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Pre-Operative History of Depression and Cognitive Changes in Bariatric Surgery Patients

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Abstract

Obesity associated cognitive impairments may be partially reversible through bariatric surgery. Depression, a prevalent comorbidity in bariatric surgery candidates, is linked with cognitive impairment and poorer surgical outcomes in other populations. No study has examined the effects of pre-operative depression on cognitive changes in bariatric surgery patients. 67 bariatric surgery patients completed a computerized cognitive test battery prior to surgery and 12-months post-operatively. The Structured Clinical Interview for the *DSM-IV* Axis I disorders assessed Major Depressive Disorder (MDD). Pre-surgery history of MDD was found in 47.8% of patients, but was not associated with greater baseline cognitive impairments. Repeated measures revealed improved cognitive abilities 12-months after surgery. Pre-surgery history of MDD did not influence post-operative cognitive function. Pre-operative history of MDD did not limit post-operative cognitive improvements. Larger studies with extended follow-ups are needed to clarify our findings and identify factors (e.g., older age) that may modify cognitive changes following surgery.

Keywords

Obesity; bariatric surgery; cognitive function; weight loss; depression

Introduction

Obesity, as defined by a body mass index (BMI) ≥ 30 , affects approximately 500 million adults worldwide (Finucane et al., 2011) and is most prevalent among the high-income

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Conflict of Interest

All author declare that they have no conflict of interest

western countries. In particular, the United States (US) ranks the highest among the high-income countries, as more than one-third of the US population is classified as obese (Ogden, Carroll, Kit, & Flegal, 2012). Nonetheless, Canada and other westernized countries have also experienced a rapid increase in obesity over the past few decades. Obesity increases are also beginning to be observed in developing countries theorized to be a consequence of a shift to the overeating Western-type diets (Popkin, Adair, & Ng, 2011).

The global rise in obesity rates presents as a significant societal concern. Obesity is associated with health consequences (e.g., diabetes, hypertension) and increased mortality and morbidity risk; Must et al., 2006; Haslam & James, 2005). Recent work also demonstrates that obesity is an independent risk factor for poor neurocognitive outcomes, including neurodegenerative conditions such as Alzheimer's disease (Fitzpatrick et al., 2009). Even before dementia onset, a rich literature demonstrates that obesity is associated with deficits on formal cognitive testing. As, an example, past work shows that obese persons of nearly all ages (i.e., 21 to 82 years) exhibited worse performances on neuropsychological tasks assessing memory abilities (Gunstad, Paul, Cohen, Tate, & Gordon, 2006). Lokken and colleagues (2009) extended these findings to show that obesity is also associated with impairments in attention and executive function. This pattern is concerning, as cognitive impairment may interfere with the functional ability to adhere to treatment recommendations that target weight loss in severely obese populations (Spitznagel et al., 2013).

Bariatric surgery has become an increasingly recognized treatment option for weight loss in severely obese individuals (Shinogle, Owings, & Kozak, 2005). In fact, annual bariatric surgery procedures in the US increased by 800% from 1998 and 2004 and surgery rates currently stand at approximately 113,000 cases each year (Zhao et al., 2007; Livingston et al., 2010). The rise in bariatric surgery is largely attributable to the effectiveness of this weight loss intervention. As an example, in a meta-analysis of 136 studies bariatric surgery was shown to be associated with a 61.2% excess weight loss two years post-operatively (Buchwald et al., 2004). Bariatric surgery also results in lower morbidity and mortality risk (Masoomi, Nguyen, Stamos, & Smith, 2012) and improved quality of life (Miranda et al., 2013).

An emerging line of research now also suggests that bariatric surgery may partially reverse cognitive deficits found in obese individuals. Gunstad and colleagues (2011) first showed that 24% of bariatric surgery patients exhibited memory impairments pre-operatively relative to non-surgery obese controls; however, no memory impairments were found in the bariatric surgery patients 12-weeks post-operatively. This study triggered a line of research that has further explored the nature and duration of cognitive benefits following weight loss surgery. Indeed, recent studies now demonstrate that bariatric surgery patients exhibit post-operative improvements in attention, executive function, and memory and such gains appear to last 2- to 3- years after surgery (Alosco et al., 2013a; Alosco et al., 2013b).

Post-surgery cognitive gains is likely not ubiquitous and dependent upon a range of pre-operative medical and clinical factors. Supporting this notion is past work that shows pre-operative medical (e.g., hyperinsulinemia, insulin resistance) and psychological factors (e.g.,

personality disorders, emotional eating severity) are key modifiers of post-bariatric surgery outcomes (Livhits et al., 2012; Dixon, Dixon, & O'Brien, 2001; Castellini et al., 2014). Pre-surgery psychiatric status appears to be particularly sensitive to post-surgery outcomes (Rutledge, Groesz, & Savu, 2011). Specifically, depression is a common comorbid condition in bariatric surgery candidates and approximately 40% of patients report pre-operative treatment for depression (Mitchell et al., 2012; Mitchell et al., 2014). Depression is a significant contributor to poor post-surgery outcomes such as decreased quality of life, higher risk of a major adverse event, and decreased weight loss (Masheb et al., 2007; Brunault et al., 2012; Mitchell et al., 2014).

