

Review Article

Cognitive Function in Bariatric Surgery

Mohammed Ezzi M.D, FRCSc

Jazan University, College of Medicine, Jazan, Saudi Arabia

***Corresponding Author:**

Mohammed Ezzi

Email: mdme2007@yahoo.com

Abstract: Obesity is a noticeable public health problem worldwide. It is well known that obesity affects physical health and cognitive function. It impairs all domains of cognitive function. Moreover, obesity affects both metabolic activity and cerebral structure of the brain. Bariatric surgery is surgical procedures that help patients with extreme obesity to lose weight. Multiple domains of cognitive function improve 24 to 36 months after bariatric surgery. Mechanism of such improvement is still questionable. It may be related to improvement of underlying medical condition, improved glucose regulation and insulin sensitivity, or correction of leptin and ghrelin systems. In this article, we review the effect of bariatric surgery on cognitive function and its possible mechanism.

Keywords: Obesity, leptin, bariatric surgery

INTRODUCTION

Obesity is an obvious public health problem. Its prevalence in the United States estimated to be 35.1% in 2011–2012 (1) and 33.7 in 2014 [2].

It is well known that obesity leads to multiple medical conditions [3]. Diabetes, hypertension, and coronary artery disease are comorbidities associated with obesity [4]. Also, obesity is connected to increased mortality and morbidity [5]. Moreover, those with morbid or extreme obesity (body mass index [BMI] ≥ 40 kg/m²) have the highest risk of psychiatric comorbidities. Additionally, obesity is linked to Alzheimer's disease and vascular dementia [6].

Obesity affects multiple domains of cognitive function including attention, executive function, and memory [7, 8]. Gunstad *et al.* found that learning and memory are affected by obesity in young to middle-aged persons [9]. Another study stated that 23.9% of severely obese persons showed learning deficit and 22.9% showed declined memory performance [10]. Binge eating disorder (BED), described by the American Psychiatric Association in 2013, is the recurrence of binge eating episodes involving the consumption of an objectively large amount of food with a simultaneous subjective sense of loss of control over eating. Obese individuals with BED showed executive function and decision making deficits more than obese non-BED controls [11, 12]. Moreover, there is theory of emotional eating which describes that overeating episodes with loss of control on over eating

is associated with emotional distress in obese adults [13, 14].

Both Positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) measure metabolic activity within the brain and show cerebral structure. Obesity affects both metabolic activity and cerebral structure [6]. The grey matter volume of the hypothalamus, prefrontal, anterior temporal and inferior parietal cortices, and the cerebellum was decreased with increased BMI and waist circumference with the waist circumference is a more important than BMI, mainly in females [15]. Functional magnetic resonance imaging shows that morbidly obese patients suffer from deterioration in functional connectivity of appetite control networks, which also mediate executive functions [16]. Recent studies confirmed that morbidly obese patients show decrease in white and grey matter densities in brain regions which associated with impaired food intake control and cognitive-emotion regulation [17, 15, 18- 21].

Overview of bariatric surgery

NIH Consensus Development Conference Panel [22] recommended bariatric surgery for those with class 3 obesity (BMI ≥ 40 kg/m²) and for those with class 2 obesity (BMI=35-39.9 kg/ m²) associated with high-risk comorbid conditions such as type 2 diabetes or cardiovascular disease [22]

There are different Bariatric surgical procedures which include Roux-en-Y gastric by-pass (RYGB), sleeve gastrectomy (SG), vertical banded

gastroplasty (VGB), adjustable gastric banding (AGB), laparoscopic adjustable gastric band (LAGB), biliopancreatic diversion with duodenal switch (BPD/DS) and laparoscopic mini gastric by-pass (MGB).

Roux-en-Y gastric by-pass is an irreversible procedure, which leads to restriction of food intake and malabsorption of consumed food [23]. The procedure is typically done through laparoscopic approach. Staples are used to first create a 15- to 30-mL gastric pouch. The jejunum is then divided and connected to the gastric pouch, effectively bypassing sections of the small intestine. The SG leads to the restriction of food intake via the creation of a gastric sleeve but, unlike the RYGB, does not involve malabsorption as the small intestine remains fully intact [24].

