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Surgical and Non-Surgical Interventions for Obesity in Service of Preserving Cognitive Function

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Abstract

Objective—The purpose of this article is to highlight what is currently known about the mechanisms of obesity-related cognitive impairment and weight-loss-related cognitive improvement, and discuss the benefits and drawbacks of available treatments.

Methods—The manuscript is based on a live debate, presenting the main advantages and disadvantages of exercise interventions and bariatric surgery as related to cognitive functioning. The live debate took place during a one-day conference on Diabetes, Obesity and the Brain, organized by the American Psychosomatic Society in October of 2013.

Results—While it is well established that bariatric surgery tends to lead to greater weight loss, better glycemic control, and cognitive improvement (effect sizes ranging between 0.61 to 0.78) during the first one to two years post intervention than non-surgical treatments, medical complications are possible, and follow-up data beyond five years is limited. In contrast, non-surgical therapies have been extensively studied in a variety of clinical settings and have proved that they can sustain positive health outcomes up to 10 years later, but their cognitive benefits tend to be more modest (effect sizes ranging from 0.18 to 0.69) and long-term regimen compliance, especially in obese individuals is uncertain.

Conclusions—Rather than focusing on debating whether surgical or no-surgical interventions for obesity are better, additional research is needed to identify the most efficient and practical combination of approaches to ensure sustained positive health outcomes for the largest number of patients possible.

Keywords

obesity; cognitive function; exercise; bariatric surgery

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Conflict of Interest

The authors declare no conflict of interest.

Obesity & Cognitive Function

Obesity is a well-known risk factor for a multitude of health problems including hypertension, diabetes, dyslipidemia and certain forms of cancer (1). Within the past ten years, numerous studies have raised awareness of the deleterious effects of obesity on brain structure and function throughout the lifespan. Higher body mass index (BMI) has been associated with lower verbal fluency in very young children (ages 6–8 years of age) (2). Obese BMI and greater visceral adipose tissue mass have also related to poorer performance on cognitive control tasks and lower academic achievement among preadolescents (3), and weaker executive function among mature adults (18–82 years of age) (4, 5). Last but not least, several large epidemiological studies have reported links between midlife obesity and severe late-life cognitive impairment (6–8). In those studies, higher BMI in middle age was related to increased risk of developing dementia 18 to 27 years later, independent of other risk factors such as higher midlife blood pressure, total cholesterol levels, smoking, and apolipoprotein E genotype (6–8). The risk increase was non-trivial, up to 72% higher than the risk for the general population (7). These findings have been corroborated by reports of obesity-related changes in brain volumes (2), white matter integrity (9), functional brain activation in response to a cognitive challenge (5, 10), and cerebral neurochemistry (11, 12). The purpose of this article is to present the highlights of what is currently known about the mechanisms via which visceral fat may negatively affect brain function, and impartially discuss the benefits and drawbacks of available treatments, including lifestyle modification and surgical interventions. Continued research on these topics is also extremely important, as it will guide the development of new interventions to preserve cognitive function throughout the lifespan.

Mechanisms

One potential mechanism linking obesity to declines in cognitive function could be vascular in nature. It is plausible that midlife obesity, through the development of insulin insensitivity, may lead to impairments in vascular endothelial function. Since the vascular endothelium is responsible for regulating vessel response to changes in blood pressure and flow, endothelial dysfunction, could impair cerebrovascular or functional brain response to cognitive challenges, eventually leading to reduced cognitive performance (**Model 1**: obesity → insulin insensitivity → endothelial dysfunction → diminished cerebrovascular response to a cognitive challenge → cognitive decline) (13). This model is supported by a study documenting that higher BMI is associated with lower functional brain activation in response to a working memory task in middle-aged adults, and this relationship is fully mediated by insulin sensitivity (10). Further support for a vascular pathway connecting obesity to cognitive impairment comes from studies linking insulin resistance to endothelial dysfunction (14) as well as evidence that better endothelium-dependent, flow-mediated vasodilatation is related to a more robust cerebrovascular response to a working memory task (15). All this evidence points towards modification of endothelial function as a potentially fruitful avenue in the pursuit of interventions to maintain cognitive health in obese and overweight individuals.

