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Obesity, Fitness, and Brain Integrity in Adolescence

Naima Ross¹, Po Lai Yau, PhD¹, and Antonio Convit, MD^{1,2,3,4}

¹ Department of Psychiatry, New York University School of Medicine, New York, New York.

² Departments of Medicine and Radiology, New York University School of Medicine, New York, New York.

³ Nathan Kline Institute for Psychiatric Research, Orangeburg, New York.

Abstract

Objective—We set out to ascertain the relationship between insulin resistance, fitness, and brain structure and function in adolescents.

Design and Methods—We studied 79 obese and 51 non-obese participants who were recruited from the community, all without type 2 diabetes mellitus. All participants received medical, endocrine, neuropsychological, and MRI evaluations as well as a 6-minute walk test that was used to estimate fitness (maximal oxygen consumption).

Results—Obese adolescents had significantly thinner orbitofrontal cortices and performed significantly worse on Visual Working Memory tasks and the Digit Vigilance task. Insulin sensitivity and maximal oxygen consumption (VO₂ max) were both highly correlated with central obesity and orbitofrontal cortical thickness, although insulin sensitivity was the stronger predictor for orbitofrontal cortical thickness. We also found that VO₂ max was the only significant physiological variable related to visual working memory.

Conclusions—This is the first study to report positive associations between insulin resistance, VO₂ max, and frontal lobe brain integrity in adolescents. Given the importance of brain health for learning and school performance, we conclude that schools should also emphasize physical fitness in order to maintain structural and functional brain integrity and facilitate academic achievement.

Keywords

Obesity; fitness; VO₂ max; adolescence; orbitofrontal cortex

⁴**Corresponding Author:** Antonio Convit, M.D. Brain, Obesity, and Diabetes Laboratory (BODYLab) New York University School of Medicine 145 East 32nd Street, 8th Floor, New York, NY 10016 212 263-7565 (phone), 212 263-4886 (fax) antonio.convit@med.nyu.edu.

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Author contributions:

Each author made substantial contributions to this manuscript. Dr. Convit designed, performed and supervised the study. Ms. Ross, Dr. Yau, and Dr. Convit acquired and analyzed the data. Ms. Ross drafted the manuscript, and Drs. Yau and Convit edited it. All authors have seen and approved of the final version of the manuscript.

Introduction

Childhood and adolescent obesity rates have reached epidemic proportions, with recent reports indicating that 17% of children and adolescents in the United States are obese, with the prevalence of severe obesity continuing to rise (1,2). Although childhood obesity in general appears to be leveling off, this has not been the case among minority groups (3). Childhood obesity increases the risk of cardiovascular disease, type 2 diabetes, and structural brain impairments, contributes to social and emotional problems, and is estimated to account for \$14.2 billion in yearly medical costs (4). Given that sedentary lifestyles and childhood obesity are predictors of adult obesity (5), preventive efforts that incorporate physical activity among young people are critical to address this public health crisis (4).

VO₂ max, or maximal oxygen consumption, is often used as a measure of cardiovascular fitness, with higher levels of fitness associated with healthier metabolic profiles that include lower plasma fasting insulin and glucose levels, lower deposition of central body fat, and lower body mass index (BMI) (6,7). Gains in aerobic fitness are known to improve weight status, blood pressure, and cholesterol profiles in adolescents, whereas low cardiovascular fitness is associated with the development of cardiovascular disease later in life (6,7). In addition to preventing weight gain, physical activity has been shown to increase VO₂ max in adolescents (8). Although many interventions aimed at preventing obesity in adolescents focus on aerobic fitness, few have ascertained the impact of fitness on brain integrity.

