Improved Memory Function Two Years After Bariatric Surgery

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Keywords: Obesity, bariatric surgery, cognitive function, weight loss
What is Already Known?

- Obesity is an independent risk factor for poor neurocognitive outcomes
- Bariatric surgery has recently been shown to provide short-term cognitive benefits
- Mechanisms underlying improved cognitive function following bariatric surgery may involve resolution of medical comorbidities
What this Study Adds?

- Bariatric surgery is associated with long-term improvements in memory relative to obese controls.
- The cognitive benefits that emerge shortly after bariatric surgery are sustained up to 24-months.
- Post-operative weight loss partly accounts for the cognitive benefits of bariatric surgery, though contribution of resolved medical conditions are mixed.
Abstract

Objective: Obesity is an independent risk factor for poor neurocognitive outcomes, including Alzheimer’s disease. Bariatric surgery has recently been shown to result in improved memory at 12-weeks post-operatively. However, the long-term effects of bariatric surgery on cognitive function remain unclear.

Design and Methods: 86 individuals (63 bariatric surgery patients, 23 obese controls) were recruited from a prospective study examining the neurocognitive effects of bariatric surgery. All participants completed self-report measurements and a computerized cognitive test battery prior to surgery and at 12-week and 24-month follow-up; obese controls completed measures at equivalent time points.

Results: Bariatric surgery patients exhibited high rates of pre-operative cognitive impairments in attention, executive function, memory, and language. Relative to obese controls, repeated measures ANOVA showed improvements in memory from baseline to 12-weeks and 24-months post-operatively ($p < .05$). Regression analyses controlling for baseline factors revealed that a lower BMI at 24-months demonstrated a trend toward significance for improved memory ($\beta = -.30, p = .075$).

Conclusion: These findings suggest that cognitive benefits of bariatric surgery may extend to 24-months post-operatively. Larger prospective studies with extended follow-up periods are needed to elucidate whether bariatric surgery decreases risk for cognitive decline and possibly the development of dementia.
Introduction

More than one-third of Americans are currently obese and prevalence rates are expected to double in the next 20 years [1,2]. This pattern is concerning, as obesity is associated with increased risk for morbidity and mortality, psychosocial distress, and depression, to name a few [3,4]. Rapidly growing evidence also links obesity with poor neurocognitive outcomes. Indeed, elevated body mass index (BMI) has been identified as an independent risk factor for Alzheimer’s disease, vascular dementia, and abnormalities on neuroimaging [5,6]. Obesity has also been linked with milder impairments across multiple domains of cognition prior to the onset of these conditions, including deficits in attention, executive function, and memory [7,8].

Bariatric surgery has become an important treatment option for weight loss among morbidly obese individuals. Bariatric surgery is effective and has been shown to result in lower morbidity and mortality risk [9] and improved health-related quality of life [10,11]. Rates of cognitive dysfunction are elevated among bariatric surgical candidates [12] and increasing attention has been paid to the effects of bariatric surgery on cognitive function. Indeed, weight loss accompanying surgical intervention usually results in the resolution or improvement in co-morbid medical conditions that adversely affect cognitive function such as hypertension [13], diabetes [14], sleep apnea [15] and depression [16]. In addition, the documented evidence for the independent effects of obesity on cognitive function [17] suggest that the substantial weight loss alone may be sufficient to improve cognitive function.

In response to these findings, a recent study from our group examined cognitive function in bariatric surgical patients compared to obese controls at baseline and a 12-week post-operative follow-up [12]. The results showed that bariatric surgical patients demonstrated improved
memory at the 12-week follow-up while no changes or declines in cognitive function were found in obese controls. Although these findings suggest that obesity-related cognitive deficits may be partly reversible through surgical intervention, the lasting impact of bariatric surgery on cognitive function remains unclear. The purpose of the current study was to examine the effects of bariatric surgery on cognitive function relative to obese controls at a 12-week and 24-month post-operative follow-up. Because body weight reaches its lowest point at 18-24 months after many bariatric surgery procedures [18], sustained cognitive benefits at 24-months were expected. We also sought to examine predictors of post-operative cognitive changes at 24-months, including BMI and comorbid medical conditions.