Depression is also well known to influence cognitive outcomes (Papazacharias, & Nardini, 2012) characterized by deficits in frontal lobe mediated mental abilities (Veiel, 1997). Although limited work has examined the association between depression and cognitive function in obese samples, a past study suggests that depression mediates the relationship between obesity and deficits in attention and executive function (Cserjesi et al., 2009). These findings raise the possibility that a pre-operative history of depression may be an important modifier of pre- and post-operative cognitive function in bariatric surgery patients. Pre-operative depression is also associated with increased severity of medical co-morbidities in bariatric surgery candidates (Ali et al., 2009) and also attenuates post-operative weight loss (Brunault et al., 2012)—both contributors to cognitive improvements post-bariatric surgery.

No study to date has examined the effects of pre-operative depression on cognitive changes following bariatric surgery. We sought to determine whether a pre-operative history of depression attenuates the cognitive gains associated with bariatric surgery. Specifically, the current study investigated group differences in cognitive function between bariatric surgery patients with and without lifetime history of depression over a 12-month period following weight loss surgery. Based on past work, we hypothesized that cognitive function would improve following surgery, but a pre-operative history of depression would attenuate post-surgery cognitive gains.

Methods

Trial Design and Participants

A total of 67 participants were recruited into a multi-site National Institutes of Health prospective study examining the effects of bariatric surgery on cognitive function. All bariatric surgery patients were part of the Longitudinal Assessment of Bariatric Surgery (LABS) parent project and were recruited from existing LABS sites (Columbia, Cornell, and Neuropsychiatric Research Institute) (Belle et al., 2007). For study inclusion, bariatric surgery patients were required to be enrolled in LABS, between 20–70 years of age, and English-speaking. All participants were indeed bariatric surgery candidates scheduled for surgery and thus met the necessary clinical, medical, and weight eligibility criteria for weight loss surgery. In particular, to be eligible for bariatric surgery participants must have met criteria for entry into the parent LABS project. These criteria were determined by clinicians at each center, typically requiring a BMI > 40 or BMI > 35 accompanied by severe negative health consequences.

Exclusion criteria included history of neurological disorder or injury (e.g. dementia, seizures), moderate or severe head injury (defined as >10 minutes loss of consciousness), 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. All participants underwent Roux-en-Y gastric bypass surgery with the exception of one participant that underwent a gastric banding procedure. The present sample represents all individuals that completed baseline and 12-month post-operative cognitive testing. Participants averaged 42.90 (SD = 10.58) years of age and were 89.6% female. Medical and demographic characteristics were ascertained through participant self-report and medical record review. Table 1 presents baseline demographic and clinical characteristics of the sample.

Major Depressive Disorder

History of Major Depressive Disorder (MDD) was assessed using the Structured Clinical Interview for the *DSM-IV* Axis I disorders (SCID-I) (First, Spitzer, Gibbon, & Williams, 1996) that was administered by trained research assistants under the supervision of a licensed clinician. Only participants that met full criteria were classified as having a history of MDD (i.e., this did not include participants meeting subthreshold criteria). Participants were categorized into one of two groups: those with or without a lifetime history of MDD. We chose to examine a lifetime history of MDD (as opposed to current depressive symptoms) as this approach captures those individuals that have met the clinical threshold for depression and are thus most likely to experience the negative effects of a life long history of depression, including heightened cognitive vulnerabilities. Moreover, only 3 participants met criteria for MDD in the past month, suggesting that current depressive symptoms in this sample are minimal.

Interventions and Clinical Follow-Up

The appropriate Institutional Review Board approved all procedures and participants provided written informed consent prior to study involvement. At baseline, all bariatric surgery patients were administered the SCID-I to assess for psychiatric disorders, including history of MDD. Bariatric surgery patients completed a series of self-report instruments and a computerized cognitive test battery within 30 days prior to surgery and at 12-months after surgery. Participant's height and weight were measured at each time point and used to calculate body mass index (BMI). Medical records were also reviewed by research staff to corroborate and supplement participant self-report.

Outcomes

The IntegNeuro cognitive test battery assessed cognitive function in the present sample. The IntegNeuro is a brief computerized battery that assesses performance in multiple cognitive domains and can be completed in 45–60 minutes. It demonstrates strong psychometric properties, including good convergent and divergent validity with paper and pencil neuropsychological tasks and strong test re-test reliability (i.e., up to $r = 0.89$) (Paul et al., 2005; Williams et al., 2005). Alternate versions of the IntegNeuro were also used at subsequent time points in order to limit the possibility of practice effects.

