Correlating cognitive and executive functions to BMI

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Objective
Cognitive and executive dysfunction is related to BMI. The present study seeks to correlate cognitive functions to BMI.
Participants and methods
An observational study included 60 patients who underwent laboratory and clinical evaluation including BMI and a series of psychometric tests, a standardized mini-mental state examination, the Wechsler adult intelligence scale, and the Wisconsin card sorting test.
Results
BMI has stronger significant inverse correlation to performance intelligence quotient than the significant inverse correlation to verbal and total intelligence quotient. Also, BMI has significant inverse correlation to executive functions.
Discussion
Our results indicate that higher BMI is correlated to lower cognitive and executive functions. Patients with obesity had low scores on general intelligence and executive functions, particularly abstraction ability and the ability to shift cognitive strategies in response to a changing environment. Future research should incorporate brain imaging techniques to further elucidate the effects of obesity on cognition.

Keywords:
body mass index, cognitive dysfunction, cognitive profile, executive functions, uncomplicated obesity

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Introduction

The health consequences of high BMI extend to cognitive function. High BMI can disturb planning functions, problem solving, mental flexibility, and inhibitory processes; these findings reflect alterations in the frontal lobe (Fagundo *et al.*, 2012). A recent study by Kittel *et al.* (2017) studied the executive functions in adolescents with high BMI and binge eating disorders. The authors concluded that adolescents with binge eating disorders and high BMI displayed significantly poorer inhibitory control than normal-weight adolescents.

Possible pathways linking high BMI and cognitive deficit may be metabolic imbalance, clinically silent stroke, atherosclerotic changes, altered distribution of cerebral blood flow, demyelination, or microinfarction in the cerebral white matter (Elias *et al.*, 2001). It is also important to consider that the relationship between high BMI and cognition may have a reverse direction such that specific cognitive attributes increase the risk of obesity (Cortese and Castellanos, 2014).

There is increasing evidence for the role of inflammatory process, an important characteristic of obesity. Recent clinical findings indicate that increased systemic expression of inflammatory markers (e.g. cytokines) in individuals with obesity correlates with neuropsychiatric status, specifically, mood, and cognitive function (Castanon *et al.*, 2014).

Consistent with this last point, inflammatory factors can induce the synthesis of the enzymes indoleamine 2,3-dioxygenase in monocytes/macrophages and dendritic cells. This hinders the biosynthesis of key monoamines (e.g. serotonin, dopamine) known to play a major role in mood regulation and cognitive function (Raison *et al.*, 2010).

In sum, previous studies on cognitive function in individuals with obesity suggest that cognitive dysfunction might be pronounced in such individuals (Gunstad *et al.*, 2006; Fitzpatrick *et al.*, 2013; Gaillard, 2015; Santangeli *et al.*, 2015; Cheke *et al.*, 2016). However, results are often mixed. These mixed findings may be explained by Prickett *et al.* (2015), who identified five design considerations for studies linking obesity and cognition: control of confounders (e.g. age, education); appropriate study design (e.g. appropriate exclusion criteria and adequate sample size); appropriate control groups; assessment of cognitive functions relevant to the specific research question; and valid, reliable psychometric tools for assessment of cognition. Most of these design features have been incorporated in the current study.

This study uses a series of established neuropsychological tests to investigate the interplay of obesity and cognitive function in Egyptian individuals with obesity. We hypothesized that patients with uncomplicated obesity would demonstrate greater difficulties with cognitive function (general intelligence, concentration, abstract thinking, strategic planning, the ability to use environmental feedback to shift cognitive sets, and visuomotor coordination) than normal-weight controls. Furthermore, we hypothesized that the more severe the uncomplicated obesity, the more intensely the cognitive function would be affected.

