RETRACTED: THE EFFECTS OF OVERWEIGHT AND OBESITY ON COGNITIVE FUNCTIONS AND PSYCHOLOGICAL WELL-BEING

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ABSTRACT

Recent findings showed that obesity represent a risk factor to developingbrain illness such as cognitive impairments and psychopathological disorders. Weight increase additively afflicts brain structure of cognitively impaired patients but is linked with poor brain volumes even in healthysubjects. Further, several studies show that subjects with psychiatric disorders are more likely than general population to be obese. Hovewer, the process by which weight gain injures cognitive abilities and psychological well-being remain unclear.In this review we analyze the relationships between obesity andbrain illness and underline the role played by covariates to determine this link.

Keywords*: Obesity, cognitive decline, mood disorders.*

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Introduction

In the past decades, worldwide obesity gradually increased and World Health Organization (WHO) formally recognized this condition as a global epidemic[1,2].

Recent readings estimate worldwide incidence of overweight and obese adults at 27,5% and increased from 857 million in 1980 to 2,1 billion in 2013 for both developing and developed countries. In the same timeframe, overweight peoples increase from 28,8% to 36,9% for men and from 29,8% to 38% for women. However, different sex and age patterns between countries are observed.

The prevalence is also rising in children and adolescents increasing from 8.1% in 1980 to 12.9% in 2013 for boys and 8.4% to 13.4% in girls[3].

Obesity negatively affects most bodily systems and boosts risk of many chronic diseases[4-9].

Recent findings showed that obesity also affect brain function and higher Body Mass Index

(BMI) increase the risk of developing cognitive impairments such as dementia and psychiatric disorders[10-13].

Currently, are still unknown how weight increase and brain functioning could be linked, and the process by which obesity injures cognitive abilities and psychological well-beingremain unclear.

To establish the independent role of body fat on central nervous system and brain functioning, is required to clarify the role played by several factors and understand their interaction is essential.

This review focuses on relationship between obesity and brain functions.

Obesity and brain physiology

Recent findings showed that obesity additively afflicts brain structure of cognitively impaired patients and is linked with poor brain volumes even in healthysubjects[14].

Structural integrity is reflected by brain substructures volumes and represents a major hallmark of underlying neuronal health. Tissue loss occurs with normal aging but it's more marked in dementia cases[15-16].

Exploratory studies performed with whole brain analysis estimate brain tissue reduction from 0.5% to 1.5% for each BMI unit increase[17]. In a structural brain mapping cohort's studies from 700 cognitively impaired patients, higher BMI was related to decreased brain volume in frontal, temporal, parietal, and occipital lobes regions. In a longitudinal study group, temporal lobe atrophy was estimated from 13 to 16% for each BMI unit increase[18].

Brain scanning techniques showed that obese individuals had significantly lower gray matter density in post-central gyrus, frontal lobe, putamen, and middle frontal gyrus[19] and greater body adiposity in otherwise healthy subjects was related with lower brain volumes in hippocampus area, orbital frontal cortex and parietal lobes[14].

Cross-sectional studies showed that elevated waist hip ratio and greater BMI, were linked with reduced hippocampal volume and tissue loss of temporal lobe[20-22].

A further analysis in over 1400 healthy Japanese, showed negative correlation between brain volume and weight gain, highlighting lower brain gray matter ratio of temporal, occipital and frontal lobes and the anterior lobe of cerebellum[23].

Several studies have found that obesity, especially in mid-life, is related with an increased risk of cognitive decline in elderly and consistent neuropathological studies showed either hippocampal brain atrophy and executive disfunction in mid-life obesity[24]. It's well recognized that hippocampal formation played a key role for learning and memory[25,26], it is particularly frailty to aging[27-29] and that poor volume in this regions predict cognitive impairment and dementia in general people[30-35].

However, the exact underlying mechanisms by which overweight and obesity increase risk of cognitive decline remain to be fully understood, but some explanations are available.

High levels of adipose tissue may modify beta-amyloid metabolism and it is suggestive of increased risk of weight gain for dementia[36]. A neuropathologicalfeatures of Alzheimer's disease (AD), such as amyloid plaques and neurofibrillary tangles[37], are even more stated in elderly obese people when compared to normal weight subjects. In a cohort study, greater levels of beta - amyloid, the main component of amyloid plaques, protein precursor and expression of tau, were present in hippocampal of morbidly obese patients without cognitive damage when compared to non-obese controls[38-40].

In a prospective study from 939 individuals aged 65 and over, greater caloric intake was related to higher AD risk in over subsequent 6.3 years follow-up[41].

