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Review Article

Evidence for Neurocognitive Improvement After Bariatric Surgery: A Systematic Review

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Background: *Bariatric surgery is an effective means of weight reduction in severely obese patients and correlates with improvements in quality of life, mental health outcomes, and neurocognition, especially in those with high psychosocial burden.* **Objective:** *The primary purpose of this systematic review was to evaluate the impact of bariatric surgery on long-term neurocognitive functioning and neuropsychological outcomes.* **Methods:** *OVID Medline and PsychInfo databases from January 1990 to August 2015 were searched with key terms and phrases: "bariatric surgery" and "cognition." The inclusion criteria for the studies included the following: $n \geq 10$, minimum postoperative follow-up of 12 months, and use of formal neurocognitive assessment tools presurgery and postsurgery.* **Results:** *Of 422 identified abstracts, a total of 10 studies met inclusion criteria and sample sizes ranged from 10–156. Postsurgical follow-up time ranged from 12–36 months. All 10 studies documented significant improvements of statistical significance ($p < 0.05$) in at least 1 neurocognitive domain following bariatric surgery; 9 studies showed improvements in memory, 4 studies showed improvement in executive function, and 2 studies showed improvements in language, and 1 study showed no improvement in any neurocognitive domain.* **Conclusion:** *Mental health care providers should consider the effect of neurocognitive performance on presurgery psychiatric assessments for bariatric surgery and implications for psychosocial functioning postsurgery. The aforementioned effect that bariatric surgical intervention has on neurocognition underscores the complex interrelationship between metabolism and brain function. Future research should validate the use of neurocognitive screening tools presurgery and evaluate the impact of neurocognitive changes on neurocognitive, bariatric, and functional outcomes.*

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Key words: bariatric surgery, obesity, cognitive dysfunction, mental disorders, weight loss.

INTRODUCTION

The increasing rate of obesity is of growing concern in North America.[1] Obesity has been acknowledged as a chronic health condition as well as a known risk factor for many other health comorbidities including but not limited to heart disease, stroke, and diabetes.[2–5] In Canada alone, 20.2% of Canadians aged 18 years and older—roughly 5.3 million adults— were obese, according to self-reported measures from data collected in 2014.[6] More than one-third of U.S. adults are obese and from 33.9–35.5% are overweight.[7]

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Moreover, 6.4% of adults aged 20 years or more are classified as extremely obese.[7]

Concerns about morbidity and mortality related to obesity are a significant concern in those with psychiatric conditions; obesity prevalence rates are as high as 60% in patients with severe mental illness.[8] Moreover, lifetime prevalence rates of psychiatric illness in patients with severe obesity, namely weight loss candidates, approach 70%.[9] Furthermore, there is no clear evidence that having a psychiatric diagnosis before bariatric surgery (BS) affects the rate, amount, or sustainability of weight loss after surgery. There is fair evidence that there is a significant initial decrease in the prevalence of psychiatric illnesses following BS, although there is no evidence of causality.[10]

In addition to specific psychiatric disorders, neurocognitive deficits have been linked to obesity in studies.[11–14] As a result, current weight loss interventions, such as BS, may also have a role in improving neurocognition. The most consistent deficits reported are in the area of executive functioning: response inhibition, decision-making, set shifting, planning, problem-solving, and mental flexibility.[14–19] In addition, deficits in executive functions persist after controlling for confounders[16] and obesity-related comorbidities including but not limited to cardiovascular disease.[18] Other cognitive areas studied that have been negatively affected by obesity include memory, language, motor performance psychomotor performance and speed, visual construction, and concept formation.[14,18] It was found that in bariatric patient population, nearly 25% of patients show clinically meaningful levels of neurocognitive impairment (defined as >1.5 SD less than average) and 40% show more subtle cognitive impairment (>1 SD) in learning and memory, attention, executive functions, and language.[20,21] Studies have also reported a predictive longitudinal association of obesity with the development of age-related neurocognitive deficits, with studies showing an association between increased body mass index and accelerated neurocognitive decline in middle-aged adults.[11,19,22]

