Evaluation of Cognitive Improvement After Bariatric Surgery Using a Virtual Reality Program and the Neuropsi Neuropsychological Battery

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Title: "EFFECT OF BARIATRIC SURGERY ON COGNITIVE PERFORMANCE EVALUATED USING A VIRTUAL REALITY PROGRAM AND THE BATTERY NEUROPSI"

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BACKGROUND

Obesity is a chronic, systemic, and multifactorial disease that affects individuals across all age groups, ethnicities, and social classes, and is not limited to economically disadvantaged countries (1). In adults, obesity is typically assessed and classified using the Body Mass Index (BMI), calculated by dividing body weight in kilograms by height in meters squared (kg/m²). According to the World Health Organization (WHO), an individual is considered obese when their BMI is ≥ 30 kg/m². Obesity is further classified into three categories: grade I (30.0–34.9 kg/m²), grade II (35.0–39.9 kg/m²), and grade III, or morbid obesity (≥ 40.0 kg/m²) (2).

Globally, obesity has reached epidemic proportions and is often referred to as "the epidemic of the 21st century." The WHO reports that more than 650 million people worldwide are affected by obesity (3), as noted in the World Obesity Atlas (2023). Projections estimate a 50% global increase by 2035 (4).

In Mexico, the National Health and Nutrition Survey (ENSANUT 2022) documented a sustained rise in overweight and obesity rates. Among children aged 5–11 years, prevalence increased by 7% between 2006 and 2020–2022. In adolescents aged 12–19, the rate rose from 24% to 41.1% over the same period. The trend continues into adulthood, with obesity being more prevalent among women (76.9%) than men (73.5%). Adults aged 40–60 years show the highest prevalence at 85%.

As obesity rates continue to rise, the incidence of associated comorbidities has also increased, including diabetes mellitus, hypertension, dyslipidemia, cardiovascular disease, and certain types of cancer. Moreover, obesity has been linked to neurodegenerative conditions such as dementia (5).

On the other hand, the WHO estimates that more than 46.8 million patients worldwide have neurodegenerative diseases, a figure that doubles every twenty years. In Mexico, approximately 800,000 older adults suffer from some neurodegenerative disease with an incidence ranging from 16.6 to 34.2 per 1000 inhabitants/year (6). The annual cost of dementia care per capita in Mexico can reach $6,157.00.

Cognitive impairment represents an intermediate clinical state between normal cognition and dementia. Cognitive decline has been attributed to the normal aging process. However, several factors have been associated with the prevalence of cognitive impairment, among which we found the educational level, cardiovascular risk (high blood pressure and obesity) (7).

Studies using murine models have described theories linking obesity to cognitive deterioration. Diets high in fat and carbohydrates, which commonly induce obesity, have been associated with cognitive

impairment due to structural lesions observed in various brain regions, including the hypothalamus (8). Furthermore, research in rodents has shown that increased adiposity can alter brain structure and function through mechanisms such as synaptic loss, reduced dendritic spine density, and changes in microglial morphology. These alterations contribute to deficits in attention, information processing speed, and memory (9).

Structural alterations in architecture have been reported in brain imaging studies, including neuronal atrophy in the gray matter of the temporal, frontal, and occipital cortices, as well as the hippocampus, thalamus, and midbrain, and a reduction in white matter. These damages suggest that obesity is associated with neuronal atrophy, regardless of the patient's chronological age. A decrease in regional blood flow was also observed in the prefrontal cortex, along with a reduction in the functional activity of cortical areas associated with episodic or sensory memory, working memory, or operational memory. However, it remains unclear whether this affects long-term memory (10).

Alterations in brain function do not exclusively affect cognition, but also the capacity for understanding, expressing, and experiencing emotions (for example, emotional lability, bipolar disorders, etc.), as well as the very structure of personality (e.g., organic personality disorder) (11). Currently, there are general neuropsychological assessment batteries (Neuropsi Attention and Memory), which are a set of tests or elements that explore the main cognitive functions in a systematic form, to detect and classify the existence of brain damage (12).

Bariatric surgery has become an increasingly common and effective intervention for achieving significant weight loss in individuals with morbid obesity. It is currently the most widely used and successful treatment for obesity, primarily because it reduces appetite, induces a negative energy balance, and promotes sustained weight loss. This weight reduction is closely associated with the remission of obesity-related comorbidities. Moreover, bariatric surgery has been linked to lower rates of mortality and morbidity, fewer hospitalizations, and a decreased need for pharmacological treatment (1).

