TITLE: Program for the comprehensive neurocognitive treatment of excess weight (TRAINEP)

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Brief Summary: The present study aims to determine the effectiveness of a comprehensive neurocognitive program for the treatment of excess weight. The program will include sessions to improve multiple cognitive processes implicated in weight gain and obesity. These cognitive processes include approach-avoidance bias, inhibition control, implementation intentions and episodic future thinking. Participants will be randomly allocated to one of three groups: 1) the experimental group will receive active neurocognitive sessions, 2) an active control group that will receive sham sessions and 3) a usual treatment control group. All three groups will receive a motivational interviewing session, along with personalized diet and physical exercise recommendations. We hypothesized that the neurocognitive program will decrease body mass index in people with overweight and obesity. In addition, the neurocognitive program will improve other anthropometric measures (waist circumference, waist-to-hip and waist-to-height ratios), lifestyle behaviors (eating behavior and physical activity), as well as cognitive processes (approach-avoidance bias, food inhibition, food liking and delay of gratification). Finally, the program will show its efficiency in the economic balance of cost-effectiveness and cost-utility.

1. STARTING HYPOTHESES AND GENERAL OBJECTIVE

HYPOTHESIS: The treatment of excess weight with a comprehensive program based on experimental knowledge about the functioning and modification of the impulsive and executive systems will be effective for the treatment of overweight and obesity. Thus, the neurocognitive training will reduce body mass index (BMI) in people with overweight and obesity, compared to a sham treatment and to only usual treatment. In addition, the neurocognitive program will improve other anthropometric measures (waist circumference, waist-to-hip and waist-to-height ratios), lifestyle behaviors (eating behavior and physical activity), as well as cognitive processes (approach-avoidance bias, food inhibition, food liking and delay of gratification). Finally, the program will show its efficiency in the economic balance of cost-effectiveness and cost-utility.

GENERAL OBJECTIVE: To determine the effectiveness of a comprehensive neurocognitive program for the treatment of excess weight.

1.1. Specific Aims:

Objective 1: To examine the effectiveness of a comprehensive neurocognitive training to reduce BMI in the short, medium and long term (post-treatment, 3-month follow-up and 6-month follow-up).

Objective 2: To study the effectiveness of the comprehensive neurocognitive program to change food behaviors, physical activity and body measures.

Objective 3: To investigate which active ingredients have an impact on the results of the program as outlined below:

3.1. To study the effectiveness of the impulsive training (approach-avoidance bias modification and improvement of inhibitory control) to reduce the approach bias to appetitive foods, increase the inhibitory control, improve the food decision making and modify the valuation of healthy and unhealthy foods.

3.2. To study the effectiveness of reflexive training (implementation of intentions and episodic future thinking) to improve behaviors related to implementation of intentions in healthy eating and physical activity, and to increase delay of gratification.

3.3. To compare the effectiveness of the neurocognitive training (impulsive and reflexive) to reduce BMI and body measures, and to improve food behaviors and physical activity.

3.4. To study the variables related to cognition, affect, stress and non-homeostatic food intake, motivation and personality to predict or mediate the intervention results.

Objective 4: To conduct an economic evaluation analysis of cost-effectiveness and cost-utility of the neurocognitive training in people with overweight and obesity, and analyze what budgetary impact would imply for the Spanish National Health System.

2. METHODOLOGY

2.1. Design: Randomized controlled trial of parallel groups.

2.2. Participants:

Sample size and statistical power:

The calculation of the sample size has been made from Objective 1, which focuses on detecting a clinically significant difference in BMI that is the primary outcome measure. Based on previous work that explored weight change in follow-ups after the application of neurocognitive training in people with overweight and obesity (Bazzaz et al., 2017, Kakoschke et al., 2018, Sze et al., 2015), we have selected the smaller sample size (Cohen's $d = 0.46$). With this data, considering the statistical method (models of repeated measures inter and intra subjects), the number of groups ($g = 3$), and assuming an alpha level of 0.05 and a power of 0.80, the resulting sample size calculated with G-Power was 105 participants. To date, no study has conducted a program based on the combination of different neurocognitive tasks that have been proposed as effective for the treatment of obesity, with a 6-month follow-up period. Thus, we opted for a conservative estimate increasing the number of participants to 150. Then, the study could suffer a sample loss of 30% from the initial session to the follow-up at 6 months and the statistical power would be still guaranteed. Previous studies that explored neurocognitive training to lose weight with different follow-up periods have showed smaller attrition rates [i.e., 16% in a 3-month follow up (Carbine et al., 2021); 12.3% in a 2-month follow-up (Forman et al., 2019); 3.4% in a 6-month follow-up (Lawrence et al., 2015)].

