

## Surgical Weight Loss and Cognition in Obesity

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The prevalence of obesity is increasing worldwide, and the burden for the patients, and for the health system is acknowledged. The influence of obesity on aging and its impact on cognition is much less known. However, obesity is linearly associated with cognitive impairments (1), including executive functions, memory, inhibition and language (2) and is also associated with neurodegenerative diseases by exacerbating brain injury and brain aging.

The complex and multifactorial etiology of obesity creates challenges for its effective long-term management. In the context of the failure to prevent obesity, and/or induce long-term weight-loss, obesity surgery [mainly sleeve gastrectomy and gastric bypass] and the new pharmacological treatments of obesity generate the hope that comorbidities, personal and the health systems burden could be reduced, and that quality of life may improve and contribute to successful aging.

Some but not all longitudinal studies suggest that weight loss diet may have a beneficial effect on brain aging and cognition (3). It appears that adding aerobic exercise and resistant exercise prevent weight loss associated muscle dysfunction but may also impact on cognitive outcomes in older adults living with obesity (4).

Long term interventions such as The Lookahead trial [randomizing 5145 people with a BMI over 25 to intensive intervention lifestyle vs. placebo] demonstrated positive effects and studied cognition as the cohort aged (5). Several composite indices (multimorbidity, geriatric syndromes, disability-free life years) were positively impacted. Cognition improvement was limited to some groups, suggesting that not all interventions may be efficient on cognition (4).

Systematic review and meta-analysis of studies about the impact of obesity surgery and cognition (mainly with gastric bypass) showed an improvement in memory, but little effects on attention, cognitive speed, or executive functions (6). Another review showed an improvement in cognition as measured by different assessment tools (7).

The study by Reynolds et al. (8) involved 113 participants who completed baseline assessments and 87 completed two-year follow-up assessments after bariatric surgery mainly sleeve gastrectomy (88.5% of participants). Cognition was assessed using the NIH toolbox cognitive battery (NIHTB-CB) and the Rey Auditory Verbal Learning Test (AVLT). The primary outcome, NIHTB-CB composite score, was stable following bariatric surgery (-0.4 (13.9),  $p=0.81$ ,  $n=66$ ). Among secondary outcomes, the NIHTB-CB dimensional card sorting test (executive function assessment), improved (+6.5 (19.9),  $p=0.01$ ,  $n=66$ ) while the Rey AVLT delayed recall test

(memory assessment) declined (-0.24 (0.83),  $p=0.01$ ,  $n=87$ ) following surgery. Improvements to metabolic risk factors and diabetes complications were not associated with improvements to NIHTB-CB composite score. The other 4 NIHTB-CB subtests and Rey AVLT assessments of auditory learning and recognition were stable at follow-up.

This suggests that bariatric surgery (here mainly sleeve gastrectomy) may mitigate the natural history of cognitive decline in individuals with obesity, but confirmatory randomized controlled trials are needed. The decline in delayed recall also warrants further studies to determine potential differential effects on cognitive subtests.

What makes the difference between this study mainly with sleeve gastrectomy, and the previous reviews? It may be that parameters other than weight change may be involved in cognitive impairment, and may be affected by surgery. These are gut microbiome, which we know is influenced by surgery (9-11), inflammation of brain blood barrier, oxidative stress, sirtuin activity, neurotrophic factors, and neurogenesis (1). The gut microbiome likely contributes to the metabolic, inflammatory, and satiety benefits and sustained weight-loss effects following bariatric procedures such as sleeve gastrectomy but very few studies are presently available (10). Koulas SG et al (11) reviewed recent experimental evidence outlining the alterations of gut microbiota composition and function in recovery from bariatric surgical operations with an emphasis on sleeve gastrectomy and gastric bypass.

Considering the strategic aspect of healthy aging, the increase in the prevalence of obesity, more studies will be helpful to understand the mechanism involved in cognitive impairment, and those that are affected by bariatric surgery [and by the new treatments] hoping that innovation will provide means to prevent cognitive impairment.

*Conflicts of interest:* The author declares that there is no conflict of interest.

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