Materials and Methods

Trial Design and Participants

A total of 86 participants were recruited into this multi-site prospective study examining the neurocognitive effects of bariatric surgery (63 bariatric surgery patients and 23 obese controls). All participants were part of the Longitudinal Assessment of Bariatric Surgery (LABS) parent project and were recruited from three LABS sites [11]. Individuals participating in the parent project who were eligible for the current study were approached at the time of enrollment regarding this ancillary cognitive study. Greater than 80% of participants approached opted to enroll. The current sample represents those individuals completing 24-month follow-up data and due to attrition the current sample size was reduced to the final sample of 86. Participants excluded as a result of attrition and subsequent missing data across time points were not different from the current sample in terms of age ($t(191) = -.55, p = .58$), gender ($\chi^2 (1, N = 191) = .15, p = .70$), baseline BMI ($t(191) = .95, p = .35$), or baseline cognitive function in attention ($t(191) =$...
1.11, \( p = .27 \), executive function \( t(191) = .93, p = .35 \), memory \( t(193) = -.23, p = .82 \), or language \( t(191) = -1.57, p = .12 \).

For study inclusion, participants were required to be enrolled in LABS, between the ages of 20-70, and English-speaking. Exclusion criteria included history of neurological disorder or injury (e.g. dementia, stroke, seizures), moderate or severe head injury (defined as >10 minutes loss of consciousness) [19], past or current history of severe psychiatric illness (e.g. schizophrenia, bipolar disorder), past or current history of alcohol or drug abuse (defined by DSM-IV criteria), history of a learning disorder or developmental disability (defined by DSM-IV criteria), or impaired sensory function that precluded cognitive testing (e.g. visual deficits preventing adequate perception of test stimuli) per participant report or examiner observation.

Inclusion/exclusion criteria were the same for the matched controls except obese controls were not enrolled in the LABS project, had not undergone bariatric surgery, and had no reported intent to undergo bariatric surgery following 2 years. Physician diagnosed medical history pre- and post surgery was obtained via medical record review from the LABS study as well as participant self-report. Within the sample, almost all patients underwent Roux-en-Y gastric bypass surgery (RYGB). Only 1 bariatric surgery patient underwent a gastric banding procedure and thus no comparisons for type of surgery were conducted.

**Interventions and Clinical Follow-Up**

This study is registered with clinical trials.gov and all procedures were approved by the appropriate Institutional Review Boards. All participants provided written informed consent prior to study involvement. The bariatric surgery participants completed a series of self-report instruments and a computerized cognitive test battery at baseline (within 30 days prior to surgery), 12 weeks (± 5 days), and 24 months (± 14 days) following surgery. The same
procedures were followed for the obese controls. Pre- and post medical records were reviewed by research staff to corroborate participant self-report and ascertain physician diagnosed comorbid medical condition status, including hypertension, diabetes, and sleep apnea.

### Outcomes

The Integneuro cognitive test battery was chosen based upon previous work from our lab, demonstrating that Integneuro tasks of attention, executive function and verbal memory are sensitive to the cognitive difficulties manifested in this population [20,21]. This cognitive test battery consists of estimated premorbid intellectual abilities as well as performance in multiple cognitive domains (e.g., attention, executive Function, verbal memory) and can be completed in 45-60 minutes. Several benefits are associated with this cognitive test battery, including auditory and visual explanations, practice trials, semi-automated scoring, and language and non-language tests (Paul et al., 2005). Moreover, it has good psychometric properties and as described above, has been employed in past studies examining obesity and cognitive function [12]. The Integneuro battery has demonstrated strong convergent and divergent validity with commonly used paper and pencil measures of cognitive function [22] and also exhibits sensitivity to deficits in neurological populations, including Alzheimer’s disease and vascular dementia [23]. Specific tests were categorized into attention, executive function, memory, and language domains and included:

**Attention and Executive Function**

**Digit Span:** This test assesses basic auditory attention and working memory. Participants are presented with a series of digits on the touch-screen, separated by a one-second interval. The subject is then immediately asked to enter the digits on a numeric keypad on the touch-screen.
The number of digits in each sequence is gradually increased from 3 to 9, with two sequences at each level. The participants complete these same procedures in a backward sequence. The dependent measure is total number correct forwards and backwards.