The cognitive domains assessed by the IntegNeuro included attention/executive function, memory, and language. The measures that comprise these domains are described in detail below. All tasks within their respective domain were highly correlated [attention/executive function: up to $r = 0.65$; memory: up to $r = 0.67$; and language: $r = 0.60$], suggesting these measures represent an appropriate conglomerate of tasks to define their respective domain.

Attention/Executive Function

Digit Span Total: This test assesses auditory attention and working memory. Participants are presented with a series of digits on the touch-screen, separated by a one-second interval. The participant is asked to immediately enter the digits on a numeric keypad on the touch-screen in the order presented. The number of digits in each sequence is gradually increased from 3 to 9, with two sequences at each level. Participants are then asked to enter the digits in a backward sequence. The total number of correct forward and backward trials was used in the current analyses.

Switching of Attention: This test is a computerized adaptation of the Trail Making Test A and B (Reitan, 1958). First, participants are asked to touch a series of 25 numbers in ascending order as quickly as possible. Then, an array of 13 numbers (1–13) and 12 letters (A–L) is presented. Participants are asked to alternately touch numbers and letters in ascending order. The first part of this test assesses attention and psychomotor speed and the second part assesses executive function. Time to completion served as the outcome measure in the current study.

Verbal Interference: This task taps the ability to inhibit automatic and irrelevant responses and has similarities to the Stroop Color Word Test (Golden, 1978). 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 subject is required to name the color of each word as quickly as possible, assessing executive functioning. Total number of words correctly identified was used as the dependent variable in this study.

Maze Task: This is a computerized adaptation of the Austin Maze (Walsh, 1985) 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.

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. 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 non-target words is completed. Total learning, Long Delay Free Recall, and Recognition of these verbal list items were used to assess memory.

Language

Letter Fluency: Participants are asked 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 served as the dependent variable.

Animal Fluency: In this task, participants generate as many animal names as possible in 60 seconds. Total correct served as the dependent variable.

Statistical Analysis

All analyses were conducted using SPSS software, version 22. Raw scores of all neuropsychological measures were transformed to T-scores (a distribution with a mean of 50, and a standard deviation of 10) using normative data correcting for age, gender, and estimated intelligence. A T-score < 35 (i.e., 1.5 SD below the mean) was operationalized as being reflective of impairment. Composite scores were computed for attention, executive function, memory, and language that consisted of the mean of T-scores of the respective neuropsychological measures that comprise each domain. Independent samples *t*-tests and chi-square analyses examined differences between those with and without a history of MDD on demographic and medical variables.

Repeated measures analysis of variance (ANOVA) examined changes in BMI from baseline to 12-months following bariatric surgery with MDD entered as grouping variable. Due to missing height and weight data across the time points the sample size for analyses examining BMI over time was reduced to 63. Independent samples *t*-tests examined the association between baseline MDD history and baseline cognitive function in each domain. Repeated measures were then conducted to determine changes in cognitive function over the 12-month post-operative period in each domain (e.g., attention, executive function, memory, and language). For each cognitive domain, pre-operative history of MDD was also entered as a grouping variable into the models to determine the effects of baseline MDD history on cognitive function from baseline to 12-months post-bariatric surgery.

Results

Baseline MDD History and Demographic and Clinical Characteristics

47.8% of the sample met criteria for a lifetime history of MDD and all participants in the current study that had a history of MDD were females. However, independent samples *t*-tests and chi-square analyses showed no differences between those with and without a history of MDD in terms of age, baseline BMI, or current diagnostic history of hypertension, diabetes, or sleep apnea ($p > 0.05$ for all). See Table 1. Based on these findings, no medical variables were included as covariates in primary analyses below. Moreover, prevalence of comorbid medical conditions between patients with and without an MDD history was similar at 12-months post-surgery: hypertension (N = 64): MDD 12-month = 40.6% versus 40.0%; diabetes (N = 64): MDD 12-month = 12.5% versus 17.1%; sleep apnea (N = 63): MDD 12-month = 15.6% versus 17.1%.

In the overall sample, the average baseline BMI was 46.35 (SD = 6.08) kg/m², placing the sample in the very severely obese category. BMI declined to 29.96 (SD = 5.11) kg/m² at 12-months post-surgery, placing the sample in the overweight category and representing a significant decline ($F(1, 62) = 910.58, p < 0.001$) from pre-operative levels. However, changes in BMI over the 12-month period were equivalent in patients with and without a history of MDD (Group $\times$ Time interaction, $F(1, 61) = 0.88, p = 0.35$).

MDD History and Baseline Cognitive Function

When using a T-score cutoff of 35, baseline impairments were common in memory and language abilities. See Table 2. Specifically, 16.4% of the sample exhibited impairments on total learning, 11.9% on long delayed free recall, and 16.4% on the recognition task. For language, 13.4% of the sample demonstrated impairments on the letter fluency task.