Interventions: Exercise

A highly promising intervention with potential to ameliorate endothelial dysfunction is aerobic exercise. Studies have shown that even a brief moderate-intensity aerobic exercise intervention, such as brisk daily walk for 12 weeks, can improve vascular compliance and restore vascular endothelial function in formerly sedentary middle-aged adults (average age 53) (16, 17). Evidence from the animal literature provides further support for the beneficial cognitive effects of daily exercise by documenting exercise-related neurogenesis in the hippocampus in conjunction with improvements in hippocampally-mediated memory functions in rats who are allowed to voluntarily run for food for 18 weeks as opposed to sedentary controls who are fed *ad libitum* (18). Fitness training has been successfully implemented as an intervention to improve cognitive function in older human volunteers as well. Meta-analytic findings reveal that participants in aerobic forms of exercise such as water aerobics exhibit greater gains in cognitive performance than sedentary controls and even participants in non-aerobic forms of exercise such as stretching (19). The benefits are modest but significant, covering multiple domains of cognitive function with particularly robust effects on executive functions including planning, working memory, and multitasking. Not surprisingly, the effects of fitness training on cognitive task performance appear to be modulated by several variables, including the type of exercise, length of training sessions, and intervention duration (20). Cognitive performance of participants in combined aerobic and resistance-training conditions shows greater improvements than the performance of participants undergoing aerobic training alone (effect size 0.59 vs. 0.41, SE = 0.043, $n = 101$, $p < 0.05$).

Naturally, a logical question is how much exercise is sufficient to maintain or enhance cognitive performance. This question appears to be a bit of a moving target, but current guidelines by the American College of Sports Medicine for a healthy active lifestyle, recommend a regiment that includes moderate-intensity cardiorespiratory exercise training for at least 30 minutes per day on at least five days per week for a total of at least 150 minutes per week (21). While ACSM recommendations do not necessarily translate directly into fitness training requirements for improvement of cognitive performance, they are remarkably consistent with the results of a meta-analytic study of exercise effects on cognitive function in older adults (average age > 55), published by Colcombe and Kramer in 2003 (20). The study noted significantly higher effect sizes for exercise session durations of moderate length (31–45 minutes; effect size = 0.61, SE = 0.05, $n = 24$, $p < 0.05$) as compared to short duration sessions of 15–30 minutes (effect size 0.18, SE = 0.09, $n = 11$, $p < 0.05$). Similarly, interventions longer than six months (effect size = 0.67, SE = 0.05, $n = 27$, $p < .05$) produced greater effect sizes than brief (effect size = 0.52, SE = 0.07, $n = 38$, $p < .05$) and medium length (effect size = 0.27, SE = 0.05, $n = 36$, $p < .05$) programs.

Drawbacks of Exercise: Lack of Adherence/ Modest Long-Term Effects

Unfortunately, despite the known benefits of exercise, 50% of individuals who begin an exercise program discontinue within 6 months (22). Therefore, weight loss and subsequent cognitive benefits associated with exercise interventions tend to be short-lived and relatively modest. Siervo and colleagues (23) conducted a systematic review of 7 randomized

controlled trials and 5 case-controlled studies that examined behavioral weight loss interventions and cognitive function. The results of this review revealed very small effect sizes for memory (0.13) and attention/executive function (0.14). Effect sizes in exercise intervention studies, however, should be interpreted with great caution considering the overarching issues with lack of adherence to the prescribed interventions.