**Switching of Attention:** This test is a computerized adaptation of the Trail Making Test and consists of two parts [24]. Participants are asked to touch a series of 25 numbers in ascending order as quickly as possible. An array of 13 numbers (1-13) and 12 letters (A-L) is presented. Participants are asked to touch numbers and letters alternately in ascending order. The first part of this test assesses attention and psychomotor speed and the second part assesses executive function. The dependent measure is total time of completion.

**Verbal Interference:** This task taps the ability to inhibit automatic and irrelevant responses and has similarities to the Stroop Color Word Test [25]. Participants are presented with colored words one at a time. Below each colored word is a response pad with the four possible words displayed in black and in fixed format. In the first part, the subject is required to name each word as quickly as possible, assessing attention. In the second part, the subject is required to name to the color of each word as quickly as possible, assessing executive function. The dependent measure is total number of words correct.

**Maze Task:** This task is a computerized adaptation of the Austin Maze [26] and assesses executive function. Participants are presented with a grid (8x8 matrix) of circles and asked to identify the hidden path through the grid. Distinct auditory and visual cues are presented for correct and incorrect responses. The trial ends when the subject completed the maze twice without error or after 10 minutes has elapsed. Number of errors committed served as the dependent measure.

**Memory**
Verbal List-learning: Participants are read a list of 12 words a total of 4 times and asked to recall as many words as possible following each trial. After a 20-minute filled delay, participants are again asked to recall target words. Finally, a recognition trial comprised of target words and foils is completed. Total learning, Long Delay Free Recall, and Recognition of these verbal list items were used to assess memory.

Language

Animal and Letter Fluency: This test asks individuals to generate words beginning with a given letter of the alphabet for 60 seconds. A different letter is used for each of the three trials. Finally, participants were then asked to generate as many animals as possible within 60 seconds.

Data Analyses

To facilitate clinical interpretation, all neuropsychological measures were transformed to T-scores (a distribution with a mean of 50 and standard deviation of 10) using existing normative data correcting for age, gender, and premorbid intelligence. Composite scores were computed for attention, executive function, memory, and language that consisted of the mean of the T-scores of neuropsychological measures within each cognitive domain. Consistent with clinical convention, a T-score ≤ 35 (1.5 SD below the mean) was reflective of cognitive impairment.

Descriptive and frequency statistics were first conducted to examine cognitive test performance in bariatric surgery patients at baseline and at the 24-month post-operative follow-up. Chi-square analyses also compared rates of cognitive impairment at baseline and rates of cognitive decline from baseline to 24-months between bariatric surgery patients and obese controls. Repeated measures analysis of variance (ANOVA) was then performed to determine group differences between bariatric surgery patients and obese controls on attention, executive function, memory, and language over time (i.e., baseline, 12-weeks, and 24-months). For those
domains exhibiting a main effect, separate follow-up repeated measures ANOVA for both bariatric surgery patients and obese controls were performed to clarify the pattern of change for each group across each time point (i.e., baseline to 12-weeks, baseline to 24-months, and 12-weeks to 24-months).

Lastly, a series of hierarchical regression analyses were conducted to examine the predictive validity of BMI on cognitive function over time in the bariatric surgery patients. As a result of missing data at 24 months, 4 cases were listwise deleted from these analyses. Attention, executive function, language, and memory at 24-month follow-up each served as the dependent variable in four separate regression models. For all analyses, baseline BMI, BMI at 12-weeks, and baseline test performance were entered in block 1. BMI at 24 months was then entered in block 2 to determine whether decreased BMI over time predicted improved cognitive function in each domain. Finally, a separate series of regression analyses were performed to examine the predictive validity of medical comorbidities on cognitive function in each domain over time in the bariatric surgery patients. Specifically, baseline and 12-week diagnostic status of hypertension, diabetes, and sleep apnea and baseline cognitive test performance were entered in block 1 and 24-month diagnostic status of each comorbidity was then entered in block 2. For these analyses, 11 cases were excluded due to missing data for diagnostic medical comorbidity status at 24-months.

Results

Sample Demographic and Medical Characteristics

At baseline, the bariatric surgery patients and obese controls were generally similar in terms of demographics, though the bariatric surgery group had a higher BMI and were more
likely to have sleep apnea. At the 24-month follow-up, the bariatric surgery patients had lost a
greater proportion of their body weight than the obese controls and were no more likely than the
obese controls to have hypertension, diabetes, or sleep apnea. See Table 1.

