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## Cognitive Function Predicts 24-Month Weight Loss Success Following Bariatric Surgery

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### Abstract

**Background**—Clinically significant cognitive impairment, particularly in attention/executive and memory function, is found in many patients undergoing bariatric surgery. These difficulties have previously been linked to decreased weight loss 12 months post-surgery, but more protracted examination of this relationship has not yet been conducted.

**Objectives**—The current study prospectively examined the independent contribution of cognitive function to weight loss 24 months following bariatric surgery. Given the rapid rate of cognitive improvement observed following surgery, postoperative cognitive function (i.e., cognition 12 weeks following surgery, controlling for baseline cognition) was expected to predict lower body mass index (BMI) and higher percent total weight loss (%WL) at 24-month follow-up.

**Setting**—Data were collected by three sites of the Longitudinal Assessment of Bariatric Surgery (LABS) parent project.

**Methods**—Fifty-seven individuals enrolled in the LABS project undergoing bariatric surgery completed cognitive evaluation at baseline, 12 weeks, and 24 months. %WL and BMI were calculated for 24-month postoperative follow-up.

**Results**—Better cognitive function 12 weeks following surgery predicted higher %WL and lower BMI at 24 months, and specific domains of attention/executive and memory function were robustly related to decreased BMI and greater %WL at 24 months.

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**Conclusions**—Results demonstrate that cognitive performance shortly after bariatric surgery predicts greater long-term %WL and lower BMI 24 months following bariatric surgery. Further work is needed to clarify the degree to which this relationship is mediated by adherence to postoperative guidelines.

### Keywords

memory; cognition; executive function; adherence

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### Introduction

Bariatric surgery is viewed as the most effective intervention for severe obesity, though up to 30% of patients experience failure to lose weight or regain a significant amount of weight at extended follow-up.<sup>1</sup> A growing number of predictors for suboptimal postoperative weight loss have been identified. These include demographic variables (e.g., education level,<sup>2</sup> socioeconomic status, and ethnicity<sup>3</sup>), medical variables (e.g., type 2 diabetes mellitus, cholesterol level, and preoperative weight loss<sup>2</sup>), and psychosocial factors (e.g., restraint,<sup>4</sup> binge eating,<sup>5</sup> depression,<sup>2</sup> coping skills,<sup>6</sup> and social support<sup>5</sup>). However, even in combination, these factors fail to account for a substantial amount of the variance in weight loss outcomes.

Converging lines of research suggest that cognitive impairment may also contribute to suboptimal weight loss following bariatric surgery. Poorer attention/executive functioning skills and memory are consistently demonstrated in obese relative to lean individuals.<sup>7,8</sup> Specifically, higher body mass index (BMI) is associated with poorer performance on measures of response inhibition, working memory, planning, and ability to shift cognitive set.<sup>7</sup> Similarly, verbal learning and delayed recall are lower in obese individuals when compared to both lean and overweight individuals.<sup>8</sup> Clinically significant cognitive impairment of this nature is present in up to 23% of patients undergoing bariatric surgery, and approximately 40% exhibit more subtle cognitive deficits on testing.<sup>9</sup> Similar cognitive dysfunction is associated with reduced adherence to medical recommendations in other patient populations, including those with type 2 diabetes,<sup>10</sup> hypertension,<sup>11</sup> HIV,<sup>12</sup> and heart failure.<sup>13</sup> The presence of cognitive impairment may be particularly problematic in the bariatric population, given the many lifestyle changes required following surgery.<sup>14</sup>

Consistent with this pattern, we recently demonstrated that preoperative baseline cognitive impairment predicts weight loss outcome at one year.<sup>15</sup> Specifically, we examined the independent contribution of baseline cognitive function to weight loss in 84 individuals undergoing bariatric surgery. After accounting for medical and demographic variables, executive function and verbal learning/memory performances predicted percent excess weight loss and body mass index (BMI) at 12-month follow-up; poorer baseline cognitive function in these domains was associated with reduced weight loss.<sup>15</sup>

However, less is known about the possible influence of cognitive function on weight loss at later postoperative follow-up. Although cognitive function predicted weight loss at 12 months, 24 months may better reflect enduring surgical outcomes, as this time point is more closely related to long-term weight maintenance or early regain.<sup>16</sup> We hypothesized that better cognitive function at 12 weeks (specifically, higher performance on measures of executive/attention and memory abilities, after controlling for baseline cognitive function) would predict higher percent weight loss (%WL) and lower BMI 24 months following surgery.

