



Published in final edited form as:

*Surg Obes Relat Dis.* 2011 ; 7(4): 465–472. doi:10.1016/j.soard.2010.09.015.

## Improved Memory Function 12 Weeks after Bariatric Surgery

John Gunstad, PhD<sup>1,2</sup>, Gladys Strain, PhD<sup>3</sup>, Michael J. Devlin, MD<sup>4</sup>, Rena Wing, PhD<sup>5</sup>, Ronald A. Cohen, PhD<sup>5</sup>, Robert H. Paul, PhD<sup>6</sup>, Ross D. Crosby, PhD<sup>7,8</sup>, and James E. Mitchell, MD<sup>7,8</sup>

<sup>1</sup> Kent State University, Kent, OH

<sup>2</sup> Summa Health System, Akron OH

<sup>3</sup> Weill Cornell Medical College

<sup>4</sup> Columbia University Medical Center

<sup>5</sup> Brown Medical School

<sup>6</sup> University of Missouri-St. Louis

<sup>7</sup> Neuropsychiatric Research Institute, Fargo, ND

<sup>8</sup> University of North Dakota School of Medicine and Health Sciences, Fargo ND

### Abstract

**Background**—There is growing evidence that obesity is associated with poor neurocognitive outcome. Bariatric surgery is an effective intervention for morbid obesity and improves many comorbid medical conditions that are associated with cognitive dysfunction. The effects of bariatric surgery on cognition are unknown.

**Methods**—Prospective study total of 150 individuals (109 bariatric surgery patients enrolled in the Longitudinal Assessment of Bariatric Surgery (LABS) project and 41 obese controls that did not undergo surgery) completed cognitive evaluation at baseline and 12 week follow-up. Demographic, medical, and psychosocial information was also collected to elucidate possible mechanisms of change.

**Results**—Many bariatric surgery patients exhibited impaired performance on cognitive testing at baseline (range from 4.6%–23.9%). However, surgery patients were no more likely to exhibit decline on two or more cognitive tests at 12-week follow-up than obese controls [12.84% vs. 23.26%;  $\chi^2(1) = 2.51, p = .11$ ]. Group comparisons using repeated measures MANOVA showed surgery patients had improved memory performance at 12 week follow-up [ $\lambda = .86, F(4, 147) = 5.88, p < .001$ ], whereas obese controls actually declined. Regression analyses showed surgery patients without hypertension had better short delay recall at 12 weeks than those that did [ $\beta = 0.31, p = .005$ ], though other demographic and medical variables were largely unrelated to test performance.

---

Address correspondence to: John Gunstad, PhD, Department of Psychology, Kent State University, 221 Kent Hall Addition, Kent, OH 44242, Telephone: 330.672.2589, Fax: 330.672.3786, jgunstad@kent.edu.

No author has a conflict of interest for this work.

**Trial Registration:** clinicaltrials.gov Identifier: NCT00671775

**Publisher's Disclaimer:** This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

**Conclusion**—The current results suggest that cognitive impairment is common in bariatric surgery patients, though these deficits may be at least partly reversible. Future studies are needed to clarify underlying mechanisms, particularly longitudinal studies employing neuroimaging and blood markers.

### Keywords

obesity; cognitive function; bariatric surgery; Integneuro

## INTRODUCTION

More than one-third of American adults are obese<sup>1</sup> and there is growing evidence that excess weight is associated with poor neurocognitive outcome. Elevated body mass index (BMI) has been identified as an independent risk factor for Alzheimer's disease, stroke, and vascular dementia.<sup>2-3</sup> Recent work extends these findings and indicates that elevated BMI is associated with cognitive dysfunction and cognitive decline prior to these severe neurological disorders.<sup>4-5</sup> Though the pattern varies somewhat across studies, deficits on tests of memory and executive function are commonly reported.<sup>4-6</sup>

Bariatric surgery is a safe and effective intervention for morbid obesity,<sup>7-8</sup> though its effects on cognition are unknown. All major surgeries involve some risk of cognitive dysfunction<sup>9</sup> and the nutritional deficiencies that can emerge post-operatively in this population<sup>10-11</sup> may confer greater risk. However, it is also possible that bariatric surgery provides cognitive benefits to many individuals. Post-operative weight loss improves or resolves many comorbid medical conditions with reversible cognitive deficits, including hypertension,<sup>12-13</sup> Type 2 diabetes,<sup>14</sup> reduced cardiovascular fitness,<sup>15-16</sup> sleep apnea,<sup>17</sup> and depression.<sup>18-19</sup> Perhaps most obviously, bariatric surgery also results in substantial weight loss.<sup>20</sup> As described above, there is growing evidence that obesity is an independent risk factor for reduced cognitive performance. Resolution of these conditions in other populations is known to improve cognitive performance, suggesting bariatric surgery may provide cognitive benefits.