Baseline and 24-month Post-Operative Cognitive Function in Bariatric Surgery Patients

At baseline, when compared to normative data, cognitive test performance in the bariatric
surgery patients fell within the low average for memory and in the average range for all other
cognitive domains. See Table 2. However, when using a T-score cutoff of 35 many bariatric
surgery patients exhibited impairments in cognitive function at baseline. Impairments were
commonly observed in memory (15.9%), executive function (7.9%), and language (7.9%).
Impairments in attention were less common (4.8%). A similar pattern emerged for the obese
controls with baseline impairments noted in memory (17.4%), executive function (13.0%), and
language (4.3%). No baseline impairments in attention were observed.

At 24-month follow up, both bariatric surgery patients and obese controls test
performance for memory and language was within the average ranges and high average range for
attention and executive function. Examination of the cognitive domain composites revealed that
no bariatric surgery patients exhibited a 1.5 SD post-operative cognitive decline for attention or
executive function while 3.6% showed declines in memory and 1.2% for language. Obese
controls did not demonstrate cognitive decline in attention, executive function, language, or
memory ($p > .05$ for all).

Between Group Cognitive Test Differences for Bariatric Surgery Patients and Obese Controls

Repeated measures ANOVA examined between group differences for bariatric surgery
patients and obese controls on each cognitive domain across the time points (baseline, 12-weeks,
and 24-months). See Table 3. For memory, repeated measures ANOVA showed a significant main effect for time ($p < .01$) and group X time interaction ($p = .02$). The group X time interaction demonstrated a significant quadratic effect ($F(1, 84) = 5.64, p = .02$), as bariatric surgery patients exhibited significant improvements in memory from baseline to 12-weeks, and from baseline to 24-months, but not from 12-weeks to 24-months post-operatively. No significant changes in memory were noted for the obese controls from baseline to 12-weeks, baseline to 24-months, or 12-weeks to 24-months. See Table 4 for a full summary of repeated measure ANOVA analyses.

For the attention domain, there was a significant effect for time ($p < .001$). Although there was no group by time interaction ($p = .43$), follow-up analyses revealed that bariatric surgery patients showed improved attention from baseline to 12-weeks, and to 24-months, and from 12-weeks to 24-month postoperatively. Obese controls also showed trends for improved attention over time: baseline to 12-weeks, baseline to 24-month, and 12-weeks to 24-months.

For executive function, there was also a significant main effect for time ($p < .001$), but there was no group X time interaction ($p = .90$). Both bariatric surgery patients and obese controls exhibited improvements in executive function from baseline to 12-weeks and to 24-months, but not from 12-weeks to 24-months. For language, there was no significant main effect for time ($p = .14$) or group X time interaction ($p = .89$).

*Weight Loss and Cognitive Function in Bariatric Surgery Patients*

After controlling for baseline test performance, baseline BMI, and BMI at 12-weeks, a lower BMI at 24-months demonstrated a trend with improved memory ($p = .075$). No such pattern emerged for attention, executive function, or language. See Table 5.
hypothesis, diabetes, or sleep apnea at 24-months did not predict cognitive function in any domain ($p > .05$ for all). Of note, there were no significant differences in the proportion of bariatric surgery patients with hypertension ($\chi^2 (1, N = 52) = 2.10, p = .15$), diabetes ($\chi^2 (1, N = 53) = 1.46, p = .23$), or sleep apnea ($\chi^2 (1, N = 53) = .03, p = .87$), from baseline to 24-months.

**Discussion**

Consistent with past work, pre-operative impairments in cognitive function were common in this sample of bariatric surgical patients relative to normative standards. In contrast, performances in all domains of cognitive function were within the normatively average and high average range 24-months following surgery. Recent work shows that bariatric surgery is associated with cognitive benefits 12-weeks post-operatively compared to obese controls and the current study demonstrates that the effects of bariatric surgery on memory may be sustained at a 24-month follow-up. While such improvements were unrelated to change in comorbid medical condition status in this sample, there was a trend for post-operative decreases in BMI and better cognitive function. Several aspects of these findings warrant brief discussion.