The most common and the gold standard procedure done in USA and Canada is RYGB [25, 23, 26]. Regarding weight loss outcomes, RYGB and SG show similar results, so SG done when RYGB is contraindicated [24].

Twenty five percent and thirty two percent are the average 2-year weight losses with VSG and RYGB. Also, bariatric surgery associated with dramatic improvement in type 2 diabetes, hypertension, sleep apnea, hyperlipidemia, hospitalizations, and reduced uses of medications among others [27, 28].

Cognitive function measurement

There are multiple domains of cognitive functions which include perception, attention, memory and executive function. The latter includes higher order processes such as planning, regulation and goal-oriented behavior [29].

The Neuropsychological assessment battery (NAB) is a comprehensive modular battery of tests normed for adults between the ages of 18–97 years. The full NAB consists of 36 individual tests across five cognitive domains: (a) Attention, (b) Language, (c) Memory, (d) Spatial, and (e) Executive Functions [30, 31]. These tests measure pre-intervention and post-intervention performance on tests.

To assess the cognitive function after bariatric surgery, several studies used the following tests: Attention/executive function: Digit span total, Switching of attention, Verbal interference, Maze task, Memory: Verbal list-learning, Language: Letter fluency, Animal fluency [32-35]. Other studies used California Verbal Learning Test II, Wechsler Memory Scale III, Brief Visuospatial Memory Test—Revised, Controlled Oral Word Association Task (COWAT), Stroop Colour and Word Test (Golden version), Wisconsin Card Sorting Task, Colour Trails Test Part A

and B, Paced Auditory Serial Attention Test [36] Iowa Gambling Task, Rey Auditory Verbal Learning Test, Rey Complex Figure Test, and Trail Making Test [37].

The cognitive function after bariatric surgery

In the last few decades, a considerable increase of performing bariatric surgeries was recorded. In 1990s, about 16,000 procedures were carried out compared to more than 103,000 and 220,000 procedures in 2003 and 2008 respectively [38].

Such records raise concerns about the effect of these procedures on overall health and cognitive function. The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) establish Longitudinal Assessment of Bariatric Surgery (LABS) project, which is a multicenter longitudinal follow-up examination of the outcome of bariatric surgery [6]

Group of researchers published series of studies that show the relation between cognitive function and bariatric surgery over 4 years. They concluded that cognitive impairment improved after the surgery on memory, executive function, and attention domain up to 36 months but the attention domain may slightly decline after 24 months with weight regain [33, 39, 10, 40, 6].

Waldstein SR *et al.* stated that high blood pressure coupled with central or total obesity showed decline in the performance of participants in tests of motor speed and manual dexterity as well as executive function [41].

Most of studies reveal that cognitive function recovers after bariatric surgery but this recovery may be affected by premorbid factors. Cases with history of depression are anticipated to have reduced cognitive recovery. Also, there is a positive association between the depression and anxiety scores and weight loss [42]. Interventions by counseling may be useful in ameliorating depression, but further studies are needed [43]. Moreover, bariatric surgery patients with family history of Alzheimer's disease did not show recovery in memory performance after surgery in comparison to those without family history [44]. On the other hand, history of binge eating disorder and older age did not show effect on postoperative cognitive improvement [32, 45]

Although, the mechanisms by which postoperative cognitive recovery occur, explained in different studies, there is inconsistent conclusion about it. One of the early explanations is that the medical conditions associated with obesity which resolve after surgery may be linked to postoperative cognition improvement [39, 46]. Another study owes the decrease of depressive symptoms after bariatric surgery to

several factors. These include deactivation of inflammatory pathways, normalization of hypothalamic pituitary adrenal axis functioning, reversal of insulin resistance, and reduction of psychological distress due to massive weight loss [47]. Improvement in glucose regulation and insulin sensitivity, as early as one month and one year, respectively, after bariatric surgery may related to improved cognitive function [48, 49, 34]. Improved liver function and decrease preoperative Alkaline Phosphatase (ALP) accompanied by postoperative cognition improvement [50, 51]. Leptin and ghrelin systems are appetitive hormones responsible for regulation of food intake, energy, and weight, these hormones disturbed in obese adults [52]. After bariatric surgery serum leptin and ghrelin levels improved [53, 54]. Increased serum ghrelin levels were associated with recovered attention/executive function at the 12-month after surgery [35]. As well, serum leptin levels were decreased and brain's sensitivity to its level is increased via increased its brain permeability. This is linked to improved cognitive function postoperatively [55, 35].