Recent reports indicate that aerobic fitness, in addition to boosting metabolism, can enhance brain function and structure in adults (9). Excess weight among elderly individuals has been linked to increased global brain atrophy and cognitive impairments (10), while fitness in middle-age individuals is known to protect against brain volume loss and improve neurocognitive function (11). Metabolic syndrome and excess weight in adolescents have been linked to reductions in cognitive performance and structural brain abnormalities, such as hippocampal and overall cerebral volume loss (12). Executive function, attention and psychomotor efficiency and working memory have been found to be associated with physical fitness in older adults (13) but these associations are not as clear in adolescents (14). Research suggests that because the adolescent brain is still maturing, the relationship between physical fitness and cognitive performance may not be as pronounced as it is in adults (15). Physical fitness has been shown to improve brain health over time by increasing gray matter volume in the prefrontal cortex and hippocampus in older adults; higher physical fitness levels are associated with greater improvements in hippocampal volume size (16,17). Given that aerobic exercise can attenuate volume loss over time, it may be an effective strategy for reversing the significant brain volume deficits in obese individuals (10,16). While gross brain volume reductions have been observed in individuals with type 2 diabetes mellitus (T2DM) and metabolic syndrome, more sensitive measures, such as cortical thickness, may be necessary to detect the impact of more subtle forms of metabolic disease on the brain in adolescents (18).

Previous neuroimaging studies of obesity found structural brain abnormalities in the orbitofrontal cortex (OFC) and the anterior cingulate cortex (ACC), two areas that are

involved in the reward circuit (19,20,21). We recently described brain abnormalities in adolescents with uncomplicated obesity and found reduced brain structural integrity in the OFC and ACC cortices (18). Insulin sensitivity and fitness are linked, thus, we wanted to contrast how a simple measure of fitness would explain brain structure and function relative to measures of insulin sensitivity and abdominal obesity, which are associated to brain integrity. The present investigation examined the relationships between cardiovascular fitness measured by an estimate of VO_2 max, insulin sensitivity measured by the quantitative insulin sensitivity check index (QUICKI), neurocognitive performance, and measures of cerebral integrity in those two brain regions that have been reported to be affected in obesity.

Methods and Procedures

Study Participants

A total of 130 non-diabetic adolescents (15-21 years of age) were evaluated in the Brain, Obesity, and Diabetes Laboratory (BODYLab) of NYU School of Medicine as part of an ongoing study on brain integrity in obesity-associated metabolic disease. All participants were recruited via internet advertisements or because they were friends or relative of other participants. This study was approved by the NYU School of Medicine Institutional Review Board. All study participants underwent medical, endocrine, cognitive, and brain MRI evaluations. Exclusion criteria were a diagnosis of T2DM or other significant medical conditions (other than insulin resistance, polycystic ovary disease, dyslipidemia, and/or hypertension), Tanner stage less than 4, use of psychoactive medications, a diagnosis of depression or attention deficit disorder, a history of significant learning disability, or pregnancy. All information about drug use was obtained via self-disclosure.

There were 79 obese participants (defined as having a $\text{BMI} \geq 30 \text{ kg/m}^2$) and 51 non-obese participants (defined as having a $\text{BMI} < 30 \text{ kg/m}^2$). Our hypothesis testing did not involve contrasting the two weight groups; however, we present the characteristics of these two groups separately in Table 1.

All study participants had a blood sample taken after a 10-12 h overnight fast to assess glucose and insulin levels in addition to cholesterol profile, electrolytes, liver function, and blood count. Glucose was measured using a glucose oxidase method (VITROS 950 AT; Ortho Clinical Diagnostics, Amersham, England) and insulin by chemiluminescence (Advia Centaur; Siemens). Fasting glucose and insulin blood levels were utilized to compute the quantitative insulin sensitivity check index (QUICKI) (22).

Physical Assessment

All participants received a physical examination to determine their height, weight, waist circumference, heart rate, blood pressure (BP), and body composition. Height and weight were assessed using a Seca 700 beam scale of 500 lbs capacity, calibrated prior to each measurement. Height and weight were then used to calculate $\text{BMI} (\text{kg/m}^2)$, and the waist circumference was used as an estimate of abdominal (central) obesity. Waist-to-height ratio (WHR) has been shown to be superior to BMI as a predictor of cardiometabolic risk (23) and is known to be a better measure of central obesity than BMI because it is not

confounded by muscle mass. Additionally, WHR is superior to waist-to-hip ratio because some racial/ethnic groups often have relatively larger hips, making waist-to-hip a better measure of lower body obesity than central obesity (24,25).