Following bariatric surgery, patients often exhibit a reduction in systemic inflammation and notable changes in adipokine profiles. Adipose tissue is now recognized not merely as an energy reservoir but as an active endocrine organ that synthesizes and secretes various adipokines, including leptin and insulin.

Insulin plays a critical role in facilitating glucose uptake by most cells in the body; however, the brain—despite its high energy demands—does not require insulin for glucose transport. Nonetheless, insulin does reach the brain, particularly the hippocampus, where it binds to specific receptors and modulates synaptic plasticity mechanisms that underlie learning and memory processes. Likewise, leptin also exerts a significant influence on these synaptic mechanisms, contributing to the regulation of cognitive functions (10) (13).

Several studies have demonstrated a relationship between adiposity and cognitive decline, showing that excessive body fat is associated with reduced cognitive performance and an increased risk of developing neurological disorders such as gray matter atrophy and Alzheimer's disease (14). This relationship may help explain why reducing systemic inflammation can lead to cognitive improvement; however, the underlying physiological mechanisms remain incompletely understood.

Furthermore, numerous studies have examined the association between preoperative mental health status and postoperative outcomes following bariatric surgery. These studies have consistently reported reductions in depressive symptoms, including lower frequency and severity of episodes, with significant improvements observed as early as six months post-surgery (15,16). In some cases, a decrease in antidepressant use of up to 18% has been documented at 12 and 36 months after surgery, with these improvements maintained for up to three years. In contrast, other mental health conditions—such as psychosis, stress-related disorders, post-traumatic stress disorder, and personality disorders—have shown no significant changes following the intervention (15). Despite the growing body of literature, the specific predictors of mental health improvement after bariatric surgery are not well established (16).

The Longitudinal Assessment of Bariatric Surgery (LABS) study utilizes subjective data from standardized questionnaires and a cognitive battery of their own design, which evaluates attitudes, motivations, and needs, using the outcomes as predictors of post-operative improvement in attention/executive function and short-term memory (17). However, other studies focused on observing non-surgical and psychological factors acting as predictors of short- and long-term outcomes through a program of National Institute of Mental Health diagnostic interviews (Version III-R, DIS III-R) and the Structured Clinical Interview for DSM-IV Axis II personality disorders (Version 2.0, SCID-II) (18).

One of the most widely used instruments for assessing the overall cognitive functioning of a person is the "Neuropsi: Attention and Memory," which consists of a series of tests that evaluate orientation, attention, memory, language, visual perception, and executive functions. Neuropsi has been validated in the Latin American Spanish-speaking population and incorporates relevant cultural factors into its evaluation process (11).

Another aspect to consider is the patient's quality of life after undergoing surgical obesity treatment (18) (19). Despite the multiple instruments designed to assess quality of life in this population, there is no consensus on the most suitable instrument to measure it (19). The battery BAROS (Bariatric Analysis and Reporting Outcome System) has been validated as the most comprehensive evaluation system and objective measure of the benefits of bariatric surgery, as it enables an objective evaluation and standardized assessment of changes in quality of life after bariatric surgery (20). Includes the Moorehead-Ardelt Quality of Life Questionnaire, developed specifically for patients

undergoing surgical obesity treatment (20). This questionnaire consists of five questions about self-esteem, physical activity, social life, working, and sexual conditions (21).

Today, Virtual Reality is a novel approach to cognitive and/or assessment. Patient rehabilitation is based on a dynamic three-dimensional simulation in which the user feels immersed in an artificial environment that they perceive as real based on stimuli of the sensory organs (22). Virtual Reality technology is based on numerous applications that employ the theory that knowledge is retained better when it is experienced directly, rather than when one sees or hears it. The basis of this theory is the concept of first-person knowledge, according to which an individual acquires most of their knowledge of daily life through natural, direct experiences, not reflective and subjective (23).

Motivated by these considerations, the present project aims to evaluate the impact of bariatric surgery on cognitive performance across different domains by employing computational techniques based on virtual reality. The virtual reality platform used for this purpose is NeuroTracker X (NT), a software system developed and patented by CogniSens Innovation Inc. in collaboration with the Visual Psychophysics and Perception Laboratory at the University of Montreal, Canada.

