# NEUROPSYCHOLOGICAL ASSESSMENT IN SEVERE OBESITY: COMPARISON BETWEEN OBESITY CLASS

# Evaluación Neuropsicológica en la obesidad grave: Comparación Entre clases de obesidad

# Avaliação Neuropsicológica na Obesidade Grave: Comparação entre classes de obesidade

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*Palabras clave:* atención; funciones cognitivas; memoria; clase de obesidad obesidad severa, estudio tramversal.

Palavras-chave: atenção; funções cognitivas; memória; classe de obesidade; obesidade severa

#### ABSTRACT

Neuropsychology has been studying the effects of obesity on cognition and its relationship with dementia and factors that may be related to the difficulty of losing weight. Objective: Neuropsychological assessment of cognitive functions in patients with severe obesity. Method: 99 patients were selected from the outpatient clinic of the Bariatric and Metabolic Surgery Unit of the Hospital das Clínicas, Faculdade de Medicina da USP, between 2018 and 2020. The patients were divided according to the class of obesity in G1 (40.0 < BMI < 49.9 Kg/m2; n=56) and G2 (BMI  $\geq$  50 Kg/m2; N=43). Results: Patients showed mild cognitive deficits in executive functions, short- and long-term verbal memory, and retrieval of recall memory. There was no significant difference in cognitive functions related to obesity class (G1 vs. G2). Conclusions: Severely obese patients showed mild cognitive impairment compared to the general population in short- and long-term verbal memory and executive functions unrelated to obesity class.

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#### RESUMEN

La neuropsicología viene estudiando los efectos de la obesidad sobre la cognición y su relación con la demencia y los factores que pueden estar relacionados con la dificultad para perder peso. Objetivo: Evaluación neuropsicológica de las funciones cognitivas en pacientes con obesidad severa. Método: 99 pacientes fueron seleccionados del ambulatorio de la Unidad de Cirugía Bariátrica y Metabólica del Hospital das Clínicas, Faculdade de Medicina da USP, entre 2018 y 2020. Los pacientes fueron divididos según la clase de obesidad en G1 (40,0 < IMC < 49,9 Kg/m2; n=56) y G2 (IMC  $\ge$  50 Kg/m2; N=43). Resultados: Los pacientes mostraron déficits cognitivos leves en las funciones ejecutivas, la memoria verbal a corto y largo plazo y la recuperación de la memoria. No hubo diferencia significativa en las funciones cognitivas relacionadas con la clase de obesidad (G1 vs. G2). Conclusiones: Los pacientes con obesidad severa mostraron deterioro cognitivo leve en comparación con la población general en memoria verbal a corto y largo plazo y funciones ejecutivas no relacionadas con la clase de obesidad.

#### RESUMO

A neuropsicologia vem estudando os efeitos da obesidade sobre a cognição e sua relação com a demência, além dos fatores que podem estar associados à dificuldade de perda de peso. Objetivo: Avaliação neuropsicológica das funções cognitivas em pacientes com obesidade severa. Método: 99 pacientes foram selecionados no ambulatório da Unidade de Cirurgia Bariátrica e Metabólica do Hospital das Clínicas da Faculdade de Medicina da USP, entre 2018 e 2020. Os pacientes foram divididos de acordo com a classe de obesidade em G1 (40,0 < IMC < 49,9 Kg/m<sup>2</sup>; n=56) e G2 (IMC  $\geq$  50 Kg/m<sup>2</sup>; n=43). Resultados: Os pacientes apresentaram déficits cognitivos leves nas funções executivas, memória verbal de curto e longo prazo e recuperação de memória. Não houve diferença significativa nas funções cognitivas em relação à classe de obesidade (G1 vs. G2). Conclusões: Pacientes com obesidade severa demonstraram leve comprometimento cognitivo em comparação com a população geral, em memória verbal de curto e longo prazo e funções executivas, não relacionadas à classe de obesidade.

Obesity is defined as an excessive accumulation of body fat, and is considered to be a chronic, multifactorial disease<sup>1,2,3</sup>. Several factors contribute to increased body weight, such as environmental, genetic, behavioral, social, and economic factors, causing physical and psychological problems and changes in cognitive functions<sup>4</sup>.