Counter to expectations, independent samples *t*-tests showed history of MDD was not associated with greater baseline impairments in any of the cognitive domains: attention ($t(51.01) = 0.79, p = 0.43$), executive function ($t(65) = 0.56, p = 0.58$), memory ($t(65) = 0.78, p = 0.44$), or language ($t(65) = 0.38, p = 0.70$).

Pre-Operative MDD History and Post-Surgery Cognitive Changes

See Table 3 for cognitive test performance from baseline to 12-months post-surgery in patients with and without a history of MDD. At 12-months post-operatively, impairments were less prevalent relative to pre-operative test performance on many measures of attention/executive function, memory, and language (see Table 2). Repeated measures ANOVA showed a significant effect for improved function over the 12-months following surgery in most cognitive domains: attention ($F(1,65) = 27.31, p < .001$), executive function ($F(1,65) = 37.60, p < .001$), and memory ($F(1,65) = 45.48, p < .001$). However, performance on tests of language functioning remained stable over time ($F(1,65) = 0.01, p = 0.94$).

There was no MDD history by time interaction for any of the cognitive domains over the 12-month period: attention ($F(1,65) = 0.06, p = 0.80$), executive function ($F(1, 65) = 0.42, p = 0.52$), memory ($F(1, 65) = 0.77, p = 0.38$), or language ($F(1, 65) = 0.43, p = 0.52$). Bariatric surgery patients with and without MDD both demonstrated significant improvements in attention, executive function, and memory ($p < 0.05$ for all). Language function remained stable in both groups over time.

Discussion

Consistent with past work (Mitchell et al., 2012), history of MDD was prevalent in this sample of bariatric surgery candidates. Although previous work in other populations suggests that pre-operative history of depression may adversely impact pre- and post-operative cognitive function in bariatric surgery patients, we found no such pattern. These findings are contrary to findings in other populations and warrant brief discussion.

Our hypothesis that a pre-surgery history of depression would negatively impact pre- and post-operative cognitive function was not supported. In fact, both patients with and without MDD demonstrated similar and significant rates of cognitive impairment prior to surgery

and cognitive improvement at 12-month follow-up. Taken in combination, such findings suggest that history of depression does not exacerbate impairment in cognitive function in severely obese persons. This pattern is inconsistent with the extant literature that demonstrates the negative association between current levels of depression and cognitive function in medical (e.g., cardiovascular disease) and elderly populations (Parerniti, 2002; Garcia et al., 2011).

The exact reason for these differences across studies is not entirely clear. One possibility is that the current study assessed lifetime history of clinical depression and current depressive symptoms may be more sensitive to bariatric surgery cognitive outcomes. Alternatively, the cognitive effects of depression may at least partly moderated by obesity and comorbid medical conditions (Ali et al., 2009) and these conditions were similar in persons with and without MDD in the current study. In addition, a likely mechanism of cognitive impairment in obese individuals is believed to involve cerebral hypoperfusion and adverse brain changes (Alosco et al., 2012; Gunstad et al., 2008). Given the severe levels of obesity in this sample, it is unlikely that depression would have effects on the brain that are not accounted for or extend beyond the impact of obesity. Moreover, the young age of this sample may have also limited the susceptibility of the bariatric surgery patients to cerebral structure insult and neuropsychiatric conditions. For instance, advancing age has been shown to modify the association between depression and neurocognitive outcomes, including brain volume, cerebral blood flow, and cognitive function (Dotson, Resnick, & Zonderman, 2008; Dotson et al., 2009; Doston et al., 2009; Sackeim et al., 1990; Lockwood, Alexopoulos, & van Gorp, 2002). Future studies should examine the effects of pre-operative depression history on cognitive changes following bariatric surgery using extended follow-ups (e.g., 15–20 years) and/or among an older adult sample.

Regardless of MDD history, cognitive function improved in nearly all domains following bariatric surgery. These findings are noteworthy given the existing literature that demonstrates midlife obesity is a risk factor for neurodegenerative conditions like Alzheimer's disease and vascular dementia (Hassing et al., 2009; Whitmer et al., 2008; Kivipelto et al., 2005). The noted improvements in cognitive function suggests the possibility that bariatric surgery may be able to reduce the risk of dementia associated with obesity, possibly through reduced inflammation and/or expression of Alzheimer's disease related proteins (Ghanim et al., 2012). Other mechanism for post-operative cognitive improvement includes resolution of comorbid medical conditions that adversely impact cognitive function (e.g., hypertension, diabetes) (Papademetriou, 2005; Awad, Gagnon, & Messier, 2004) or even from the independent effects of substantial weight loss (Alosco et al., 2013; Lee, 2011; Troller et al., 2012; Diniz & Teizeira, 2011). Prospective studies with extended follow-ups are needed to elucidate underlying mechanisms and determine whether bariatric surgery can decrease risk of dementia.