NeuroTracker involves a dynamic visual task in which participants are required to track specific target objects moving within a 3D virtual space among multiple identical distractors. Functional magnetic resonance imaging (fMRI) studies investigating the neural correlations of object tracking have shown activation in the frontal, parietal, and temporal brain regions, each associated with distinct cognitive functions. The frontal lobe contributes to movement processing, attention, planning, decision-making, language, and emotional regulation. The parietal lobe is involved in integrating sensory information and supporting reasoning, motivation, and behavior. Meanwhile, the temporal lobe plays a critical role in auditory processing, language recognition, and memory formation (24). NeuroTracker X has emerged as a valuable tool for assessing and enhancing the efficiency of neural networks underlying key cognitive processes such as working memory, attention, executive function, and processing speed.

Problem statement

Obesity is a chronic disease that is progressively increasing worldwide. It is estimated that approximately 38% of the world's adult population will be overweight by 2030. Adiposity is linked to cognitive impairment, reducing cognitive abilities and increasing the risk of developing neurological disorders such as brain gray matter atrophy and Alzheimer's disease.

Bariatric surgery is an effective and increasingly popular method for weight loss among people with severe obesity. The loss of adipose tissue appears to have a positive effect on cognitive functioning; however, predictors of improvement are not yet well established. This study seeks to quantify the impact of bariatric surgery on cognitive function using virtual reality-based computing tools and

evaluate the changes in quality of life after bariatric surgery.

Justification

Bariatric surgery is a set of surgical interventions designed to produce significant weight loss. It has also been the most widely used and successful procedure for treating obesity, as it produces a decrease in appetite in patients, causing the energy balance to become negative and thus leading to weight loss, which in turn is related to the remission of comorbidities. After bariatric surgery, a reduction in inflammation and changes in adipokines have been observed, indicating that the reduction of inflammation may improve cognition after bariatric surgery. Although there is scientific evidence indicating that the post-operative outcome of this group of patients has been even superior to the improvement achieved by lifestyle modifications and/or pharmacological therapy, the data are inconsistent (14). The use of computerized tools, Virtual Reality-based assessments, is a novel approach to cognitive and/or Patient rehabilitation. Using Neutrotracker (NT) and the Neuropsi Attention test and memory, this study seeks to evaluate the effect of bariatric surgery on performance in domains of post-operative cognitive impairment in patients from the Comprehensive Patient Care Clinic service with diabetes and obesity (CAIDO).

Hypothesis

Patients with obesity undergoing bariatric surgery will present statistically significant differences ($p \leq 0.05$) in their scores on the Neuro Tracker and the Neuropsi Attention and Memory battery before and after surgery.

Objectives:

General

Evaluate using virtual reality software (NeuroTracker) and the neuropsychological battery (Neuropsi Attention and Memory) improvements in the performance of cognitive domains of patients, candidates for bariatric surgery, before and after the surgical procedure.

Secondary

- Evaluate the cognitive performance of obese patients undergoing bariatric surgery 3 and 6 months after the intervention through NT and Neuropsi Attention and Memory (the latter after 6 months to avoid the effect of learning the battery).
- To study the impact of bariatric surgery on the quality of life of patients who underwent the intervention using the BAROS battery.

Methodology

Type and design of study: Quasi-experimental, prospective study.

Population and sample size:

The sample size was determined using the difference of means method for paired samples. The effect size used (Cohen's d) was 0.6575741 (25), with a two-tailed (bilateral) test at a 95% confidence level and 80% statistical power. With these characteristics, the sample size is 21 patients.

The software used for determining the sample size was Gpower version 3.1.9.7.

INCLUSION, EXCLUSION AND ELIMINATION CRITERIA.

Inclusion Criteria

A. Age (18-65 years)
B. Diagnostic of morbid obesity with a body mass index (BMI) > 40 kg/m2, or,
C. Obesity grade II (BMI > 35 kg/m2) and associated comorbidities (Diabetes Mellitus type 2, Hypertension, Ischemic Cardiopathy, Hyperlipidemia, Hepatic Steatosis, Metabolic Syndrome, Obstructive Sleep Apnea, Pickwick Syndrome)
D. Bariatric surgery criteria.