BP was measured twice while sitting in a standardized way. The two measurements were then averaged and used to compute the mean arterial blood pressure (MBP), which is calculated as the sum of the diastolic blood pressure (DBP) and one third of the difference between the systolic blood pressure (SBP) and DBP ($MBP = DBP + [SBP - DBP]/3$).

Bio-Electrical Impedance Analysis (BIA)

Body composition was assessed by a bioelectrical impedance method, using a body composition 2.1 RJL Portable System and the Quantum IV Bioelectrical Impedance Analyzer (RJL Systems, Clinton Township, MI); estimates of fat mass and body fat percentage were derived.

Six Minute Walk Test (6MWT)

For the 6MWT participants were instructed to walk back and forth between two cones that were placed 20 meters apart. Participants were told to wear comfortable shoes and to walk as fast as possible (without running or jogging) for 6 minutes as per American Thoracic Society guidelines (26). The total distance covered was measured in meters, by the number of full and partial laps completed; this value was then recorded as the 6MWT score. Heart rate, blood pressure, and blood oxygen saturation (using a finger oximeter) were measured prior to the beginning and immediately after the end of the test. One hundred and seventeen participants underwent the 6MWT.

VO₂ max Calculation

The standard measurement of maximal oxygen uptake is complex and requires sophisticated equipment and a fair amount of inconvenience for the participant. Instead, we chose to estimate VO₂ max by a simpler and less intrusive method using an algorithm based on results of the 6MWT (27). The main components of the formula are the total distance walked during the 6MWT, the participant's age, sex, weight in kg, and baseline heart rate. It is important to note that the estimate of VO₂ max obtained by this formula provides excellent equivalency to VO₂ max evaluated with direct measures of O₂ consumption and CO₂ production during an exercise paradigm (28).

Insulin Resistance Assessment

We chose to estimate insulin sensitivity utilizing a simple method that has been validated against the hyperinsulinimic euglycemic clamp (22). All participants had a morning blood draw for glucose and insulin levels performed after a 10-12 hour overnight fast and insulin sensitivity was estimated by the quantitative insulin sensitivity check index (QUICKI) value: $(1/(\log \text{fasting glucose [mg/dL]} + \log \text{fasting insulin [microU/mL]}))$ (22). Participants with a QUICKI value of less than 0.350 are considered insulin resistant. Please note that the QUICKI is log scale, so small numerical changes indicate fairly large changes in insulin sensitivity.

Neuropsychological Assessment

We conducted a standardized neurocognitive assessment focusing on the evaluation of executive function, attention, and memory (29). Given the prior literature linking frontal lobe function deficits to obesity, we hypothesized that fitness and VO_2 max would be associated with frontal lobe functions and therefore restricted our analyses to eight neurocognitive tests that reflect performance in frontal lobe-mediated functions including: 1.) executive function (Tower of London Test, Category Test, Stroop Interference Trial, and Trail Making Test B-A); 2.) attention and psychomotor efficiency (Digit Vigilance Test and Digit Symbol Substitution Test); and 3.) working memory (Wechsler Memory Scale IV Visual Working Memory Index Score and Letter-Number Sequencing task). With the exception of the Stroop Test, which provides age corrected standard scores, raw scores were utilized.

MR Image Acquisition and Image Analysis

All participants were studied on the same 3.0T Siemens Trio System utilizing an identical protocol that had been programmed on the console. The magnetization-prepared rapid acquisition gradient echo (MPRAGE; TR 2,300 ms; TE 2.3 ms; TI 1,100 ms; FOV 240×240; slice thickness 0.90 mm; flip angle 12°; matrix size 256×256; 192 coronal slices) sequence was used for volumetric assessment. To rule out primary neurological disease and to quantify WM disease, the fast fluid-attenuated inversion recovery (FLAIR; TR 9,000 ms; TE 81 ms; FOV 220×220; one average and three concatenations; flip angle 120°; slice thickness 3 mm; matrix size 256×256; 60 axial slices) sequence was used with the MPRAGE. Please note that not all study participants had an MRI. Sixty-three obese and forty-three non-obese participants underwent brain MRI evaluations. Those few adolescents without MRI failed to keep their appointments for the MRI, had claustrophobia, or were too large to fit in the gantry.

