Clinical Science

Cognitive function after bariatric surgery: evidence for improvement 3 years after surgery

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KEYWORDS:
Bariatric surgery; Obesity; Cognitive function; Weight loss

Abstract
BACKGROUND: Bariatric surgery is associated with improved cognition, and it is possible that such improvements are found at extended follow-ups. We hypothesized that cognitive improvement would be maintained 3 years after bariatric surgery.

METHODS: Fifty bariatric patients were recruited from the Longitudinal Assessment of Bariatric Surgery parent project. Participants completed a computerized cognitive test battery to assess cognitive function at 12 weeks, 12 months, 24 months, and 36 months after surgery.

RESULTS: Repeated measures revealed main effects for attention, executive function, and memory. Attention improved up to 24 months and then slightly declined although it still fell within the average range at 36 months. Improvements in executive function reached their peak at 36 months after surgery. Short-term improvements in memory were maintained at 36 months. No main effect emerged for language.

CONCLUSIONS: Bariatric surgery may lead to lasting improvements in cognition. Prospective studies with extended follow-ups (eg, 10 years) should examine whether bariatric surgery can attenuate cognitive decline in severely obese patients.

Obesity has reached epidemic proportions, with up to 35.5% of adult men and 35.8% of adult women categorized as obese.1 It is well established that obesity leads to poor health (eg, diabetes, hypertension, and coronary artery disease)2 and outcomes (eg, increased mortality and morbidity risk).3 Extant evidence also shows that obesity adversely affects the brain. For example, obesity has been linked with an increased risk for neurologic changes, including Alzheimer disease, vascular dementia, and brain atrophy.4,5 Indeed, obese persons also exhibit impairments on formal cognitive testing, including tasks of attention, executive function, and memory.6,7

Bariatric surgery has become an increasingly popular and effective treatment option for weight loss among severely...
obese people. Bariatric surgery is associated with lower mortality and morbidity risk, decreased hospitalizations, and reduced need for medications. Recent work also shows that bariatric surgery is associated with cognitive improvement at 12 weeks and 24 months postoperatively, particularly in memory abilities.

Despite these findings, the long-term impact of bariatric surgery on cognitive function remains poorly understood. This is unfortunate because the acute improvements in cognitive function after surgery and the substantial weight loss may reduce the known cognitive decline in obese people or even the risk of Alzheimer disease. The purpose of the current study was to determine the effects of bariatric surgery on cognitive function up to 3 years after surgical intervention. Based on past studies, we hypothesized that bariatric surgery patients would exhibit improved cognitive function immediately after surgery and such improvements would be maintained at the long-term follow-up, including 36 months postoperatively. Exploratory analyses among a subsample also examined the hypothesis that cognitive benefits would last up to 4 years after bariatric surgery.

Methods

Trial design and participants

A total of 50 consecutive bariatric patients were recruited into this multisite 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 3 LABS sites. Patients 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. For study inclusion, participants were required to be enrolled in LABS, between the ages of 20 and 70 years, and English speaking. Exclusion criteria included a history of neurologic disorder or injury (e.g., dementia, stroke, or seizures), moderate or severe head injury (defined as >10 minutes loss of consciousness), past or current history of severe psychiatric illness (e.g., schizophrenia or bipolar disorder), past or current history of alcohol or drug abuse (defined by Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition), history of a learning disorder or developmental disability (defined by Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition 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.

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 gastric banding procedure, and, thus, no comparisons for type of surgery (Roux-en-Y gastric bypass vs gastric banding) were conducted.

The present sample represents all participants that have completed ≥36 months of follow-up data. Participants excluded as a result of attrition and/or subsequent missing data across time points were not different in terms of age ($t_{127} = .63, P = .53$); baseline body mass index (BMI) ($t_{127} = .54, P = .59$); or baseline cognitive function in attention ($t_{127} = .42, P = .68$), executive function ($t_{127} = .14, P = .89$), memory ($t_{127} = 1.14, P = .26$), or language ($t_{127} = -9.8, P = .33$).

In addition, exploratory analyses also examined cognitive function 48 months after bariatric surgery. For these analyses, the sample size was reduced to 21 as a result of further participant attrition. Participants excluded as a result of incomplete data at 48 months did not differ in terms of age or baseline medical history of diabetes (chi-square 1 [N = 50] = .49, $P = .49$) or sleep apnea (chi-square 1 [N = 50] = 2.79, $P = .10$). However, participants excluded were more likely to have a diagnosis of hypertension at baseline (chi-square 1 [N = 50] = 6.65, $P = .01$; 65.5% vs 28.6%). Table 1 provides demographic and clinical characteristics.