Attrition rates in exercise intervention studies range between 25% and 50% and adherence is poor even among those participants that do complete the study (24). Specifically, only 5% of participants have been shown to engage in the recommended 150 minutes per week of exercise during study periods (25). These high rates of attrition and non-adherence are in part due to the overwhelming exercise protocols (e.g., 3–5 days per week of exercise participation) among samples of unfit individuals (see (26)). Exercise intervention studies also tend to be short in duration and short bouts of exercise is unlikely to confer meaningful health benefits to severely obese persons with a lifelong history of an unhealthy lifestyle. Indeed, the most effective exercise interventions appear to consist of frequent (e.g., 5 to 6 times per week) moderate to vigorous intensity levels of long-term duration (27). However, obese persons are highly unlikely to adhere to these behaviors or continue this level of intensity after study conclusion. Thus, improving adherence with exercise intervention programs is a crucial step towards making physical activity a viable option for enhancing cognitive function in obese individuals.

Exercise Interventions: Addressing Adherence

Team-based interventions relying on social networks for initiating and maintaining positive health behavior changes have shown real promise in improving adherence to lifestyle modification including increased physical activity and improved nutrition. For example, in a large statewide weight loss initiative, *Shape Up Rhode Island*, Leahey and colleagues enrolled over 3,000 individuals into more than 900 teams to compete on either weight loss or physical activity (28). Self-appointed team captains organized teams, provided encouragement, and monitored progress without any formal training by the investigators. The results showed that clinically significant weight loss (5%) tended to cluster within teams and was predicted by greater number of teammates achieving substantial weight reduction and higher social influences towards weight loss. The authors concluded that health behavior outcomes could be improved on a large scale by capitalizing on teammate influence within team-based interventions.

Other research teams have explored interdisciplinary programs, combining cognitive behavioral therapy with nutrition and exercise counseling to improve long-term maintenance of positive health behavior changes in diet and physical activity. Göhner and colleagues demonstrated that the addition of skilled psychological support focused on goal setting, action planning, and barrier management can result in significantly better long-term outcomes for the participants in a weight loss intervention including higher level of physical activity, better food choices, and lower follow-up weight as compared to non-participating controls (29). Two years post program completion; the intervention group adults who received the extra assistance in formulating a personal weight loss goal and support in pursuing the goal, reported an average of two extra hours of physical activity per week than

the comparison group. They also received a significantly higher healthy eating habits score following diet analysis. Finally, the exhibited significantly lower follow-up BMI and a significantly higher percent sustained-weight loss.

Exercise Interventions: Enhancement by Bariatric Surgery

Interestingly, it appears bariatric surgery may serve as a motivational tool to increase physical activity levels in obese individuals. For instance, a majority of bariatric surgery patients have been shown to exhibit increased physical activity levels post-operatively (30). This pattern of findings may be a consequence of post-surgery improvements in psychological factors that influence physical activity in at-risk older adults, most notably depression (31). Furthermore, exercise-related study concerns such as significant attrition appear to be attenuated in bariatric surgery research. Recent work shows that 100% of bariatric surgery patients were retained in study procedures at a 14 year follow-up (32). Bariatric surgery is discussed in greater detail below.

Exercise: It is Not All About Fitness

Last but not least, it is worth discussing that while cardiovascular fitness undeniably plays a role in brain health (33–35), the link between obesity and cognitive performance does not appear to be solely reliant on vascular compliance and endothelial function. Rather, evidence suggests that obesity can also alter cerebral metabolism in middle age (**Model 2**: obesity → dyslipidemia → cerebral neurochemical alterations → cognitive decline) (13). Increased BMI in midlife was recently linked to significantly elevated levels of the cerebral metabolite *myo*-inositol, an organic osmolyte and precursor to the second messenger inositol triphosphate (11). More importantly, elevated *myo*-inositol in that study had a significant indirect effect connecting midlife obesity to poorer memory performance. Since *myo*-inositol elevations are hallmark signs of the prodromal stages of known cognitive disorders such as amnesic Mild Cognitive Impairment, Alzheimer's disease (36), Multiple Sclerosis (37) and HIV-related cognitive decline (38), midlife *myo*-inositol increases in obesity are a serious concern. They raise the possibility that visceral fat could negatively affect cognitive function in individuals with higher BMIs by disrupting cerebral metabolic processes. On the optimistic side, *myo*-inositol elevations in obesity appear to be driven by dyslipidemia, more specifically, increases in peripheral triglyceride levels and decreases in high-density lipoprotein (HDL) cholesterol levels (39), both of which are treatable. Much like recommendations for treating endothelial dysfunction, guidelines for treating hypertriglyceridemia include smoking cessation, increases in physical activity, limiting the consumption of saturated fats and increasing the consumption of fruits/vegetables and whole grains, but options also include medications such as statins, fibrates, niacin, and fish oil (40, 41).