Gunstad and colleagues (2011) [12] found improved memory at 12-weeks following bariatric surgery and the current study suggests that these improvements may be sustained at 24-months. Taken together, these findings continue to support the possibility that obesity-related cognitive dysfunction may be partly reversible. However, it is noted that the effect sizes for the differences in cognitive function between obese controls and bariatric surgery patients in this sample were small and larger studies are needed to help clarify the clinical significance of our findings. Interestingly, memory performance in the current sample of bariatric surgical candidates remained stable from 12-weeks to 24-months post-operatively. The impact of
Bariatric surgery and improved memory

Bariatric surgery on cognitive function may occur the immediate months following surgical intervention, as this is the time of the most substantial weight loss and resolution of medical comorbidities that negatively affect cognitive function [27,28]. However, significant decreases in total cardiovascular disease disorders have also been observed up to 3 years post bariatric surgery and maximal excess weight loss has been shown to occur at 18-months post-operatively [18,27]. It is likely that cognitive benefits are sustained if weight regain is avoided or minimized, though future studies are needed to confirm this notion.

The prevalent baseline impairments in memory among the bariatric surgical patients and resulting post-operative improvement is noteworthy. Midlife obesity is a known independent risk factor for Alzheimer’s disease [5,29]. Moreover, obesity has been linked with similar neuropathological changes found in Alzheimer’s disease patients, including increased amyloid beta and amyloid beta precursor protein in the hippocampus [30]. The current sample of bariatric surgery patients demonstrated several baseline risk factors that place them at future risk for Alzheimer’s disease, including high BMI, baseline impairments in memory, and comorbid vascular risk factors. However, the observed sustained improvements in memory at 24-months following surgical intervention suggest that it is possible that bariatric surgery may actually prevent pathological cognitive decline and even the development of dementia. For instance, a recent study showed that bariatric surgery was associated with reduced inflammation and expression of Alzheimer’s disease related proteins (e.g., amyloid precursor protein) [31]. Prospective studies that use extended follow up periods (e.g., 15-20 years) are needed to help clarify whether bariatric surgery reduces risk of the development of neurological conditions associated with obesity, particularly Alzheimer’s disease [5].
No relationship emerged between post-operative change in status of comorbid medical conditions and improved cognitive function in this sample of bariatric patients. This is surprising in light of the adverse effects of medical comorbidities (e.g., diabetes, hypertension) on neurocognitive outcomes. The low rates of resolution in comorbid medical conditions may help to explain these findings. For instance, past work with similar post-operative follow up shows resolution rates post-bariatric surgery of 71% for diabetes, 33% hypertension, and 100% sleep apnea [32] compared to 21% for hypertension, 56% diabetes, and 46% for sleep apnea in this study. In addition, it is also possible that the comorbid medical conditions produced lasting irreversible effects on the brain (e.g., small vessel disease) that prevented improved cognition post-bariatric surgery. In contrast, the present study found a trend for decreased BMI and improvements in memory at 24-months. These findings highlight the possibility that improved post-operative neurocognitive outcomes may be a result of the effects of bariatric surgery on unique pathophysiological mechanisms associated with obesity. For instance, bariatric surgery has been shown to alter insulin resistance, circulating biomarkers (e.g., leptin, brain derived neurotrophic factor) and endothelial function [33-36]—all factors that have been linked with cognitive function. Other work suggests amyloid beta and inflammatory processes may play a key role [31]. Clearly, future work is much need to elucidate underlying mechanisms of the effects of obesity on cognitive function and the modifying impact of bariatric surgery on such processes.

Bariatric surgery patients in the current sample exhibited baseline impairments in all domains of cognitive function, including attention, executive function, memory, and language. Pre-operative cognitive impairment may predict poor outcomes following surgery, as work from our group has shown that baseline cognitive function plays an important role in post-operative
weight loss [37]. These findings may involve the association between cognitive function and treatment adherence. To optimize weight loss, bariatric surgical patients are asked to adhere to complex post-operative treatment regimens such as self-monitoring, tracking physical activity levels and caloric intake, and managing multiple medications [38]. The simultaneous performance of these tasks is challenging and requires higher order cognitive processes (e.g., executive function) that are responsible for the ability to organize, plan, and monitor behavior [39]. Indeed, cognitive impairment has been shown to be a significant contributor to poor treatment adherence in other medical populations (e.g., diabetes) [40]. Pre-operative cognitive screening may provide key insight into long-term outcomes following surgery and future studies should examine this possibility, particularly as it involves post-operative treatment adherence.