Interventions and clinical follow-up

All procedures were approved by the appropriate institutional review boards before study onset. All participants provided written informed consent before study involvement. Bariatric surgery participants completed a series of self-report instruments and a computerized cognitive test battery at baseline (within 30 days before surgery), 12 weeks (± 5 days), 12 months (± 30 days), 24 months (± 30 days), 36 months (± 30 days), and 48 months (± 30 days) after surgery. Medical records were reviewed by research staff to corroborate and supplement self-report.

Outcomes

The IntegNeuro (Brain Resource Company Ltd, San Francisco, CA) cognitive test battery assesses estimated premorbid intellectual abilities as well as performance in multiple cognitive domains (e.g., attention, executive function, and verbal memory) and can be completed in 45 to 60 minutes. It has excellent psychometric properties and has been shown to be sensitive to the effects of obesity in past work. Specific tests were categorized into attention, executive function, memory, and language domains.

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 1-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 2 sequences at each level. The participants complete these
same procedures in a backward sequence. The total digit span for both forwards and backwards served as the dependent variable.

Switching of attention: This test is a computerized adaptation of the Trail Making Test and consists of 2 parts. Participants are asked to touch a series of 25 numbers in ascending order as quickly as possible. An array of 13 numbers (1 to 13) and 12 letters (A to 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.

Verbal interference: This task taps the ability to inhibit automatic and irrelevant responses and is similar to the Stroop Color Word Test. Participants are presented with colored words 1 at a time. Below each colored word is a response pad with the 4 possible words displayed in black and in a 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 the color of each word as quickly as possible, assessing executive function.

Maze task: This task is a computerized adaptation of the Austin Maze 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 had elapsed.

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 after each trial. After the 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. 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 participants to generate words beginning with a given letter of the alphabet for 60 seconds. A different letter is used for each of the 3 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 normative data correcting for age, sex, 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 standard deviation [SD] below the mean) was reflective of cognitive impairment.

Repeated measures analysis of variance (ANOVA) was performed to determine change in cognitive function after bariatric surgery. Specifically, analyses examined changes in attention, executive function, memory, and language across the following time points: baseline, 12 weeks, 12 months, 24 months, and 36 months. Separate exploratory analyses were then conducted to examine cognitive function in each domain from baseline to 48 months after bariatric surgery. These analyses were conducted separately because of reduced sample size due to participant attrition from 36 to 48 months after bariatric surgery (see Methods section). Repeated measures and bivariate correlation analyses also examined the possible effects of weight regain on cognitive function.

Results

Baseline and 36-month BMI and comorbid medical status

Based on conventional BMI categories, the current sample of bariatric surgery patients were classified as very severely obese at baseline (mean BMI = 46.61 [SD = 5.27]). However, the average BMI reduced to 32.35 (SD = 6.57) (ie, moderately obese) at 36 months, which represents a significant decline (t = 14.55, P < .001). A similar pattern emerged with comorbid medical status. Specifically, relative to baseline, significantly fewer participants had hypertension (chi-square = 4.49, P = .03) or diabetes (chi-square = 14.55, P < .001; Table 1).
Baseline and 36-month postoperative cognitive function in bariatric surgery patients

At baseline, when compared with normative data, cognitive test performance in the bariatric surgery patients fell within the low average range for memory and in the average range for all other cognitive domains (Table 2). Bariatric surgery patients had clinically significant impairments in cognitive function at baseline. When using a t score cutoff of 35, 12.0% and 8.0% of patients showed impairments in memory and executive function. Impairments in attention and language were less common (4.0% of patients for both domains). At the 36-month postoperative follow-up, bariatric surgery patients' cognitive test performance for all domains of cognitive function fell within the average range, and the prevalence of impairment was also less prevalent.