Overall, neurocognition, in particular executive functioning, seems to improve after weight loss, independently of the method, although the level of functioning is still not equivalent to that of a healthy person.[17,23–25] The duration for these dates does not exceed 24 months post-BS. Therefore, it is likely that BS potentially plays an important role in improving patient neurocognitive outcomes postsurgery. The primary aim of our review article is to examine the impact that BS intervention played in neurocognitive outcomes. The secondary aims of this article have set to summarize the following: (1) the role of the gut microbiome and gut-brain interactions in relation to specific adipokines, namely, leptin and ghrelin on neurocognitive outcomes after BS; and (2) the evidence for using specific cognitive assessment tools to evaluate neurocognition in patients undergoing BS.

METHODS

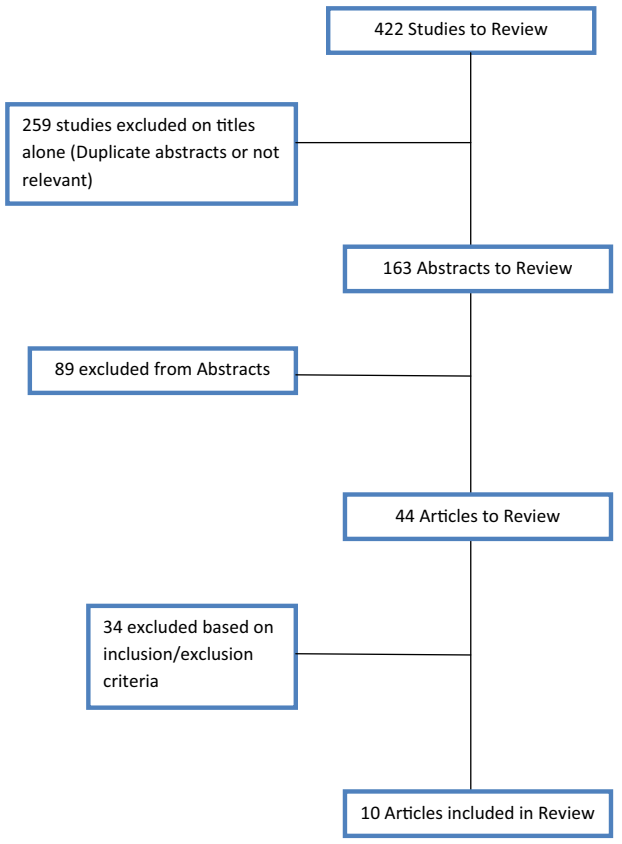
OVID Medline and PsychInfo databases from January 1990 to August 2015 were searched with the key terms and phrases: "bariatric surgery" and "cognition. "The inclusion criteria for the studies included the following: $n \geq 10$, minimum postoperative follow-up of 12 months, and the use of formal neurocognitive assessment tools presurgery and postsurgery. This inclusion criterion was established to ensure clinical relevance and rigor given the number of studies included in the review. Three investigators independently reviewed all abstracts and full-text copies of articles were further assessed for inclusion in this review (Figure). Any disagreements related to either inclusion or exclusion criteria were resolved by discussion among 3 reviewers.

Our search yielded 422 abstracts of which 44 warranted further review. A total of 10 studies met the inclusion criteria and sample sizes ranged from 10–156. Additional literature related to the areas of focus was used to supplement findings from these 10 studies.