Bariatric surgery candidates exhibit impairments on cognitive testing,<sup>21</sup> though no study has examined changes following surgery. The current study did so to determine the risk of cognitive impairment following bariatric surgery and to identify possible cognitive benefits associated with these procedures.

## METHODS

### Trial Design and Participants

A total of 150 participants were recruited into this multi-site prospective examination of the cognitive effects of bariatric surgery, 109 Bariatric Surgery Patients and 41 Obese Controls. All Bariatric Surgery patients were part of the Longitudinal Assessment of Bariatric Surgery (LABS) parent project and all participants were recruited from existing LABS sites (Columbia, Cornell, and Neuropsychiatric Research Institute).<sup>7</sup> For study inclusion, Bariatric Surgery Patients were required to be enrolled in LABS, between 20–70 years of age, 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>21</sup>), 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. Inclusion/exclusion criteria for matched control participants included the above criteria for surgical patients, except they were not

enrolled in the LABS project, had no history of bariatric surgery procedures, and no reported interest in pursuing bariatric surgery in the next two years.

Within the sample, just 5 Bariatric Surgery patients underwent an adjustable gastric banding procedure and thus no comparisons for type of surgery were conducted. At baseline, Bariatric Surgery Patients were generally similar to Obese Controls, though they had higher BMI and were more likely to have hypertension, type 2 diabetes, and sleep apnea. See Table 1. At follow-up, Bariatric Surgery Patients lost a greater proportion of initial body weight than Obese Controls (−16.80% vs. −1.24%,  $t(150) = 10.40$ ,  $p < .001$ ). Importantly, no individual was identified by clinical care providers regarding new onset of significant neurologic or psychiatric disorder post-operatively.

### Interventions and Clinical Follow-Up

All procedures were approved by the appropriate Institutional Review Boards and all participants provided written informed consent prior to study involvement. Bariatric Surgery Patients completed a series of self report instruments and a computerized cognitive test battery within 30 days prior to and 12 weeks after surgery ( $\pm 14$  days). Obese Controls completed these measures at equivalent intervals. Medical records were reviewed by research staff to corroborate and supplement participant self-report.

### Outcomes

The primary endpoint was change in cognitive test performance as measured by alternate forms of the Integneuro test battery. This cognitive test battery consists of estimated premorbid intellectual abilities as well as performance in multiple cognitive domains (e.g. executive function, memory) and can be completed in 45–60 minutes. It has good psychometric properties and has been employed in past studies examining obesity and cognitive function.<sup>6,22–23</sup> Specific tests included:

**Digit Span Forward**—This test assesses basic attention. 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 dependent measure is the total number of correct trials forward and backward.

**Switching of Attention**—This test is a computerized adaptation of the Trail Making Test<sup>24</sup> and consists of two parts. In the first part, participants are presented with a pattern of 25 numbers in circles and asked to touch them in ascending order. In the second part, 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 whereas the second part taps these abilities as well as executive function. Time to completion for each test is used as the dependent variable.

**Verbal Interference**—This task taps the ability to inhibit automatic and irrelevant responses and has similarities to the Stroop Color Word Test.<sup>25</sup> 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. The test has two parts. In part 1, the subject is required to identify the name of each word as quickly as possible after it is presented on the screen, thus providing a measure of attention. In part 2, the subject is required to name the color of each word as quickly as possible, assessing executive functioning. Each part lasts for 1 minute. The dependent variable will be the number of words correctly identified in each trial.

**Maze Task**—This task is a computerized adaptation of the Austin Maze26 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 is the number of total errors on the task.

**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. Four dependent variables are generated from this task, specifically Total Learning (sum of words recalled on all learning trials), Short Delay Free Recall, Long Delay Free Recall, and Recognition.

**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 will serve as the dependent variable.

**Animal Fluency**—Participants are asked to generate as many animal names as possible in 60 seconds. Total correct serves as the dependent variable.