Brain Volumetric Assessment

All brain volumes were determined utilizing unbiased methods blind to participants' identity and diagnosis. We manually traced the outline of the intracranial vault (ICV) on the MPRAGE image by following the dural and tentorial margins. An intensity threshold which identified cerebrospinal fluid (CSF) voxels within the ICV was used to determine the overall CSF volume, which was then used as a measure of global cerebral atrophy (30). To account for inter-participant variability in brain size, measured brain volumes and global cerebral atrophy were adjusted (residualized) to the ICV volume using linear regression.

We used the FreeSurfer image analysis toolkit (<http://surfer.nmr.mgh.harvard.edu>) to perform cortical reconstruction and volumetric segmentation of the MPRAGE images. The standard options for the procedure included the removal of non-brain tissue, automated Talairach transformation, segmentation of the subcortical white matter and construction of a model boundary of the cortical gray and white matter (31). We used an algorithm to parcel the cerebral cortex into units based on gyral and sulcal structures (32). We computed GM volumes and cortical thickness for the two regions we hypothesized would be affected, the OFC (lateral and medial combined) and anterior cingulate cortex (ACC; rostral and caudal combined).

Statistical Analysis

For descriptive purposes and to ensure group equivalency, we conducted two-tailed statistics of socio-demographic measures. In addition, to examine group differences in endocrine data, measures of brain integrity, and neurocognitive performance we also performed t-tests. To account for individual brain size differences, the CSF volume and all brain measures were adjusted (residualized) to the ICV volume using linear regression. We did not have specific localization of lateralization hypotheses, therefore we averaged the cortical thickness of the OFC and ACC subregions and combined the right and left hemispheres weighted by their corresponding surface areas.

Partial correlational analyses (controlling for sex) were used to assess the relationship between VO_2 max, QUICKI value, WHR, and the brain and cognitive variables. Please note that we controlled for sex in all of our analyses because other studies have found sex-related differences in the impact of metabolic disease on brain (33) and because our measure of VO_2 max may be biased towards males as males typically have higher VO_2 max values due to their lower body fat percentage and higher hemoglobin content relative to females (34,35). In order to establish which of our metabolic predictors (VO_2 max, QUICKI, or WHR) best predicted the brain variables we used stepwise linear regression after accounting for age and sex. Follow-up mediation analyses examined whether the relationship between WHR and the cognitive variables was mediated by either VO_2 max or QUICKI using the Sobel test and the bootstrapping method with 5000 bootstrapped samples at 95% confidence interval.

Results

Demographics

Table 1 shows the demographic data for the study participants, separated into the two groups based on BMI. All obese participants had fasting glucose levels in the normal range. Fasting insulin levels as well as mean arterial BP were significantly higher among obese adolescents. Obese adolescents also had significantly lower QUICKI values, indicating higher insulin resistance and also had significantly lower VO_2 max values.

Associations between VO_2 max and Obesity/IR

After controlling for sex, we found significant inverse associations between VO_2 max and measures of obesity (BMI, $r_p[114]=-0.861$, $p<.01$; WHR, $r_p[114]=-0.836$, $p<.01$; and percent body fat, $r_p[110]=-0.783$, $p<.01$). Higher VO_2 max also correlated with insulin sensitivity as reflected by higher QUICKI value ($r_p[114]=0.593$, $p<.01$). See Figures 1A-1C which show the relationships between the metabolic variables.

Brain and Associations with VO_2 max and QUICKI

There were no brain abnormalities noted on the MPRAGE or FLAIR images. Consistent with expectation, and as depicted in Table 2, obese adolescents had significant reductions in OFC thickness ($t[128]=2.66$, $p<0.05$; Cohen's $d=0.53$, medium effect size) but the groups did not differ on OFC volume, ACC volume, ACC cortical thickness, or global brain atrophy.