The classification of obesity is performed by calculating the body mass index (BMI), an internationally accepted standard for assessing the nutritional status of patients. In recent years the prevalence of obesity has increased progressively in Brazil and worldwide, and approximately one third of the world population can be considered obese today<sup>5</sup>. Obesity affects all social classes, age groups, genders, ethnicities, regardless of geographic location, being more prevalent among women and the elderly <sup>1,6</sup>.

Other conditions related to obesity are cognitive problems, especially in executive functions, where patients, due to lack of inhibitory control and compulsive behavior, may have difficulty losing/maintaining the weight<sup>7</sup>.

Bariatric surgery promotes short-term results, as improvement of clinical conditions and comorbidities, and long-term benefits, with improvement in quality of life, physical, psychological and cognitive aspects, preventing the onset of neurodegenerative diseases such as dementia<sup>6</sup>. It is important for the patient to follow the postoperative recommendations, through medical, nutritional and psychological follow-ups, to obtain success in the treatment<sup>8</sup>.

Bariatric surgery can improve cognitive function rapidly<sup>9</sup>, reducing the risk of obesity-associated dementia, possibly by reducing inflammation and/or expression of Alzheimer's disease-related proteins<sup>10,11</sup>.

There is evidence that cognitive function plays an important role in adherence to postoperative recommendations, leading to sustained long-term weight loss results after bariatric surgery. Possibly, such results are associated with improvement in some functions such as memory, attention, inhibitory control, goal setting, and planning<sup>12,13</sup>.

Neuropsychology is an area of psychology and neuroscience that studies the brain organization of individuals, establishing differences between healthy and pathological cognitive functioning<sup>14</sup>. The main objective of the Neuropsychological evaluation is to identify possible alterations in cognitive functions<sup>15,16</sup>.

The cognitive functions act together to properly complete their functions, the executive functions use the working memory responsible for the momentary storage of information, which will be used in other cognitive processes. Attention, in turn, involves the attentional processes related to engagement, alternation and sustaining, inhibition of influences and manipulation of information<sup>17,18</sup>.

The association between obesity and cognitive dysfunction is receiving increasing attention<sup>19</sup>. Patients with severe obesity often have cognitive dysfunction and are a risk for the development of neurodegenerative diseases<sup>9,20</sup>.

Obesity in adults may be a predictor for the development of Alzheimer's disease and vascular dementia at older age<sup>20,21</sup>. Thus, it is suggestive that obesity may determine changes in cognitive functions before age-related decline occurs in the elderly<sup>22</sup>. The changes observed in obese adults are related to executive functions, memory and attention, causing an impact on social and professional relationships of the individual<sup>23,24,25</sup>.

Recognition of the preclinical phase of dementia is of paramount importance, to identify future risk in asymptomatic individuals<sup>26</sup>. The impairment in cognitive functions in individuals with severe obesity<sup>27,28</sup> may determine binge eating, difficulty in decision making, related to the choice of the most appropriate diet<sup>29,30</sup> and changes in cognitive flexibility with decreased inhibitory control, causing lack of adherence to treatments and recommendations for weight loss<sup>31,32 33</sup>. The most prevalent deficits reported in obese individuals were in the domains of attention, memory, and executive function,

regardless of gender and age<sup>10</sup>.

The performance of immediate memory in obese individuals seems to be influenced by the level of education, where individuals with low education present a worse performance in relation to individuals with high education. Therefore, schooling may have a protective function on immediate memory in obese individuals<sup>34</sup>.

Finally, although there are several studies related to obesity and cognitive changes, there are no studies evaluating neuropsychological changes according to obesity class.

### **METHODS**

This was a cross-sectional study conducted at the Outpatient Clinic of the Bariatric and Metabolic Surgery Unit of the Hospital das Clínicas, School of Medicine, USP, between 2018 and 2020. Individuals with BMI above 40 kg/mg, age between 18 and 60 years, with minimum education of 4 years with acceptance and signature on the Informed Consent Form were included.

