical and Cognitive Functions in Middle-Aged and Older Obese Participants*

	All (n = 21)			Middle-Aged (n = 9)			Older Aged (n = 12)		
	Baseline	Post-WL	Δ	Baseline	Post-WL	Δ	Baseline	Post-WL	Δ
Age (years)	56.9 (9.7)	—	—	47.8 (7.5)	—	—	63.7 (3.5)	—	—
M/F	4/17	—	—	4/5	—	—	0/12	—	—
Education									
Primary	3	—	—	2	—	—	1	—	—
Secondary	6			2			4		
High school	8			4			4		
Degree	4			1			3		
Number of days on WL treatment	115.5 (27.2)	—	—	102.5 (15.5)	—	—	122.5 (30.5)	—	—
Weight (kg)	92.6 (16.5)	83.6 (14.9)	−9.0 (2.7)[c]	99.3 (15.5)	89.5 (14.3)	−9.8 (2.4)[b]	87.6 (16.1)	79.2 (14.2)	−8.4 (3.0)[b]
BMI (kg/m^2)	36.4 (5.7)	32.9 (5.3)	−3.5 (0.9)[c]	36.4 (4.2)	32.9 (4.3)	−3.5 (0.42)[b]	35.9 (6.0)	32.4 (5.4)	−3.5 (1.2)[b]
Waist circumference (cm)	111.6 (12.6)	102.2 (12.3)	−9.4 (4.5)[c]	112.0 (10.3)	102.0 (10.8)	−10.0 (3.7)[b]	111.4 (14.6)	102.4 (13.8)	−9.0 (5.2)[b]
Hip circumference (cm)	112.6 (8.9)	107.9 (9.5)	−4.7 (4.9)[b]	113.6 (8.7)	109.0 (8.8)	−4.6 (2.8)[b]	112.0 (9.3)	107.1 (10.4)	−4.8 (6.1)[a]
Skinfold triceps (mm)	28.1 (10.8)	24.1 (8.7)	−3.9 (3.7)[b]	24.3 (12.7)	22.6 (10.1)	−1.7 (3.2)	30.9 (8.6)	25.3 (7.8)	−5.6 (3.3)[b]
Fat mass (kg)	38.1 (9.7)	30.6 (10.0)	−7.5 (3.4)[c]	35.7 (8.1)	27.3 (9.8)	−8.4 (3.8)[b]	39.9 (10.7)	33.2 (9.8)	−6.7 (3.0)[b]
Fat mass index (kg/m^2)	15.1 (4.3)	12.3 (4.4)	−2.8 (1.1)[c]	13.5 (3.9)	10.5 (4.5)	−3.0 (0.9)[b]	16.3 (4.3)	13.6 (4.0)	−2.7 (1.2)[a]
Fat-free mass (kg)	54.5 (13.8)	52.9 (14.0)	−1.5 (2.0)[b]	63.6 (15.9)	62.2 (16.1)	−1.4 (2.3)	47.6 (6.9)	46.0 (5.8)	−1.7 (1.8)[a]
Fat-free mass index (kg/m^2)	21.2 (3.9)	20.5 (3.7)	−0.7 (0.8)[b]	23.4 (4.5)	22.9 (4.4)	−0.5 (0.9)	19.5 (2.3)	18.7 (1.7)	−0.8 (0.7)[a]
Hand-grip strength (kg)	28.2 (11.4)	29.8 (9.8)	+1.6 (3.2)[a]	35.6 (12.2)	36.3 (10.6)	+0.7 (2.8)	22.6 (7.2)	24.9 (5.8)	+2.2 (3.5)
SPMSQ	0.90 (0.83)	0.38 (0.86)	−0.5 (0.9)[a]	1.1 (0.7)	0.6 (1.1)	−0.4 (0.7)	0.8 (0.8)	0.1 (0.6)	−0.6 (1.1)
MMSE	28.6 (1.4)	29.5 (0.9)	+0.9 (1.2)[b]	28.8 (1.2)	29.6 (0.7)	+0.8 (1.3)	28.4 (1.7)	29.3 (1.0)	+0.9 (1.1)[a]
TMT-A	55.2 (27.5)	40.6 (15.2)	−14.6 (22.9)[b]	51.2 (24.8)	31.4 (9.1)	−19.7 (22.2)[a]	58.3 (30.1)	47.5 (15.4)	−10.8 (23.1)
TMT-B	114.4 (32.5)	86.2 (27.0)	− 28.1 (28.1)[b]	107.5 (28.8)	81.4 (23.8)	−26.1 (27.0)[a]	119.5 (35.3)	89.9 (29.7)	−29.6 (30.0)[a]

* Data are shown as mean (SD). Δ = mean change from baseline. Significant change relative to baseline: [a] $p < 0.05$; [b] $p < 0.01$; [c] $p < 0.001$. WL = weight loss, M = male, F = female, BMI = body mass index, SPMSQ = Short Portable Mental Status Questionnaire, MMSE = Mini Mental State Examination, TMT = Trail-Making Test. Wilcoxon signed-rank test was used to test changes from baseline.