Interventions: Bariatric Surgery

Bariatric surgery is the most effective weight loss intervention for severe obesity. Given the link between exercise-related weight loss and cognitive improvements, research has also sought to determine whether bariatric surgery may provide cognitive benefits to many individuals. Below, we first highlight the rising popularity of bariatric surgery and then

review the literature that has examined cognitive outcomes following bariatric surgery and discuss possible mechanisms for this relationship, as well as potential drawbacks of surgical weight loss interventions. Of note, the review of bariatric surgery and cognitive outcomes is primarily from data that has been collected through the Longitudinal Assessment of Bariatric Surgery consortium, a multisite NIH-funded center study that has been the leader in research examining outcomes associated with bariatric surgery. The sample from this project was largely young to middle aged women (N= 125; mean age 45 years) with a mean BMI > 45.

Bariatric Surgery: Popularity & Sustainability

Bariatric surgery has become a popular intervention for long-term weight loss. Specifically, annual bariatric surgery procedures in the United States increased from 13,386 in 1998 to 121,055 in 2004, representing an 800% increase (42). A similar trend was also found worldwide (Buchwald et al., 2004). Although the annual rates of bariatric surgery slightly decreased from 2004 to 2007 (93,733 procedures), this appeared to be subsequent to insurance-related restrictions because 22,151,116 class III obese persons were potentially eligible for surgical intervention in 2007 (43). Regardless, the annual incidence of bariatric surgery procedures since 2007 in the US may have plateaued around 113,000 cases per year (44).

The rising popularity of bariatric surgery can largely be attributed to the increasing recognition of surgery as an effective intervention for dramatic weight loss reductions. In a meta-analysis of 136 studies, bariatric surgery was shown to yield a 61.2% excess weight loss across all surgical interventions two years post-operatively (45). While there was minimal variability among the various interventions (i.e., gastric banding, gastric bypass, gastropasty, and/or biliopancreatic diversion or duodenal switch), gastric bypass appeared to be the most effective with an excess weight loss of nearly 75% (45). The weight loss efficacy of bariatric surgery is indeed longstanding. Nearly 80% of gastric bypass patients display between 60%–80% excess weight loss in the first year following surgery and long-term rates stabilize at approximately 50%–60% excess weight loss (45–47). Among a sample of 1,035 bariatric surgery patients and 5,746 matched controls, initial excess weight loss of 67.1% among the bariatric surgery patients was largely maintained for up to 16 years post-operatively (48). More recent evidence also shows maintenance of 50% excess weight loss approximately 14 years after surgery (32). Such long-term weight loss may help to explain the lasting benefits in cognition following bariatric surgery. However, it should be noted that strict adherence to post-operative treatment guidelines is necessary in order for successful and sustainable weight loss. Yet, treatment regimens are complex and post-surgery non-adherence is indeed common (see (49)), particularly to postoperative dietary recommendations and eating behaviors. Such poor adherence can preclude sustainable weight loss and ultimately counter the initial health and cognitive benefits of bariatric surgery.