The brain volumes and thicknesses presented are the absolute measurements; for the analyses, the ICV adjusted values were used and are reflected in the statistical results. As hypothesized, and after adjusting for sex, OFC thickness was correlated with better fitness, ($r_p[79]=0.228$, $p<.05$) and insulin sensitivity ($r_p[90]=0.320$, $p<.05$) and negatively correlated with WHR ($r_p[90]=-0.311$, $p<.05$). Figures 2A-2C show the relationships between orbitofrontal cortex thickness and metabolic variables.

After accounting for age and sex, ($R^2 = 0.08$, $\beta_{age} = .004$, $\beta_{sex} = .077$, $F(2,79)=3.444$, $p<.05$), the stepwise regression showed that the QUICKI value was the most significant predictor of OFC thickness ($R^2 = 0.112$, $F(1,78)=10.860$, $p<.05$). The other two metabolic predictors did not reach the significance threshold required to enter the model.

Cognition and Associations with VO₂ max and QUICKI

Table 3 shows the descriptives for the cognitive variables split by BMI groups. Visual Working Memory Index Score ($t[116]=2.70$, $p<.05$) and Digit Vigilance total time ($t[127]=-2.08$, $p<.05$) were the only measures that significantly differentiated the groups, with obese participants performing poorer than non-obese participants.

Again, after adjusting for sex we examined the relationships between the two cognitive variables that differed between groups and the metabolic variables. Visual Working Memory Index Score was significantly associated with VO₂ max ($r_p[103]=0.280$, $p<.05$) but not with the QUICKI value ($r_p[115]=0.164$, $p>.05$) or WHR ($r_p[115]=-0.177$, $p>.05$). See Figures 3A-3C which show the relationships between Visual Working Index Score and the metabolic variables. However, Digit Vigilance Total Time was not significantly associated with any of the metabolic variables (VO₂ max ($r_p[113]=-0.113$, $p>.05$), QUICKI value ($r_p[126]=-0.069$, $p>.05$), or WHR ($r_p[126]=0.160$, $p>.05$)). Given the slight difference in socioeconomic status between the groups, we repeated these analyses adjusting for both sex and socioeconomic status and the results remained the same. Plots are not shown.

We performed a mediation analyses to ascertain whether fitness or insulin sensitivity mediated the effects of obesity on the neurocognitive measures. Results indicated that the total effect of obesity on the Visual Working Memory Index Score was significant ($TE=-27.2697$, $SE=10.4984$, $p=.0108$) and that the relationship was partially mediated by VO₂ max (Sobel test, $Z=-3.4819$, $p=.0005$; bootstrapping, indirect effect= -41.2882 [95% CI, -63.0952 to -23.4507]; $SE=9.9143$). QUICKI was not a significant mediator. We confirmed that the relationship between WHR and Digit Vigilance total time was not mediated by either VO₂ max or QUICKI.

Discussion

To our knowledge, this is the first study demonstrating clear associations between insulin sensitivity, VO₂ max, and the structural and functional integrity of brain frontal lobe areas in adolescents. We selected to ascertain the strength of the relationships between VO₂ max and very selected brain variables, namely the OFC and ACC volumes and cortical thickness and a measure of global brain atrophy, given their reported associations to obesity and to limit the number of comparisons. As hypothesized, we identified differences in the OFC thickness

between obese and non-obese adolescents but did not identify differences in the OFC and ACC volumes or in the overall level of brain atrophy. Furthermore, we did not see group differences in the ACC cortical thickness. With the exception of the Category Test, obese adolescents performed descriptively worse on all frontal-lobe based measures examined and had significantly lower visual working memory and attention.

VO₂ max was associated with better weight status and metabolic profile and brain integrity in adolescents, which is a novel finding since only cognition had been associated with VO₂ max in adolescents (14). Similarly, QUICKI was associated with better weight status and brain integrity. As anticipated, both VO₂ max and QUICKI are strongly associated with one another and with obesity and its correlates. Other studies of fitness, insulin sensitivity and weight status have found that fitness impacts insulin sensitivity in both lean and obese weight groups (36) as well as reduces their risk of cardiovascular disease mortality (37).