Participants and methods

Design observational design

Ethical approval of the research protocol was obtained by the authority of Ain Shams University Ethics and Research Committee. The researchers explained the details of the research goals to the participants, ensured that the obtained data would be confidential, and informed participants that they could withdraw from the study at any time. Those who refused to participate were excluded. Then, a written informed consent was sought from all participants. The recruitment continued until 30 uncomplicated obese individuals and 30 matched healthy controls were enrolled. Subsequently, participants were asked to complete a series of neuropsychological tasks in a fixed order. The research was performed from April 2015 until the end of July 2016.

Participants and sample size

A total of 60 individuals were calculated using Epi-Info (centers for disease control and prevention, Atlanta Georgia USA SPSS 22, International Business machines corporation IBM, New York, USA) program version 6 assuming: 95% confidence interval, 80% power of the test. Accordingly, the following equation was used:

$$n=(z/e)^2\ (p)\ (1-p)$$

where n is the sample size, P the expected prevalence, z the critical value of 1.96, and e is the margin of sample error tolerated, which is 0.05.

The expected prevalence according to Yaffe *et al.* (2009) is 4.1%. Therefore, the sample size was calculated to be 60.

Sample selection

Inclusion criteria

A convenient sample was collected from patients who visited the outpatient eating clinic of the Institute of Internal Medicine at Ain Shams University twice weekly for 4 months and were enrolled in the study. The institute is located in eastern Cairo and serves about a third of greater Cairo. It serves both urban and rural areas, including areas around greater Cairo. Age of the patients was between 30 and 50 years, normal or corrected-to-normal vision, and sufficient Arabic language skills.

Exclusion criteria

Participants who come under the following were excluded:

(1) Significant medical conditions (e.g. cardiovascular or metabolic diseases, including type 2 diabetes) were excluded; they were identified through a standardized medical screening questionnaire, laboratory investigations (fasting blood glucose and fasting lipid profile), and radiological investigations (duplex on carotid arteries to exclude atherosclerotic changes);
(2) Neurological or other psychiatric conditions, the current use of medications (e.g. anticholinergic agents, anticonvulsants, antiparkinsonian agents, antihypertensive/cardiac medications, corticosteroids, narcotic analgesics) and/or substances known to alter mood, reaction time, or cognitive capacity, including smoking, alcohol consumption ($\geq$50 g/week), and recreational drug use. Exclusion of psychiatric disorders was done using the Arabic version of GHQ (Thabet and Vostanis, 2005) (Goldberg and Williams, 1978).
(3) Patients with vision, hearing, or motor coordination problems that could impair the ability to complete the computerized version of cognitive function testing.

Procedures

Anthropometric measurements were taken. Height was measured to the nearest 0.1 cm with a stadiometer; weight was recorded on a digital platform scale accurate to 0.1 kg [BMI=weight (kg)/ height (m^2)) (Dorian, 2010). Obesity was diagnosed according to the WHO guidelines (WHO, 2015) (BMI $\geq$30.0 kg/m^{-2}).

Cognitive dysfunction was diagnosed using the Wechsler adult intelligence scale (WAIS) and the Wisconsin card sorting test (WCST). Cognitive performance was measured by a standardized mini-mental state examination (SMMSE).

Standardized mini-mental state examination (Molloy et al., 1991).

The SMMSE is a clinical assessment tool which is used as a screening test for cognitive impairment. It consists of 12 items or questions which cover a range of cognitive domains. Each item has a maximum score. The test items have limits of allowable score values. The scores are summed for the 12 items and can range from a minimum of 0 to a maximum of 30. Interpretation of results include four possibilities: normal cognition (25–30 points), mild cognitive impairment (19–24 points), moderate cognitive impairment (10–18 points), and severe cognitive impairment (≤9 points).

Wechsler adult intelligence scale (Wechsler, 1981)

The WAIS is the most commonly administered general intelligence test for adults and is also viewed as a broad assessment of cognitive function. It is an individually administered measure of intelligence, intended for adults aged 16–89 years. It is the most widely used intelligence test in clinical practice and is intended to measure human intelligence in both verbal and performance abilities.