In obese patients, increase of long-term cerebral metabolic activity is associated with structural brain abnormalities which causes cognitive decline. All of this is reversible with weight loss after bariatric surgery [37]. Interestingly, recent study discovered that there is acute recovery of brain structural abnormalities in obese patients within one month postoperatively [56].

CONCLUSION

In conclusion, obesity is accompanied by cognitive impairment in all domains. All research studies prove that bariatric surgery shows obvious improvement in cognitive function after 24 and 36 months follow-up. The mechanism of such improvement is inconclusive till now. Further research is needed to detect the long term effect of these surgeries on the cognition and to identify the possible mechanism.

Compliance with Ethical Standards:

Funding: None

Conflict of Interest: None declared

Ethical approval: This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent: None needed

REFERENCES

1. Bastert, G. B. (1982). Clinical trials in West Germany: adjuvant therapy for breast cancer patients. *Experientia. Supplementum*, 41, 618.
2. <http://apps.who.int/gho/data/node.main.A900A?lang=en>
3. Hensrud, D. D., & Klein, S. (2006, October). Extreme obesity: a new medical crisis in the United States. In *Mayo Clinic Proceedings* (Vol. 81, No. 10, pp. S5-S10). Elsevier.
4. Must, A., Spadano, J., Coakley, E. H., Field, A. E., Colditz, G., & Dietz, W. H. (1999). The disease burden associated with overweight and obesity. *Jama*, 282(16), 1523-1529.
5. Ogden, C. L., Carroll, M. D., Kit, B. K., & Flegal, K. M. (2014). Prevalence of childhood and adult obesity in the United States, 2011-2012. *Jama*, 311(8), 806-814.
6. Spitznagel, M. B., Hawkins, M., Alosco, M., Galioto, R., Garcia, S., Miller, L., & Gunstad, J. (2015). Neurocognitive effects of obesity and bariatric surgery. *European Eating Disorders Review*, 23(6), 488-495.
7. Cournot, M. C. M. J., Marquie, J. C., Ansiau, D., Martinaud, C., Fonds, H., Ferrieres, J., & Ruidavets, J. B. (2006). Relation between body mass index and cognitive function in healthy middle-aged men and women. *Neurology*, 67(7), 1208-1214.
8. Gunstad, J., Lhotsky, A., Wendell, C. R., Ferrucci, L., & Zonderman, A. B. (2010). Longitudinal examination of obesity and cognitive function: results from the Baltimore longitudinal study of aging. *Neuroepidemiology*, 34(4), 222-229.
9. Gunstad, J., Paul, R. H., Cohen, R. A., Tate, D. F., & Gordon, E. (2006). Obesity is associated with memory deficits in young and middle-aged adults. *Eating and Weight Disorders-Studies on Anorexia, Bulimia and Obesity*, 11(1), e15-e19.
10. Gunstad, J., Strain, G., Devlin, M. J., Wing, R., Cohen, R. A., Paul, R. H., ... & Mitchell, J. E. (2011). Improved memory function 12 weeks after bariatric surgery. *Surgery for obesity and related diseases*, 7(4), 465-472.
11. Monica, D., Paulo, M., Appolinário, J. C., Freitas, S. R. D., Coutinho, G., Santos, C., & Coutinho, W. (2010). Assessment of executive functions in obese individuals with binge eating disorder. *Revista brasileira de psiquiatria*, 32(4), 381-388.
12. Svaldi, J., Brand, M., & Tuschen-Caffier, B. (2010). Decision-making impairments in women with binge eating disorder. *Appetite*, 54(1), 84-92.
13. Leehr, E. J., Krohmer, K., Schag, K., Dresler, T., Zipfel, S., & Giel, K. E. (2015). Emotion regulation model in binge eating disorder and obesity-a systematic review. *Neuroscience & Biobehavioral Reviews*, 49, 125-134.
14. Goldschmidt, A. B., Crosby, R. D., Cao, L., Engel, S. G., Durkin, N., Beach, H. M., ... & Peterson, C. B. (2014). Ecological momentary assessment of eating episodes in obese adults. *Psychosomatic medicine*, 76(9), 747.
15. Kurth, F., Levitt, J. G., Phillips, O. R., Luders, E., Woods, R. P., Mazziotta, J. C., ... & Narr, K. L. (2013). Relationships between gray matter, body