Our findings are limited in several ways. First, the current study was observational and randomized control studies are needed to confirm our findings. Prospective studies that examine cognitive function at a more distant post-operative follow up (e.g., 36- and 48-months) would also help to further elucidate whether bariatric surgery can reduce risk of cognitive decline. In addition, the mechanisms of improved cognitive function following bariatric surgery remain unclear. Obesity has been linked with both functional and structural abnormalities and future studies should examine whether bariatric surgery also affects brain integrity and/or the biomarkers such as adipokines. The current study also found no significant relationship between change in comorbid medical condition status and improved cognitive function. The relatively small sample size and indirect assessment of medical comorbidities may account for these findings. Future studies that implement more direct assessments of medical status (e.g., blood pressure readings, continuous glucose monitoring) would help clarify mechanisms underlying improved cognition post-bariatric surgery. Although our findings suggest reduced adiposity may
be a plausible explanation for improved cognition, the relatively small sample size of the current study limited the ability to test whether the trend between lower 24-month BMI and improved cognition was independent from the effects of the resolution of medical comorbidities (i.e., comorbid medical conditions were not included as covariates in these analyses). Likewise, the small sample size of the current study may have comprised the power of analyses and larger randomized controlled studies with equal number of controls are needed to replicate our findings. The homogeneity of the current sample (e.g., 90-95% female) also limits the generalizability of the findings and larger more diverse studies would help to increase the external validity of this study.

Several other limitations deserve further discussion. The current study recruited obese controls from weight control centers and these participants presented with fewer comorbid conditions (e.g., sleep apnea, hypertension), perhaps due to lower disease severity (e.g., lower BMI). Future studies that use tightly controlled experiments (e.g., treatment wait-list) are needed to examine cognitive function in bariatric surgery patients and bariatric surgery controls with similar medical history. Such studies should also examine the influence and efficacy of preoperative weight loss activities on post bariatric surgical outcomes, including cognitive function. Similar to this notion, the obese controls did not demonstrate a change in weight over two years and this may account for the lack of improvement in certain domains of cognitive function (e.g., memory) in this group. Future studies should compare the effects of surgical vs. behavioral weight loss interventions on cognitive function. For example, it is possible that the physiological benefits (e.g., cardiovascular fitness) resulting from adjusted health habits (e.g., exercise) or other confounding factors (e.g., medication status) following surgery may have also contributed to improved cognitive function in this sample. Finally, while it is possible that
practice effects and improved computer familiarity may have contributed to the improvements in memory over time, this is unlikely given the presence of a control group in addition to our findings replicating past work showing improved memory 12-weeks post bariatric surgery [12]. Future work should examine the aims of the current study using paper and pencil neuropsychological test batteries.

In brief summary, the current study suggests that bariatric surgery may have lasting effects on improved memory. The mechanisms for these effects may involve the impact of bariatric surgery on physiological processes associated with obesity. Larger and more diverse prospective studies with extended follow-up periods are needed to elucidate whether bariatric surgery prevents cognitive decline and decreases risk for the development of neurological conditions (e.g., Alzheimer’s disease).
Conflict of Interests

The authors report no conflict of interest.
Acknowledgments

Author Contributions:

Study Concept and Design: MA, MBS, JG
Acquisition of Subjects: GS, MD, RP, RDC, JEM
Data Analysis and Interpretation: MA, MBS, JG, RC
Manuscript Preparation: MA, MBS, GS, MD, RC, RP, RDC, JEM, JG
Funding:

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References


Table 1. Demographic and Medical Characteristics

<table>
<thead>
<tr>
<th>CHARACTERISTICS</th>
<th>BASELINE PATIENTS</th>
<th>BARIATRIC SURGERY PATIENTS</th>
<th>OBESE CONTROLS</th>
<th>Test Statistic</th>
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<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>42.29 (11.42)</td>
<td>41.13 (12.55)</td>
<td>.40</td>
<td></td>
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<tr>
<td>Female (%)</td>
<td>90.5</td>
<td>95.7</td>
<td>.60</td>
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<tr>
<td>Body Mass Index, mean (SD)</td>
<td>46.52 (5.26)</td>
<td>40.90 (5.24)</td>
<td>4.35**</td>
<td></td>
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<tr>
<td>Hypertension (%)</td>
<td>44.4</td>
<td>21.7</td>
<td>3.43</td>
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<tr>
<td>Diabetes (%)</td>
<td>25.4</td>
<td>13.0</td>
<td>1.49</td>
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<tr>
<td>Sleep Apnea (%)</td>
<td>34.9</td>
<td>4.3</td>
<td>8.04**</td>
<td></td>
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</table>