However, obesity is increasing at an alarming rate, in the US as well as elsewhere. The World Health Organization estimates that within the next year, 1.5 billion people worldwide will be overweight, more than 21% of the world's population (50). It is not difficult to see

that faced with potential patient numbers in the millions, spread across countries of varying wealth and access to health care, a surgical solution to the obesity epidemic is not feasible. In the US alone, the estimated workload for providing surgery to the 22 million eligible patients is for 5500 bariatric surgeons to complete 400 procedures a year for 10 years (51). These numbers are not sustainable even in the US, a country that spends over 2.2 trillion dollars per year on personal health care (52). Therefore, while surgical options for the most extreme cases of morbid obesity are important, it is also imperative that substantial resources are focused on improving non-surgical interventions and prevention.

Bariatric Surgery: Cognitive Improvements

An emerging literature now suggests that obesity-related cognitive impairments may be partially reversible via bariatric surgery. Specifically, a series of studies from the Longitudinal Assessment of Bariatric Surgery (LABS) consortium demonstrates that bariatric surgery confers both acute and long-term cognitive gains. In 2011, Gunstad and colleagues (53) first demonstrated that relative to obese controls bariatric surgery patients exhibited improved memory abilities 12-weeks following surgery; in contrast, memory for the non-surgery obese controls declined. Clinically meaningful memory impairments in the bariatric surgery patients improved from nearly 24% pre-operatively to 0% at the 12-week follow-up. In a subsequent study, these findings were extended to show that memory continued to improve 12-months post-surgery among a sample of 95 bariatric surgery patients relative to 42 obese controls (54). These findings are noteworthy, as memory impairment is a clinical hallmark of Alzheimer's disease.

Continued examination of the LABS cohort has shown long-term cognitive changes following bariatric surgery. When compared to non-surgery obese controls, bariatric surgery patients exhibited improvements in memory 2 years after surgery (55, 56). For example, relative to obese controls, bariatric surgery patients were shown to demonstrate improvements in memory at 12-weeks and 24-months postoperatively. Preliminary work also reveals cognitive gains 3 years post-operatively, including among domains other than memory, including attention and executive function (55). Specifically, Alosco and colleagues (2014) conducted repeated measures analyses over four time points after bariatric surgery (12-weeks, 12-months, 24-months, and 36-months) and found main effects for attention, executive function and memory. Despite initial differences in cognitive trajectories, benefits were observed in all domains at the 36-month follow-up. Interestingly, cognitive benefits associated with bariatric surgery are robust even in the presence of older age and a genetic history of Alzheimer's disease, suggesting bariatric surgery benefits cognition even in obese persons at high risk for neurological impairment (57, 58). In brief summary, there is reason to believe that bariatric surgery may attenuate cognitive decline or even reduce the known risk for Alzheimer's disease in severely obese persons.

Bariatric Surgery & Cognitive Improvement: Resolution of Comorbid Medical Conditions

As previously described, bariatric surgery is associated with significant weight loss, which is associated with an array of physiological health improvements that likely underpin the post-operative cognitive gains. Specifically, similar to that associated with exercise, bariatric surgery and subsequent weight loss is associated with improved and/or resolved vascular

medical comorbidities (53), including improved cardiac function, lower blood pressure, better glucose control, to name a few. Weight loss also yields improvements in novel physiological biomarkers (e.g., adipokines, inflammation) that are uniquely linked with adiposity and known to influence cognitive outcomes. The below reviews the possible role of comorbid medical conditions as well as other adiposity-related factors in post-bariatric surgery cognitive improvements.

Vascular Improvements—Severe obesity is nearly always accompanied by type 2 diabetes mellitus (T2DM), sleep apnea, hypertension, and/or hyperlipidemia. These medical conditions are well known to negatively affect the brain and cognitive abilities, and also increase risk for severe neurological conditions such as Alzheimer’s disease. Specifically, cardiovascular disease and related risk factors negatively affect blood perfusion to brain via cardiac deficiency, micro- and macrovascular insult, and reduced arterial plasticity. Cerebral hypoperfusion can lead to oxygen and glucose deprivation to the brain and thus result in structural brain alterations (e.g., white matter hyperintensities, brain atrophy) that ultimately produce cognitive impairment.