### Statistical Analysis

A series of analyses were conducted to determine the effects of bariatric surgery on cognitive function. First, distributions of key variables were examined for violations of normality. None were identified and no transformations were applied. Descriptive statistics and frequency counts were used to determine the prevalence of cognitive impairment at baseline, 12-weeks, and change from pre- to post-operative assessments in Bariatric Surgery Patients. Repeated measures MANOVA compared cognitive test performance in Bariatric Surgery Patients and Obese Controls in each cognitive domain (i.e. memory, attention, executive function, language). Bonferroni-corrected post-tests were used to clarify any significant omnibus tests. Finally, hierarchical regression identified predictors of improved test performance in Bariatric Surgery Patients. Test performance at 12-week follow-up served as the dependent variable. In Step 1, baseline values for age, BMI, test performance at baseline, and absence/presence of medical conditions associated with cognitive impairment (i.e. hypertension, type 2 diabetes, and sleep apnea) were entered. In Step 2, 12-week values for BMI and these medical conditions were entered to determine those variables most closely associated with change in cognitive test performance.

## RESULTS

### Clinical Interpretation of Cognitive Test Performance in Bariatric Surgery Patients

At baseline, the average cognitive test performance in Bariatric Surgery Patients generally fell within the low average to average range when compared to normative test data. See Table 2. However, there was substantial variability in test performance, as a number of Bariatric Surgery Patients exhibited impaired performance ( $\geq 1.5$  SD below normative data). For example, 23.9% of patients exhibited impaired test performance on Learning, and 22.9% Recognition Memory. In contrast, just 7.3% had deficits on Verbal Interference-Color.

At 12-week follow-up, the average performance for the Bariatric Surgery group was within the average or above average range for all cognitive tests. The proportion of Bariatric

Surgery Patients who showed a  $\geq 1.5$  SD post-operative decline on each test ranged from 0.0% for Recognition Memory to 9.5% for Digit Span. Importantly, Bariatric Surgery Patients were no more likely to exhibit decline on two or more cognitive tests than were than Obese Controls [12.84% vs. 23.26%;  $\chi^2(1) = 2.51, p = .11$ ]. This finding was confirmed through a series of Chi-Square analyses, as the proportion of participants that declined was equivalent across all tests (all  $p > .05$ ).

### Cognitive Differences between Bariatric Surgery Patients and Obese Controls

Repeated measures MANOVA was used to compare the cognitive test performance of Bariatric Surgery Patients to Obese Controls from baseline to 12 weeks. See Table 3. On memory tests, repeated measures MANOVA indicated a main effect for timepoint [ $\lambda = .76, F(4, 147) = 11.36, p < .001$ ], though not for group [ $\lambda = .99, F(4, 147) = 0.32, p = .87$ ]. However, a significant group  $\times$  timepoint interaction emerged [ $\lambda = .86, F(4, 147) = 5.88, p < .001$ ], with Bariatric Surgery Patients showing improved performance on all four memory indices at 12 week post-operative. More specifically, Bonferroni-corrected posttests revealed improved test performance on Learning [ $F(1, 150) = 10.99, p = .001$ ], Short Delay Free Recall [ $F(1, 150) = 12.18, p = .001$ ], Long Free Delay Recall [ $F(1, 150) = 19.53, p < .001$ ], and Recognition [ $F(1, 150) = 9.60, p = .002$ ] indices. Unexpectedly, control participants showed a *decline* in memory performance in Short Delay Free Recall [ $F(1, 42) = 5.59, p = .023$ ] and Long Delay Free Recall [ $F(1, 42) = 9.90, p = .03$ ], though not for Learning [ $F(1, 42) = 3.37, p = .07$ ] or Recognition [ $F(1, 42) = 2.60, p = .11$ ].

For the attention domain, no effect for group [ $\lambda = .98, F(3, 144) = 0.99, p = .40$ ] or group  $\times$  timepoint interaction emerged [ $\lambda = .98, F(3, 144) = 0.83, p = .48$ ]. A main effect for timepoint emerged [ $\lambda = .89, F(2, 144) = 5.86, p = .001$ ]. Follow-up analyses indicated that the Bariatric Surgery group improved on Switching of Attention [ $F(1, 104) = 9.63, p = .002$ ] and Obese Controls on Verbal Interference—Text [ $F(1, 42) = 4.81, p = .03$ ].

For the executive function domain, no significant effects emerged for group [ $\lambda = .99, F(3, 146) = 0.46, p = .71$ ] or group  $\times$  timepoint interaction [ $\lambda = .98, F(3, 146) = 0.77, p = .52$ ]. A significant main effect for timepoint emerged [ $\lambda = .67, F(3, 146) = 24.56, p < .001$ ]. Follow-up analyses indicated that both groups improved on all measures, specifically: Bariatric Surgery Patients, Switching of Attention-Number/Letter [ $F(1, 108) = 26.34, p < .001$ ], Verbal Interference—Color/Word [ $F(1, 108) = 32.30, p < .001$ ], and Maze Errors [ $F(1, 108) = 21.83, p < .001$ ]; Obese Controls, Switching of Attention-Number/Letter [ $F(1, 40) = 8.42, p = .006$ ], Verbal Interference—Color/Word [ $F(1, 40) = 9.91, p = .003$ ], and Maze Errors [ $F(1, 40) = 14.44, p < .001$ ].