Wisconsin card sorting test, computerized version (Heaton et al., 2003)

The WCST was developed to assess abstraction ability and the ability to shift cognitive strategies in response to changing environmental contingencies. It is considered a measure of executive function that requires strategic planning, organized searching, the ability to use environmental feedback to shift cognitive sets, goal-oriented behavior, and the ability to modulate impulsive responding. It provides information on several aspects of problem-solving behavior beyond basic indices of task success or failure, such as the number of perseverative errors, the failure to maintain set, and the number of categories achieved.

Data analysis plan

Data analysis was performed using the Statistical Package for Social Sciences Version-22 (SPSS-22). Student's *t*-test was used to determine the significance of an independent variable if there were only two values of this variable (to compare between independent means). Pearson's χ^2 was used for comparison between qualitative variables. The correlation coefficient (*r*) was used to measures the strength and direction of a linear relationship between two variables on a scatterplot. The *P* value was used to indicate the level of significance, where *P* less than or equal to 0.05 is considered significant; *P* less than or equal to 0.01 is highly significant; *P* less than or equal to 0.001 is very highly significant.

Results

Sociodemographic assessment

Obese individuals were of highly significant older age than the nonobese (P=0.009) and had significant higher rates of marital status (P=0.04). There were no significant differences in sex (P=0.20) between the obese and the nonobese (Table 1).

Cognitive and executives domains

(1) Cognitive performance (SMMSE) showed no significant difference between obese and nonobese individuals, indicating that obese individuals had no impaired general cognitive performance (Table 1).
(2) Cognitive and executive functions (WAIS and WCST) showed highly significant lower scores of the obese compared with the nonobese in all parameters, except for the similarities domain (Table 1).
(3) Significant inverse correlations were found between BMI and all parameters of executive functions and cognitive function except verbal intelligence quotient (IQ) (P>0.05) (Table 2).
(4) Picture completion showed the strongest inverse correlation with BMI (−0.53), followed by performance IQ (−0.49), total IQ (−0.42), conceptual level responses (−0.41), categories completed (−0.31), preservative responses (−0.38), arithmetic (−0.38), digital span (−0.33), comprehensive (−0.31), coding (−0.30), block design (−0.29), and similarities (−0.25) (Table 2).

Discussion

Obesity is a risk factor for lowered cognitive function in obese individuals without clinically diagnosed stroke and dementia. Obesity is associated with cognitive dysfunction in adults, as shown by an increasingly large number of cross-sectional, case–control, longitudinal, and weight management intervention studies (Jartti *et al.*, 2009; Van den Berg *et al.*, 2009; Siervo *et al.*, 2011; Smith *et al.*, 2011; Fitzpatrick *et al.*, 2013; Prickett *et al.*, 2015).

Table 1 Demographic data, SMMSE, WAIS, and WCST of the obese and nonobese individuals