24-MONTH FOLLOW-UP

<p>| Body Mass Index, mean (SD) | 31.34 (6.42) | 40.90 (5.64) | -5.41** |</p>
<table>
<thead>
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<th>Condition</th>
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<th>Time 2</th>
<th>P-value</th>
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<td>Hypertension (%)</td>
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<td>34.8</td>
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<tr>
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<td>11.1</td>
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<tr>
<td>Sleep Apnea (%)</td>
<td>19.0</td>
<td>4.3</td>
<td>.20</td>
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Note. Statistics were based on complete data for each time point.
Table 2. Baseline, 12-Week, and 24-Month T-Score Neuropsychological Test Performance among Bariatric Surgery Patients

<table>
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<tr>
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<th>Baseline M(SD)</th>
<th>12-week M(SD)</th>
<th>24-month M(SD)</th>
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<td>Digit Span Total</td>
<td>49.14 (9.00)</td>
<td>50.73 (9.66)</td>
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<td>SOA-A</td>
<td>54.71 (13.59)</td>
<td>57.24 (15.04)</td>
<td>58.91 (13.60)</td>
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<td>SOA-B</td>
<td>51.73 (16.83)</td>
<td>57.34 (13.69)</td>
<td>58.17 (13.09)</td>
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<tr>
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<td>52.92 (11.34)</td>
<td>54.01 (13.27)</td>
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<td><strong>Verbal Interference-Color</strong></td>
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<tr>
<td>Word</td>
<td>53.78 (11.49)</td>
<td>61.81 (12.86)</td>
<td>65.26 (11.50)</td>
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<td><strong>Maze Errors</strong></td>
<td>49.93 (12.75)</td>
<td>56.15 (11.98)</td>
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<td><strong>Memory</strong></td>
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<td><strong>Total Recall</strong></td>
<td>46.70 (14.02)</td>
<td>46.03 (15.37)</td>
<td>48.57 (15.10)</td>
</tr>
<tr>
<td><strong>LDFR</strong></td>
<td>46.61 (11.76)</td>
<td>49.35 (13.56)</td>
<td>49.92 (12.76)</td>
</tr>
<tr>
<td><strong>Recognition</strong></td>
<td>41.02 (11.19)</td>
<td>52.26 (11.03)</td>
<td>51.02 (9.05)</td>
</tr>
<tr>
<td><strong>Language</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Animal Fluency</strong></td>
<td>49.59 (11.16)</td>
<td>49.38 (10.43)</td>
<td>49.27 (11.96)</td>
</tr>
<tr>
<td><strong>Letter Fluency</strong></td>
<td>45.15 (11.44)</td>
<td>45.77 (10.24)</td>
<td>49.03 (11.47)</td>
</tr>
</tbody>
</table>

**Note.** Averages were based on complete data for each time point.

**Abbreviations**—SOA-A = Switching of Attention A; SOA-B = Switching of Attention B; LDFR = Long Delay Free Recall
### Table 3. Cognitive Function for Bariatric Surgery Patients and Obese Controls Over Time