Participants:

The participants (N=150) will be randomly allocated to three groups: experimental group (neurocognitive intervention; n=50), active control group (sham intervention; n=50), and control group (treatment as usual; n=50).

People between 18 and 55 years old will be candidates to participate in the study, with a good command of the Spanish language, a range of BMI between 25 and 39.9 kg/m^2, and with at least two electronic devices available (one tablet, computer or smartphone to attend the online meeting and one smartphone with a gyroscope to do the training with the apps). All candidates will be screened for medical and psychological disorders and excluded if they have: (i) traumatic, digestive, metabolic or systemic disorders that affect the central nervous system, autonomic or endocrine, (ii) cardiovascular or any other disorders that prevent physical exercise; (iii) psychopathological disorders or presence of severe symptoms in the Depression Anxiety and Stress Scale-21 (DASS-21); (iv) eating disorders or presence of criteria in the Questionnaire on Eating and Weight Patterns-5 (QEWP-5); (v) pharmacological or any other kind of treatment for losing weight at present; (vi) candidates for bariatric surgery; (vii) food conditions that could interfere with the stimulus of the program (allergies, sprue, vegetarianism, veganism); (viii) current pregnancy or breastfeeding (or expected pregnancy in the following six months); (ix) weight loss >5% on the 3 months previous to the program; (x) use of medication that affects weight; (xi) frequent use of alcohol or other drugs that affects food intake.

Sampling context:

The recruitment will be carried out through social media and the web of the project.

Randomization and blinding:

A randomization (minimization) through the software Minimizer® will be performed to avoid imbalances between the groups in age, sex, and BMI (Stout et al., 1994). The psychologists that conduct the assessments (screening, evaluation sessions and follow-ups) will be blinded to the group allocation during the whole project. Moreover, since all assessments will be computerized and online, they are not subject to the biases of the evaluator. Further, all participants will be blind to their condition. Also, the people who perform the statistical analyses will be blind to the condition of the groups, through the coding of the interventions. Only the therapist performing the interventions will not be blind to the allocation of the participants.

2.3. Interventions:

Pre-treatment interventions (all groups).

Before the neurocognitive training, all participants will participate in a Motivational Interviewing group session to maximize motivation and adherence to the program. In the session, participants will be guided through open questions and empathic reflections and affirmations to promote change talk. Participants will share their personal aims to reduce weight, improve their diet and increase their level of physical activity. Further, participants will talk about obstacles they have had on previous occasions, their expectations, and their motivations in regards to weight loss. When needed, information about obesity and nutrition will be provided with the elicit-provide-elicit format. Sessions will end with an individual empathic summary for each participant's interventions.

Importantly, all participants will receive an individualized diet (by a Ph.D. nutritionist) and a physical exercise planning (by a Master's degree physical exercise professional) for the following 6 weeks.

Furthermore, with the aim of equating their knowledge before starting the program, all participants will be provided with 20-minute videos on basic ideas and frequent myths about nutrition and physical exercise. Also, brochures made by the research team about basic nutrition and physical exercise will be provided. Further, participants will have the opportunity if they wish so to attend a group session with a nutritionist and another group session with a physical exercise instructor to ask questions about their individualized diet and physical exercise recommendations and solve any doubt they could have about healthy habits, and thus match and complete relevant information on nutrition and excess weight. These two meetings will be recorded and made available for all participants.

A Whatsapp group will be created for each group of participants to promote their social interactions.

Neurocognitive interventions (experimental and active control groups).

Duration: 4 weeks

Note: The order of phases 1 & 2 will be counterbalanced. One task will be trained in each session, and participants will practice the tasks daily at home for one week (until the next session). Daily training will last approximately 5 minutes. Participants will receive daily reminders to practice via instant messaging on their mobile phones. A weekly pre-post assessment will be conducted for each trained task.

Phase 1: Impulsive training will consist of 2 weekly group sessions of about 60-90 minutes.

a. Approach-avoidance bias modification with the Tilt Task app (Kakoschke et al., 2018). In this task participants must zoom in or zoom out a food image according to its format (vertical or horizontal) using their smartphone device. Specifically, 90% of healthy food images will appear in the format to be approached (for example, vertical), while only 10%

of unhealthy images will appear in that format (to ensure concentration on the task). The format to be approached will be counterbalanced. For the sham training, the approach-avoidance ratio of the healthy and unhealthy food images will be 50%.
b. Inhibition training with the Food Trainer task (Lawrence et al., 2018). In this App participants are instructed to touch green circle items as quickly as possible, but to withhold their response and not to press on the red circle items, using their smartphone device. Some images are food, some non-foods. Participants in the experimental condition can choose which food categories they would like to train to resist (sweets, cakes, chocolate, biscuits, alcohol, crisps/chips, bread, cheese, fast food (burger, takeaways), fizzy (soft) drinks, meat, pizza, fruit, vegetables, crispbread/ricecakes). The food-specific inhibition training condition included pictures of high-calorie foods always paired with the no-go signal. Regarding the sham training, high-calorie and low-calorie foods will be paired with the go signal on 50% of trials and with the no-go signal on 50% of trials.