Fortunately, bariatric surgery can alleviate or even resolve these conditions and thus improve cognitive abilities in severely obese persons possibly through vascular-related benefits such as improved cardiac and endothelial function. Given this possibility, much attention has been paid to the effects of bariatric surgery on comorbid medical conditions. In particular, there is much research that has investigated the effects of bariatric surgery on T2DM resolution given the detrimental outcomes linked with T2DM, including nearly a 2-fold elevated risk for dementia (59). Bariatric surgery improves glycemic control and results in long-term improvement and remission of T2DM (60). As an example, as many as 86% of bariatric surgery patients exhibit resolution of T2DM 2 years after surgery (61), nearly 70% demonstrate partial remission of T2DM 3 years post-operatively (62), and almost 25% of bariatric surgery patients have been shown to exhibit complete resolution of T2DM 6 years after surgery (60). These remission rates have led to recent attention to bariatric surgery as an alternate treatment option for T2DM rather than lifestyle interventions.

The health benefits of bariatric surgery extend beyond T2DM. Fredheim and colleagues (63) also demonstrated that sleep apnea resolves 1 year after bariatric surgery in 66% of patients, which was significantly more than the 40% remission rate associated with lifestyle intervention. Recent work from the LABS consortium also demonstrates remission of hypertension in up to 38.2% of bariatric surgery patients 3 years after surgery; dyslipidemia also resolved in as many as 61.9% of patients (62). While the above highlights a few of the most common medical comorbidities well documented to influence cognition, bariatric surgery is associated with a diverse range of other health benefits (e.g., improved liver and renal function) that may also benefit cognitive function.

Adiposity-related Health Improvements—As discussed above, obesity is linked with cognitive deficits in healthy individuals (4), suggesting that adiposity introduces several independent mechanisms for cognitive impairment. Specifically, severe obesity is associated with increased inflammation (64) and disturbed serum concentrations of appetite hormones (e.g., leptin, ghrelin), brain derived neurotrophic factor (BDNF), and amyloid beta (65–68).

These factors are linked with poor neurocognitive outcomes, including increased risk for neurodegenerative conditions (e.g., Alzheimer's disease (69–74). Yet, bariatric surgery is known to reduce inflammation and improve serum concentrations of appetite hormones, BDNF, and amyloid beta (75–77). Most notably, gastric bypass has been shown to reverse heightened inflammation in obesity to subsequently reduce expression of Alzheimer's disease-related pathology, including concentrations of amyloid precursor protein (76). These findings further support the possibility that bariatric surgery can attenuate risk for dementia in severely obese individuals and future studies are needed to confirm the role of novel mechanisms in post-surgery cognitive changes.

Summary of Bariatric Surgery and Cognitive Outcomes

Bariatric surgery is growing in popularity and associated with dramatic weight loss. An extant literature now shows that bariatric surgery confers cognitive benefits, particularly in memory. These findings raise the possibility that obesity-related cognitive impairments may be reversible via bariatric surgery and weight loss surgery may even attenuate or reverse the risk for dementia that is associated with severe obesity. Although bariatric surgery is associated with significant improvements in vascular function, the exact mechanism by which weight loss surgery improves cognitive function remains poorly understood. Future work is much needed to clarify the mechanisms by which bariatric surgery improves cognitive abilities, including the role of improvements in cerebrovascular function such as cerebral hemodynamics.