RESULTS

The times when patients were measured for neurocognitive function ranged from baseline (presurgery) up to 48 months (and included 3, 12, 24, and 36 months). All studies measured their patients' neurocognitive function at baseline presurgery, but postsurgery measurements varied along the aforementioned time points. Five studies measured neurocognitive function in patients 3 months postsurgery.[26–30] Six studies measured neurocognitive function 12 months postsurgery,[28,29,31–34] 3 studies measured neurocognitive

FIGURE. PRISMA Flow Diagram



function 24 months postsurgery,[27,29,30] 2 studies measured neurocognitive function 36 months postsurgery,[26,29] and only 1 study measured neurocognitive function 48 months postsurgery.[29] Those studies that indicated time deviation at measurement time points pointed out that patients were measured within 30 days before surgery for baseline measurements, ±5 days at 3 months, and ±30 days for all the following cognitive function measurements, except for[30] those that had a ±14-day deviation for cognitive function measurements at 24-months follow-up.

Postsurgical follow-up duration for 10 identified studies from this systematic review ranged from 12–36 months, with 8 studies having a 12-month follow-up. The neurocognitive domains being assessed included the following: attention and executive function, memory, and language. All 10 studies documented significant improvements of statistical significance ($p < 0.05$) in at least 1 neurocognitive domain following BS; 10 studies showed improvements in memory, 4 studies showed improvement in attention/executive function, and 2 studies showed improvements in language. Of the 10 studies, only 1 study ($n = 84$) measured adipokine levels; after controlling for age, sex, and baseline factors, 12-month serum leptin ($p = 0.03$) and ghrelin ($p = 0.03$) levels predicted 12-month attention/executive function (Table).

Metabolic, Inflammatory, and Vascular Mechanisms for Change in Cognition Post-BS

A rationale for an observed improvement in neurocognition after weight loss surgery is the reduction in medical comorbidities (e.g., hypertension, type 2 diabetes, and chronic obstructive airway disease). However, recent clinical studies show that resolution of comorbidities does not alone account for improved neurocognition observed in patients after weight loss surgery.[29] Previous studies have discussed in great detail potential metabolic and vascular mechanisms by which underlying physiology alters neurocognition in obese individuals. Such examples include reduced cerebral blood flow[17,35] and impaired metabolism, mainly in prefrontal cortex being responsible for the decline in neurocognition.[18,36] In addition, glucose and insulin dysregulation in the brain have been implicated as a potential cause described as metabolic syndrome driving the cognitive changes.[14] Other studies have attributed cognitive changes to elevated leptin levels,[18,37,38] dysregulation of inflammation,[14,18,19] structural brain changes (greater brain atrophy, decreased gray matter volumes, and increased white matter hyperintensities).[18,39–42]

Effect of Adipokines on Neurocognition

A secondary purpose of our review was to further evaluate changes in adipokine levels, namely, leptin and ghrelin and their effect on neurognition. Of the 10 studies included in this review, only 1 study ($n = 84$) measured adipokine levels.[40] In this particular study, the reduction in serum leptin level and increase in serum ghrelin level following BS was accompanied by improved attention and executive function. There are many theories elucidating both neurochemical and physiologic mechanisms explaining the role adipokine levels play in altering neurocognition, among