The OFC cortical thickness was the only measure that was significantly different between the obese and non-obese groups. This is consistent with previous reports from our laboratory, where, in a separate adolescent sample, we described associations between obesity and the OFC, a brain region which is important for impulse control and is known to be an integral part of the reward network (19). We found that although QUICKI and VO₂ max were both individually associated with OFC thickness, the association was strongest with QUICKI. Given that VO₂ max shares significant variance with QUICKI, our findings suggest that although both contribute to brain integrity, insulin sensitivity plays a larger role. This finding is consistent with prior reports from our lab that demonstrated that insulin resistance was the strongest predictor of brain volume changes, indicating that metabolic status is an important indicator of structural brain integrity (12).

We found that the Visual Working Memory Index Score, but not the Digit Vigilance Test, was significantly associated with VO₂ max, suggesting a relationship between fitness and working memory. The QUICKI value was not significantly associated with either of the cognitive variables. We suspect that the lack of association between glycemic control (QUICKI) and cognitive test performance is likely due to differences in scatter in the distributions of VO₂ max and QUICKI in our sample and therefore in our ability to discern effects. Given the relatively modest sample size, we cannot conclude whether this difference is a physiologically meaningful result. While higher levels of physical fitness have been linked to greater prefrontal cortex volume, it is possible that physical fitness may have a stronger effect on working memory than on other frontally-mediated tasks such as attention (38). We further explored this relationship using mediation analyses and found that VO₂ max partially mediates the relationship between central obesity and the Visual Working Memory Index Score. While further studies that examine this mechanism are warranted, this finding underscores the importance of physical fitness for cognitive performance and academic achievement.

Based on the effect sizes from previous results in our laboratory we expected to have adequate power to test our hypotheses. With that said, our sample size is only modest. However, our groups were well matched on socioeconomic status, age, sex, and education and we were able to identify clear differences in the OFC cortical thickness. Additionally,

our participants were recruited from the community and were not part of a clinical population, thus improving our ability to generalize. Further, the brain evaluations were unbiased, which gives greater credence to our findings. Given the prevalence of drug use among adolescents and the associated stigma, the accuracy of self-reported drug use may affect our findings. Future studies should use more detailed assessments of drug use, conduct prospective longitudinal evaluations, and include a larger sample size in order to determine whether physical activity interventions could lead to structural brain improvements in adolescents. Lastly, we recognize that our simple measure of VO_2 max, although validated against the much more involved direct measure, is only an estimate; future studies should utilize direct assessment of VO_2 max.

Fitness has been associated with school performance in children. In a large scale study of over 500,000 children investigators reported that students who performed in the top five percent on a standards-based fitness assessment scored thirty-six percentile points higher on standardized academic tests than students who performed in the bottom five percent on the fitness assessment (39). Furthermore it has been demonstrated that physically active lifestyles can increase VO_2 max and maintain brain health over time (17). Although we did not find evidence that VO_2 max levels can predict brain integrity independent of insulin sensitivity, physical fitness is important for brain health. For example, exercise and improvements in physical fitness have been associated with increases in brain derived neurotrophic factor (BDNF), which is very important for brain repair and maintenance (16). While improvements in lifestyle, including better nutrition and weight loss are key to reversing insulin resistance (40), the focus of clinical interventions aimed at improving brain health should include improvements in fitness and reductions in central obesity as targets.

In these data, insulin sensitivity is a stronger predictor of brain integrity than fitness. But, VO_2 max can be easily measured in school settings and used to track adolescents' fitness levels, and this could perhaps be used as a surrogate marker of brain health when measurements of insulin sensitivity are not feasible. Due to budget cuts, physical education in schools has been steadily decreasing, even as reports show the benefits of fitness carry over into the classroom. Given the obesity epidemic it is imperative that policymakers consider the importance of physical fitness when making decisions about distribution of resources. There is emerging evidence that brain deficits associated with obesity may be reversible and improved fitness may help ensure that brain function and structure are protected even in the presence of excess weight.

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Highlights

- We examine fitness, insulin resistance, and brain integrity in adolescents.
- Fitness and insulin resistance correlated with orbitofrontal cortex integrity.
- Fitness does not predict brain integrity independent of insulin resistance.
- Fitness correlated significantly with visual working memory but not attention.
- Physical fitness may play an important role in maintaining brain integrity.