Variables	Obese (*n*=30) [mean ±SD or *n* (%)]	Nonobese (*n*=30) [mean ±SD or *n* (%)]	*t*	*P*
BMI (kg/m^2)	35.29±3.88	23.36±1.05	16.27	<**0.001****
Age (years)	39.57±6.25	35.2±6.32	**2.69**	**0.009****
Sex				
Male	22 (73.3)	26 (86.7)	1.67	0.20
Female	8 (26.7)	4 (13.3)		
Marital status				
Married	30 (100)	26 (86.7)	**4.29**	**0.04***
Unmarried	0	4 (13.3)		
SMMSE	28.8±1.28	29.68±0.83	1.18	0.12
VIQ	93.6±8.24	109.33±8.24	**7.39**	<**0.001****
Comprehensive	11.8±2.52	15.03±1.81	**5.70**	<**0.001****
Arithmetic	5.9±1.86	9.37±2.33	**6.37**	<**0.001****
Similarities	9.73±2.82	10.57±2.31	1.25	0.06
Digital span	5.6±1.31	9.23±2.06	**6.42**	<**0.001****
PIQ	94.13±9.58	104.6±11.64	**3.80**	<**0.001****
Picture completion	7.97±1.75	9.9±1.4	**4.73**	<**0.001****
Block design	7.27±1.98	9.73±2.05	**4.74**	<**0.001****
Coding	8.5±2.6	10.37±2.62	**2.77**	**00.007****
Total IQ	92.13±8.82	106.5±9.57	**6.04**	<**0.001****
Borderline IQ	2 (6.7)	0	χ^2	
Dull average	11 (36.7)	1 (3.3)	**22.33**	<**0.001****
Average	17 (56.7)	17 (56.7)		
Above average	0	10 (33.3)		
Superior	0	2 (6.7)		
WCST			χ^2	
No difficulties on concentration, abstract thinking, and visuomotor coordination	1 (3.3%)	26 (86.7%)	**42.09**	<**0.001****
Difficulties in concentration, abstract thinking, and visuomotor coordination	29 (96.7)	4 (13.3)		
Abnormal categories completed	28 (93.3)	3 (10)	**41.71**	<**0.001****
Normal categories completed	2 (6.7)	27 (90)		
No frontal lobe function difficulties	2 (6.7)	27 (90)	**41.71**	<**0.001****
Frontal lobe function difficulties	28 (93.3)	3 (10)		
			Mann–Whitney test	*P*
Perseverative responses	24.1±16.3	15.6±9.1	**311.5**	**0.04***
Conceptual level responses	39.1±13.7	72.6±13.8	**54**	<**0.001****
Categories completed	2.9±1.2	5.7±0.8	**56.5**	<**0.001****

IQ, intelligent quotient; PIQ, performance intelligence quotient; SMMSE, standardized mini-mental state examination; VIQ, verbal intelligence quotient; WCST, Wisconsin card sorting test; WAIS: Wechsler adult intelligence scale.

In keeping with previous limitations identified in studies investigating obesity and cognition (Crichton *et al.*, 2012), inconsistencies related to poor study design, small sample size, limited consideration of confounders, and the array of psychometric tests used make it difficult to compare studies (Cheke *et al.*, 2016).

In using the standardized mini-mental state examination to assess cognitive performance of both groups. No significant difference was found between obese individuals and nonobese controls. This was in accordance with previous studies that did not find any significant differences between groups (normal, overweight, and obese) on the MMSE. The MMSE was designed as a screening tool for dementia and is not sensitive to mild cognitive deficits, particularly attention and executive dysfunction. Accordingly, there appears to be no evidence to support impaired general cognitive performance in obese adults (Nichelli *et al.*, 1993).

In this study, IQ was assessed in the groups using the WAIS as a method of assessing general intelligence. We found a highly significant difference between obese individuals and nonobese controls in all parameters ($P<0.001$), except for the domain similarities, which had no difference ($P>0.05$). Intellectual function in obese adults was assessed in seven previous studies. Three studies utilizing data from the Danish draft board between 1956 and 1977 reported a significant

Table 2 Correlation of BMI to cognitive function parameters in individuals with obesity

Variables	BMI	
	r	*P* value
WAIS		
Total IQ	–0.42	0.02*
PIQ	–0.49	0.01*
Picture completion	–0.53	<0.001**
Block design	–0.29	0.04*
Coding	–0.30	0.03*
VIQ	–0.10	0.56
Comprehensive	–0.31	0.03*
Arithmetic	–0.38	0.02*
Similarities	–0.25	0.04*
Digital span	–0.33	0.03*
WCST		
Preservative responses<	–0.38	0.02*
Conceptual level responses	–0.41	0.02*
Categories completed	–0.31	0.03*

IQ, intelligence quotient; PIQ, performance intelligence quotient; *r*, correlation coefficient; VIQ, verbal intelligence quotient; WAIS, Wechsler adult intelligence scale; WCST, Wisconsin card sorting test.

relationship between intellectual function and obesity. Four studies, two of which utilized normative comparisons, found no significant differences in general intelligence between obese individuals and normative or control comparisons (Pignatti *et al.*, 2006). Our research is in keeping with the Danish studies.