## Materials and Methods

### Trial Design and Participants

A total of 57 bariatric surgery patients were recruited into this multi-site prospective study examining the neurocognitive effects of bariatric surgery. All participants were part of the Longitudinal Assessment of Bariatric Surgery (LABS) parent project and were recruited from three LABS sites.<sup>17</sup> 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 the individuals completing 24 month follow-up data. 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),<sup>18</sup> past or current history of severe psychiatric illness (e.g. schizophrenia, bipolar disorder), past or current history of alcohol or drug abuse, history of a learning disorder or developmental disability, or impaired sensory function that precluded cognitive testing (e.g. visual deficits preventing adequate perception of test stimuli) per participant report or examiner observation. Medical history was obtained via medical record review from the LABS study as well as participant self-report. Within the sample, just 1 bariatric surgery patient underwent a lapband procedure, thus no comparisons for type of surgery were conducted. Participants averaged 43.65 (Standard deviation (SD) = 11.24) years of age and were 87.7% female. See Table 1 for baseline demographic and clinical characteristics.

### Interventions and Clinical Follow-Up

This study is registered with clinicaltrials.gov and all procedures were approved by the appropriate Institutional Review Boards. All participants provided written informed consent prior to study involvement. Participants completed self-report measures of demographic and medical characteristics and a computerized cognitive test battery at baseline (within 30 days prior to surgery), 12 weeks ( $\pm$  5 days), and 24 months ( $\pm$  30 days) following surgery. Weight and height were measured in the research office with shoes removed, but clothes on. Height measurement was taken twice, or until equal values were obtained on consecutive trials. Medical records were reviewed by research staff to corroborate and supplement participant self-report.

### Outcomes

The current study examined whether cognitive function 12 weeks following bariatric surgery predicted %WL and BMI at 24 month follow-up. The Integneuro cognitive test battery demonstrates strong psychometric properties<sup>19</sup> and was chosen based upon previous work from our lab showing its sensitivity to the cognitive difficulties manifested in obese persons.<sup>20</sup> This cognitive test battery consists of estimated premorbid intellectual abilities as well as performance in cognitive domains most sensitive to deficits in this population (i.e., Attention/Executive Function, Verbal Memory) and can be completed in 45–60 minutes. Specific tests were categorized into Attention/Executive Function and Verbal Memory domains and included:

#### Attention/Executive Function

**Digit Span Backward:** 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 immediately asked to enter the digits in a backward sequence on a numeric keypad on the touch-screen. The number of digits in each sequence gradually

increases from 3 to 9, with two sequences at each level. The total number of trials correct was used in the current analyses.

**Switching of Attention:** This test is a computerized adaptation of the Trail Making Test B.<sup>21</sup> An array of 13 numbers (1–13) and 12 letters (A–L) is presented. Subjects are asked to touch numbers and letters alternately in ascending order. This test assesses attention and psychomotor speed as well as executive function. Time to completion served as the dependent variable.

**Verbal Interference:** This task taps the ability to inhibit automatic and irrelevant responses and is similar to the Stroop Color Word Test.<sup>22</sup> Participants are presented with color words one at a time, printed in a different color ink. Below each color word is a response pad with the four possible words displayed in black and in fixed format. The subject is required to name the color of each word as quickly as possible, assessing cognitive inhibition. Total number of words correctly identified served as the dependent variable in this study.

**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. Total number of correct words generated across the three trials was the dependent variable.

**Maze Task:** This task is a computerized adaptation of the Austin Maze<sup>23</sup> and assesses executive function. Participants are presented with a grid (8×8 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. The dependent variable was the number of total errors on the task.

### 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. Following presentation and recall of a distraction list, participants are asked to recall words from the original list. 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. Short Delay Free Recall, Long Delay Free Recall, and Recognition of these verbal list items were used to assess memory.

### Data Analyses

To facilitate clinical interpretation and maintain directionality within scales, all raw scores of neuropsychological measures assessing cognitive function were transformed to T-scores (a distribution with a mean of 50, and a standard deviation of 10) using existing normative data correcting for age, gender, and estimated premorbid intelligence. A global cognitive function composite score for baseline and 12-week postoperative time points was then created that consisted of the mean of the T-scores for each task listed above. A higher score on this composite was reflective of better performance. BMI and %WL were calculated using the standard formulas.