- mass index, and waist circumference in healthy adults. *Human brain mapping*, 34(7), 1737-1746.
16. Tuulari, J. J., Karlsson, H. K., Hirvonen, J., Salminen, P., Nuutila, P., & Nummenmaa, L. (2015). Neural circuits for cognitive appetite control in healthy and obese individuals: An fMRI study. *PloS one*, 10(2), e0116640.
 17. Karlsson, H. K., Tuulari, J. J., Hirvonen, J., Lepomäki, V., Parkkola, R., Hiltunen, J., ... & Nuutila, P. (2013). Obesity is associated with white matter atrophy: A combined diffusion tensor imaging and voxel-based morphometric study. *Obesity*, 21(12), 2530-2537.
 18. Maayan, L., Hoogendoorn, C., Sweat, V., & Convit, A. (2011). Disinhibited eating in obese adolescents is associated with orbitofrontal volume reductions and executive dysfunction. *Obesity*, 19(7), 1382-1387.
 19. Pannacciulli, N., Del Parigi, A., Chen, K., Le, D. S. N., Reiman, E. M., & Tataranni, P. A. (2006). Brain abnormalities in human obesity: a voxel-based morphometric study. *Neuroimage*, 31(4), 1419-1425.
 20. Raji, C. A., Ho, A. J., Parikshak, N. N., Becker, J. T., Lopez, O. L., Kuller, L. H., ... & Thompson, P. M. (2010). Brain structure and obesity. *Human brain mapping*, 31(3), 353-364.
 21. Shott, M. E., Cornier, M. A., Mittal, V. A., Pryor, T. L., Orr, J. M., Brown, M. S., & Frank, G. K. (2015). Orbitofrontal cortex volume and brain reward response in obesity. *International Journal of Obesity*, 39(2), 214-221.
 22. Hubbard, V. S., & Hall, W. H. (1991). Gastrointestinal Surgery for Severe Obesity. *Obesity surgery*, 1(3), 257-265.
 23. Franco, J. V. A., Ruiz, P. A., Palermo, M., & Gagner, M. (2011). A review of studies comparing three laparoscopic procedures in bariatric surgery: sleeve gastrectomy, Roux-en-Y gastric bypass and adjustable gastric banding. *Obesity surgery*, 21(9), 1458-1468.
 24. Padwal, R., Klarenbach, S., Wiebe, N., Hazel, M., Birch, D., Karmali, S., ... & Tonelli, M. (2011). Bariatric surgery: a systematic review of the clinical and economic evidence. *Journal of general internal medicine*, 26(10), 1183-1194.
 25. Malli, C. P., Sioulas, A. D., Emmanouil, T., Dimitriadis, G. D., & Triantafyllou, K. (2016). Endoscopy after bariatric surgery. *Annals of Gastroenterology: Quarterly Publication of the Hellenic Society of Gastroenterology*, 29(3), 249.
 26. Tice, J. A., Karliner, L., Walsh, J., Petersen, A. J., & Feldman, M. D. (2008). Gastric banding or bypass? A systematic review comparing the two most popular bariatric procedures. *The American journal of medicine*, 121(10), 885-893.