TABLE. Summary of included studies

Number	Study	Number of patients	Cognitive tests	Adipokine changes included	Type of surgery	Follow-up time (mo)	Study design	Cognitive domain improved	Results: postsurgery
1	Spitznagel et al.[26]	55	Digit span backward, switching of attention (SOA), verbal interference, verbal fluency, maze task, verbal list-learning and memory	No	Roux-en-Y, 1 patient—banding	12, 24, 36	Prospective cohort	Memory	Adjusting for sex, baseline cognitive function, and 12-wk %WL, 12-wk global cognitive test performance predicted 36-mo postoperative %WL and BMI. Partial correlations revealed recognition memory, working memory, and generativity were most strongly related to weight loss
2	Spitznagel et al.[27]	57	Digit span backward, switching of attention, verbal interference, letter fluency, maze task, verbal list-learning	No	Roux-en-Y	12, 24	Prospective cohort	Attention/executive function, memory	Better cognitive function 12 wk after surgery predicted higher %WL and lower BMI at 24 mo, and specific domains of attention/executive and memory function were robustly related to decreased BMI and greater %WL at 24 mo
3	Miller et al.[28]	137	Cognitive test battery, verbal list, digit span switching of attention, maze task, verbal interference, letter fluency	No	Roux-en-Y bypass procedure or adjustable gastric banding surgery	12	Prospective cohort	Memory	Patients who underwent bariatric surgery exhibited cognitive deficits relative to well-established standardized normative data before surgery, and obese controls demonstrated similar deficits. Analyses of longitudinal change indicated an interactive effect on memory indices, with patients who underwent bariatric surgery demonstrating better performance postoperatively than obese controls
4	Alosco et al.[29]	50	Digit span, switching of attention, verbal interference, maze task, verbal list-learning, verbal and letter fluency	No	N/A	36	Prospective cohort	Memory, attention/executive function	Exploratory analyses for cognitive test performance at 48-mo post–bariatric surgery showed that attention, memory, and language functioning fell within the average range, whereas executive function fell within the high average to above average range. Repeated measures ANOVAs showed significant improvements from baseline to 48-mo post–bariatric surgery in the following domains: executive function ($\Lambda = 0.49$, $F(1, 20) = 20.58$, $p < 0.001$; baseline executive function M (SD) = 53.84 (10.88) vs executive function at 48-mo M (SD) = 62.75 (10.32)) and memory ($\Lambda = 0.39$, $F(1, 20) = 31.60$, $p < 0.001$; baseline memory M (SD) = 46.60 (5.54) vs memory at 48-mo M (SD) = 55.19 (8.11). No such pattern emerged for attention ($\Lambda = 0.99$, $F(1, 20) = 0.29$, $p = 0.60$; baseline attention M (SD) = 55.02 (6.61 vs attention at 48-mo M (SD) = 54.14 (8.41) or language ($\Lambda = 0.99$, $F(1, 49) = 0.14$, $p = 0.71$; baseline language M (SD) = 49.44 (11.41 vs language at 48-mo M (SD) = 50.20 (10.94).
5	Alosco et al.[31]	78	The IntegNeuro cognitive test battery assessed cognitive function in multiple domains: switching of attention, maze task, verbal list-learning, letter fluency, verbal fluency	No	N/A	12	Prospective cohort	Attention/executive function, memory	Relative to baseline, impairments on cognitive testing were less prevalent 12-mo following surgery on many measures of attention/executive function, memory, and language. As a whole, repeated measures ANOVA revealed significant improvements in attention/executive function ($F(1,77) = 70.16$, $p < 0.001$) and memory ($F(1,77) = 28.85$, $p < 0.001$) 12-mo postoperatively. There were no significant preoperative to postoperative changes in language abilities ($F(1,77) = 0.68$, $p = 0.41$)
6	Alosco et al.[32]	84	Cognitive function: the IntegNeuro cognitive test battery was administered to assess cognitive function. Digit span backwards, switching of attention, verbal interference, verbal listing	Yes gherlin and serum leptin	Gastric banding procedure (1), Roux-en-Y gastric bypass surgery	12	Prospective cohort	Attention/executive function, memory, language	Repeated measures ANOVA revealed a significant and positive effect on cognitive function over the 12 mo following surgery regarding attention/executive function ($F(1, 83) = 36.20$, $p < 0.001$) and memory ($F(1, 83) = 54.90$, $p < 0.001$). In contrast, performance on tests of language abilities remained stable over time ($F(1, 83) = 0.19$, $p = 0.67$). The prevalence of impairments in many