Phase 2: Reflexive training will also consist of 2 weekly group sessions of about 60-90 minutes.
c. Implementation of Intentions technique. Following the process described by Benyamini et al. (2013), each participant establishes one intention related to food and one related to exercise, and writes when, where and how they will implement each one, possible inconveniences to do it, and how they will overcome them. Furthermore, according to Adriaansen et al. (2009), motivational cues (why I eat) will be considered (negative emotions –I'm bored; social motives –eat a piece of cake you are offered in a party; politeness/conformity with others' expectations; pleasure). The implementation of intentions related to food will be written in format: "if… then…" [e.g., "If I come home from work hungry in the evening, then I will eat an apple" (Adriaansen et al., 2009)]. This format allows for the consideration of the health goals and medium and long-term objectives for each of the participants. The intention related to food will focus on unhealthy snacking habits whenever possible. For participants without snacking behaviors personalized food goals will be used. The sham condition participants will choose 10 items of healthy foods to eat in the moment that they want to eat unhealthy food and they will order a list of physical activities that they would like to do.
d. Episodic Future Thinking. Participants will decide health-related goals and anticipate future personal events at various time points (e.g., next month, 2-3 months and 4-6 months), from which contextual, temporal and emotional cues should be obtained. Goals and future events will be matched to generate episodic future thinking that includes the necessary keys to facilitate their effectiveness (O'Neill et al., 2016). For the sham training, habits and positive recent past events (1 day ago, 2 days ago, 1 week ago) unrelated to food or exercise will be considered. Participants will write their three cues on paper and/or their cell phones, and they will read and visualized them daily at home.

Post-treatment interventions (all groups): Participants will have the opportunity to attend a second group meeting with the nutritionist and another with the physical activity professional to receive information and ask questions about how to maintain long-term healthy habits on diet and physical exercise. These meetings will be recorded and made available for all participants. They will also be provided with new videos with guidelines about how to maintain a healthy long-lasting eating and exercise. The aim is that participants be autonomous and can develop their own diet and exercise planning.

Different strategies will be implemented to improve adherence to intervention protocols throughout the program. First, all groups will attend a motivational interview session to promote adherence to the program. All of the intervention sessions will be opened with an explanatory exposition to ensure that participants understand the task perfectly. In addition, the correct execution of each task will be assured in each session: The Tilt Task app has an initial trial with no-food images to test and practice the task before proceeding with the real trial. Furthermore, in both Tilt Task and Food Trainer task sessions, the researcher will ask participants to show their smartphone screen to ensure that movement is detected correctly. As well, if any participant has problems perceiving colors, the Food Trainer app allows to substitute this variable for another one (continuous vs. discontinuous line). Regarding reflexive training sessions, the researcher will ask the participants to send her the worksheets after the group session ends. Thus, she will be able to check the correct execution and suggest improvements to each participant individually. Also, about the homework compliance, the daily reminders will be sent by Whatsapp (thus, the researcher will be able to check that they are received correctly). Daily training at home will be recorded in different ways: Each practice with Tilt Task and Food Trainer apps will be automatically recorded in the online database; referring to implementation of intentions, participants will have to complete a daily self-registration; Lastly, during the EFT training week, they will have to answer some questions on WhatsApp every day. In addition, to monitor the daily task execution, at the beginning of each intervention session participants will answer a short debriefing about their practice over the previous week.

2.4. Outcome measures:

Note: The measures have been selected attending to ADOPT (Accumulating Data to Optimally Predict Obesity Treatment), to generate evidence about the efficacy for obesity interventions (MacLean et al., 2018). These measures are marked with an asterisk (*).

(1) Main outcome measure

a. BMI*: Height and weight will be measured to determine BMI. The weight and height for the calculation of the BMI (kg/m2) will be obtained with a pharmacy digital scale

BMI will check for the results of the whole program (the 4 intervention sessions), and will be registered weekly from session 1 to post-treatment assessment, and will be also registered at follow-ups (3- and 6-months post-treatment). In addition, the week before the pre-treatment assessment session, it will be recorded daily to obtain the baseline weight and then averaged.