Cognitive function after bariatric surgery

Fig. 1 shows the trajectory of cognitive function for each domain from baseline to 36 months after bariatric surgery. Repeated measures ANOVA examined changes in attention, executive function, memory, and language after bariatric surgery at 12 weeks, 12 months, 24 months, and 36 months (Table 3). There was a significant main effect for attention across the 5 time points (A = .32, F_{4,46} = 24.15, P < .001). As shown in Fig. 1, attention generally improved up until 12 months and then declined between 24 and 36 months after bariatric surgery (A = .40, F_{1,49} = 72.38, P < .001). Consistent with this pattern, follow-up analyses showed significant improvements in attention from baseline to 12 weeks (A = .85, F_{1,49} = 8.47, P < .01), 12 months (A = .69, F_{1,49} = 22.20, P < .001), and 24 months (A = .60, F_{1,49} = 33.37, P < .001).

For executive function, there was also a significant main effect for time (A = .41, F_{4,46} = 16.75, P < .001). The most significant improvement in executive function was found 12 weeks after bariatric surgery (A = .56, F_{1,49} = 38.60, P < .001), and after a slight nonsignificant decline from 12 weeks to 12 months (A = .98, F_{1,49} = .91, P = .35), executive function continued to improve until it reached its peak at 36 months postoperatively (Fig. 1). Of note, executive function significantly improved from baseline to each of the distant time points (baseline to 12 months [A = .65, F_{1,49} = 26.76, P < .001]; baseline to 24 months [A = .53, F_{1,49} = 44.09, P < .001]; and baseline to 36 months [A = .45, F_{1,49} = 60.89, P < .001]).

For memory, there was a significant main effect across the 5 time points (A = .57, F_{4,46} = 15.16, P < .001). Examination of Fig. 1 shows that memory gradually improved up until 12 months and then remained largely unchanged from 12 to 36 months after bariatric surgery. Follow-up analyses showed significant improvements in memory from baseline to each of the distant time points (12 weeks [A = .62, F_{1,49} = 30.31, P < .001], 12 months [A = .44, F_{1,49} = 63.40, P < .001], 24 months [A = .72, F_{1,49} = 19.32, P < .001], and 36 months [A = .68, F_{1,49} = 23.56, P < .001]). No significant main effect emerged for language (A = .83, F_{4,46} = 2.32, P = .07).

48-month postoperative cognitive function

Exploratory analyses for cognitive test performance at 48 months after bariatric surgery showed that attention, memory, and language functioning fell within the average range, whereas executive function fell within the high average to above average range. Repeated measures ANOVA showed significant improvements from baseline to 48 months after bariatric surgery in the following

<table>
<thead>
<tr>
<th>Cognitive domains and measures</th>
<th>Baseline, mean (SD)</th>
<th>12 weeks, mean (SD)</th>
<th>12 months, mean (SD)</th>
<th>24 months, mean (SD)</th>
<th>36 months, mean (SD)</th>
<th>48 months*, mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attention/executive function</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digit span total</td>
<td>49.30 (8.41)</td>
<td>50.63 (9.78)</td>
<td>53.01 (10.76)</td>
<td>55.56 (11.15)</td>
<td>51.15 (10.46)</td>
<td>53.47 (12.41)</td>
</tr>
<tr>
<td>SOA-A</td>
<td>55.17 (14.12)</td>
<td>58.83 (14.39)</td>
<td>61.65 (16.39)</td>
<td>59.76 (13.31)</td>
<td>52.54 (12.99)</td>
<td>58.53 (10.65)</td>
</tr>
<tr>
<td>SOA-B</td>
<td>52.28 (17.80)</td>
<td>58.42 (12.69)</td>
<td>57.68 (15.09)</td>
<td>58.80 (13.44)</td>
<td>58.48 (13.02)</td>
<td>61.90 (11.43)</td>
</tr>
<tr>
<td>Verbal Interference word</td>
<td>51.98 (11.45)</td>
<td>54.10 (12.95)</td>
<td>56.09 (15.31)</td>
<td>59.15 (11.42)</td>
<td>45.75 (19.10)</td>
<td>50.41 (11.50)</td>
</tr>
<tr>
<td>Verbal interference color/word</td>
<td>52.78 (11.84)</td>
<td>60.98 (13.81)</td>
<td>60.54 (12.38)</td>
<td>64.60 (11.21)</td>
<td>65.49 (11.06)</td>
<td>67.81 (12.79)</td>
</tr>
<tr>
<td>Maze errors</td>
<td>50.51 (12.86)</td>
<td>56.32 (12.83)</td>
<td>54.96 (11.58)</td>
<td>53.52 (11.04)</td>
<td>55.68 (13.37)</td>
<td>58.55 (14.19)</td>
</tr>
<tr>
<td>Memory</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total learning</td>
<td>43.19 (14.07)</td>
<td>47.09 (14.94)</td>
<td>51.86 (14.05)</td>
<td>49.28 (15.42)</td>
<td>46.37 (16.22)</td>
<td>55.24 (12.62)</td>
</tr>
<tr>
<td>LDFR</td>
<td>46.78 (11.80)</td>
<td>50.59 (13.40)</td>
<td>56.21 (10.08)</td>
<td>51.72 (12.87)</td>
<td>51.49 (13.98)</td>
<td>56.80 (12.77)</td>
</tr>
<tr>
<td>Recognition</td>
<td>42.12 (10.57)</td>
<td>53.06 (10.10)</td>
<td>51.65 (8.67)</td>
<td>50.76 (9.26)</td>
<td>54.14 (9.68)</td>
<td>53.53 (7.69)</td>
</tr>
<tr>
<td>Language</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verbal fluency</td>
<td>45.45 (10.43)</td>
<td>45.99 (9.79)</td>
<td>47.02 (10.27)</td>
<td>49.71 (9.92)</td>
<td>48.41 (9.33)</td>
<td>47.55 (9.23)</td>
</tr>
<tr>
<td>Animal fluency</td>
<td>50.26 (10.83)</td>
<td>50.33 (10.82)</td>
<td>51.09 (11.91)</td>
<td>50.74 (11.53)</td>
<td>50.18 (12.48)</td>
<td>52.86 (14.61)</td>
</tr>
</tbody>
</table>