Several limitations of the current study deserve brief discussion. First, the lack of a control group of severely obese participants that does not undergo bariatric surgery limits the external validity of our findings due to the possibility of practice effects. However, the use of alternate computerized test versions and the extant literature that shows cognition improves following bariatric surgery relative to obese controls argues against this potential confound.

Regardless, to fully eliminate practice effects as a possible confound, future case-controlled studies are needed to confirm our findings. Similarly, the reduced sample size may have also precluded significant effects and larger studies are needed to examine the impact of depression on cognitive function in bariatric surgery patients. Likewise, more demographically diverse studies that examine the aims of the current study are needed to replicate our findings. In particular, a majority of this sample was female (i.e., 89.6%) and such gender composition may introduce certain biases, as females tend to exhibit better outcomes following bariatric surgery relative to their male counterparts (Tiwari et al., 2011).

The categorical approach to assess depression in this study also deserves brief discussion. We used the SCID to examine the impact of a clinical history of depression on bariatric surgery cognitive outcomes that is not permitted via the use of depression symptom screening measures. Although this approach precluded examination of depressive symptoms along a continuum (i.e., mild to severe), current depressive symptoms appeared to be minimal in this sample as only 3 participants met criteria for past month MDD. Past work also shows minimal differences between current and past history of depression on cognitive function in elderly populations (Reppermund et al., 2011). Lastly, the present study sought to determine whether a pre-operative life history of depression limits post-surgery cognitive improvements and did not necessarily target the mechanisms of cognitive gains; that is, whether improvements in depression predict better cognitive abilities. Bariatric surgery has indeed been shown to improve depressive symptoms subsequent to weight loss, as operationalized by continuous measures such as the Beck Depression Inventory (Mitchell et al., 2014), and larger samples that meet the necessary statistical power requirements to perform mediation models and employ measures of depressive symptoms should examine the role of weight loss and resulting improvements in depression in cognitive changes.

Past studies show that depression is common in bariatric surgery patients and associated with poorer clinical outcomes (Dixon et al., 2001; Mitchell et al., 2012). The current findings show that a pre-operative history of MDD does not increase the prevalence of cognitive impairment prior to surgery or limit post-operative gains in cognitive function in bariatric surgery patients. Case-controlled studies that utilize extended follow-ups (e.g. 5 years) and neuroimaging are needed to confirm these findings and further clarify the mechanisms for adverse neurocognitive outcomes in obese adults.

References

- Ali MR, Rasmussen JJ, Monash JB, Fuller WD. Depression is associated with increased severity of co-morbidities in bariatric surgical candidates. *Surgery for Obesity and Related Disorders*. 2009; 5:559–564.
- Alosco ML, Spitznagel MB, Strain G, Devlin M, Cohen R, Paul R, Crosby RD, Mitchell JE, Gunstad J. Improved memory function two years after bariatric surgery. *Obesity*. 2013a; 22:32–38. [PubMed: 23625587]
- Alosco ML, Galioto R, Spitznagel MB, Strain G, Devlin M, Cohen R, Crosby RD, Mitchell JE, Gunstad J. Cognitive function after bariatric surgery: Evidence for improvement 3 years after surgery. *American Journal of Surgery*. 2013b
- Alosco ML, Spitznagel MB, Raz N, Cohen R, Sweet LH, Colbert LH, Josephson R, van Dulmen M, Hughes J, Rosneck J, Gunstad J. Obesity interacts with cerebral hypoperfusion to exacerbate

cognitive impairment in older adults with heart failure. *Cerebrovascular Disorders EXTRA*. 2012; 2:88–98.