(2) Secondary outcomes (changes in cognitive measures, changes in eating and physical exercise behaviors and body measures).

(2.1) Changes in cognitive measures.

a. Approach-avoidance bias: The approach-avoidance bias will be calculated before and after the 1-week training with the Tilt Task app. Participants should zoom in or out the appetizing and healthy food images that appear on the screen, depending on the presentation format of the image (horizontal or vertical). Approach and avoidance trials will be 50% for each type of image (healthy vs. unhealthy). The average reaction time of the approach (pull) and avoidance (push) trials will be subtracted separately for healthy and unhealthy foods, with the positive and

negative scores representing approximation and avoidance bias, respectively (see Kakoschke et al., 2018 for a full description).

b. Food inhibition assessment: Using the Food Trainer task, reaction time for the high-calorie and low-calorie foods paired 50% with the go and 50% with the no-go signal will be measured before and after the 1-week training with the app. The average response time for go and no-go items will be calculated according to the type of images (appetizing and healthy foods), and commission errors will be recorded (see Lawrence et al., 2015).
c. Food Liking Task (Lawrence et al., 2015): Participants will be asked to imagine that different foods are in their mouth and to rate how much they like the taste with a visual analogue scale (VAS) anchored at the extremes with "not at all" and "very much". Participants will move a cursor along the scale using a mouse and press the mouse button to confirm their rating, and the score between 0 and 100 will be recorded.
d. Delay of gratification*: Score on the questionnaire Now or Later (Kirby et al., 1999) will be used pre-intervention to measure the sensitivity relative to immediate rewards versus higher value rewards delayed at different time intervals. At post-intervetion, for the experimental group each item of the questionnaire will be applied immediately after reading the episodic future thinking cue trained, attending to the temporary interval of the item (Dassen et al., 2016). For the active control group, each item of the questionnaire will be applied immediately after reading the recent episodic thinking cue trained, attending to the temporary interval of the item. The control group will respond to the Now or Later questionnaire without any modification.

(2.2) Changes in lifestyle behaviors (eating and physical activity)

(2.2.1) Food preferences

a. Food Choice Task (Kakoschke et al., 2018): In this task, 16 pictures of different healthy and unhealthy snack foods will be presented. Participants will select 8 of these foods. They will have 15 seconds to make their choices. The scores will be the number of healthy foods selected.

(2.2.2) Short-term healthy behavior achievements

b. Self-reported diary: Participants will complete a self-reported diary for 7 days to register frequency and quantity of foods in the snacking behavior, and frequency and time of physical exercise. The desire to snack and do physical exercise will be also recorded, as well as the achievement of intentions in the experimental/sham groups.
c. Self-reported 72 hours food intake: Units and quantities on the amounts of foods and drinks that the participants eat and drink along these hours will be transformed into the number of calories for carbohydrates, sugars and fat.
d. Mediterranean Diet Adherence Screener (MEDAS; Schröder et al., 2011): Score on the 14 items that evaluate nutritional habits.
e. International Questionnaire about physical activity (IPAQ; www.ipaq.ki.se): Score on this questionnaire with 7 questions about physical activity during the last week, as well as time walking and sitting down.
f. Number of daily steps (pedometer): A pedometer will be used to register daily number of steps through the whole program.

(2.2.3) Adherence to healthy eating and exercise

g. Healthy eating with a Visual Analog Scale, with the question: During the last week, how healthy do you think your diet has been? Healthy eating is understood

as that according to the information received in the program: low amount of ultra-processed food, added sugar or alcohol; high amount of whole grain products, fruits and vegetables; etc. (0= no healthy at all; 100= 100% healthy).

h. Exercise habits with a Visual Analog Scale, with the question: During the last week, what has been your level of activity and physical exercise? (0= no activity at all; 100= maximum level of activity that I would be able to do).

(2.3) Changes in body measures (body fat distribution):

a. Waist circumference* (WC): Participants should stand with heels close together and trunk erect, and put the tape measure around the waist, just above the navel, to measure the waist circumference in centimeters.

b. Waist-to-hip ratio* (WHR): Participants should stand with heels close together and trunk erect. To measure waist circumference, participants should put the tape measure around the waist, just above the navel. To measure hip circumference, participants should place the tape measure at the maximum gluteal prominence. The hip-to-waist ratio is determined by dividing the waist circumference (in cm) by the hip circumference (in cm).

c. Waist-to-height ratio (WHtR): Participants should stand with heels close together and trunk erect, and put the tape measure around the waist, just above the navel, to measure the waist circumference in centimeters. The height in centimeters will be measured with a digital weight. The waist to hip ratio is determined by dividing the waist circumference by the height.