A repeated measures analysis of variance (ANOVA) was first conducted to determine whether cognitive function improved from baseline to 12 weeks following surgery, as previous work has shown this type of improvement.<sup>9</sup> If early postoperative cognitive change is present in the current sample, utilizing preoperative baseline data would not accurately capture cognitive function during the period of interest (i.e., 24 months following surgery). Early cognitive effects of surgical intervention on weight loss were thus accounted for in a series of regression analyses examining whether cognitive function at 12 weeks predicts

long-term weight loss. Specifically, regression analyses examined the predictive validity of the 12-week global cognitive composite score on %WL and BMI at 24 months. For analyses examining %WL at 24-months as the dependent variable, the baseline global cognitive composite, %WL at 12 weeks, gender (1 = male; 2 = female), and diagnostic history of depression were entered in block 1. We controlled for depression (history of or current depression as diagnosed by a mental health professional or use of antidepressant medication) to account for its known effects on long-term weight loss in bariatric patients following surgery.<sup>2</sup> The global cognitive function composite score at 12-weeks was then entered into block 2. This same analysis was conducted for BMI at 24-months except baseline BMI was entered in block 1 rather than %WL at 12-weeks.

## Results

### Baseline, 12-week, and 24-month BMI and %WL

The average baseline BMI within the sample was 46.49 (SD = 5.22) kg/m<sup>2</sup>. There was a significant decrease in BMI from baseline to 12 weeks following surgery ( $F(1,56) = 573.29$ ,  $p < .001$ ; Mean 12-week BMI = 38.43 (SD = 4.81) kg/m<sup>2</sup>) and from 12 weeks to 24 months following surgery ( $F$ -statistic ( $F$ ) (1,56) = 119.59,  $p$ -value ( $p$ ) < .001; mean 24-month BMI = 31.17 (SD = 6.46) kg/m<sup>2</sup>). Consistent with this pattern, there was a significant increase in %WL ( $F(1,56) = 120.77$ ,  $p < .001$ ) from 12 weeks (Mean (M) = 17.30 (SD = 5.25) %) to 24 months (M = 33.00 (SD = 10.90) %) following surgery.

### Cognitive function at baseline and 12 weeks following surgery

Consistent with clinical interpretation, cognitive impairment was defined as a T-score < 35 (i.e., 1.5 SD below the mean). At baseline, 8.8% of the sample exhibited impairments on short delay free recall, 14.0% on long delay free recall, and 19.3% demonstrated impairments on the recognition task. For attention/executive function, 22.8% of the sample exhibited impaired performance on the letter fluency task. Impairments on the other tasks of attention/executive function were less common. When using the global cognitive composite score, repeated measures ANOVA showed significant improvements in cognitive function from baseline to 12 weeks following surgery ( $F(1,56) = 56.29$ ,  $p < .001$ ). Refer to Table 2 for baseline, 12 week, and 24 month cognitive test performance in the sample.

### 12 Week Cognitive Function Predicts %WL and BMI at 24 Month Follow-Up

Regression analyses showed that after controlling for baseline cognitive function, 12 week %WL, gender, and diagnostic history of depression, the 12 week global cognitive composite demonstrated significant predictive validity for %WL at 24 months ( $F(1,51) = 4.16$ ,  $p < .01$ ). The global cognitive composite score at 12 weeks also predicted BMI 24 months following surgery ( $F(1,51) = 11.64$ ,  $p < .001$ ) after accounting for baseline cognitive function, baseline BMI, gender, and diagnostic history of depression. In each case, better cognitive function 12 weeks following surgery predicted greater %WL ( $\beta = .64$ ,  $p < .01$ ) and lower BMI 24 months following surgery ( $\beta = -.60$ ,  $p < .001$ ). See Table 3 and 4 for a summary of %WL and BMI hierarchical regression analyses.

### Correlations between 24 Month %WL/BMI and Specific Cognitive Domain Scores

Partial correlations were conducted to clarify the relationship between specific measures of cognitive function at 12 weeks and %WL and BMI at 24 months. After adjusting for baseline cognitive function, diagnostic history of depression, gender, and 12 week %WL, a significant association emerged between digit span backwards performance at 12-weeks (Pearson's correlation ( $r$ )(51) = .32,  $p = .02$ ) and verbal interference at 12-weeks ( $r$ (51) = .27,  $p = .047$ ) with 24-month %WL. A strong trend also emerged for long delay free recall

( $r(51) = .24, p = .08$ ). Improved performance on these cognitive tasks at 12 weeks predicted greater %WL 24 months following surgery. This pattern did not emerge for the other cognitive tasks ( $p > .05$ ).