Further, high fat diet (fatty acids and sugars) may also interact with brain physiology, harming the integrity of Blood Brain Barrier (BBB) which play a key role to protecting Central Nervous System (CNS) from blood-borne toxins. Alzheimer's disease and vascular dementia are linked with blood brain barrier (BBB) dysfunction and longitudinal study showed that mid-life obesity was related with lower BBB integrity[43-45].

Finally, higher levels of white adipose tissuecould increase systemic inflammation. Adipocytes, lymphocytes and macrophages leading to production of pro inflammatory cytokines and subsequent increase of tumor necrosis factor (TNF-α). Central inflammation is observed after high fat feeding, especially in the hypothalamus regions and was linked to vascular disease, poorer cognitive performance and dementia. It was demonstratedthat outcomes of metabolic syndrome on cognitive performance were mediated by inflammation, and that combined effects of high inflammation and metabolic syndrome had a greater risk of cognitive decline. However, the direction of the associations between inflammation and dementia is unclear[45-54].

Obesity and Psychopatology

Several studies show that subjects with severe psychiatric disorders are more likely than general

population to be obese[55]. However, the link between weight gain and psychiatric illness is widely discussed.

There are several studies that account the risk of psychiatric disorders in obese individuals such as mood disorders, anxiety disorders, low self-esteem, body dissatisfaction, eating disorders and emotional problems. Hovewer an extensive body of literature show that mood disorders are most frequently related to obesity and the incident risk of lifetime depression is significantly higher in obese persons when compared to non-obese peers,with a range from 29% to 56%[56,60].

In a study performed with more than 40,000 people,the relationship between obesity and depression varied by sex and obese men, when compared with normal-weight people, report less symptom of major depression and suicidal ideation. A different pattern was seen for women that was 37% more likely to report depressive symptom when compared with normal weight peers[61].

However, regard to direction of relationships between obesity and psychopathology, the studies failed to find clinically significant results. Studies that investigate whether obesity precedes depression or whether an existing mood disturbance predispose to weight increase, showed conflicting results.

In a nationally representative adolescents sample, obesity condition did not increase depression incidence one year later. However, depression at baseline, doubled the risk of developing obesity at follow up[62].

Apparently, results from longitudinal studies suggest that depression precedes obesity in adolescents' girls, but not boys, and that obesity precedes depression in older adults. In a sample of 1037 New Zealanders, boys who were depressed at age 18 or 21 were less likely to be obese at age 26. Girls with late-adolescent depression, however, were twice as likely to be obese at age 26[63].

However, other studies showed that obesity is not strongly associated with depression or any abnormal personality characteristics and psychological traits are more widely varied within the population of obese individuals than between obese and non-obese[64-66].

The reason for controversial results seems to be a lack of consensus as to how to measure psychological functioning and a growing body of studies reminder the importance of considering the role played by co-morbidity of morbid obesity.

Actually further research on this issue are needed.

Conclusion

It is unclear whether obesity predisposes to cognitive impairments or psychopathological disorderindependent of other risk factors, given that some experimental studies are limited by study design, variable follow-up and limited adjustment-for considerable comorbidities.

The experimental investigations that explore the link between obesity and brain illness shall include all covariates that may have great bearing on this relation, such as sex, lifestyle factors (diet, physical activity, level of education, smoking, alcohol consumption), vascular diseases, genetics and inflammatiory processes. Moreover, obesity increaserisk of hypertension, diabetes, stroke and leptin dysregulation which directly affectsbrain functions[67-68].

Body fat contains leptin and estrogen, which are proposed to play a neuroprotective role for cognitive performance, enhancing hippocampal plasticity and inhibiting cell death0[69,70]. However, it is also been show that leptin dysregulation negatively impact on cognitive function[71-72].

The effects of metabolic syndrome have also been identified as a risk factor for neurocognitive disorders and recent findings from obese adolescents, showed significantly smaller hippocampal volumes wich interacts with cognitive performance, such as attention and mental flexibility[73].

Recent finding report also an important role of both hypothalamic - pituitary - adrenal axis (HPA-) dysfunction and systemic low-grade inflammation to explain the relationship between psychiatric diseases and obesity.

Finally, alternative anthropometric tools to assess obesity could be more effective. Body Mass Index (BMI) was first described in 1832 by Adolphe Quetelet but involve some limitations[80]. Ethnicity and age, for example, affect this index because fat-free mass ratio decreases with age, especially among women[74,75]. Aging process implied that lean body mass decrease, while adipose tissue increase without weight gain.

Therefore, this ratio may not be captured by BMI and not represent, in the elderly, a reliable index of adiposity. In other words, BMI may underestimate adiposity because in aging lean body mass is replaced by fat. Thus, this index is a better

measure of adiposity only for younger peoples while, during old age, it is possible to report low BMI despite relatively high body fat. Sagittal abdominal diameter, waist circumference and waist-hip ratio have been proposed as a better adiposity marker[76-100].

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