Exclusion Criteria

A. Age < 18 years, > 65 years
B. Visual impairment
C. Personal history of CVE
D. Drug addiction.

Variables

VARIABLE	TYPE	OPERATIONAL DEFINITION	UNIT OF MEASUREMENT	STATISTICAL ANALYSIS
Sex	Nominal	Biological differences between males and females of a species, including differences in chromosomes and reproductive structures.	Male/Female	Frequencies %
Age	Nominal	It is the time elapsed since birth.	Years	Frequencies %
Body Mass Index (BMI)	Quantitative	A measure that assesses the relationship between a person's weight and height to determine their level of adiposity.	Kg/m^2	Frequencies %
Visual perception	Quantitative	Execution value: Stimulus detection threshold.	Seconds	Linear regression, Student's t-test, ANOVA, time-frequency and multiscale entropy

				spectra
Neuropsychological Battery: Attention and Memory	Quantitative	Score obtained on the Battery Neuropsychological Neuropsychology Attention and Memory.	Normalized punctuation	Student's t-test
NT	Quantitative	Tracking speed.	m/s	Linear Regression, Student's t-test, ANOVA
Quality of Life	Qualitative/ Quantitative	A measure that assesses a person's overall well-being.	Numeral	Student's t-test

Information on the Neuropsi Neuropsychological Battery for Attention and Memory

The Neuropsi Attention and Memory Neuropsychological Battery [11] is a compilation of tasks most used in neuropsychological literature to assess attention and memory (verbal and visual, both in its encoding and recall modes). It also includes subtests that allow for the assessment of executive functioning. It was developed in a Spanish-speaking Latin American population, so it takes important cultural aspects into account in its implementation.

It has a total of 17 profiles and three educational levels: low (0-3 years of schooling), medium (4-9 years), and high (10-24 years).

To assess skills and disabilities, it has a total of 29 subtests that are converted into normalized scores with a mean of 10 and a standard deviation of 3. The battery allows obtaining two partial scores, one from the Attention subdivision and another from memory, with a third factor being the total score (Attention and Memory). Neuropsi allows a classified score into one of the following levels of alteration: 1) high normal, 2) normal, 3) mild alterations, 4) severe alterations.

The test is administered individually and lasts approximately 1.5 hours.

NEUROPSI: NEUROPSYCHOLOGICAL ASSESSMENT TEST	
Author	Dr. Feggy Ostrosky-Solis
Aim	Evaluates cognitive functioning in the attention and memory areas. Provides a quantitative and objective assessment of these key cognitive functions.
Application Context	Clinics, hospitals, doctor's offices and neuropsychological research centers.
Description	A brief neuropsychological test for assessing various cognitive domains (e.g., attention, memory, language, perception, and executive functions).
Procedure	Individual administration and subtests application following the established protocol.
Target Population	Mexican population, considering age and educational level.
Duration	90 minutes (1 hour and 30 minutes).
Material	Application Manual, Record Form/Protocol, Pencil and Paper.
Scoring and Interpretation	Each subtest is scored, and composite scores are obtained for each cognitive domain. These can be interpreted using z-scores or percentiles.
Advantages	This test allows for the identification of alterations or difficulties in attention and memory. It can be applied in a group or individually. It is suitable for any clinical setting with patients who have suffered or are suffering from an illness (e.g., stroke, Alzheimer's, schizophrenia, neurodevelopmental disorders,

Technical information about the training programs and devices to be used NeuroTracker (NT):

NeuroTracker (NT) is a computer tool that assigns cognitive tasks involving multiple visual tracking of 3D objects on the screen, under increasing difficulty. Each training session consists of a series of mini-tests where the patient needs to remember the target objects and follow their movement among distractors for several seconds before identifying them.

NT is a product validated and patented by the Cogni Sens Applied Research Center (ARC), which has been used in Hospitals, Specialized Care Centers, and centers specialized in vision, schools, and the general population.

We will use the rate threshold protocol NeuroTracker (NT), established under only one condition: tracking 4 targets. Each block (referred to as a “ladder”) will last approximately 10 minutes. Participants will complete three sets of ladders in one session, for a total duration of 30 minutes. Each block has five phases (see Figure 1).