Drawbacks of Bariatric Surgery: Complications

Bariatric surgery is a medical procedure and complications do occur in 10–20% of all cases (78). These complications, when they do occur, tend to be quite serious including stomal stenosis, bowel obstruction, nutrient malabsorption and death (78). While mortality is relatively rare, 0.1–2% (78), the percentages translate to thousands of individuals when we consider that approximately 113,000 patients in the US receive bariatric surgery each year (44). Another important point to consider is that the complication rates reported in the literature are likely underestimated as discussed in a large review recently published in the *Journal of the American Medical Association* (79). Maggard-Gibbons and colleagues examined over 1290 articles covering 32 surgical and 22 non-surgical interventions for obesity. They pointed out a few drawbacks of the studies included in their systematic review including the fact that none were specifically designed to assess complications, data came mostly from a few select centers specialized in providing bariatric surgery, and serious adverse events in general tend to be underreported in the medical literature. The authors concluded that surgery complications may be expected to rise as the procedures become more ubiquitous and are offered by a larger number of less experienced providers.

Bariatric Surgery: Addressing the Risk of Complications

A very important consideration in weighing the risk of complications from bariatric surgery is the fact that it is linked with longer survival rates in obese individuals relative to diet and exercise therapies (80). Although risk for health complications accompany any surgical procedure, contemporary surgical methods (i.e., laparoscopic gastric bypass approaches)

have become less invasive, improved in safety, and reduced the length in hospital stays (see (81). Inhospital mortality secondary to bariatric surgery has decreased by a total of 79% between the years of 1998 and 2004 (see Elder et al., 2007). Moreover, in a recent meta-analysis of 164 studies between 2003 and 2012 that included 161,756 patients, mortality rates within 30 days of bariatric surgery was <0.1% and this rate continued to be <0.5% 30 days after surgery (82). Complication rates have also steadily declined over the years (44). A recent retrospective study showed that out of 299 bariatric surgery patients only 7 were readmitted and there was a complication rate of 2.6%; 30-day mortality was 0 (83).

In addition, the risks for complications and/or mortality following bariatric surgery often have little to do with the surgical procedure itself. Instead, adverse bariatric surgery outcomes are often a product of other non-surgical factors such as preexisting medical and/or psychological comorbidities (e.g., sleep apnea, T2DM, depression), impaired functional status, and/or inter-individual differences in surgeon skill, among others (83–87). Regardless, bariatric surgery is considered relatively safe even among those at high-risk (88) and the rates of health complications and mortality that may occur after bariatric surgery ultimately pale in comparison to the negative outcomes associated with untreated severe obesity (89).

Conclusions

Within the past ten years, multiple studies have established links between midlife obesity and late-life cognitive impairment. While the mechanisms underlying this association are not well understood, both vascular and non-vascular pathways connecting increased body mass and visceral adiposity with alterations in brain integrity have been proposed, and multiple intervention strategies to reduce body weight in service of preserving cognitive function have been explored. Among the most popular ones are exercise interventions, diet, and bariatric surgery, each with its own set of benefits and drawbacks. While it is well established that bariatric surgery tends to lead to greater weight loss, better glycemic control, and cognitive improvement (effect sizes ranging between 0.61 to 0.78) during the first one to two years post intervention than non-surgical treatments, medical complications are possible, and follow-up data beyond five years is limited. Therefore, the long-term health outcomes of bariatric surgery patients are at this point largely unknown. In contrast, non-surgical therapies have been extensively studied in a variety of clinical settings and have proved that they can sustain positive health outcomes up to 10 years later, but their cognitive benefits tend to be more modest (effect sizes ranging between 0.18 and 0.69). Long-term adherence to rigorous exercise regimens is also difficult to sustain for anyone, and unproven for obese individuals. Unfortunately, bariatric surgery alone is by no means sufficient to address the health problems related to obesity. Post-surgical patients are still required to implement life-style modifications and carefully monitor their nutrition in order for the surgical intervention to succeed. Pre-existing mental health issues and behavioral factors such as binge eating may play a role in determining the success of bariatric surgery. Therefore, rather than focusing on debating whether surgical or no-surgical interventions for obesity are better, additional research is needed to identify the most efficient and practical combination of approaches to ensure sustained positive health outcomes for the largest number of patients possible.

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