The WCST is one of the most widely used psychological testing tools to assess executive functioning skills such as problem solving, decision making, inhibitory control, and working memory. Our assessment of study groups using the WCST showed that obese individuals had more perseverative responses and more conceptual level responses, required more trials to complete categories, and had more difficulties in concentration, abstract thinking, and visuomotor coordination. This shows that patients had impairment in nearly all aspects of executive functions. These results were in accordance with the results of Elias *et al.* (2003), who examined the effects of obesity on cognitive functioning in older adults without a history of clinical stroke, dementia, or cardiovascular disease. There was a significant multivariate effect of obesity for men, namely, after considering all the covariates in the model. Obese men performed more poorly on the Logical Memory Immediate Recall, Visual Reproductions, Digit Span Backward, Word Fluency, and Logical Memory Delayed Recall tests. A cross-sectional longitudinal study of more than 2000 middle-aged workers supported a linear association between BMI and cognitive function. The authors assessed the cognitive function using the word-list learning test, which evaluates verbal learning and memory, and the digit-symbol substitution test, which assesses attention, response speed, and visuomotor coordination. Individuals with obesity recalled fewer words in the word-list learning test and took longer to complete the digit-symbol substitution test relative to normal-weight individuals (Cournot *et al.*, 2006). Across studies, the different cognitive domains analyzed make it difficult to draw absolute comparisons, but impairment of specific cognitive domains such as executive function and short-term memory have been consistently identified in obese individuals when compared with normal-weight counterparts (Cournot *et al.*, 2006; Mond *et al.*, 2007; Lokken *et al.*, 2009).

In an attempt to determine a relationship between the severity of obesity and degree of cognitive impairment in obese individuals using WAIS and WCST, there was a positive correlation between BMI and all parameters of the WAIS except for verbal IQ. BMI positively correlated with perseverative responses, conceptual level responses, and categories completed, indicating that with increasing obesity there is more cognitive impairment. Other studies that assessed severity of obesity and degree of cognitive impairment support our findings in the following domains: intellectual functioning, psychomotor performance and speed, visual construction, concept formation and set shifting, and decision making. Limited evidence was available for the domain of time estimation. Available evidence was equivocal for a relationship between obesity and visual memory, verbal memory, complex attention, delay discounting, and inhibition. There was no evidence of deficits in areas of general cognitive performance, time judgment, working memory, and verbal fluency. While these results support the conclusions from a previous review that found consistent evidence that mid-life obesity was associated with impaired cognitive function, specifically in the area of executive functioning, it also provides evidence for a relationship between obesity and intellectual functioning, psychomotor performance and speed, and visual construction (Smith *et al.*, 2011).

There are a number of novel strengths in this study that support the reliability and validity of our findings. First, this research directly compared specific domains of cognitive function to enable more direct comparisons between studies, and we provide a more detailed reflection of how such methodological issues may influence interpretation of results. Second, since this paper specifically addressed mid-life, strict inclusion criteria were used to minimize variability in findings, which improves the quality of our results.

Our study is limited by its comparatively small sample size, which necessitates careful conclusions. Second, we did not include overweight adults, so we are unable to speculate on the cognitive performance of this group.

Future directions for research should take into consideration that, although the cross-sectional design of our study precludes causal relationships from being determined, our findings of reduced general intelligence and executive function in obese individuals deserve further examination via longitudinal research. Large epidemiological studies across the BMI spectrum and clinical trials examining the effect of acute and longer-term weight loss on the cognitive function of young adults with obesity are also warranted. Further, it would be interesting to speculate on possible mechanisms as to why obesity affects intellectual functioning.

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Conflicts of interest

There are no conflicts of interest.

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