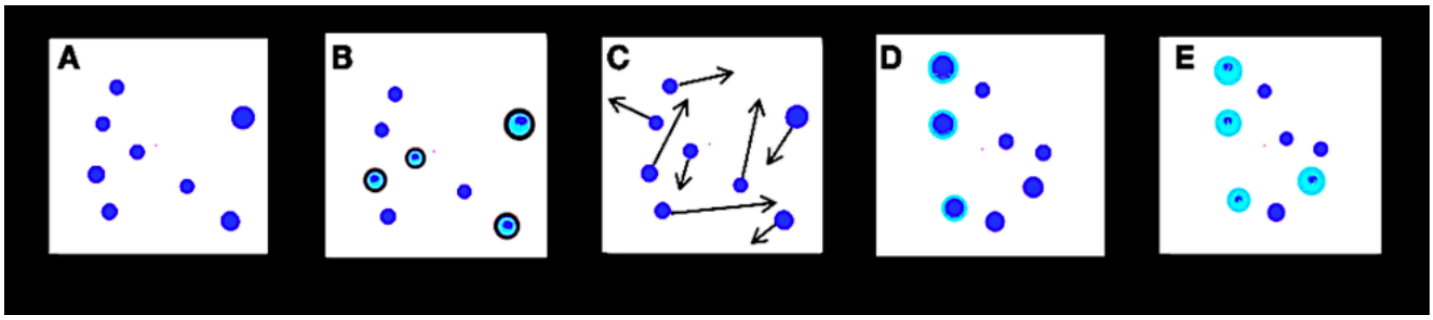


Figure 1. 5 Phases of NT.

- Phase 1, presentation: Eight static balls are presented for 2.5 s in random positions.
- Phase 2, indexing: Four red spheres for 2 seconds for target identification, before returning to their original color.
- Phase 3, tracking: all spheres begin to move in random directions at the speed defined

by the staircase procedure (see below), bouncing between them and with the virtual walls for 8 seconds.

- Phase 4, identification: the spheres stop moving, each one has a label of unique identification from 1 to 8. The task of the participants is to identify the 3 numbers corresponding to the three target spheres that had been indexed.
- Phase 5, feedback: feedback is given, showing the observer the spheres which were initially indexed. Speed thresholds will be evaluated using an ascending ladder procedure, that is, after a response is correct, the displacement of the ball's speed will increase by 0.05 units. record and will decrease in the same proportion after each incorrect answer, resulting in a threshold criterion of 50%. The ladder is interrupted after eight investments, and the threshold is estimated by the geometric mean velocity of the last four inversions. The initial virtual velocity is set at 3.75 cm/s. To obtain a correct answer, participants must report all objectives correctly.

Instrument for measuring Quality of Life using (BAROS)

BAROS (Bariatric Analysis and Reporting Outcome System) is an instrument that permits the objective and standardized evaluation of changes in the quality of life of patients undergoing bariatric surgery.

This evaluation includes the validated Moorehead-Ardelt Quality of Life Questionnaire, specifically designed for this population. The questionnaire consists of 5 simple questions aimed at measuring self-esteem, physical activity, social life, working, and sexual conditions.

Each question offers five answer choices with illustrations, scored from -1 to +1 points depending on whether it worsens, remains the same, or improves. This approach yields a total score between -3 and +3, which is incorporated into the comprehensive evaluation conducted by the BAROS system.

The Moorehead-Ardelt questionnaire is brief, easy to understand, and easy to complete. Autonomous monitoring by the patient enables independent quantification of potential changes in five key areas related to quality of life after surgical treatment. In this way, the instrument provides an objective and comparable measure of the effects of subjective aspects of bariatric surgery from the patient's own perspective. Their results form an integral part of the overall ranking, which is based on the system's assessment of the achieved results.