 27. Buchwald, H., Avidor, Y., Braunwald, E., Jensen, M. D., Pories, W., Fahrenbach, K., & Schoelles, K. (2004). Bariatric surgery: a systematic review and meta-analysis. *Jama*, 292(14), 1724-1737.
 28. Sjöström, L., Narbro, K., Sjöström, C. D., Karason, K., Larsson, B., Wedel, H., ... & Bengtsson, C. (2007). Effects of bariatric surgery on mortality in Swedish obese subjects. *New England journal of medicine*, 357(8), 741-752.
 29. Sternberg, R. J. (Ed.). (1984). *Mechanisms of cognitive development*. Freeman.
 30. Brooks, B. L., & Iverson, G. L. (2010). Comparing actual to estimated base rates of "abnormal" scores on neuropsychological test batteries: Implications for interpretation. *Archives of Clinical Neuropsychology*, 25(1), 14-21.
 31. Brooks, B. L., Iverson, G. L., & White, T. (2009). Advanced interpretation of the neuropsychological assessment battery with older adults: base rate analyses, discrepancy scores, and interpreting change. *Archives of Clinical Neuropsychology*, acp061.
 32. Lavender, J. M., Alosco, M. L., Spitznagel, M. B., Strain, G., Devlin, M., Cohen, R., ... & Gunstad, J. (2014). Association between binge eating disorder and changes in cognitive functioning following bariatric surgery. *Journal of psychiatric research*, 59, 148-154.
 33. Alosco, M. L., Galioto, R., Spitznagel, M. B., Strain, G., Devlin, M., Cohen, R., ... & Gunstad, J. (2014). Cognitive function after bariatric surgery: evidence for improvement 3 years after surgery. *The American Journal of Surgery*, 207(6), 870-876.
 34. Galioto, R., Alosco, M. L., Spitznagel, M. B., Strain, G., Devlin, M., Cohen, R., ... & Gunstad, J. (2015). Glucose regulation and cognitive function after bariatric surgery. *Journal of clinical and experimental neuropsychology*, 37(4), 402-413.
 35. Alosco, M. L., Spitznagel, M. B., Strain, G., Devlin, M., Cohen, R., Crosby, R. D., ... & Gunstad, J. (2015). Improved serum leptin and ghrelin following bariatric surgery predict better postoperative cognitive function. *Journal of Clinical Neurology*, 11(1), 48-56.
 36. Restivo, M. R., McKinnon, M. C., Frey, B. N., Hall, G. B., & Taylor, V. H. (2016). Effect of obesity on cognition in adults with and without a mood disorder: study design and methods. *BMJ open*, 6(2), e009347.
 37. Marques, E. L., Halpern, A., Corrêa Mancini, M., de Melo, M. E., Horie, N. C., Buchpiguel, C. A., ... & Cunha-Neto, E. (2014). Changes in neuropsychological tests and brain metabolism after bariatric surgery. *The Journal of Clinical Endocrinology & Metabolism*, 99(11), E2347-E2352.
 38. <https://www.niddk.nih.gov/health-information/health-topics/weight-control/Bariatric-Surgery/Pages/labs.aspx>