Figure 1.

A and C show the relationships between VO_2 max and QUICKI values and VO_2 max and WHR, respectively. B shows the relationship between WHR and QUICKI values.

Metabolic Variables Relationships

Figure 2.

A-C shows the relationships between orbitofrontal cortex thickness and the metabolic variables. Orbitofrontal Cortex Thickness and Metabolic Variables

Figure 3.

A-C shows the relationships between Visual Working Memory Index Scores and the metabolic variables. Relationships between Visual Working Memory Index Score and Metabolic Variables

Table 1

Demographic and Endocrine Data

	Non-Obese (n=51)	Obese (n=79)	t	p	Cohen's d
	Mean ± SD	Mean ± SD			
Age (years)	19.41 ± 1.66	19.59 ± 1.62	-0.61	0.54	-0.11
Socioeconomic Status	3.47 ± 1.10	3.13 ± 1.20	1.61	0.11	0.29
Sex^a	26 M / 25 F	28 M / 51 F	3.08	0.08	
Race (Black/White/Asian/Hispanic/Other)^a	18/8/9/15/1	27/8/6/36/2	5.61	0.23	
Education (years completed)	12.63 ± 1.71	12.75 ± 1.57	-0.41	0.68	-0.07
Body Mass Index (kg/m²)	22.89 ± 3.09	35.60 ± 4.98	17.96	0.000	-2.93
Fasting Glucose (mg/dL)	80.98 ± 6.00	85.23 ± 7.08	-3.54	0.01	-0.64
Fasting Insulin (microIU/mL)	7.66 ± 3.80	17.52 ± 9.51	-8.25	<.001	-1.26
Mean Blood Pressure (mm Hg)	76.56 ± 7.56	83.58 ± 7.95	-5.00	<.001	-0.90
VO₂ maximum (mL/kg/min)	44.14 ± 8.46	30.31 ± 8.57	8.58	<.001	1.62
% Body Fat	26.77 ± 8.53	41.21 ± 7.22	-9.93	<.001	-1.86
Waist Height Ratio	0.48 ± 0.04	0.66 ± 0.09	-15.55	<.001	-2.46

^a Categorical variables were evaluated with the chi-square test.

Table 2

Brain Data

	Non-Obese (n=51)	Obese (n=79)
	Mean $\pm$ SD	Mean $\pm$ SD
Intracranial Vault Volume (cc)	1258.33 $\pm$ 111.63	1235.58 $\pm$ 129.53
Global Atrophy (cc)	48.21 $\pm$ 13.84	47.34 $\pm$ 14.67
Orbitofrontal Cortex Volume (cc)	28.84 $\pm$ 3.12	28.39 $\pm$ 2.99
Anterior Cingulate Volume (cc)	9.51 $\pm$ 1.52	9.45 $\pm$ 1.59
Orbitofrontal Cortical Thickness (mm)^a	2.85 $\pm$ 0.14	2.78 $\pm$ 0.13
Anterior Cingulate Cortical Thickness (mm)	2.87 $\pm$ 0.15	2.88 $\pm$ 0.17

^a
p<.05

Table 3

Cognitive Data

	Non-Obese (n=51)	Obese (n=79)
	Mean $\pm$ SD	Mean $\pm$ SD
Tower of London Excess Moves	9.66 $\pm$ 8.32	11.47 $\pm$ 11.34
Category Test Number of Errors	34.53 $\pm$ 21.18	33.32 $\pm$ 21.25
Stroop Interference Score	5.89 $\pm$ 7.46	4.81 $\pm$ 8.74
Trails B-A Time (s)	35.59 $\pm$ 30.12	37.61 $\pm$ 25.44
Digit Symbol Substitution Test	64.02 $\pm$ 11.68	61.24 $\pm$ 8.96
Digit Vigilance Total Time (s)^a	356.86 $\pm$ 78.47	387.54 $\pm$ 84.02
Visual Working Memory Index Score^a	103.36 $\pm$ 12.66	97.18 $\pm$ 11.83
Letter Number Sequencing	11.00 $\pm$ 2.51	10.89 $\pm$ 2.03

^a p<.05