Averages were based on complete data for each time point.
LDFR = long delay free recall; SD = standard deviation; SOA-A = switching of attention number; SOA-B = switching of attention letter number.
*N = 21.
domains: executive function ($\alpha = .49, F_{1,120} = 20.58, P < .001$; baseline executive function: mean [SD] = 53.84 [10.88] vs executive function at 48 months: mean [SD] = 62.75 [10.32]) and memory ($\alpha = .39, F_{1,20} = 31.60, P < .001$; baseline memory: mean [SD] = 55.19 [8.11]) vs memory at 48 months: mean [SD] = 55.19 [8.11]). No such pattern emerged for attention ($\alpha = .99, F_{1,20} = .29, P = .60$; baseline attention: mean [SD] = 54.14 [8.41] vs attention at 48 months: mean [SD] = 50.20 [10.94]).

Weight regain and cognitive function

Participants exhibited significant declines in BMI from baseline to 36 months after bariatric surgery ($F_{1,46} = 300.06, P < .001$). However, significant weight regain was observed between 24 and 36 months postoperatively ($F_{1,46} = 14.42, P < .001$; BMI: mean [SD] = 31.07 [6.67] vs 32.25 [6.66]). Specifically, 74.5% of participants exhibited an increase in BMI during this time period, with an average increase of 1.27 ± 2.30 (range from −5.16 to 8.15, 17.0% with a >3.0 BMI unit increase). Participants who exhibited weight regain from 24 to 36 months postoperatively also showed significant declines in attention ($F_{1,34} = 67.24, P < .001$). No changes were noted for any of the other cognitive domains ($P > .05$). Bivariate correlations also revealed a trend for an increase in BMI from 24 to 36 months after surgery and poorer 36-month performance in attention ($r_{47} = −.27, P = .069$). No such pattern emerged for the other cognitive domains ($P > .10$).

Comments

The current study hypothesized that bariatric surgery patients would show postoperative improvements in cognitive function that would be maintained at a 36-month follow-up. Our findings support this hypothesis and extend previous work by showing the long-term cognitive benefits of bariatric surgery. Specifically, the current findings show that improvements in memory are maintained at 36 months postoperatively and further indicate that executive function improves up to this time point. Exploratory analyses at longer follow-up visits also yielded promising results, indicating that these cognitive benefits may be maintained.