For the language domain, no significant effects emerged for group [ $\lambda = .99, F(2, 149) = 0.86, p = .42$ ], timepoint [ $\lambda = .96, F(2, 149) = 2.83, p = .06$ ], or group  $\times$  timepoint interaction [ $\lambda = .99, F(2, 149) = 0.88, p = .42$ ].

### Predictors of Improved Cognitive Function in Bariatric Surgery Patients

Regression analyses were used to identify possible predictors of improved test performance in the Bariatric Surgery Patients. Significant incremental prediction after control variables was found for Short Delay Free Recall [ $R^2$  change = .09,  $F(4, 97) = 3.67, p = .008$ ], as patients without hypertension at 12 week post-operative exhibited better test performance than those that did [ $\beta = 0.31, p = .005$ ]. See Table 4. No incremental prediction was found for Learning [ $R^2$  change = .05,  $F(4, 97) = 1.97, p = .11$ ], Long Delay Free Recall [ $R^2$  change = .02,  $F(4, 97) = 0.92, p = .45$ ], Recognition [ $R^2$  change = .02,  $F(4, 97) = 0.89, p = .47$ ], or Switching of Attention—Numbers [ $R^2$  change = .04,  $F(4, 97) = 1.54, p = .20$ ].

## COMMENT

Consistent with past studies, results indicate that cognitive deficits are common in candidates for bariatric surgery. Interestingly, Bariatric Surgery Patients showed improved memory function 12 weeks post-operatively, though this improvement was largely unrelated to medical conditions or change in weight status. Several aspects of these findings warrant brief discussion.

Obesity is now recognized as an independent risk factor for cognitive dysfunction<sup>4-5</sup> and bariatric surgery candidates have been shown to exhibit impairments on neuropsychological testing.<sup>21</sup> A similar pattern emerged in the current sample, as 18.3% of patients exhibited deficits on a measure of executive function and 23.9% on a memory index. These findings encourage screening for cognitive dysfunction in bariatric surgery candidates to promote optimal outcomes, as deficits in these cognitive abilities are associated with poorer adherence to medical regimen in patients with medical conditions like type 2 diabetes and HIV.<sup>27-28</sup> For example, it is easy to imagine that the problems with organization, planning, or self-monitoring found in persons with executive dysfunction would make adhering to the post-operative medical regimen more difficult. Similarly, given the risk of neurological dysfunction due to vitamin deficiency in bariatric surgery patients,<sup>29</sup> the value of brief screening for cognitive dysfunction both pre- and post-operatively should be examined.

Analyses also showed that several tests improved in bariatric surgery patients relative to obese controls, including multiple memory indices and a test of psychomotor speed. Should they be replicated, these findings suggest that obesity-related cognitive dysfunction is at least partly reversible in some persons. Prospective studies are needed to examine cognitive function at a longer post-operative time period in bariatric surgery patients, especially as body weight often reaches its nadir 18–24 months post-surgery. Our ongoing project will determine whether these cognitive benefits are maintained at 12 and 24 months over time and examine whether cognitive dysfunction helps to predict weight re-gain. Though estimates vary, some bariatric surgery patients exhibit significant weight re-gain<sup>30</sup> and given its importance for adherence to medical regimen in other populations, it appears likely that cognitive impairment might help predict those patients at highest risk. Similarly, prospective studies will help determine whether bariatric surgery patients are at lower risk for cognitive decline and Alzheimer's disease than obese individuals that do not undergo surgery. Such studies are particularly needed given the growing number of older adults that undergo bariatric surgery.<sup>31</sup>

Less clear are the possible mechanisms for the improvements in cognitive function in bariatric surgery patients. Bariatric surgery improves many medical conditions with reversible cognitive deficits.<sup>12-17</sup> In the current study, regression analyses showed that the absence of hypertension at 12 week follow-up was associated with better performance on one memory index (Short Delay Free Recall). No additional predictors emerged for this or any other cognitive test, highlighting a need to determine the contribution of novel risk factors such as insulin resistance, biomarkers like brain derived neurotrophic factor and leptin, and endothelial function. Each of these are associated with cognitive function and altered following bariatric surgery.<sup>32-35</sup>

Future studies should also clarify the mechanisms for the decline in memory performance of obese controls. Recent work has shown that obesity can interact with age to exacerbate cognitive decline<sup>4</sup>, though that observed decline occurred over a period of years, not months. Exploratory analyses within our sample did not identify a clear mechanism for the reduced performance over time, as 79.1% declined on at least one memory test and almost 48.9% on two or more. No available demographic (e.g. age, gender) or medical variable

(e.g. hypertension, type 2 diabetes) distinguished controls who declined from those that did not. One speculative explanation could involve differences in glycemia control following meal ingestion, as poorer glucose tolerance after eating has been linked to acute impairments in cognitive function.<sup>36–37</sup> Another might involve the neuropathological changes of morbidly obese individuals that show similarities to Alzheimer's disease,<sup>38</sup> a condition typified by memory impairment. Future work in this area may shed key insight into the physiological processes linking obesity and poor neurocognitive outcome..