(3) Mediating/moderating variables:

(3.1) Affect, stress and nonhomeostatic eating:

a. *State affect.* Positive and Negative Affect Schedule* (PANAS; Watson et al., 1988): Score in this questionnaire that contains 10 items to evaluate negative affect experienced in the last week, and other 10 items to evaluate positive affect. Two questions about the number of binges and overeating episodes will be included at the end of the questionnaire.

b. *Perceived stress.* Perceived Stress Scale* (PSS; Cohen et al., 1983). Score in this scale with 10 items that evaluates stress feelings experienced during the last month.

c. *Emotional eating.* Coping subscale of the Palatable Eating Motives Scale* (PEMS; Burgess et al., 2014): Score on 4 items that evaluate the intentionality for eating palatable foods to face negative emotions.

d. *Trait food craving.* The Food Craving Questionnaire Trait-reduced* (FCQ-T-r; Meule, et al., 2014): Score on this questionnaire that evaluates the tendency to experience craving.

e. *Reward-related eating.* Reward-Based Eating Scale* (RED; Mason et al., 2017): Score on this scale with 13 items that evaluate worries about foods, losing intake control and absence of satiety.

f. *Nonhomeostatic eating.* Dutch Eating Behavior Questionnaire (DEBQ; Van Strien et al., 1986): Score on this questionnaire that assesses restrictive eating behaviors related to external cues and emotional states.

(3.2) Executive function:

g. Behavior Rating Inventory of Executive Function-Adult Version* (BRIEF-A Spanish version; Roth et al., 2005): Score on this questionnaire that assesses cognitive dysfunction in behavioral and emotional actions in everyday life. Consists of 75 items divided in 9 subscales: inhibition, changes, self-monitoring, initiation, working memory, planning, monitoring task and material organization.

h. Consideration of Future Consequences scale- short food version (CFC; Vilar et al., 2020): Score on 6 items that assess temporal perspective related to health and nutrition, with items oriented to the immediate ("I only act to satisfy immediate concerns, figuring the future will take care of itself") and the future ("I consider how things might be in the future, and try to influence those things with my day-to-day behavior").

(3.3) Motivation:

i. *Behavioral intention.* Dieting Intentions Scale* (DIS; Cruwys et al., 2013): Score on this 7-item scale about the intentions to follow a diet.

j. *Behavioral intention.* Physical Exercise Intentions Scale (EIEF): Score on this 7-item scale about the willingness to do physical exercise. This scale is an adaptation from DIS, Cruwys et al. (2013).

k. *Self-efficacy.* Weight Lose Self-efficacy scale* (WLSE; Wilson et al., 2016): Score obtained in 12 items that assess self-confidence to eat healthy food, do physical exercise and lose weight.

l. *Hedonic response to 'liking' for food.* Visual Analogue Scale to measure liking* (VAS liking; Berridge & Robinson, 2003): Participants will answer the question: How do you like ultra-processed food (high calorie foods, high in sugars and fats, like pizza, hamburgers, chocolate cake, chips…). Responses have a 0 to 100 scale, where 0= I don't like it, and 100= I absolutely like it.

m. *Hedonic response to motivation for food.* Visual Analogue Scale to measure wanting* (VAS wanting; Berridge & Robinson, 2003): Participants will answer the question: How do you want ultra-processed food (high calorie foods, high in sugars and fats, like pizza, hamburgers, chocolate cake, chips…). Responses have a 0 to 100 scale, where 0= I don't want it at all, and 100= I absolutely want it.

n. *Hunger.* Visual Analogue Scale to evaluate hunger* (VAS hunger) through the question: "How hungry do you feel?", with a 0 to 100 scale, where 0= not hungry at all, and 100= absolutely hungry.

o. *Motivation to change.* The Stages of Change Readiness and Treatment Eagerness Scale (SOCRATES 00; Vieira da Silva et al., 2019): Score in this questionnaire about motivation to change adapted to excess weight. It has 18 items that score readiness to change in people with abusive food use.

(3.4) Personality:

p. *Big Five factors.* Mini International Personality Item Pool* (mini-IPIP; Goldberg et al., 2006): Score in 20 items that evaluate the big five factors of Personality (extraversion, agreeableness, conscientiousness, neuroticism and openness.

q. *Impulsivity.* Impulsive behavior scale (UPPS-P; Lyman et al., 2006, Spanish adaptation by Verdejo-García et al., 2010). This scale evaluates five personality factors that can trigger impulsive behaviors: negative and positive urgency, lack of premeditation, lack of perseverance and sensation seeking.

r. *Inhibition and activation systems.* Sensitivity to punishment and reward. Punishment Sensitivity and Reward Sensitivity Questionnaire (PSRSQ;Torrubia et al., 2001): Score on this questionnaire with 48 dichotomous response items (Yes/No). The instrument has two subscales of 24 items each: The Punishment Sensitivity subscale, related to the inhibition behavioral system; and the Reward Sensitivity subscale, related to the activation behavioral system of Gray's theory.