The following were excluded from the study: individuals with concomitant diagnoses of active neurological diseases, previously documented conditions (traumatic, metabolic, vascular, or degenerative) that make it difficult to assess neurological symptoms and signs (e.g. senile or vascular dementia, central nervous system infections, etc.), current use of psychoactive substances for pathologies such as schizophrenia, inability to understand the content required for neurological assessment and application of the tests included in this study.

This study was approved by the Ethics Committee for Analysis of Research Projects - CAPPESQ (number: 81329817.5.0000.0068). This study was conducted in accordance with the HELSINK declaration of 1964 and its subsequent amendments, respecting the ethical norms and principles that govern research with human beings.

The general objective was to evaluate the cognitive functions, through neuropsychological evaluation, of patients with severe obesity compared to the general population and the specific objective was to evaluate the cognitive functions according to obesity class: G1 (BMI: 40.0 - 49.9) vs. G2 (BMI  $\ge 50$ ).

The tests applied were: Phonological Verbal Fluency - FAS, Semantic or Categorical Verbal Fluency with animals, Hopkings Verbal Learning Test - HVLT, Rey's Complex Figure and the Weschsler Intelligence Scale for Adults - WAIS III tests: Matrix Reasoning, Vocabulary, Codes and Digits direct order and reverse order and Beck's Depression Inventory (BDI). The raw scores obtained in the above tests were converted into Z-scores according to the normative tables for each test. Table 1 describes the Z score classification in relation to the general population.

#### Table 1 - Z Score classification in relation to the general population

| Maximum | Minimum | Classification |
|---------|---------|----------------|
| Above 3 | 3       | Much Higher    |
| 2.5     | 1.4     | Higher         |
| 1.3     | 0.7     | Upper Average  |
| 0.6     | -0.6    | Average        |
| -0.7    | -1.3    | Lower Average  |
| -1.4    | -1.9    | Borderline     |
| -2      | -3      | Deficit        |

Source: WAIS III<sup>35</sup>.

#### STATISTICAL ANALYSIS

Continuous variables were expressed as mean and standard deviation, while categorical variables were expressed in terms of frequencies and percentages. For comparison of two groups on continuous variables, the nonparametric Mann-Whitney test and Fisher's Exact test were used. The significance level adopted was 0.05. Two-tailed hypotheses were considered. R software (version 4.0.2) was used to perform all analyses.

0.417

3 (7.32%)

3 (7.32%)

## RESULTS

Our sample consisted of 99 research participants: 56 in G1 and 43 in G2. The age of the total group (TG) was 43 ± 9 years, in G1 44 ± 8 years and in G2 43 ± 10 years. There was no significant difference between groups (p=0.944). The TG had a BMI of 48 ± 7 Kg/m<sup>2</sup>, G1 43 ± 2 Kg/m<sup>2</sup>, and G2 54 ± 6 Kg/m<sup>2</sup>. 75% (n=74) of the TG, 73% (n=41) of the G1 and 77% (n=33) of the G2 were female. There was no significant difference between groups (p=0.816).

The results of the BDI are shown in Table 2. There was no significant difference regarding the degree of depressive symptoms between groups (p=0.417).

5 (9.43%)

2 (3.77%)

| Degree  | GT          | G1         | G2        |
|---------|-------------|------------|-----------|
| Minimum | 62 (65.96%) | 38 (71.7%) | 24(58.5%) |
| Light   | 19 (20.21%) | 8 (15.09%) | 11(26.8%) |

#### Table 2 - Beck's Depression Inventory – BDI

Fisher's exact test.

Moderate

Serious

GT: total group; G1:40.0 < BMI < 49.9 Kg/m<sup>2</sup>; G2: BM ≥ 50 Kg/m<sup>2</sup>; P = P value.