39. Alosco, M. L., Spitznagel, M. B., Strain, G., Devlin, M., Cohen, R., Paul, R., ... & Gunstad, J. (2014). Improved memory function two years after bariatric surgery. *Obesity*, 22(1), 32-38.
40. Miller, L. A., Crosby, R. D., Galioto, R., Strain, G., Devlin, M. J., Wing, R., ... & Gunstad, J. (2013). Bariatric surgery patients exhibit improved memory function 12 months postoperatively. *Obesity surgery*, 23(10), 1527-1535.
41. Waldstein, S. R., & Katzel, L. I. (2006). Interactive relations of central versus total obesity and blood pressure to cognitive function. *International journal of obesity*, 30(1), 201-207.
42. Karlsson, J., Sjöström, L., & Sullivan, M. (1998). Swedish obese subjects (SOS)—an intervention study of obesity. Two-year follow-up of health-related quality of life (HRQL) and eating behavior after gastric surgery for severe obesity. *International Journal of Obesity & Related Metabolic Disorders*, 22(2).
43. Ghoneim, M. M., & O'Hara, M. W. (2016). Depression and postoperative complications: an overview. *BMC surgery*, 16(1), 5.
44. Alosco, M. L., Spitznagel, M. B., Strain, G., Devlin, M., Crosby, R. D., Mitchell, J. E., & Gunstad, J. (2014). Family history of Alzheimer's disease limits improvement in cognitive function after bariatric surgery. *SAGE open medicine*, 2, 2050312114539477.
45. Alosco, M. L., Cohen, R., Spitznagel, M. B., Strain, G., Devlin, M., Crosby, R. D., ... & Gunstad, J. (2014). Older age does not limit postbariatric surgery cognitive benefits: a preliminary investigation. *Surgery for Obesity and Related Diseases*, 10(6), 1196-1201.
46. Abu-Abeid, S., Keidar, A., & Szold, A. (2001). Resolution of chronic medical conditions after laparoscopic adjustable silicone gastric banding for the treatment of morbid obesity in the elderly. *Surgical endoscopy*, 15(2), 132-134.
47. de Zwaan, M., Enderle, J., Wagner, S., Mühlhans, B., Ditzgen, B., Gefeller, O., ... & Müller, A. (2011). Anxiety and depression in bariatric surgery patients: a prospective, follow-up study using structured clinical interviews. *Journal of affective disorders*, 133(1), 61-68.
48. Kashyap, S. R., Daud, S., Kelly, K. R., Gastaldelli, A., Win, H., Brethauer, S., ... & Schauer, P. R. (2010). Acute effects of gastric bypass versus gastric restrictive surgery on β -cell function and insulinotropic hormones in severely obese patients with type 2 diabetes. *International journal of obesity*, 34(3), 462-471.
49. Nestvold, T. K., Nielsen, E. W., & Lappegård, K. T. (2013). Bariatric surgery reduces risk factors for development of type 2 diabetes mellitus in morbidly obese, nondiabetic patients. *Metabolic syndrome and related disorders*, 11(6), 441-446.
50. Alosco, M. L., Spitznagel, M. B., Strain, G., Devlin, M., Cohen, R., Crosby, R. D., ... & Gunstad, J. (2014). The effects of cystatin C and alkaline phosphatase changes on cognitive function 12-months after bariatric surgery. *Journal of the neurological sciences*, 345(1), 176-180.
51. Spitznagel, M. B., Gunstad, J., Manderino, L., & Heinberg, L. (2015). Liver Fibrosis Predicts Cognitive Function Following Bariatric Surgery: A Preliminary Investigation. *Obesity*, 23(10), 1957-1959.
52. Klok, M. D., Jakobsdottir, S., & Drent, M. L. (2007). The role of leptin and ghrelin in the regulation of food intake and body weight in humans: a review. *Obesity reviews*, 8(1), 21-34.
53. Terra, X., Auguet, T., Guiu-Jurado, E., Berlanga, A., Orellana-Gavaldà, J. M., Hernández, M., ... & Aguilar, C. (2013). Long-term changes in leptin, chemerin and ghrelin levels following different bariatric surgery procedures: Roux-en-Y gastric bypass and sleeve gastrectomy. *Obesity surgery*, 23(11), 1790-1798.
54. Dimitriadis, E., Daskalakis, M., Kampa, M., Peppe, A., Papadakis, J. A., & Melissas, J. (2013). Alterations in gut hormones after laparoscopic sleeve gastrectomy: a prospective clinical and laboratory investigational study. *Annals of surgery*, 257(4), 647-654.
55. Lee, J. H., Reed, D. R., & Price, R. A. (2001). Leptin resistance is associated with extreme obesity and aggregates in families. *International journal of obesity*, 25(10), 1471.
56. Zhang, Y., Ji, G., Xu, M., Cai, W., Zhu, Q., Qian, L., ... & Cui, G. (2016). Recovery of brain structural abnormalities in morbidly obese patients after bariatric surgery. *International Journal of Obesity*.