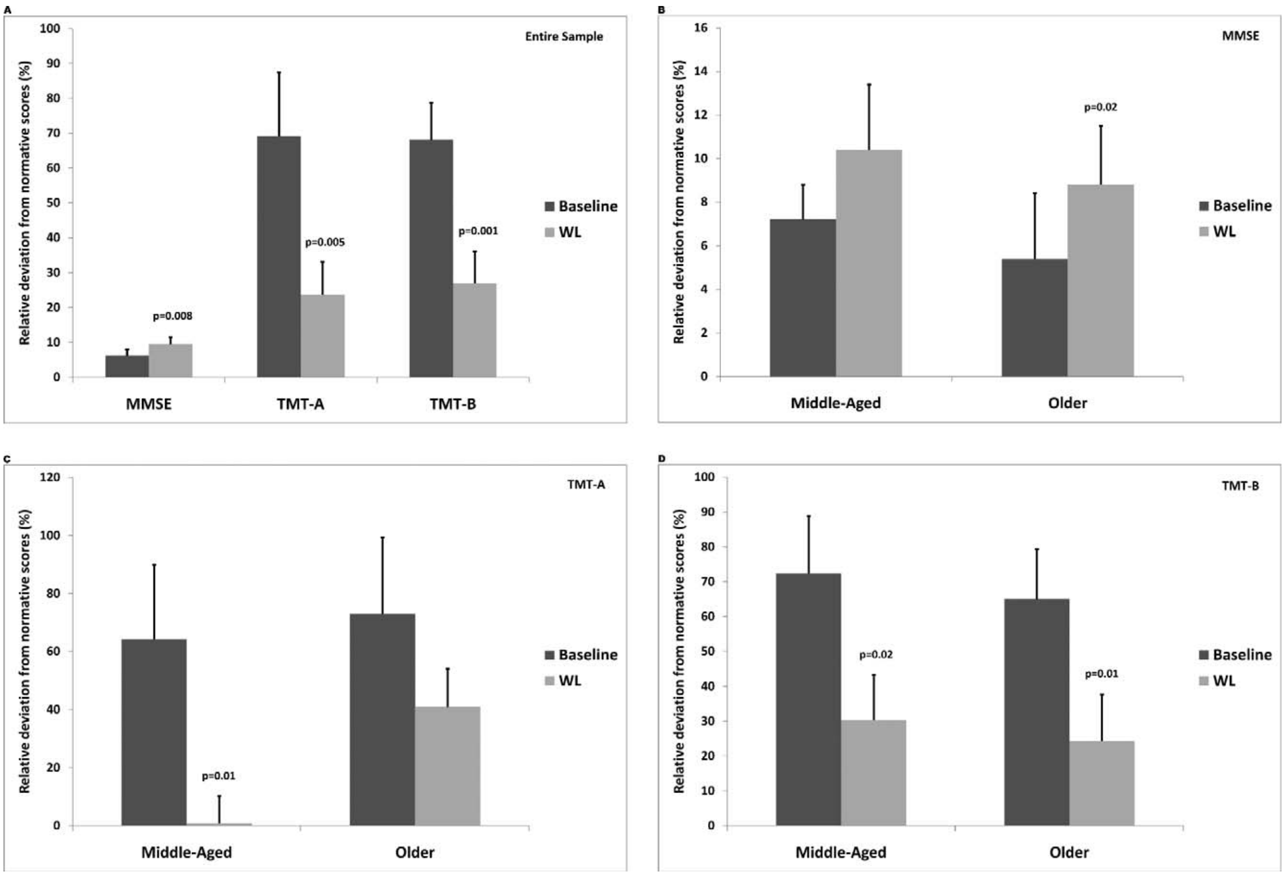

Fig. 1. Mean relative deviation from normative scores (adjusted for age and education) at baseline and after weight loss (WL) in the entire sample (A) and in middle-aged and older participants for the MMSE (B), TMT-A (C), and TMT-B (D). The Wilcoxon signed-rank test has been used to compare the baseline to WL values. Error bars are SE. Higher values are associated with improvements in MMSE scores. Lower values correspond with improvements in TMT-A and TMT-B scores.

DISCUSSION

The primary objective of this pilot study was to test the effectiveness of weight loss on cognitive function in obese middle-aged and older-aged patients attending a weight loss clinic. We report for the first time a putative beneficial effect of a standardized amount of intentional weight loss on cognitive function in middle-aged adults and older-aged obese participants. Weight loss was also found to be associated with potential improvements in physical and psychiatric functioning. All of these effects need to be confirmed in larger, more controlled weight loss interventions.