8 (8.51%)

5 (5.32%)

The results of all tests applied are summarized on Table 3. The groups had preserved functioning without significative difference according to obesity class in visuoconstructive and visuospatial skills (Rey's complex Figure test - copy; p=0.166), short-term memory for visual content (Rey's Complex Figure test - evocation after 03 minutes; p=0.458), long-term memory for visual content (Rey's complex figure test - evocation after 03 minutes; p=0.458), long-term memory for visual content (Rey's complex figure test - evocation after 20 minutes; p=0.599), concentrated attention (Trail Making Test - A; p = 0.74), alternate attention (Trail Making - B test; p= 0.294), semantic memory, ability to retrieve information stored in memory and the processing of executive functions (FAS- Verbal Phonological Fluency test; p= 0.81), selective attention and executive functions (Stroop test; p = 0.913), recognition memory (Hopkins Verbal Learning Test- HVLT - recognition; p=0.75), language (Vocabulary test- Wais III; p=0.37), attention and processing speed (Coding test-Wais III ; p=0.465), short-term and working memories (Digits-Wais III test; p=0.51). Reasoning (Matrix Reasoning test- Wais III; p=0.854).

The executive functions (EF) and categorical and semantic memory were evaluated by the Animal fluency test. There was no difference between groups (p=0.359). The groups showed a mild cognitive deficit in categorical EF (inferior mean) in relation to the general population.

The verbal short-term memory (VSTM) was evaluated through the Hopkings Verbal Learning Test- HVLT (immediate). There was no difference between groups (p = 0.245). The groups showed a mild cognitive deficit in VSTM (lower mean) in relation to the general population.

The verbal long-term memory (VLTM) was evaluated through the Hopkings Verbal Learning Test- HVLT (late). There was no difference between groups (p=0.156). The groups showed a mild cognitive deficit in VLTM (lower mean) in relation to the general population.

#### Table 3

| Group   | Z score                      | Р     | Classification     |
|---|------------------------------|-------|--------------------|
| Rey's Complex Figure- (Copy)                      |                              | 0.166 |                    |
| GT  | 0.5 (±) 1.2                  |       | Average            |
| G1  | 0.4 (±) 1.2                  |       | Average            |
| G2  | 0.6 (±) 1.3                  |       | Average            |
| Rey's Complex Figure (Evocation after 3 minutes)  |                              | 0.458 |                    |
| GT  | 0.0 (±) 1.5                  |       | Average            |
| G1  | 0,1 (±) 1.3                  |       | Average            |
| G2  | 0.1 (±) 1.6                  |       | Average            |
| Rey's Complex Figure (Evocation after 20 Minutes) | ( )                          | 0.599 | 0                  |
| GT  | 0.0 (±) 1.4                  |       | Average            |
| G1  | 0.1 (±) 1.2                  |       | Average            |
| G2  | 0.1 (±) 1.7                  |       | Average            |
| Trail Making Test - A                             | 0.2 (2) 2.7                  | 0.74  |                    |
| GT  | -0.4 (±) 1.1                 | 0.7 1 | Average            |
| G1  | -0.4 (±) 1.2                 |       | Average            |
| G2  | -0.4 (±) 1.1                 |       | Average            |
| Trail Making Test - B                             | -0.4 (±) 1.1                 | 0.294 | Average            |
| GT  | -0.4 (±) 1.2                 | 0.294 | Average            |
| G1  | -0.4 (±) 1.2<br>-0.3 (±) 1.1 |       | Average<br>Average |
| G2  | -0.5 (±) 1.1                 |       | -                  |
|   | -0.0 (±) 1,5                 | 0.81  | Average            |
| Verbal Phonological Fluency: F.A.S.               | 07/1)00                      | 0.81  |                    |
| GT  | -0.7 (±) 0.9                 |       | Lower Average      |
| G1  | -0.7 (±) 0.9                 |       | Lower Average      |
| G2  | -0.7 (±) 0.9                 | 0.250 | Lower Average      |
| Animal Testing                                    | 0.0(1)0.0                    | 0.359 |                    |
| GT  | -0,8 (±) 0,9                 |       | Lower Average      |
| G1  | -0,9 (±) 0,8                 |       | Lower Average      |
| G2  | -0,7 (±) 0,9                 | 0.040 | Lower Average      |
| Stroop test                                       |                              | 0.913 |                    |
| GT  | 0.3 (±) 1.4                  |       | Average            |
| G1  | 0.2 (±) 1.3                  |       | Average            |
| G2  | 0.4 (±) 1.5                  |       | Average            |
| HVLT- Immediate                                   |                              | 0.245 |                    |
| GT  | -0.9 (±) 0.9                 |       | Lower Average      |
| G1  | -0.8 (±) 1.0                 |       | Lower Average      |
| G2  | -1.0 (±) 0.7                 |       | Lower Average      |
| HVLT - Late                                       |                              | 0.156 |                    |
| GT  | -1.1 (±) 1.2                 |       | Lower Average      |
| G1  | -1.0 (±) 1.1                 |       | Lower Average      |
| G2  | -1.3 (±) 1.3                 |       | Lower Average      |
| HVLT- Recognition                                 |                              | 0.75  |                    |
| GT  | -0.7 (±) 1.6                 |       | Lower Average      |
| G1  | -0.9 (±) 1.3                 |       | Lower Average      |
| G2  | -0.6 (±) 1.9                 |       | Lower Average      |
| Vocabulary - WAIS III                             |                              | 0.37  |                    |
|   |                              |       |                    |