			learning, letter fluency, verbal fluency						measures of attention/executive function, memory, and language was lower at 12 mo postoperatively than preoperatively
7	Galioto et al.[33]	85	Cognitive function: the IntegNeuro cognitive test battery was administered to assess cognitive function. Digit span backwards, switching of attention, verbal interference, verbal listing learning, letter fluency, verbal fluency	No	Gastric banding procedure (1), Roux-en-Y gastric bypass surgery	12	Prospective cohort	Memory, attention/ executive function	Repeated measures ANOVA examined changes in cognitive function presurgery to postsurgery. There were no violations in statistical assumptions (e.g., univariate normality) associated with repeated measures ANOVA design. Analyses showed significant improvements in cognitive function over 12 mo for all cognitive tests except letter and verbal fluency
8	Graff-Radford et al.[12]	10 Patients/ 10 controls	Patients underwent formal neuropsychometric testing that included tests of executive function (Trail-Making Test A and B and Stroop), language function (Boston Naming Test and Category Fluency), memory (Auditory Verbal Learning Test) and visuospatial function (Rey-Osterrieth complex figure)	No	Roux-en-Y gastric bypass surgery	Variable?	Retrospective	None	Patients underwent formal neuropsychometric testing that included tests of executive function (Trail-Making Test A and B and Stroop), language function (Boston Naming Test and Category Fluency), memory (Auditory Verbal Learning Test) and visuospatial function (Rey-Osterrieth complex figure).[11] The raw scores from these neuropsychological tests were converted to MOANS values[12] that are age-adjusted to norms derived from Olmsted County population, and transformed to a standardized score with a mean of 10 and a standard deviation (SD) of 3. A MOANS score of less than 1.5 standard deviations (<5) is typically considered evidence of mild impairment. MRI findings: the patients who underwent gastric bypass surgery had significantly smaller thalamic volumes compared with age and sex-matched controls ($p = 0.003$). In fact, 7 of the these patients had thalamic volumes smaller than the smallest control subject, with only 3 gastric patient volumes overlapping with the control range
9	Lavender et al.[34]	68	Cognitive function: the IntegNeuro cognitive test battery was administered to assess cognitive function. Digit span backwards, switching of attention, verbal interference, verbal listing learning, letter fluency, verbal fluency	No	Roux-en-Y Gastric bypass	12	Prospective	Attention/executive function, memory	Results revealed that on the whole, participants displayed improvements from baseline to follow-up in attention, executive function, and memory, even after controlling for diagnostic history of depression; no changes were observed for language. However, individuals with and without a history of BED did not differ in changes in body mass index or in the degree of improvement in cognitive functioning from baseline to follow-up
10	Alosco et al.[30]	86 Individuals (63 patients who underwent bariatric surgery, 23 obese controls)	Cognitive function: the IntegNeuro cognitive test battery was administered to assess cognitive function. Digit span backwards, switching of attention, verbal interference, verbal listing learning, letter fluency, verbal fluency	No	Roux-en-Y gastric bypass, surgery, gastric banding procedure[1]	Before surgery and at 12-wk and 24-mo follow-up	Prospective cohort	Memory	Relative to obese controls, repeated measures ANOVA showed improvements in memory from baseline to 12-wk and 24-mo postoperatively ($p < 0.05$). Regression analyses controlling for baseline factors revealed that a lower BMI at 24-mo demonstrated a trend toward significance for improved memory ($\beta = -0.30$, $p = 0.075$)

which primarily focus on the role of leptin and ghrelin. One such explanation is that adipokines (such as leptin and ghrelin) seem capable of reducing glial activation in models of excitotoxicity.[43] A potential therapeutic and preventive role in neurodegenerative disorders has been hypothesized for adipokines, mainly for leptin.[43,44] More specifically, leptin has been implicated in having a protective effect against age-related cognitive decline and atrophy, Alzheimer disease and other neurodegenerative disorders, such as Parkinson disease. There appears to be a general decrease in leptin sensitivity[44–47] and higher leptin levels are associated with reduced risk of developing neurodegenerative disorders among elderly subjects.[48] Another known adipokine, ghrelin, has shown to be associated with the progression of obesity and metabolic syndrome, but it has been also linked to neuromodulation, neuroprotection, memory, and learning processes.[43]