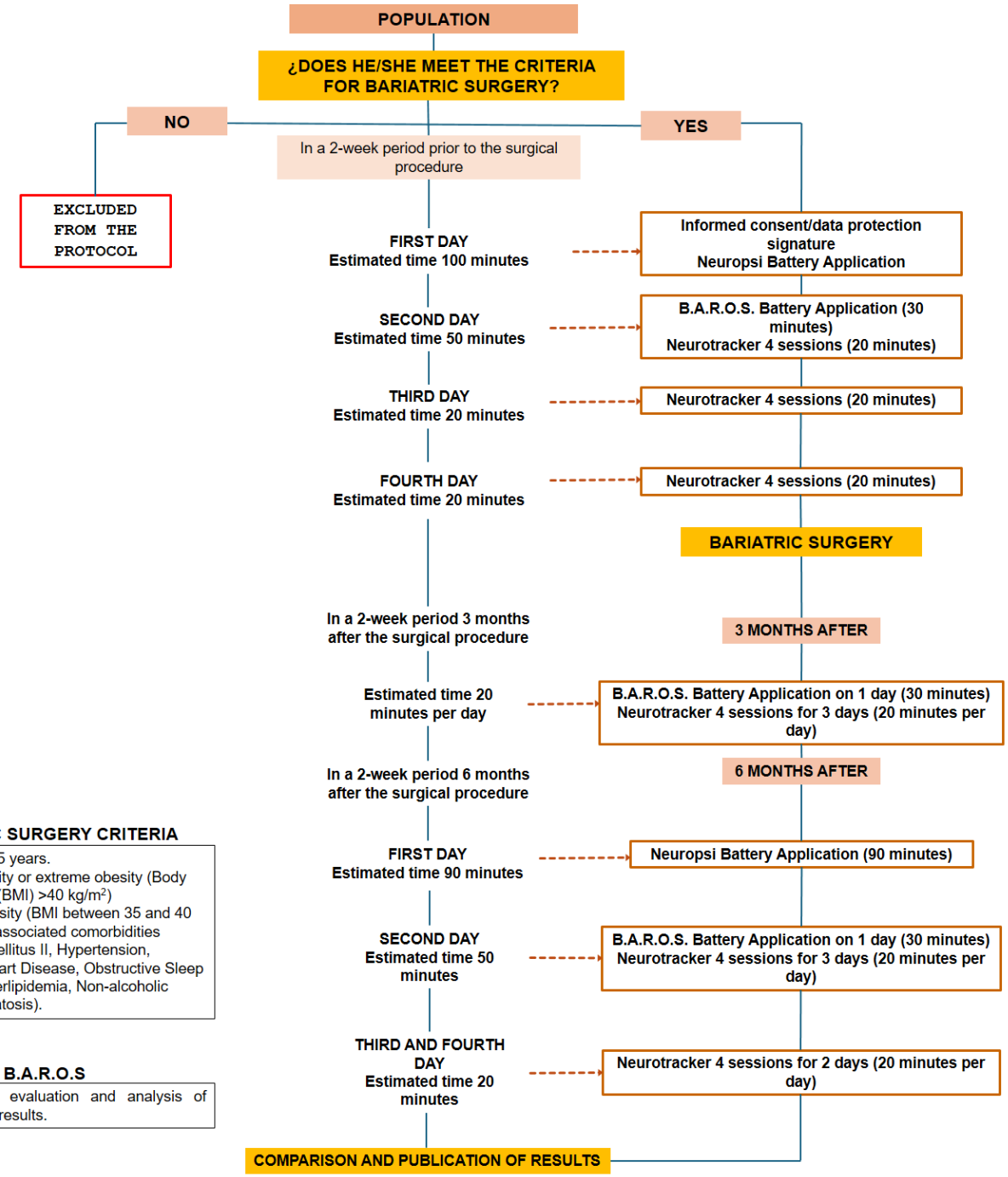
Procedure

Once the group has been identified, the patients who meet the inclusion criteria proceed with the visits described below:

1. 1) Visit 1. Explanation of the project for your subsequent informed consent, data recording, and application of the Neuropsi Attention and Memory battery.
2. 2) Visit 2. Application of the BAROS Battery and Neurotracker for four sessions.
3. In the first session, the dynamics of the virtual reality program are explained to the subject, with a trial session (5-10 minutes). Each subject performs 4 NT sessions per day until completing a total of 12 sessions. You will need to use the Virtual Reality equipment three times a day for two weeks before bariatric surgery.
4. Visit 3. Neurotracker application four sessions.
5. Visit 4: Neurotracker application four sessions.
6. Visit 5: Bariatric Surgery is performed.
7. Visit 6 (3 months after bariatric surgery): Neurotracker 4 application sessions and BAROS battery. After bariatric surgery (at 3 and 6 months). A new NT assessment will be applied at a rate of 12 sessions with a duration of each one approximately 20 minutes.
8. Visit 7 (3 months after bariatric surgery): Neurotracker 4 application sessions.
9. Visit 8 (3 months after bariatric surgery): Neurotracker 4 application sessions.
10. Visit 9 (6 months after bariatric surgery): Neuropsi Battery Application Attention and Memory.
11. Visit 10 (6 months after bariatric surgery): Neurotracker 4 application, BAROS sessions, and drums.
12. Visit 11 (6 months after bariatric surgery): Neurotracker 4 application sessions.
13. Visit 12 (6 months after bariatric surgery): Neurotracker 4 application sessions.