Findings from the current study are limited in several ways by the chosen methodology. Being an observational study, we were unable to randomize participants to surgery or control groups. Although the groups were similar in cognitive test performance at baseline, they differed on medical variables that facilitate approval for bariatric surgery from third-party payers, including type 2 diabetes and hypertension. However, our direct comparison of obese controls at each timepoint alleviates this concern somewhat and provides an ecologically valid examination of cognitive function in this population. Similarly, future studies are much needed to identify the mechanisms for cognitive benefits following bariatric surgery, including a direct comparison of gastric bypass and banding procedures. As noted above, there are numerous potential biomarkers or physiological processes that likely contribute to cognitive dysfunction in obesity. A growing body of literature also suggests both structural and functional abnormalities on neuroimaging in obese individuals<sup>39–41</sup> and studies should examine possible post-operative changes in these indices. Mechanistic studies will benefit from following bariatric patients for a longer period of time to maximize weight loss. Finally, future studies should compare the potential cognitive benefits of behavioral weight loss to that found in surgery patients, as cardiovascular fitness is associated with better cognitive function in both healthy and patient groups.<sup>15–16</sup> The low levels of physical activity found in many bariatric surgery patients<sup>42</sup> may also contribute to the observed cognitive dysfunction.

Results from the current study suggest that uncomplicated bariatric surgery does not confer significant risk of cognitive dysfunction at 12 weeks post-operatively and may actually provide some cognitive benefits. Additional studies are needed to examine this possibility at longer post-surgery intervals and clarify mechanisms for change.

## Acknowledgments

Funding/Support: This work supported by DK075119 and indirect support from HL089311.

## References

1. Flegal KM, Carroll MD, Ogden CL, Curtin LR. Prevalence and trends in obesity among US adults, 1999–2008. *JAMA*. 2010; 303:235–41. [PubMed: 20071471]
2. Fitzpatrick A, Kuller LH, Lopez O, et al. Midlife and late-life obesity and the risk of dementia: cardiovascular health study. *Arch Neurol*. 2009; 66:336–42. [PubMed: 19273752]
3. Strazzullo P, D'Elia L, Cairella G, Garbagnati F, Cappuccio F, Scalfi L. Excess body weight and incidence of stroke: meta-analysis of prospective studies with 2 million participants. *Stroke*. 2010; 41:e418–26. [PubMed: 20299666]
4. Gunstad J, Lhotsky A, Wendell CR, Ferrucci L, Zonderman AB. Longitudinal examination of obesity and cognitive function: results from the Baltimore longitudinal study of aging. *Neuroepidemiology*. 2010; 34:222–29. [PubMed: 20299802]
5. Waldstein SR, Katzell LL. Interactive relations of central versus total obesity and blood pressure to cognitive function. *Int J Obes*. 2006; 30:201–07.
6. Gunstad J, Paul RH, Cohen RA, Tate DF, Spitznagel MB, Gordon E. Elevated body mass index is associated with executive dysfunction in otherwise healthy adults. *Compr Psychiatry*. 2007; 48:57–61. [PubMed: 17145283]