Types of Cognitive Measures in Patients Undergoing BS

Of the 10 studies, 9 used an IntegNeuro cognitive test battery that comprised the following tests: digit spin forward, digit spin backward, switching of attention, verbal interference, verbal fluency, maze task, and verbal list used to assess cognitive functioning in patients undergoing BS, preoperation and postoperation. One study did not use the aforementioned test but had patients undergo "formal neuropsychometric testing that included tests of executive function (Trail-Making Test A and B and Stroop), language function (Boston Naming Test and Category Fluency), memory (Auditory Verbal Learning Test), and visuospatial function (Rey-Osterrieth complex figure)." Although the IntegNeuro Cognitive Test Battery and the other less formalized combination of tests share many similarities, there are still many discrepancies between their selection choices in specific tests. It should also be noted that there are internal differences among various studies that used the IntegNeuro Cognitive Test Battery regarding the operating definitions that explained what was being used to test cognition, how many components of the test were used, the strengths and limitations of the test and each of its components, and assessment timings.

Limitations of Cognitive Assessments

Neurocognitive tests have their strengths, however, several factors may confound the effects BS has on neurocognitive function, including (1) age, (2) sex, and (3) years of education. To minimize the confounds of age, it was suggested by Clark et al.[49] to norm cognitive tests over age to "help ensure cross-sectional validity in clinical assessments," "to represent aging associated cognitive change across a continuum to detect sensitively abnormal variation that may occur in such conditions," and use a normalization model based on age regression to "demonstrate the sensitivity of the battery across the age range." Sex differences in cognitive assessment results were of only moderate strength, but it should be noted that evolutionary psychology literature shows substantial sex differences on specific task performance (i.e., maze task).[49] Lastly, the effect of education on cognitive function depends on the age range examined, the range of measures used, specific sex testing, and the categorization of education level by the researchers. As expected, individuals with high levels of education will perform better on specific neurocognitive tests, specifically tests that analyze measures of language, as higher education stresses effective communication skills in writing and speaking. In addition, repeat testing of subjects may influence the raw scores on the assessments; however, this process was standardized among all subjects in the studies included in the review.

Timing of Cognitive Assessments Post-BS

The current literature suggests there are no established standards for cognitive assessment for patients before and after undergoing BS; however, there have been some suggestions made about its possible creation. Sptiznagel et al.[72] suggest that "a thorough preoperative and brief postoperative series of evaluations [be used] to help identify those patients at highest risk for poor [cognitive] outcomes." Furthermore, these authors recommend that the cognitive assessment of patients undergoing BS should include "all primary neurocognitive domains, including global neurocognitive function, attention, executive function, memory, language, visuospatial and motor function."[72] It should be noted that these neurocognitive domains can be measured with the IntegNeuro Cognitive Test Battery.

DISCUSSION

Our review was limited to 10 studies with very different study designs and outcomes, thus preventing us from doing a meta-analysis. However, all 10 studies included in the review documented significant improvements of statistical significance ($p < 0.05$) in at least 1 neurocognitive domain following BS. The domains most significantly improved were memory ($N = 9$), attention/executive function ($N = 4$), and language ($N = 2$). The studies included in our review enrolled both patients with and without baseline neurocognitive impairment that was adjusted for baseline neurocognitive deficits.

As a result, it is evident that overall neurocognition improves following BS intervention in obese patients. There exist multiple mechanisms in the literature that may explain the results of this review including but not limited to the following: metabolic changes, increased inflammation, adipokine changes (namely, leptin and ghrelin), vascular changes and hypoperfused states in the brain, and changes in the gut microbiome that have all been discussed in detail earlier. It is most likely that neurocognitive improvements are multifactorial given that both BS inteven-tion and weight reduction affect changes in the following: inflammatory processes, metabolism, vasculature, and gut micribiota.