Location: Comprehensive Diabetes and Obesity Care Clinic (CAIDO) located in Pavilion 401-PB, of the Outpatient Clinic, and in the laboratory of the Research Unit and Technological Development (UDIT) located in Unit 110 between Internal Medicine and Geriatrics from the General Hospital of Mexico. Duration per visit: approx. 1:30 hrs.

Flowchart



BARIATRIC SURGERY CRITERIA

A. Age: 18 to 65 years.
B. Morbid obesity or extreme obesity (Body Mass Index (BMI) >40 kg/m^2)
C. Grade II obesity (BMI between 35 and 40 kg/m^2) with associated comorbidities (Diabetes Mellitus II, Hypertension, Ischemic Heart Disease, Obstructive Sleep Apnea, Hyperlipidemia, Non-alcoholic Hepatic Steatosis).

B.A.R.O.S

System for the evaluation and analysis of bariatric surgery results.

Schedule of activities

Bimester	APRIL/MAY 24	JUNE /JUL 24	AUG/SEP 24	OCT/NOV 24	DEC/JAN 24	FEB/MAR 25	APR/MAY 25	JUN/JUL 25	AUG/SEP 25
Protocol submitted to the HGM committees for approval and signing of the agreement	X	X							
Training and space adaptation		X							
Patient evaluation before Bariatric Surgery		X	X						
Data analysis (1st evaluation of results)			X	X	X	X	X		
Patient evaluation after Bariatric Surgery							X	X	
Analysis of the 1st evaluation of results									X

Statistical analysis

Statistical analysis will be performed using SPSS statistical software. The results obtained will be interpreted in consideration of the statistical significance values ($p < 0.05$) and the corresponding confidence intervals.

Descriptive statistics will be performed for all variables, calculating means and standard deviations. Standard, medians, and interquartile ranges, frequencies, and proportions depending on the type of variable. To evaluate the improvement, comparisons will be made using the difference of means with Student's t-test (before and after bariatric surgery). In the case of the variables, Qualitative assessments will include a chi-square test (X2) before and after bariatric surgery in all evaluations and follow-up. Additionally, a pre- and post-bariatric surgery comparison will be conducted to assess the differences in performance between the Neuropsi, BAROS, and Neurotracker tests.

Ethical and biosecurity aspects

NeuroTracker is a proven computer-based cognitive training tool. Normal and laboratory conditions require nothing more than subjects being seated. In this way, the tool poses no danger to the participants' health. Therefore, this investigation is classified as minimal risk according to Article 17 of the International Guidelines for Good Medical Practice and Research, as it employs non-invasive techniques and cognitive testing. Therefore, integrity will not affect the physical health of the patients. This study will be based on the three ethical principles of justice, non-maleficence, and beneficence, in accordance with the provisions of the National Commission for the Protection of Human Subjects, in the context of Biomedical and behavioral research.

The informed consent form will be utilized to ensure that each individual who enters the protocol

understands and authorizes their participation; those who do not sign will be excluded from participation.

Relevance and expectations

The project's relevance lies in its focus on obesity and its association with cognitive deterioration. While several previous studies have attempted to evaluate this association subjectively through tests that often depend on the observer's perspective, our approach is different. The use of new technologies allows for an objective and non-invasive evaluation of Multiple Objects Tracking (MOT) performance. This will enable us to identify whether the effect of bariatric surgery helps improve cognition and quality of life in patients who have undergone the intervention. In this context, the Hospital General de México supports the use of this new type of intervention. Technologies such as the Neuro Tracker (NT) are gaining significant relevance; this project also aims to position the NT as a transferable tool to other health institutions in the country.

Available resources

The Comprehensive Care Clinic for Diabetes and Obesity (CAIDO) at HGM has the required population for this research protocol.

Support from bariatric physicians who perform the evaluation, providing a clinical diagnosis, to the patients. Likewise, the space and support of the UIDT researchers are available at HGM.

The Applied Research Center of Cognisens Inc. will grant some licenses free of charge, exclusive to the use of NeuroTracker (NT) for the duration of the study, with the possibility of renewal by prior agreement between the parties..

Resources to be acquired

The materials to be acquired include file materials, such as A4 paper sheets, a pencil, and an eraser.

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