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| GT                          | 0.0 (±) 0.9  | Average |
|-----------------------------|--------------|---------|
| G1                          | -0.1 (±) 0.8 | Average |
| G2                          | 0.1 (±) 1.0  | Average |
| Codes - WAIS III            | 0.465        | 5       |
| GT                          | 0.1 (±) 0.8  | Average |
| G1                          | 0.2 (±) 0.8  | Average |
| G2                          | 0.1 (±) 0.9  | Average |
| Matrix Reasoning - WAIS III | 0.854        | ļ       |
| GT                          | -0.5 (±) 1.0 | Average |
| G1                          | -0.5 (±) 1.0 | Average |
| G2                          | -0.5 (±) 1.0 | Average |
| Digits - WAIS III           | 0.51         |         |
| GT                          | -0.3 (±) 1.0 | Average |
| G1                          | -0.3 (±) 1.0 | Average |
| G2                          | -0.3 (±) 1.0 | Average |

Mann-Whitney test.

GT: total group; G1:40.0 < BMI < 49.9 Kg/m<sup>2</sup>; G2: BM  $\ge$  50 Kg/m<sup>2</sup>; P = P value.

The IQ stratification in comparison with the general population is shown in Table 4. There was no significant difference between the TG, G1 and G2 groups (*p*=0.949).

#### Table 4 - IQ classification

| Classification | GT          | G1          | G2          | Р     |
|----------------|-------------|-------------|-------------|-------|
| Deficit        | 3 (3.03%)   | 2 (3.57%)   | 1 (2.33%)   |       |
| Borderline     | 19 (19.19%) | 11 (19.64%) | 8 (18.6%)   |       |
| Lower Average  | 33 (33.33%) | 17 (30.36%) | 16 (37.21%) | 0.949 |
| Average        | 40 (40.4%)  | 24 (42.86%) | 16 (37.21%) |       |
| Upper Average  | 4 (4.04%)   | 2 (3.57%)   | 2 (4.65%)   |       |

Fisher's exact test.

GT: total group; G1:40.0 < BMI < 49.9 Kg/m<sup>2</sup>; G2: BM ≥ 50 Kg/m<sup>2</sup>; P = P value.

#### DISCUSSION

The cognitive changes observed in patients with severe obesity have not yet been fully elucidated<sup>31</sup>. Cognitive impairments are also observed in other chronic diseases and may result from the interaction of several factors and not only from a single specific cause<sup>07,27</sup>. Patients with obesity may present abnormalities in executive functions, attention, and memory that could determine a lack of inhibitory control and compulsive behavior. These changes may also be associated with difficulty in losing and maintaining weight <sup>7,36</sup>.

Some studies suggest that individuals with obesity have a higher risk for neurodegenerative diseases, such as Alzheimer's and vascular dementia <sup>9,20,37</sup>. Therefore, studies that can elucidate, prevent, and avoid weight gain are important.

The patients in our sample presented varied socio-demographic characteristics, with results similar to the general population, and were evaluated according to age, gender, and education.