- Awad N, Gagnon M, Messier C. The relationship between impaired glucose tolerance, type 2 diabetes, and cognitive function. *Journal of Clinical & Experimental Neuropsychology*. 2004; 26:1044–1080. [PubMed: 15590460]
- Belle SH, Berk PD, Courcoulas AP, Flum DR, Miles CW, Mitchell JE. Longitudinal Assessment of Bariatric Surgery Consortium Writing Group. Safety and efficacy of bariatric surgery: Longitudinal Assessment of Bariatric Surgery. *Surgery for Obesity and Related Disorders*. 2007; 3:116–126.
- Buchwald H, Avidor Y, Braunwald E, Jensen MD, Pories W, Fahrenbach K, Schoelles K. Bariatric surgery: a systematic review and meta-analysis. *Journal of The American Medical Association*. 2004; 292:1724–1737. [PubMed: 15479938]
- Brunault P, Jacobi D, Miknius V, Bourbao-Tournois C, Hutten N, Gaillard P, Couet C, Camus V, Ballon N. High preoperative depression, phobic anxiety, and binge eating scores and low-medium-term weight loss in sleeve gastrectomy obese patients: a preliminary cohort study. *Psychosomatics*. 2012; 53:363–370. [PubMed: 22458986]
- Castellini G, Godini L, Amedei SG, Faravelli C, Lucchese M, Ricca V. Psychological effects and outcome predictors of three bariatric surgery interventions: a 1-year follow-up study. *Eat and Weight Disorders*. 2014; 19:217–224.
- Cserjesi R, Luminet O, Poncelet AS, Lenard L. Altered executive function in obesity. Exploration of the role of affective states on cognitive abilities. *Appetite*. 2009; 52:535–539. [PubMed: 19260167]
- Diniz BS, Teixeira AL. Brain-derived neurotrophic factor and Alzheimer's disease: Physiopathology and Beyond. *Neuromolecular Medicine*. 2011; 11:217–222. [PubMed: 21898045]
- Dixon JB, Dixon ME, O'Brien PE. Pre-operative predictors of weight loss at 1-year after lap-band surgery. *Obesity Surgery*. 2001; 11:200–207. [PubMed: 11355027]
- Dotson VM, Resnick SM, Zonderman AB. Differential association of concurrent, baseline, and average depressive symptoms with cognitive decline in older adults. *American Journal of Geriatric Psychiatry*. 2008; 16:318–330. [PubMed: 18378557]
- Dotson VM, Davatzikos C, Kraut MA, Resnick SM. Depressive symptoms and brain volumes in older adults: a longitudinal magnetic resonance imaging study. *Journal of Psychiatry & Neuroscience*. 2009; 34:367–375. [PubMed: 19721847]
- Dotson VM, Beason-Held L, Kraut MA, Resnick SM. Longitudinal study of chronic depressive symptoms and regional cerebral blood flow in older men and women. *International Journal of Geriatric Psychiatry*. 2009; 24:809–819. [PubMed: 19484709]
- Finucane MM, Stevens GA, Cowan MJ, Danaei G, Lin JK, Paciorek CJ. Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group (Body Mass Index). National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9.1 million participants. *Lancet*. 2011; 377:557–567. [PubMed: 21295846]
- First, M.; Spitzer, R.; Gibbon, M.; Williams, J. Structured clinical interview for DSM-IV axis I disorders (SCID-I). Washington, D.C.: Clinician version: American Psychiatric Press; 1996.
- Fitzpatrick A, Kuller LH, Lopez O, Dieher P, O'Meara ES, Longstreth WT Jr, Luchsinger JA. Midlife and late-life obesity and the risk of dementia: cardiovascular health study. *Archives of Neurology*. 2009; 66:336–342. [PubMed: 19273752]
- Garcia S, Spitznagel MB, Cohen R, Raz N, Sweet L, Colbert L, Josephson R, Hughes J, Rosneck J, Gunstad J. Depression is associated with cognitive dysfunction in older adults with heart failure. *Cardiovascular Psychiatry and Neurology*. 2011; 2011:368324. [PubMed: 22195274]
- Ghanim H, Monte SV, Sia CL, Abuaysheh S, Green K, Caruana JA, Dandona P. Reduction in inflammation and the expression of amyloid precursor protein and other proteins related to Alzheimer's disease following gastric bypass surgery. *Journal of Clinical Endocrinology & Metabolism*. 2012; 97:E1197–E1201. [PubMed: 22508715]
- Golden, C. Stroop color and word task: a manual for clinical and experimental uses. Wood Dale: Stoelting; 1978.