(3.5) Adherence to diet and physical exercise:

s. Adherence to diet with a Visual Analog Scale, with the question: During the last week, what has been your degree of compliance with the eating guidelines given by the nutritionist of the program? (0= I did not comply with the diet at all; 100= I absolutely complied with the diet).
t. Adherence to physical exercise with a Visual Analog Scale, with the question: During the last week, what has been your degree of compliance with the physical exercise guidelines given by the physical trainer of the program? (0= I did not comply with the exercise recommendations at all; 100= I absolutely complied with the exercise recommendations).
(3.6) Clinical variables:
u. Participants' will answer having suffered weight stigma (Yes/No) (Himmelstein et al., 2017), will rate their motivation to intervention (1 to 5), and state the number of previous interventions to lose weight.

(4) Screening and descriptive measures
a. Sociodemographic (age, education, sex, socioeconomic variables) and clinical variables to consider exclusion criteria (central nervous system, autonomic or endocrine disorders; cardiovascular disorders; treatment for losing weight; bariatric surgery; conditions that interfere with the stimulus of the program, weight loss >5% on the 3 months previous to the program; medication that affects weight; use of alcohol or other drugs).
b. Depression Anxiety and Stress Scale-21 (DASS-21; Antony et al., 1998): Scores on the 3 subscales that evaluate anxiety, depression and stress.
c. Questionnaire on Eating and Weight Patterns-5 (QEWP-5; Yanovski et al., 2015): Score on the items of the questionnaire, that is adapted to DSM-5 criteria. It will be used to exclude people with binge eating problems and bulimia.

(5) Measures to calculate cost effectiveness, cost utility and budget impact analysis:
a. SF-36 Quality of Life Questionnaire: Total score on this questionnaire will be used to estimate the quality of life in terms of utility. The utility will be estimated based on the tariff validated for Spain (Abellán-Perpignan et al., 2012).
b. Years of life adjusted for quality (QALY). The QALY is the most used measure in economic evaluation. It is a measure composed of years of life and profits (collected from the SF-36) that reflect the quality of life of the population under study. This measure will be used in the cost-utility analysis of the intervention.
c. Body Mass Index (kg / m2). This measure will be used to calculate the cost effectiveness of the neurocognitive training intervention.
d. Cost of health resources that the participants spend (visits to primary care, urgencies, hospital admissions, and medicines consumed).
e. Cost of the time spent by the personnel in charge of the neurocognitive training sessions. A professional with the category of Clinical Psychology for each session of cognitive training with 5 participants, with 1 hour 30 minutes per session for 5 weeks. The cost per hour will be collected according to the salary of the personnel of health centers and institutions of the Andalusian Health Service.

3. PROCEDURE

All assessments and intervention sessions will be delivered online. Inclusion and exclusion criteria will be checked through the data collected in a questionnaire of sociodemographic and clinical variables. Further, psychopathology exclusion criteria will be tested with two questionnaires to measure depression, anxiety, and stress symptoms as