BS is considered a durable treatment for severe obesity[50] and includes a variety of different surgical procedures, such as the Roux-en-Y gastric bypass and the sleeve gastrectomy, to accomplish long-term weight reduction in severely obese patients. According to National Institutes of Health guidelines, patients are eligible for BS if they meet the following clinical criteria: body mass index of 40 kg/m^2 or higher (class III obesity); or a body mass index of 35 kg/m^2 or higher (class II obesity) with obesity-related comorbidities. BS is more effective than medical treatment and lifestyle interventions for moderate and severe obesity, both in short- and long-term follow-up studies.[51,52]

Potential mechanisms for BS-related weight loss have included hypotheses related to changes in leptin, ghrelin, and insulin sensitivity.[53,54] In general with weight loss, regardless of the method by which it is achieved, leptin levels seem to increase and there is some evidence that obese subjects may regain some leptin sensitivity, changing their neural response to food.[45,53]

BS and Gut Microbiome

Evidence shows that weight loss can reverse some of these changes in the gut microbiome, independently from BS.[55–57] Further, there is evidence for a decrease in firmicutes/bacteroidetes ratio and an increase in gene richness of gut microbiota after both surgical and nonsurgical weight loss.[58,59] The same decrease in firmicutes/bacteroidetes ratio has been observed after BS (namely, RYGB, up to 6 mo postoperatively).[56,58–61] Several mechanisms have been hypothesized to explain how BS could affect microbiota composition. One such mechanism suggests that changes in acid exposure in gastric remnant and small intestine after surgery seem to play a role, given also the attenuation of the observed changes in gut microbiota after BS in PPI users compared with nonusers.[56,62] Other mechanisms taken into account are dietary changes requested after surgery (namely restriction in the type and amount of food that can be ingested), the modest degree of nutrient malabsorption induced, the alterations of intestinal motility and the shortening of small intestine, leading both to an increased amount of oxygen (normally removed before beginning of the colon), and to relocation of some species (e.g., Enterobacteriaceae) to the large intestine.[56] The observed changes in microbiota composition could have several metabolic consequences, partly linked to weight maintenance, improvement of obesity comorbidities, and modulation of systemic inflammation.

Cognition and Gut Microbiota

Both animal models and studies on humans show an association between gut microbiome and neurocognition. In humans, alterations of gut microbiota are implicated in several diseases associated with cognitive impairment or increased vulnerability for dementia, among which chronic hepatic encephalopathy, even in the form of minimal hepatic encephalopathy, chronic inflammatory gastrointestinal diseases, multiple sclerosis, obesity, autism, and mood disorders (discussed earlier), although their causative role is not yet clear.[57,63–66] Moreover, alterations of the gut microbiome are also suspected to play a significant role in the pathogenesis of celiac disease, which shows some neurological manifestations, among which cognitive dysfunctions, often associated with a specific pattern of autoimmunity.[65]

In healthy subjects, treatment with probiotics and prebiotics reduces cognitive reactivity to sad mood, particularly in the areas of rumination and aggressive thoughts[67] and is associated with improvement in emotional processing, with reduced brain response to emotional faces attention task[55,68,69] and improved attention to positive stimuli compared with negative stimuli in emotional categorization and emotional recognition tasks.[55,70] These effects could be mediated not only by alterations in gut microbiota composition but also by changes in transcriptional state or metabolic activity.[71]

Moreover, our systematic review identified several similar reports as those recognized in a recently published review article by Spitznagel et al.[72] Spitznagel et al. identified similar methodologic limitations to the available literature as well as the many potential mechanisms to explain improvements in neurocognition following BS.[72] Another recent review article by Handley et al. investigated cognitive changes post-BS and proposed some physiologic mechanisms including physical activity, thiamine deficiency, psychiatric and medical comorbidities for theses changes.[73] However, a key addition of our review to the current litertature was our systematic approach, which resulted in the identification of additional literature and the inclusion of data on gut microbiome effects on neurocogntion following BS. In addition, fewer articles are included in this review, which is the result of searching fewer databases, and, therefore, important findings may have been missed.