The depressive mood state can interfere negatively in cognitive functions, such as memory and attention <sup>38</sup> and for this reason, we evaluated the depressive mood state, through the Beck Depression Inventory (BDI) without significant difference between groups. Thus, the depressed mood state did not interfere with the results.

Several studies confirm the presence of cognitive changes in individuals with obesity, although their origin and significance have not been fully clarified <sup>27, 28,31,32, 33.</sup>

Our study evaluated cognitive differences in patients with obesity according to their severity. Psychometric tests restricted to psychologists similar to those applied in the literature to assess cognitive functions were used.

The participants' Intelligence Quotient presented an average classification in relation to the general population with no difference according to obesity class. Thus, the patients had a preserved intellectual level without interference in results.

We observed mild cognitive deficits in verbal short and long-term memory, i.e., a reduction in the ability to retrieve and store learned information. This change may be related to the difficulty that patients with obesity have in planning healthy meals in advance, avoiding high-calorie foods, and difficulty in following an appropriate diet, causing low adherence to weight loss treatment. Patients tend not to follow medical and nutritional recommendations, as reported in some studies <sup>25, 26, 27,39</sup>. No difference was observed according to obesity class.

We also found alterations in semantic memory related to the ability to retrieve facts, knowledge of words and their expression<sup>40</sup>, hindering the patients' communication and making their understanding more difficult, similar to what was observed in other studies<sup>12,13,31</sup>. There were no differences according to obesity class.

Some studies reported alterations in the attention of patients<sup>7,10</sup>, influencing memory, executive functions, and planning. However, we did not observe alterations in concentrated, alternating, and divided attention in our sample.

we observed mild cognitive deficit <sup>29, 31, 32</sup> in executive functions, possibly related to the compulsion observed in some patients, due to the difficulty to inhibit inappropriate behaviors in relation to food, facilitating the ingestion of caloric foods that are not part of the prescribed diet. There may also be difficulty in the ability to weight loss, low commitment to achieve determined goals and to follow the recommendations to perform physical activities and lifestyle changes, which are important for both weight loss and weight maintenance<sup>12,13</sup>. We observed no statistically significant correlation between obesity severity and greater cognitive impairment. Therefore, we can conclude that the cognitive functions of attention, executive functions, memory, language, visuospatial, and visuoconstructive are not associated with obesity class.

The study has some limitations: The cross-sectional design limits conclusions about cause and effect. 73% of the subjects were female, thus the predominantly female sample may not be generalizable to the entire population. The third would be limited sample size with possible selection bias. The forth possible limitation would be that the evaluations were made close to the bariatric surgery, where the emotional factor may have influenced the performance of the patients in the execution of the tests that were applied.

It is important to emphasize that the experimental design of this cross-sectional study allowed us to examine a theme that had been little investigated, clarifying cognitive aspects that permeate the life of patients with severe obesity and we believe there are other aspects that influence or affect the cognition. This study, however, contributes to future research to better clarify other aspects that have not been studied.

In this sense, we suggest longitudinal studies that can assess changes in cognitive function over time, considering the progression of obesity, interventions such as bariatric surgery, or lifestyle changes and their effects on cognition. Inclusion of a larger, more diverse control group that better represents the general population, considering factors such as age, gender, education, and socioeconomic status, and the incorporation of the assessment of inflammatory, metabolic, and neurochemical biomarkers to explore possible mechanisms underlying the observed cognitive deficits.

Perform subgroup analyses to explore whether the relationship between obesity and cognitive function varies depending on specific factors, such as the presence of comorbidities or a family history of neurodegenerative diseases.

Employ more specific measures of executive function, such as inhibition, planning, and decision-making tasks, to better understand the deficits observed in this area, and finally include a more detailed assessment of emotional state, including anxiety, stress, and body image satisfaction levels, to explore its possible influence on cognition.

### CONCLUSION

Patients with severe obesity showed mild cognitive deficits in verbal short and long term memory, semantic memory, and the ability to retrieve information from memory and executive functions, especially those related to the ability to organize thought and strategies There was no significant difference in cognitive functions according to obesity class.

#### **CONFLICT OF INTERESTS**

The authors declare the absence of conflict of interests.

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