7. Belle SH, Berk PD, Courcoulas AP, et al. Safety and efficacy of bariatric surgery: Longitudinal Assessment of Bariatric Surgery. *Surg Obes Rel Dis.* 2007; 3:116–26.
8. Flum DR, Belle SH, et al. Longitudinal Assessment of Bariatric Surgery (LABS) Consortium. Perioperative safety in the longitudinal assessment of bariatric surgery. *N Engl J Med.* 2009; 361:445–54. [PubMed: 19641201]
9. Dijkstra J, Van Boxtel M, Houx P, et al. An operation under general anesthesia as a risk factor for age-related cognitive decline: Results from a large cross-sectional population study. *JAGS.* 1998; 46:1258–65.
10. Clegg A, Colquitt J, Sidhu M, et al. Clinical and cost effectiveness of surgery for morbid obesity: A systematic review and economic evaluation. *Int J Obesity Rel Metabol Dis.* 2003; 27:1167–77.
11. Skroubis G, Sakellaropoulos G, Pougouras K, et al. Comparison of nutritional deficiencies after Roux-en-Y gastric bypass and after bilopancreatic diversion with Roux-en-Y gastric bypass. *Obes Surg.* 2002; 12:551–58. [PubMed: 12194550]
12. Amenta F, Mignini F, Rabbia F, et al. Protective effect of anti-hypertensive treatment on cognitive function in essential hypertension: analysis of published clinical data. *J Neurol Sci.* 2002:203–204. 147–51.
13. Papademetriou V. Hypertension and cognition function. Blood pressure regulation and cognitive function: a review of the literature. *Geriatrics.* 2005; 60:20–22. [PubMed: 15700945]
14. Awad N, Gagnon M, Messier C. The relationship between impaired glucose tolerance, type 2 diabetes, and cognitive function. *Journal of Clinical and Experimental Neuropsychology.* 2004; 26:1044–80. [PubMed: 15590460]
15. Aberg MA, Pedersen NL, Toren K, et al. Cardiovascular fitness is associated with cognition in young adulthood. *Proc Natl Acad Sci.* epub ahead of print.
16. Gunstad J, MacGregor KL, Paul RH, et al. Cardiac rehabilitation improves cognitive performance in older adults with cardiovascular disease. *J Cardiopulm Rehabil.* 2005; 25:173–76. [PubMed: 15931022]
17. Aloia M, Arnedt J, Davis J, et al. Neuropsychological sequelae of obstructive sleep apnea-hypopnea syndrome: a critical review. *J Int Neuropsychol Soc.* 2004; 10:772–85. [PubMed: 15327723]
18. Biringer E, Lundervold A, Stordal K, et al. Executive function upon remission of recurrent unipolar depression. *Eur Arch Psychiatry Clin Neurosci.* 2005; 255:373–80. [PubMed: 15793669]
19. Rogers M, Kasai K, Koji M, et al. Executive and prefrontal dysfunction in unipolar depression: a review of neuropsychological and imaging evidence. *Neurosci Rev.* 2004; 50:1–11.
20. Buchwald H, Avidor Y, Braunwald E, et al. Bariatric surgery: a systematic review and meta-analysis. *JAMA.* 2004; 292:1724–37. [PubMed: 15479938]
21. Alexander M. Mild traumatic brain injury: Pathophysiology, natural history, and clinical management. *Neurol.* 1985; 45:1253–60.
22. Lokken KL, Boeka AG, Yellumahanthi K, Wesley M, Clements RH. Cognitive performance of morbidly obese patients seeking bariatric surgery. *Am Surg.* 2010; 76:55–9. [PubMed: 20135940]
23. Paul RH, Lawrence J, Williams LM, Richard CC, Cooper N, Gordon E. Preliminary validity of “integneuro”™ a new computerized battery of neurocognitive tests. *Int J Neurosci.* 2005; 115:1549–67. [PubMed: 16223701]
24. Williams LM, Simms E, Clark CR, Paul RH, Rowe D, Gordon E. The test-retest reliability of a standardized neurocognitive and neurophysiological test battery: “neuromarker”. *Int J Neurosci.* 2005; 115:1605–30. [PubMed: 16287629]
24. Reitan R. Validity of the Trail Making Test as an indicator of organic brain damage. *Percept Motor Skills.* 1958; 8:271–76.
25. Golden, C. Stroop color and word task: a manual for clinical and experimental uses. Wood Dale; Stoelting: 1978.
26. Walsh, K. Understanding Brain Damage – A Primer of Neuropsychological Evaluation. Churchill Livingstone; Melbourne: 1985.
27. Feil D, Pearman A, Victor T, et al. The role of cognitive impairment and caregiver support in diabetes management of older outpatients. *Int J Psychiatry Med.* 2009; 39:199–214. [PubMed: 19860078]