Weight loss in older obese populations is contentious [27,28], but accruing evidence from clinical investigations suggests that weight loss is associated with improvements in quality of life, frailty, and metabolic and cardiovascular functions [29–31]. Modest weight loss ($\sim$10%) is associated with changes in insulin resistance and vascular reactivity and reduction of the risk for cardiovascular and metabolic diseases [32–37]. Greater insulin resistance was associated with an Alzheimer disease (AD)–like pattern of reduced cerebral glucose metabolic rate measured by positron emission tomography in adults with prediabetes and newly diagnosed type 2 diabetics [38]. These results suggest that lifestyle modifications such as weight loss or physical exercise may be effective therapeutic strategies to prevent AD [11] because of the recognized effects on insulin sensitivity [39] and endothelial function [36,40].

A recent meta-analysis conducted by our group has shown a low-order significant effect of intentional weight loss on executive function and memory in obese participants but not in overweight participants. The meta-analysis identified several research gaps that pointed toward a lack of nutritional interventions testing the effects of weight loss in older participants [41]. To date, only 1 study has attempted to evaluate the effects of intentional weight loss in older overweight and obese participants. The study reported the positive effects of a 30% caloric restriction (weight loss of 2.4 kg after 3 months) on memory and executive functions assessed using the Rey Auditory Verbal Learning Task and the TMT [42]. Although the average age of the population was 60.5 years, the sample included participants younger than 60 years (age range, 50–80

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years), which may limit the generalizability of the results to a geriatric population [42]. A weight loss study achieving a similar amount of weight loss (7.7%) in middle-aged obese participants used the TMT-B to test the effects of weight loss on cognition [43] and amount of weight loss. The study observed a decrease in processing speed on the TMT-B of 27 seconds in 1 of the 2 groups, which is similar to the decrease recorded in this study [43]. A large randomized clinical trial investigated the effects of weight loss plus exercise on cognition in overweight and obese hypertensive middle-aged participants [44]. The study showed that the combined intervention was associated with greater improvements in cognition (memory and executive functions) compared with exercise alone [44]. Positive effects of weight loss on cognition were also observed in 109 middle-aged obese participants undergoing bariatric surgery. Obese participants reported significant improvements in memory and concentration 12 weeks after the operation and after losing 17% of their initial body weight [45].

This study has demonstrated that the modest 10% weight loss was associated with significant effects on psychological, physical, and cognitive functions. If confirmed in future studies, these results may inform current guidelines on obesity management in older participants supported by the improvement of quality of life, psychological functioning, and physical performance as well as by a reduction of the risk for cognitive decline associated with excess body weight. However, this study did not investigate whether further functional improvements may be achieved with extra weight loss or whether the positive effects would be maintained during either weight maintenance or weight regain. Also, we do not know whether these effects were due to metabolic consequences of loss of fat mass, persisting effects of the metabolism occurring during fat oxidation, or changes in self-esteem or reduced depression.

The limitations of this study are intrinsic to its pilot nature, which is reflected in the small sample size. The lack of a control group could be considered as another potential methodological drawback, but we argue that a weight maintenance group in the context of a weight loss clinic is a complicated issue. In addition, the comparison of the cognitive measures to normative cognitive scores varying for age and education could provide further support for the independent effects of weight loss on cognitive function. The clinical relevance of moderate weight loss in obese older participants can be clearly associated with a decrease in the risk-benefit ratio. This study had a high dropout rate. However, completers were not overall significantly different from noncompleters, and the middle-aged and older groups were matched at baseline for body composition and physical and cognitive functions. A larger dropout of male subjects was observed, as none were present in the older group, but gender differences in body composition and metabolic responses to weight loss may be minimized in older subjects. Nevertheless, the main limitation is that we cannot conclude that this effect was generated biologically.

This pilot study has confirmed in a clinical setting and in older obese participants the results reported in previous weight loss dietary interventions and bariatric surgery studies in younger participants [41,45]. A modest amount of weight loss using a hypocaloric, low-fat diet with an adequate protein intake results in beneficial effects on FFM, physical function, and cognition in both middle-aged and older obese participants. If confirmed in future trials, the effects can have a significant impact on public health strategies for the prevention of dementia as well as on the clinical management of obesity by assessing cognitive function alongside metabolic and cardiovascular functions as part of the diagnostic and follow-up plans of weight loss treatments.

ACKNOWLEDGMENT

We thank Dr. Emiliano Albanese for the useful comments on the manuscript.

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Received August 31, 2011; revision accepted November 11, 2011.