<table>
<thead>
<tr>
<th>Domain</th>
<th>Baseline Surgery</th>
<th>Baseline Controls</th>
<th>12-weeks Surgery</th>
<th>12-weeks Controls</th>
<th>24-months Surgery</th>
<th>24-months Controls</th>
<th>Time (A, F)</th>
<th>Group X Time (A, F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attention</td>
<td>52.26(8.02)</td>
<td>52.64(7.31)</td>
<td>53.99(9.21)</td>
<td>54.71(8.55)</td>
<td>57.45(9.76)</td>
<td>56.11(9.62)</td>
<td>.82, 9.32**</td>
<td>.98, .86</td>
</tr>
<tr>
<td>Executive</td>
<td>51.81(9.95)</td>
<td>50.64(11.85)</td>
<td>58.44(10.21)</td>
<td>57.95(9.03)</td>
<td>58.58(9.58)</td>
<td>57.51(10.59)</td>
<td>.54, 35.85**</td>
<td>.99, .10</td>
</tr>
<tr>
<td>Memory</td>
<td>43.45(10.57)</td>
<td>44.99(10.18)</td>
<td>49.21(10.78)</td>
<td>44.24(13.33)</td>
<td>49.83(10.38)</td>
<td>47.54(10.70)</td>
<td>.87, 6.50**</td>
<td>.91, 4.05*</td>
</tr>
<tr>
<td>Language</td>
<td>47.37(10.08)</td>
<td>49.19(8.99)</td>
<td>47.57(8.54)</td>
<td>49.88(8.76)</td>
<td>49.15(10.10)</td>
<td>50.75(7.65)</td>
<td>.95, 2.03</td>
<td>.99, .89</td>
</tr>
</tbody>
</table>

*Note. *p* < .05; **p* < .01*
<table>
<thead>
<tr>
<th></th>
<th>Attention ($A, F$)</th>
<th></th>
<th>Executive ($A, F$)</th>
<th></th>
<th>Memory ($A, F$)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Surgery</td>
<td>Controls</td>
<td>Surgery</td>
<td>Controls</td>
<td>Surgery</td>
<td>Controls</td>
</tr>
<tr>
<td>BL-12wk</td>
<td>.93, 4.63*</td>
<td>.87, 3.24</td>
<td>.55, 51.83**</td>
<td>.52, 20.00**</td>
<td>.67, 31.06**</td>
<td>.99, 0.09</td>
</tr>
<tr>
<td>BL-24mon</td>
<td>.70, 26.27**</td>
<td>.86, 3.70</td>
<td>.53, 55.15**</td>
<td>.49, 23.18**</td>
<td>.71, 24.79**</td>
<td>.94, 1.46</td>
</tr>
<tr>
<td>12wk-24mon</td>
<td>.25, 20.77**</td>
<td>.96, 0.82</td>
<td>.99, .04</td>
<td>.99, 0.10</td>
<td>.99, 0.25</td>
<td>.86, 3.70</td>
</tr>
</tbody>
</table>

*Note.* *p* < .05; **p* < .01
Table 5. The effects of weight loss on cognitive function 24-months post-bariatric surgery patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Attention 24mon</th>
<th>ExecFunc. 24mon</th>
<th>Memory 24mon</th>
<th>Language 24mon</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Block 1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline TestΨ</td>
<td>.71(.14)**</td>
<td>.69(.13)**</td>
<td>.59(.17)**</td>
<td>.70(.10)**</td>
</tr>
<tr>
<td>Baseline BMI</td>
<td>.59(.47)*</td>
<td>-.25(.36)</td>
<td>.11(.60)</td>
<td>.37(.44)</td>
</tr>
<tr>
<td>12-week BMI</td>
<td>-.74(.48)**</td>
<td>.05(.52)</td>
<td>-.26(.59)</td>
<td>-.32(.45)</td>
</tr>
<tr>
<td>R²</td>
<td>.53</td>
<td>.44</td>
<td>.36</td>
<td>.55</td>
</tr>
<tr>
<td>F</td>
<td>15.65**</td>
<td>10.69**</td>
<td>7.78**</td>
<td>16.78</td>
</tr>
<tr>
<td><strong>Block 2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24-Month BMI</td>
<td>.09(.24)</td>
<td>-.14(.25)</td>
<td>-.30(.27)***</td>
<td>.45(.46)</td>
</tr>
<tr>
<td>R²</td>
<td>.54</td>
<td>.45</td>
<td>.41</td>
<td>.56</td>
</tr>
<tr>
<td>F for ΔR²</td>
<td>.37</td>
<td>.78</td>
<td>3.35</td>
<td>1.10</td>
</tr>
</tbody>
</table>

*Note. *p < .05; **p < .01; ***p = .075

Ψ = Corresponding baseline test performance for each cognitive domain

Abbreviations: Numerical values for variables in Block 1 and Block 2 are standardized regression coefficients and standard error; BMI = Body Mass Index; ExecFunc. 24mon = Executive Function at 24-months post-bariatric surgery