Table 3  Cognitive function for bariatric surgery patients 36 months postoperatively ($t$ score: mean [SD])

<table>
<thead>
<tr>
<th>Time point</th>
<th>Attention (T-score)</th>
<th>Executive function (T-score)</th>
<th>Memory (T-score)</th>
<th>Language (T-score)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>52.15 (7.90)</td>
<td>51.86 (10.24)</td>
<td>44.03 (10.42)</td>
<td>47.85 (9.27)</td>
</tr>
<tr>
<td>12 weeks</td>
<td>54.52 (8.48)</td>
<td>58.58 (10.60)</td>
<td>50.25 (10.40)</td>
<td>48.16 (8.37)</td>
</tr>
<tr>
<td>12 months</td>
<td>56.92 (10.04)</td>
<td>57.73 (10.55)</td>
<td>52.95 (8.29)</td>
<td>49.06 (9.62)</td>
</tr>
<tr>
<td>24 months</td>
<td>58.16 (9.34)</td>
<td>58.98 (10.04)</td>
<td>50.59 (10.71)</td>
<td>50.23 (8.97)</td>
</tr>
<tr>
<td>36 months</td>
<td>49.81 (10.99)</td>
<td>59.88 (9.80)</td>
<td>50.67 (11.62)</td>
<td>49.49 (9.47)</td>
</tr>
<tr>
<td>$F$</td>
<td>24.15*</td>
<td>16.75*</td>
<td>15.16*</td>
<td>2.32</td>
</tr>
<tr>
<td>Partial eta</td>
<td>.68</td>
<td>.59</td>
<td>.57</td>
<td>.17</td>
</tr>
</tbody>
</table>

* $P < .001$.
up until 48 months. These findings continue to support the notion that cognitive dysfunction related to obesity may be at least partially reversible after bariatric surgery.

The implications of these findings are noteworthy in light of the extant literature that shows midlife obesity as a risk factor for Alzheimer disease and vascular dementia. Given that the current sample of participants were in midlife at study onset and showed high rates of impairment in memory and executive function, they may have been at increased risk for future dementia. However, after surgery, performance across multiple domains of cognitive function improved, suggesting that bariatric surgery may reduce risk for Alzheimer disease in obese patients. Future research should clarify this possibility by examining the cognitive benefits of bariatric surgery at very extended follow-ups (eg, 10 years), particularly given the many surgical patients that regain weight over time.

The mechanisms for improved cognition after bariatric surgery are not well understood. Although rates of medical comorbidities (ie, hypertension and diabetes) decreased in the current sample, previous research has shown that the cognitive benefits of bariatric surgery largely occur independent of changes in medical condition status. Studies using direct measurements of possible mechanisms (eg, plasma concentrations of HbA1C and ambulatory blood pressure) are much needed to elucidate whether more subtle changes are associated with cognitive improvement. Future research should also examine other potential mechanisms of change, including factors closely linked with obesity and known to impair cognitive function (eg, cerebral blood flow and vascular function).

Interestingly, we found that weight regain was associated with reduced attention from 24 to 36 months postoperatively. Although the average amount of regain was relatively small (1.27 ± 2.30 BMI units), such findings highlight the importance of maintaining weight loss in bariatric surgery patients to prevent increased risk for cognitive decline. The mechanisms for this association likely involve the return of comorbid medical conditions that adversely impact cognitive function (eg, hypertension, diabetes, and sleep apnea) or even from the independent effects of adiposity. Future research is needed to investigate factors that promote the maintenance of weight loss and clarify the differential effects of weight regain on neurocognitive outcomes.

The current findings are limited in several ways. First, the lack of a control group of obese participants limits the generalizability of these findings. For instance, it is possible that practice effects may have contributed to postoperative cognitive improvements in the current sample. However, several factors argue against practice effects as being a key contributor. First, past work that used obese controls showed improved cognitive function at 12 weeks and 24 months after bariatric surgery, suggesting this pattern is likely to continue at extended follow-ups. In addition, the long-term intervals between test administrations also diminish practice effects as a confounding variable. Nonetheless, future randomized case controlled studies are needed to confirm the current findings and fully elucidate whether bariatric surgery can attenuate cognitive decline in severely obese patients. In addition, the mechanisms for the cognitive benefits of bariatric surgery are not well understood, and prospective studies that implement laboratory work and neuroimaging are needed. Similarly, research has shown that cognition also improves after behavioral weight loss interventions, and future work is needed to clarify the differential effects of behavioral and surgical weight loss on the brain.

In summary, this study replicates past work showing improvements in cognitive function after bariatric surgery and further indicates that postoperative cognitive benefits may be maintained up to 3 years postoperatively. Future research is needed to elucidate the mechanisms for these improvements and examine whether these benefits are maintained over extended periods of time.

References