well as binge eating and bulimia (DASS-21 and QEWP-5), and a short clinical interview by phone and/or information requested by email in those cases where there are doubts about any of the aspects collected through the online instruments.
All candidates who meet the criteria will attend an information meeting about the project in which they will receive written and oral information, and will be asked for their informed consent. Then, participants will be randomly assigned to groups before the pre-treatment assessment sessions. The three groups of the study (intervention, active control and control) will complete all of the evaluations, as well as the follow-ups (see below and Figure 1). Further, all groups will received the pre-treatment interventions (Motivational Interviewing, nutrition and physical activity sessions). What will differentiate the groups will be, therefore, the treatment: neurocognitive intervention vs. sham vs. usual treatment. The control groups will be offered the treatment sessions (without the assessment components) after the end of the 6-month follow-up.
Sessions will be developed in groups of 5-6 persons. If a participant misses a session he/she can attend another one within 3-4 days. There will be 10 experimental groups of active training = 50 participants; 10 active control groups of sham training = 50 participants; and 10 control groups = 50 participants. The program will comprise 8 weeks including three assessments (pre, intermedium and post-treatment), four intervention sessions, as well as pre-treatment and post-treatment intervention sessions. Also, two follow-up sessions at 3 and 6 months after treatment (see below). Sessions will last about 1 hour and a half.
Sessions will consist of the following (see Figure 1):
1. Informative session (session 1; week 0): All participants will be informed about the aims and the procedure of the research, and they will provide written informed consent.
2. Pre-treatment assessment (session 2; week 1): All participants will complete the following instruments to assess the main and secondary outcomes, and the potential mediators/moderators, exploratory and economic measures: economic and sociodemographic questionnaire; MEDAS; visual analogue scales to evaluate liking, wanting and hunger; food choice task; food liking task; BRIEF-A; IPAQ; DEBQ; FCQ-Tr; PEMS (Coping subscale); RED; DIS; EIEF; WLSE; SOCRATES-00; PSS; mini IPIP; PANAS; UPPS-P; PSRSQ ; FCCS; SF-36, interview about used health resources. The administration order of the tasks will be counterbalanced.
3. Pre-treatment interventions (sessions 3, 4 and 5, week 2):
3.1. Motivational interviewing session: This 90-minute session will be developed in a group format of 5-6 participants.
3.2. Nutrition session: Participants will receive an individualized diet for the following 6 weeks. Videos and brochures about nutrition will be provided, and participants will assist a 60-minute group session with the nutritionist to match and complete relevant information on nutrition and excess weight.
3.3. Physical activity session: Participants will receive physical activity recommendations for the following 6 weeks. Videos and brochures about physical exercise will be provided, and participants will assist a 60-minute group session with the physical exercise instructor to match and complete relevant information on exercise and excess weight.
4. Intervention sessions (sessions 6, 7, 9 and 10; weeks 3, 4, 6 and 7): All sessions will start with Visual Analogue Scales to evaluate hunger, nutrition and physical activity. Each intervention session will be preceded by its pre-treatment evaluation, and followed by its post-treatment evaluation after a week of daily training. The pre and post-treatment evaluation of the impulsive training will be measured by the approach-avoidance bias (with the Tilt-Task app), food choice, the inhibitory control (with the Food Trainer app) and food liking. The pre and post-treatment evaluation of the reflexive training will be

measured by the Now or Later questionnaire for the episodic future thinking training, and the self-registration of nutrition and physical exercise for the implementation of intentions.
5. Intermediate assessment (session 8; week 5): This assessment will allow the comparison between the interventions for the impulsive and reflexive trainings. It will include: pedometer data; Visual Analogue Scales for liking, wanting and hunger; adherence to diet and physical exercise measured with Visual Analog Scales; Healthy eating with VAS; Exercise habits with VAS; registration of BMI; measure of waist and hip circumference, waist-to-hip ratio and waist-to-height ratio; food choice task; food liking task; PEMS (Coping subscale); DIS; EIEF; WLSE; PANAS; CFCS. The administration order of the tasks will be counterbalanced. After the session, participants will fulfill a self-reported diary with 24-hours food intake.
6. Post-treatment assessment (session 11, week 8): To evaluate the effectiveness of the whole intervention program, the measures of the pre-treatment assessment will be repeated, including: pedometer data; MEDAS, Visual Analogue Scales to evaluate liking, wanting and hunger; adherence to diet and physical exercise measured with Visual Analog Scales; Healthy eating with VAS; Exercise habits with VAS; BMI; measure of waist and hip circumference, waist-to-hip ratio and waist-to-height ratio; food choice task; food liking task; IPAQ; FCQ-Tr; PEMS (Coping subscale); RED; DIS; EIEF; WLSE; PANAS; UPPS-P; CFCS; interview about used health resources. The administration order of the tasks will be counterbalanced. After the session participants will fulfill the self-reported diary with 72-hours food intake.
7. Post-treatment interventions (session 12, week 8): After the post-treatment assessment, participants will have the opportunity to have a second 60-minute group meeting with the nutritionist and another with the physical activity professional, and they will be provided with new 20-minute videos about how to maintain a healthy long-lasting eating and exercise.
After all interventions, participants will be asked to complete a debriefing to register their thoughts and subjective experience about the program.
8. Follow-up (sessions 13 and 14; week 20 and week 32): Follow-ups at 3 and 6 months after the intervention will include the instruments to obtain the main and secondary outcome measures: pedometer data; Visual Analogue Scales to evaluate liking, wanting and hunger; adherence to diet and physical exercise measured with Visual Analog Scales; Healthy eating with VAS; Exercise habits with VAS; BMI; measure of waist and hip circumference, waist-to-hip ratio and waist-to-height ratio; IPAQ; FCQ-Tr; PEMS (Coping subscale); RED; PSS; mini IPIP; SF-36; interview about used health resources; 72 hours food intake. The administration order of the tasks will be counterbalanced.
Besides, every month after the end of the treatment, participants will be contacted by email and mobile message to explore possible difficulties in following healthy nutritional and exercise habits, and to ask them about their physical activity and healthy goals achievement. The purpose of this contact is, fundamentally, therapeutic adherence.
Participants will be instructed to eat two hours before all evaluation (pre, intermediate and post-treatment, and the two follow-ups) and neurocognitive sessions. Pre, intermediate and post-treatment assessments will be carried out at the same hour.