28. Ettenhofer ML, Hinkin CH, Castellon SA, et al. Aging, neurocognition, and medication adherence in HIV infection. *Am J Geriatr Psychiatry*. 2009; 17:281–90. [PubMed: 19307857]
29. Aasheim ET. Wernicke encephalopathy after bariatric surgery: a systematic review. *Ann Surg*. 2008; 248:714–20. [PubMed: 18948797]
30. Odom J, Zalesin KC, Washington TL, et al. Behavioral predictors of weight regain after bariatric surgery. *Obes Surg*. 2010; 20:349–56. [PubMed: 19554382]
31. Wittgrove AC, Martinez T. Laparoscopic gastric bypass in patients 60 years and older: early postoperative morbidity and resolution of comorbidities. *Obes Surg*. 2009; 19:1472–76. [PubMed: 19705206]
32. Ballantyne GH, Farkas D, Laker S, Wasielewski A. Short-term changes in insulin resistance following weight loss surgery for morbid obesity: laparoscopic adjustable gastric banding versus laparoscopic Roux-en-Y gastric bypass. *Obes Surg*. 2006; 16:1189–97. [PubMed: 16989703]
33. Beckman LM, Beckman TR, Earthman CP. Changes in gastrointestinal hormones and leptin after Roux-en-Y gastric bypass procedure: a review. *J Am Diet Assoc*. 2010; 110:571–84. [PubMed: 20338283]
34. Merhi ZO, Minkoff H, Lambert-Messerlian GM, Macura J, Feldman J, Seifer DB. Plasma brain-derived neurotrophic factor in women after bariatric surgery: a pilot study. *Fertil Steril*. 2009; 91:1544–48. [PubMed: 18950757]
35. Sturm W, Tschoner A, Engl J, et al. Effect of bariatric surgery on both functional and structural measures of premature atherosclerosis. *Eur Heart J*. 2009; 30:2038–43. [PubMed: 19502233]
36. Chui MH, Greenwood CE. Antioxidant vitamins reduce acute meal-induced memory deficits in adults with type 2 diabetes. *Nutr Res*. 2008; 28:423–29. [PubMed: 19083441]
37. Nilsson A, Radeborg K, Bjorck I. Effects of differences in postprandial glycaemia on cognitive functions in health middle-aged subjects. *Eur J Clin Nutr*. 2009; 63:113–20. [PubMed: 17851459]
38. Mrak RE. Alzheimer-type neuropathological changes in morbidly obese elderly individuals. *Clin Neuropathol*. 2009; 28:40–5. [PubMed: 19216219]
39. Gunstad J, Paul RH, Cohen RA, et al. Relationship between body mass index and brain volume in healthy adults. *Int J Neurosci*. 2008; 118:1582–93. [PubMed: 18853335]
40. Raji CA, Ho AJ, Parikshak NN, et al. Brain structure and obesity. *Hum Brain Mapp*. 2010; 31:353–64. [PubMed: 19662657]
41. McCaffery JM, Haley AP, Sweet LH, et al. Differential functional magnetic resonance imaging response to food pictures in successful weight-loss maintainers relative to normal-weight and obese controls. *Am J Clin Nutr*. 2009; 90:928–34. [PubMed: 19675107]
42. King WC, Belle SH, Eid GM, et al. Physical activity levels of patients undergoing bariatric surgery in the Longitudinal Assessment of Bariatric Surgery study. *Surg Obes Rel Dis*. 2008; 4:721–28.

**Table 1**  
Demographic and medical characteristics of 109 Bariatric Surgery Patients and 43 Obese Controls

	<b>Bariatric Surgery Patients</b>	<b>Obese Controls</b>	<b>Test Statistic</b>	<b>p</b>
<i>Baseline</i>				
Age, yrs	44.66 ± 11.03	40.42 ± 11.48	2.11	.04
Gender, women	83.48%	83.72%	0.00	.97
Race, Caucasian	88.57	63.15	12.11	.001
BMI	46.45 ± 6.65	42.12 ± 6.67	3.61	<.001
Hypertension	46.79%	23.26%	7.11	.008
Type 2 diabetes	27.52%	9.30%	5.90	.02
Sleep apnea	37.61%	6.98%	14.07	<.001
<i>12-week follow-up</i>				
BMI	38.61 ± 6.32	41.59 ± 6.80	2.57	.01
Hypertension	39.44%	27.90%	1.78	.18
Type 2 diabetes	23.85%	11.62%	2.84	.09
Sleep apnea	25.69%	2.32%	10.90	.001

**Table 2**

T scores of Cognitive Test Performance in 109 Bariatric Surgery Patients at Baseline and 12-week Follow-up