Partial correlations adjusting for baseline cognitive function, baseline BMI, gender, and diagnostic history of depression showed better 12-week performance on the following tasks predicted lower BMI at 24 months: digit span backwards ( $r(51) = -.33, p = .02$ ), long delay free recall ( $r(51) = -.31, p = .02$ ), and verbal interference ( $r(51) = -.28, p = .04$ ). This pattern did not emerge for the other cognitive measures ( $p > .05$ ).

## Discussion

The current study prospectively examined cognitive function as a predictor of weight loss following bariatric surgery. Bariatric surgery patients demonstrated baseline cognitive impairment that improved 12 weeks following bariatric surgery. In addition, cognitive function at 12 weeks postoperatively was associated with lower BMI and significantly higher postoperative %WL at 24 months.

Finding that cognitive performance shortly after surgery predicts weight loss outcomes 2 years later is particularly noteworthy. Although the mechanism for this relationship is not entirely clear, greater adherence in individuals with better cognitive performance has been previously suggested<sup>15</sup> and appears most likely. Specifically, deficits in executive functions (which include higher-order cognitive abilities such as inhibition, planning, and complex focus)<sup>24</sup> could lead to greater difficulty resisting temptation to eat desired foods. In fact, the elevated behavioral disinhibition observed in the obese population<sup>25</sup> appears to increase susceptibility to food cues and reduces control of eating behavior,<sup>26</sup> and executive dysfunction is linked to high calorie snack food intake and sedentary behavior.<sup>27</sup> Similarly, reduced memory or organizational skills might impact ability to incorporate regular exercise into daily life and correctly track physical activity. Consistent with this notion, a recent study examining pre- to postoperative changes in physical activity found postoperative decreases in objectively measured physical activity, despite patient reports of a 5× increase.<sup>28</sup> Taken together, such findings suggest that cognitive dysfunction could be responsible for reduced postoperative weight loss through a mechanism of reduced adherence to postoperative diet, eating behavior, and physical activity guidelines. Future studies are needed to clarify the influence of cognitive function on adherence in this population.

Previous studies found clinically meaningful baseline cognitive impairment in up to 23% of patients undergoing bariatric surgery.<sup>9</sup> Similarly, clinically significant baseline cognitive impairment in the current study ranges from 9–23%, with the greatest deficits in executive function and memory. This finding underscores that a notable subset of bariatric surgery patients exhibit significant cognitive impairment on testing. Particularly in light of the association between cognition and weight loss outcomes, cognitive function may be an important consideration in clinical screening of bariatric surgical candidates, as it may help identify individuals needing more intensive psychological or educational services. However, it is noted that empirical research has not yet determined the extent of benefit additional services might confer, or the nature of the services that may be most helpful for these patients. Future research should focus on interventions tailored to the nature of the cognitive impairment in the individual, and determine if adherence interventions targeting specific cognitive profiles result in better adherence and more positive weight loss outcomes.

The limitations of the current study include the small sample size. Although direct comparison of weight loss outcomes in individuals with and without cognitive impairment,

or examination of the potential contribution of medical comorbidities would be of interest, due to attrition over the course of 2 years, the sample is not sufficiently powered to conduct these analyses. Further, although a 24-month follow-up should be adequate to capture problematic weight maintenance or early regain,<sup>16</sup> greater variability in outcomes might be found at a more extended follow-up period, and thus would be helpful in determining the contribution of cognition to long-term weight loss outcomes. In addition, obtaining medical characteristics via self-report and medical record review may be suboptimal. Future research may wish to consider direct evaluation of individual comorbid medical conditions (e.g., sleep study for sleep apnea) for better understanding of participant characteristics that may be related to cognitive results. Finally, although the current study, in combination with previous research, implicates adherence to postoperative lifestyle change as a mediator for the relationship between cognitive performance and weight loss outcomes, we did not have opportunity to directly examine the relationship between adherence and cognition. Future research investigating the contribution of cognitive function to postoperative weight loss outcomes should incorporate measures of adherence to postoperative diet, eating behavior, and physical activity guidelines, optimally utilizing a combination of self-report as well as objective (e.g., accelerometry) and real-time (e.g., ecological momentary assessment) data collection. Examining cognitive factors associated with failure to follow bariatric surgical program recommendations will be of benefit in identifying not only which patients might need greater support in adherence behavior, but may also identify specific cognitive predictors of postoperative failures in adherence, thus providing a target for possible intervention. For example, it has been suggested that for the subset of individuals in this population experiencing executive dysfunction, an adherence intervention including frequent reminders regarding structured, specific, and detailed postoperative daily plans for diet, eating behavior, and physical activity might be more beneficial than general guidelines typically provided to patients.<sup>15</sup> Similar approaches utilizing technology have demonstrated positive effects in other patient populations with known executive dysfunction and memory problems (e.g., heart failure)<sup>29</sup> as well as obesity<sup>30</sup> but this has not been examined in bariatric surgery patients. If supported, this approach could help optimize outcomes and reduce costs over time.