One of the limitations of our review article is the lack of a standardized comprehensive neurocognitive assessment modality for patients undergoing BS that made it difficult to generalize these results to different neurocognitive domains. Thus, we could not determine if the reported neurocognitive gain in attention/executive function or memory could be directly comparable across the different studies. Secondly, as with any systematic review, we searched only published studies. Our results may reflect a publication bias, as negative studies for changes in neurocognition following BS are less likely to be published. Lastly, only 2 studies examined the impact of adipokines and their potential role in neurocognitive changes following BS. For the remaining studies, it was difficult to quantify the degree of neurognitive changes in each domain following surgery as different neurocognitive assessments were used in the studies. Therefore, additional research is needed to further elucidate the pathophysiological and neurochemical changes explaining the improved neurocognitve gains after surgery.

Recommendations for a comprehensive neurocognitive assessment precludes that each domain being assessed is done so under the same conditions effectively removing any variability and possible confounding factors. The comprehensive neurocognitive assessment should include the following domains: attention/executive functioning, working memory, and language as these domains have shown statistically significant changes in the studies included in this review. Many different neurocognitive measures employed across disparate studies made it very difficult to compare results in this review. More systematic review studies are needed to clarify the specific domains of neurocognition that are improved, where limited and standardized neurocognitive assessments of specific domains are systematically compared.

FUTURE CONSIDERATIONS

It is evident that there remains a gap in the current literature of clinical studies that examine the impact of gut microbiome in neurognition following bariatric surgery. Future research should consider the impact of microbiota and neurocognition after bariatric surgery based on clinical studies emerging in these two domains. Further research may elaborate on the neurocognitive results reflecting improvement in selective neural networks (e.g., memory improvement reflects better strategic learning and retrieval secondary to more efficient frontostriatal networks that would also account for improved measures on attention/executive function). The identification of set neural networks of the brain networks that show "improvement" would allow for more hypothesis driven neurocognitive testing and streamlined assessments presurgery and postsurgery.

CONCLUSIONS

This systemic review of the literature on neurocognition and BS offers new insights to physiologic and neurochemical mechanisms to further explore in clinical studies in understanding the relationship. Mental health care providers should consider the impact of these neurocognitive trends on presurgery

psychiatric assessments for BS and implications for psychosocial functioning postsurgery. It is evident that neurocognitive deficits exist across multiple domains and there are changes in measures after BS. The aforementioned effect bariatric surgical intervention has on neurocognition underscores the complex interrelationship between metabolism and brain function. Further research should further validate the use of neurocognitive screening tools presurgery and evaluate the impact of changes in neurocognition on neurocognitive, bariatric, and functional outcomes. Presently, American Society for Metabolic and Bariatric Surgery guidelines for evaluation of neurocognition in the presurgical evaluation of BS candidates suggests the following: In cases where the evaluator has significant concerns about comprehension and the potential impact on ability to give informed consent or on postsurgical self-care and/or adherence is not clear, cognitive testing may be indicated, and information should be gathered from collateral sources (parent, spouse, and other treaters) about the patient's ability to manage the demands of daily living and whether adequate supports are in place to assist the patient in doing so. The evaluator should recommend collaboration between the bariatric team and a member of the patient's social or family network to help the patient comprehend, remember, and follow the postoperative regimen."[74] The lack of a standardized neurocognitive assessment tool across clinical studies and the absence of clinical research specifically examining the role of gut micribota play in weight loss surgery relating to cognition precludes us from making more conclusive recommendations. It is recommended that a comprehensive neurocognitive assessment should be included as a part of the BS assessment process and measured at various time points postsurgical intervention. This would effectively allow for necessary data to further investigate clinical time course of neurocognitive changes present post-BS to be compared with other weight loss interventions. Until more robust evidence is made available for further exploring the relationships in the domains of neurocognition and BS, our review provides an updated summary of emerging neurochemical and physiologic mechanisms in understanding the relationship of these domains.

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