	<b>Pre-operatively</b>	<b>12-weeks post-operative</b>	<b>&gt;1.5 SD Decline</b>
<i>Memory</i>			
Learning	42.82 ± 12.52 (23.9%)	46.25 ± 13.74 (18.3%)	6.7%
Short Delay Free Recall	45.39 ± 10.86 (15.6%)	48.00 ± 12.59 (19.3%)	5.5%
Long Delay Recall	45.34 ± 10.91 (14.7%)	48.23 ± 13.18 (20.2%)	5.5%
Recognition	40.46 ± 10.65 (22.9%)	51.63 ± 10.20 (7.3%)	0.0%
<i>Attention</i>			
Digit Span	49.66 ± 11.51 (9.3%)	51.23 ± 13.08 (13.1%)	9.5%
Switching of Attention-Number	53.33 ± 15.28 (13.8%)	58.00 ± 13.73 (5.5%)	2.8%
Verbal Interference-Word	53.56 ± 11.26 (4.6%)	54.75 ± 12.36 (5.5%)	5.5%
<i>Executive Function</i>			
Switching of Attention-Letter/Number	52.57 ± 14.44 (8.3%)	57.81 ± 11.70 (4.6%)	0.9%
Verbal Interference-Color Word	55.27 ± 12.77 (7.3%)	63.36 ± 13.21 (6.4%)	2.8%
Maze Errors	48.55 ± 13.52 (18.3%)	54.51 ± 11.66 (6.4%)	1.8%
<i>Language</i>			
FAS	47.66 ± 11.60 (14.5%)	48.46 ± 11.21 (12.5%)	1.3%
Animals	50.15 ± 11.51 (6.6%)	50.17 ± 10.81 (4.6%)	5.3%

Note. T scores and % >1.5 SD below normative performance based on age, education, and estimated IQ.

**Table 3**  
Cognitive Test Performance in 109 Bariatric Surgery Patients and 43 Obese Controls at Baseline and 12-week Follow-up

Cognitive Domain/Test	Baseline		12 Week Follow-Up	
	Bariatric Surgery Patients	Obese Control	Bariatric Surgery	Obese Control
<i>Memory<sup>ab</sup></i>				
Learning	29.89 ± 5.54	32.26 ± 4.80	31.70 ± 6.81	30.67 ± 6.11
Short Delay Free Recall	7.21 ± 2.20	8.19 ± 1.92	7.76 ± 2.45	7.28 ± 2.52
Long Delay Free Recall	6.82 ± 2.26	8.12 ± 1.98	7.47 ± 2.64	6.93 ± 2.59
Recognition	10.07 ± 1.60	10.63 ± 1.24	11.24 ± 1.18	11.00 ± 1.33
<i>Attention<sup>d</sup></i>				
Digit Span	6.16 ± 1.27	6.02 ± 1.68	6.30 ± 1.55	6.28 ± 1.30
Switching of Attention-Number	21.87 ± 9.78	21.20 ± 8.59	19.52 ± 6.45	19.65 ± 6.18
Verbal Interference-Word	18.37 ± 3.38	17.09 ± 4.11	18.79 ± 3.57	18.40 ± 4.35
<i>Executive Function<sup>d</sup></i>				
Switching of Attention-Letter/Number	48.65 ± 18.36	46.63 ± 13.23	42.63 ± 14.71	42.67 ± 12.58
Verbal Interference-Color Word	11.79 ± 3.98	12.54 ± 3.40	13.79 ± 4.17	14.27 ± 3.38
Maze Errors	63.32 ± 69.58	52.15 ± 22.68	42.93 ± 44.28	40.02 ± 18.51
<i>Language<sup>d</sup></i>				
FAS	14.61 ± 3.90	14.93 ± 3.99	14.87 ± 3.64	15.73 ± 4.40
Animals	23.08 ± 5.32	22.91 ± 6.57	23.28 ± 5.30	22.77 ± 5.85

Note.

<sup>a</sup> denotes main effect for timepoint.

<sup>b</sup> denotes significant group × timepoint interaction.

**Table 4**  
Hierarchical Regression to Predict Memory Indices at 12-week Follow-up in 109 Bariatric Surgery Patients

Test	Baseline						12 Week						F Change	p
	Age	HTN	DM	SA	Test	BMI	HTN	DM	SA	BMI	R <sup>2</sup>	R <sup>2</sup> Change		
Learning	.14	.02	-.01	-.12	.57***	-.27	-.10	-.19	.04	.30	.63	.05	1.97	.11
Short Delay Free Recall	-.02	.16	.07	-.18	.49***	.28	-.31***	-.15	.17	-.32	.62	.09	3.67	.008
Long Delay Free Recall	-.03	.09	.06	-.08	.53***	.17	-.07	-.16	.02	-.21	.61	.02	0.92	.45
Recognition	-.18	-.06	-.19	-.01	.50***	-.11	.12	.13	.07	-.04	.59	.02	0.89	.47
Switching of Attention--Numbers	.10	.16	-.05	-.09	.50***	.32	-.16	.00	.20	-.21	.64	.04	1.54	.20

Note.

\*\*\* p<.01.

Abbreviations: HTN, hypertension; DM, type 2 diabetes; SA, sleep apnea; Test, baseline test performance.