## Conclusions

Results of the current study indicate that better cognitive test performance shortly after surgery predicts higher %WL and lower BMI 24 months following bariatric surgery. Further work is necessary to clarify the degree to which adherence to postoperative guidelines for diet, eating behavior, and physical activity contributes to the relationship between weight loss and cognitive function, as this approach may ultimately help identify those individuals in greatest need for intervention to optimize postoperative weight loss.

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**Table 1**

## Demographic and Clinical Characteristics of 57 Bariatric Surgery Patients

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<b>DEMOGRAPHIC CHARACTERISTICS</b>	
Age, mean (SD)	43.65 (11.24)
Female (%)	87.7
Race (% Caucasian, % Black)	80.7, 5.3
<b>BASELINE MEDICAL CHARACTERISTICS (%)</b>	
Hypertension	54.4
Diabetes	29.8
Sleep Apnea	38.6
Depression	52.6

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SD = Standard Deviation

**Table 2**

Baseline, 12-Week, and 24-Month T-Scores for Neuropsychological Test Performance in Bariatric Surgery Patients

	<b>Baseline M(SD)</b>	<b>12-week M(SD)</b>	<b>24-month M(SD)</b>
<i>Attention/Executive Function</i>			
Digit Span Backward	49.91(11.29)	51.85(11.02)	54.92(12.93)
SOA-B	52.85(16.72)	58.37(12.67)	58.95(12.67)
Verbal Interference	53.44(12.30)	60.77(13.18)	63.63(12.03)
Verbal Fluency	44.89(10.70)	46.03(10.05)	48.89(10.69)
Maze Errors	50.90(12.26)	57.01(12.02)	53.40(10.57)
<i>Memory</i>			
SDFR	46.66(10.74)	49.01(12.49)	51.13 (13.94)
LDFR	46.47(11.47)	49.98(13.58)	51.58(12.76)
Recognition	41.74(11.45)	53.17(10.72)	51.26(9.38)

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

Abbreviations—SOA-B = Switching of Attention B; SDFR = Short Delay Free Recall; LDFR = Long Delay Free Recall; SD = Standard Deviation; M = Mean

**Table 3**

Regression Model Examining the Predictive Validity of Cognitive Function at 12 Weeks on 24-Month %WL  
(*N* = 57)

	<u>24-Month %WL</u> ( <i>SE b</i> )
<u>Block 1</u>	
Baseline Cognitive Function	-.01(.19)
%WL-12-weeks	.31(.28)*
Depression (1= positive; 0 = negative)	-.01(2.86)
Gender	.26(4.46)
<i>R</i> <sup>2</sup>	.13
<i>F</i>	1.98
<u>Block 2</u>	
Cognitive Function 12-weeks	.64(.32)**
<i>R</i> <sup>2</sup>	.29
<i>F</i> for <i>R</i> <sup>2</sup>	11.32**

Note.

\* *p* < .05;

WL = Weight Loss

**Table 4**

Regression Model Examining the Predictive Validity of Cognitive Function at 12 Weeks on 24-Month BMI  
( $N = 57$ )

	<b>24-Month BMI</b> <i>(SE b)</i>
<u>Block 1</u>	
Baseline Cognitive Function	-.03(.09)
BMI Baseline	.56(.14) **
Gender (1 = Male; 2 = Female)	-.16(2.25)
Depression (1 = positive; 0 = negative)	.02(1.42)
$R^2$	.39
$F$	8.25 **
<u>Block 2</u>	
Cognitive Function 12-weeks	-.60(.15) **
$R^2$	.49
$F$ for $R^2$	15.82 **

Note.

\*\*  
 $p < .01$ ;

BMI = Body Mass Index