- Gunstad J, Paul RH, Cohen RA, Tate DF, Spitznagel MB, Grieve S, Gordon E. Relationship between body mass index and brain volume in healthy adults. *International Journal of Neuroscience*. 2008; 118:1582–1593. [PubMed: 18853335]
- Gunstad J, Paul RH, Cohen RA, Tate DF, Gordon E. Obesity is associated with memory deficits in young and middle-aged adults. *Eating and Weight Disorders*. 2006; 11:e15–e19. [PubMed: 16801734]
- Gunstad J, Strain G, Devlin MJ, Wing R, Cohen RA, Paul RH, Crosby RD, Mitchell JE. Improved memory function 12 weeks after bariatric surgery. *Surgery for obesity and related diseases*. 2011; 7:465–472. [PubMed: 21145295]
- Haslam DW, James WP. Obesity. *Lancet*. 2005; 366:1197–1209. [PubMed: 16198769]
- Hassing LB, Dahl AK, Thorvaldsson V, Berg S, Gatz M, Pedersen NL, Johansson B. Overweight in midlife and risk of dementia: a 40-year follow-up study. *International Journal of Obesity*. 2009; 33:893–898. [PubMed: 19506566]
- Kivipelto M, Ngandu T, Fratiglioni L, Vltanen M, Kareholt I, Winblad B, Nissinen A. Obesity and vascular risk factors at midlife and the risk of dementia and Alzheimer disease. *Archives of Neurology*. 2005; 62:1556–1560. [PubMed: 16216938]
- Lee EB. Obesity, leptin, and Alzheimer's disease. *Annals of the New York Academy of Sciences*. 2011; 1243:15–29. [PubMed: 22211890]
- Livhits M, Mercado C, Yermilov I, Parikh JA, Dutson E, Mehran A, Gibbons MM. Preoperative predictors of weight loss following bariatric surgery: systematic review. *Obesity Surgery*. 2012; 22:70–89. [PubMed: 21833817]
- Lockwood KA, Alexopoulos GS, van Gorp WG. Executive dysfunction in geriatric depression. *American Journal of Psychiatry*. 2002; 159:1119–1126. [PubMed: 12091189]
- Lokken KL, Boeka AG, Austin HM, Gunstad J, Harmon CM. Evidence of executive dysfunction in extremely obese adolescents: a pilot study. *Surgery for Obesity and Related Disorders*. 2009; 5:547–552.
- Must A, Spadano J, Coakley E, Field AE, Colditz G, Dietz WH. The disease burden associated with overweight and obesity. *Journal of The American Medical Association*. 2006; 295:1549–1556. [PubMed: 16595758]
- Masheb RM, White MA, Toth CM, Burke-Martindale CH, Rothschild B, Grilo CM. The prognostic significance of depressive symptoms for predicting quality of life 12 months after gastric bypass. *Comprehensive Psychiatry*. 2007; 48:231–236. [PubMed: 17445516]
- Masoomi H, Nguyen NT, Stamos MJ, Smith BR. Overview of outcomes of laparoscopic and open roux-en-Y gastric bypass in the United States. *Surg Technol Int*. 2012 [epub ahead of print].
- Miranda WR, Batsis JA, Sarr MG, Collazo-Clavell ML, Clark MM, Somers VK, Lopez-Jimenez F. Impact of bariatric surgery on quality of life, functional capacity, and symptoms in patients with heart failure. *Obesity Surgery*. 2013; 23:1011–1015. [PubMed: 23604694]
- Mitchell JE, Selzer F, Kalarchian MA, Devlin MJ, Strain GW, Elder KA, Yanovski SZ. Psychopathology before surgery in the longitudinal assessment of bariatric surgery-3 (LABS-3) psychosocial study. *Surgery for Obesity and Related Disorders*. 2012; 8:533–541.
- Mitchell JE, King WC, Chen JY, Devlin MJ, Flum D, Garcia L, Yanovski S. Course of depressive symptoms and treatment in the longitudinal assessment of bariatric surgery (LABS-2). *Obesity (Silver Spring)*. 2014; 22:1799–1806. [PubMed: 24634371]
- Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of obesity in the United States, 2009–2010. *Center for Disease Control and Prevention. National Center for Health Statistics*. Incomplete. 2012
- Papademetriou V. Hypertension and cognition function: blood pressure regulation and cognitive function: a review of the literature. *Geriatrics*. 2005; 60:20–22. [PubMed: 15700945]
- Papazacharias A, Nardini M. The relationship between depression and cognitive deficits. *Psychiatria Danubina*. 2012; 24:179–182.
- Paterniti S. Depressive symptoms and cognitive decline in elderly people. *The British Journal of Psychiatry*. 2002; 181:406–410. [PubMed: 12411266]
- Paul RH, Lawrence J, Williams LM, Richard CC, Cooper N, Gordon E. Preliminary validity of “integneuro” a new computerized battery of neurocognitive tests. *International Journal of Neuroscience*. 2005; 115:1549–1567. [PubMed: 16223701]

- Popkin BM, Adair LS, Ng SW. Global nutrition transition and the pandemic of obesity in developing countries. *Nutrition Reviews*. 2012; 70:3–21. [PubMed: 22221213]
- Livingston EH. The incidence of bariatric surgery has plateaued in the U.S. *American Journal of Surgery*. 2010; 200:378–385. [PubMed: 20409518]
- Reitan R. Validity of the Trail Making Test as an indicator of organic brain damage. *Perceptual Motor Skills*. 1958; 8:271–276.
- Reppermund S, Brodaty H, Crawford JD, Kochan NA, Slavin MJ, Trollor JN, Sachdev PS. The relationship of current depressive symptoms and past depression with cognitive impairment and instrumental activities of daily living in an elderly population: the Sydney Memory and Ageing Study. *Journal of Psychiatric Research*. 2011; 45:1600–1607. [PubMed: 21871636]
- Rutledge T, Groesz LM, Savu M. Psychiatric factors and weight loss patterns following gastric bypass surgery in a veteran population. *Obesity Surgery*. 2011; 21:29–35. [PubMed: 19847571]
- Sackeim HA, Prohovnik I, Moeller JR, Brown RP, Apter S, Prudic J, Mukherjee S. Regional cerebral blood flow in mood disorders. I. Comparison of major depressives and normal controls at rest. *Archives of General Psychiatry*. 1990; 47:60–70. [PubMed: 2294857]
- Shinogle J, Owings M, Kozak L. Gastric bypass as treatment for obesity: trends, characteristics, and complications. *Obesity Research*. 2005; 13:2202–2209. [PubMed: 16421356]
- Spitznagel MB, Alosco M, Strain G, Devlin M, Cohen R, Paul R, Crosby RD, Mitchell JE, Gunstad J. Cognitive function predicts 24-month weight loss success after bariatric surgery. *Surgery for Obesity and Related Diseases*. 2013; 9:765–770. [PubMed: 23816443]
- Tiwari MM, Goede MR, Reynoso JF, Tsang AW, Oleynikov D, McBride CL. Differences in outcomes of laparoscopic gastric bypass. *Surgery for Obesity and Related Diseases*. 2011; 7:277–282. [PubMed: 21459686]
- Trollor JN, Smith E, Agars E, Juan SA, Baune BT, Campbell L, Sachdev P. The association between systemic inflammation and cognitive performance in the elderly: the Sydney Memory and Ageing Study. *Age*. 2012; 34:1295–1308. [PubMed: 21853262]
- Veiel HO. A preliminary profile of neuropsychological deficits associated with major depression. *Journal of Clinical and Experimental Neuropsychology*. 1997; 19:587–603.
- Walsh, K. *Understanding Brain Damage – A Primer of Neuropsychological Evaluation*. Melbourne: Churchill Livingstone; 1985.
- Whitmer RA, Gustafson DR, Barrett-Connor E, Haan MN, Gunderson EP, Yaffe K. Central obesity and increased risk of dementia more than three decades later. *Neurology*. 2008; 71:1057–1064. [PubMed: 18367704]
- 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”. *International Journal of Neuroscience*. 2005; 115:1605–1630. [PubMed: 16287629]
- Zhao, Y.; Encinosa, W. *Healthcare Cost and Utilization Project (HCUP) Statistical Briefs* [Internet]. Rockville, MD: Agency for Health Care Policy and Research (US); 2006–2007. Agency for Healthcare Research and Quality AHRQ Bariatric Surgery Utilization and Outcomes in 1998 and 2004. Statistical Brief #23.

Table 1

Baseline Demographic and Clinical Characteristics of 67 Bariatric Surgery Patients

Demographic and Clinical Characteristics	Overall Sample	MDD	No MDD	χ^2/t statistic
N	67	32	35	
Age, mean (SD)	42.90 (10.58)	42.97 (10.15)	43.74 (11.04)	-0.68
Body Mass Index	46.35 (6.08)	45.82 (3.96)	46.83 (7.55)	-0.67
Hypertension (%)	41.8	40.6	42.9	0.03
Diabetes (%)	20.9	21.9	20.0	0.04
Sleep apnea (%)	37.3	40.6	34.3	0.29

Note.

*
 $p < .05$;

MDD = Major Depressive Disorder

Table 2
Neuropsychological Test Performance (T-score mean (SD)) among the Overall Sample of Bariatric Surgery Patients

	Baseline M(SD)	12-months M(SD)	Baseline % T-score < 35	12-Months % T-score < 35	Chi-square for Baseline versus 12- Month Impairment
<i>Attention/Executive Function</i>					
Digit Span Total	50.93 (8.25)	53.72 (10.51)	1.5	0.0	--
SOA-A	56.71 (13.38)	64.43 (12.95)	7.5	3.0	5.40*
SOA-B	54.69 (13.20)	60.21 (12.94)	6.0	7.5	1.90
Verbal Interference	55.29 (13.97)	64.04 (12.70)	7.5	1.5	12.59**
Maze Errors	52.52 (10.21)	55.85 (8.79)	6.0	1.5	15.99**
<i>Memory</i>					
Total Learning	44.43 (12.30)	50.82 (12.37)	16.4	7.5	15.92**
LDFR	46.98 (9.39)	53.10 (8.85)	11.9	4.5	1.37
Recognition	42.61 (10.14)	49.45 (9.46)	16.4	6.0	3.50 (p = 0.06)
<i>Language</i>					
Verbal Fluency	47.31 (11.81)	47.80 (10.82)	13.4	11.9	18.81**
Animals	50.73 (10.32)	50.43 (10.40)	3.0	6.0	32.47**

Note.

Abbreviations—SOA = Switching of Attention; LDFR = Long Delay Free Recall

Table 3

Cognitive Function (T-score, mean (SD)) among the Bariatric Surgery Patients with and without a History of MDD

	MDD (n = 32)		No MDD (n = 35)		F (time)	F (group × time)
	Baseline	12-month	Baseline	12-month		
Attention	54.68 (5.44)	59.67 (8.77)	53.04 (10.85)	58.53 (9.96)	27.31 *	0.06
Executive Function	54.82 (8.37)	60.03 (7.06)	53.57 (9.71)	60.03 (9.65)	37.60 *	0.42
Memory	45.52 (7.22)	52.85 (7.50)	43.90 (9.57)	49.54 (8.73)	45.48 *	0.77
Language	49.51 (8.59)	49.00 (8.88)	48.57 (11.06)	49.21 (9.62)	0.01	0.43

Note.

* $p < 0.001$;

MDD = Major Depressive Disorder