4. DATA ANALYSIS PLAN

Once the preliminary analyses for the detection of possible errors in the recording of the data have been made, exploratory and descriptive analyses will be carried out to study the distribution of the variables and the presence of atypical values. The applied inferential statistics will be in accordance with the characteristics of the data obtained (distribution

of the data, qualitative/quantitative nature of the data, etc.) and with the hypotheses proposed in the study. Models of repeated measures two-way ANOVA will be performed, using as dependent variables (DV):
- For objective 1, the change in the BMI between the four moments of assessment [pre (session 1), post-treatment (session 7), 3-month follow-up and 6-month follow-up];
- For objective 2: quantity, type and calories of the food intake; quantity of physical activity; degree of adherence to the diet and physical exercise recommendations; waist circumference and waist to hip ratio; food decision-making and valuation.
- For objective 3: approach-avoidance bias, inhibitory control, food choice task and food liking task will be used to assess the impulsive system; delay discounting and frequency and quantity of food and physical exercise behaviors will be used to assess the executive system. Furthermore, differences on BMI, food behaviors and physical exercise between the groups will be performed to compare the impulsive training and the reflexive training.
Effect sizes for between-group pairwise comparisons will be calculated using the following equation by Morris (2008) to estimate the magnitude of the difference between two groups at two different points in time:

$$d = c_p \left(\frac{(M_{TIME\ 2,GROUP\ 2} - M_{TIME\ 1,GROUP\ 2}) - (M_{TIME\ 2,GROUP\ 1} - M_{TIME\ 1,GROUP\ 1})}{SD_{TIME\ 1}} \right)$$

where M is the mean for each situation, and $SD_{TIME\ 1}$ refers to the pooled standard deviation of the first measurement moment:

$$SD_{TIME\ 1} = \sqrt{\frac{(n_{GROUP\ 2} - 1)SD^2_{TIME\ 1,GROUP\ 2} + (n_{GROUP\ 1} - 1)SD^2_{TIME\ 1,GROUP\ 1}}{n_{GROUP\ 2} + n_{GROUP\ 1} - 2}}$$

and c_p is a correction for bias, calculated by:

$$c_p = 1 - \frac{3}{4(n_{GROUP\ 2} + n_{GROUP\ 1} - 2) - 1}$$

where n is the sample size for the corresponding group.

Within-group effect sizes will be calculated using Cohen's d (Cohen, 1992):

$$d = \frac{M_{TIME\ 2} - M_{TIME\ 1}}{SD_{pooled}}$$

where SD_{pooled} is:

$$SD_{pooled} = \sqrt{\frac{SD^2_{TIME\ 1} + SD^2_{TIME\ 2}}{2}}$$

Based on Cohen's (1992) rule of thumb, clinical significance of change will be reflected by medium within-group effect sizes ($d \geq .5$).

Mediation and/or moderation analysis will be carried out to study the role of variables related to cognition, affect, stress and non-homeostatic food intake, motivation and personality on the program outcome measures.
In addition, possible differences in the program outcomes will be assessed based on sex and weight classification (overweight and obesity -type I and type II).
All the analyses described will be carried out following an intention to treat strategy (ITT) and analysis per protocol (PP). Corrections will always be considered to control for multiple comparisons.
- For objective 4, the average cost and effectiveness (BMI and QALY) for the 3 groups (intervention, sham and treatment as usual) will be estimated. The ratios of incremental cost effectiveness and incremental utility cost will be calculated as the cost and effectiveness difference (BMI and QALY) for the 3 groups. All the analyses will be carried out according to the methodological recommendations for Spain (López-Bastida et al., 2010). The perspective of the health system will be used, including only direct costs. The uncertainty of the results will be carried out through various deterministic sensitivity analysis (AS) and a probabilistic one using nonparametric bootstrapping methods of 1000 iterations (Luce et al., 2001) that will allow to represent the cost-effectiveness plane and the Acceptability curve. The AIP will estimate the variation that the introduction of neurocognitive training would imply for the budget of the public health system, based on the estimated costs of the alternatives compared and the estimated number of patients expected to benefit from the program. Likewise, univariate and multivariate AS will be performed to analyze different budgetary scenarios based on a possible variation in the cost variables and number of beneficiary patients.

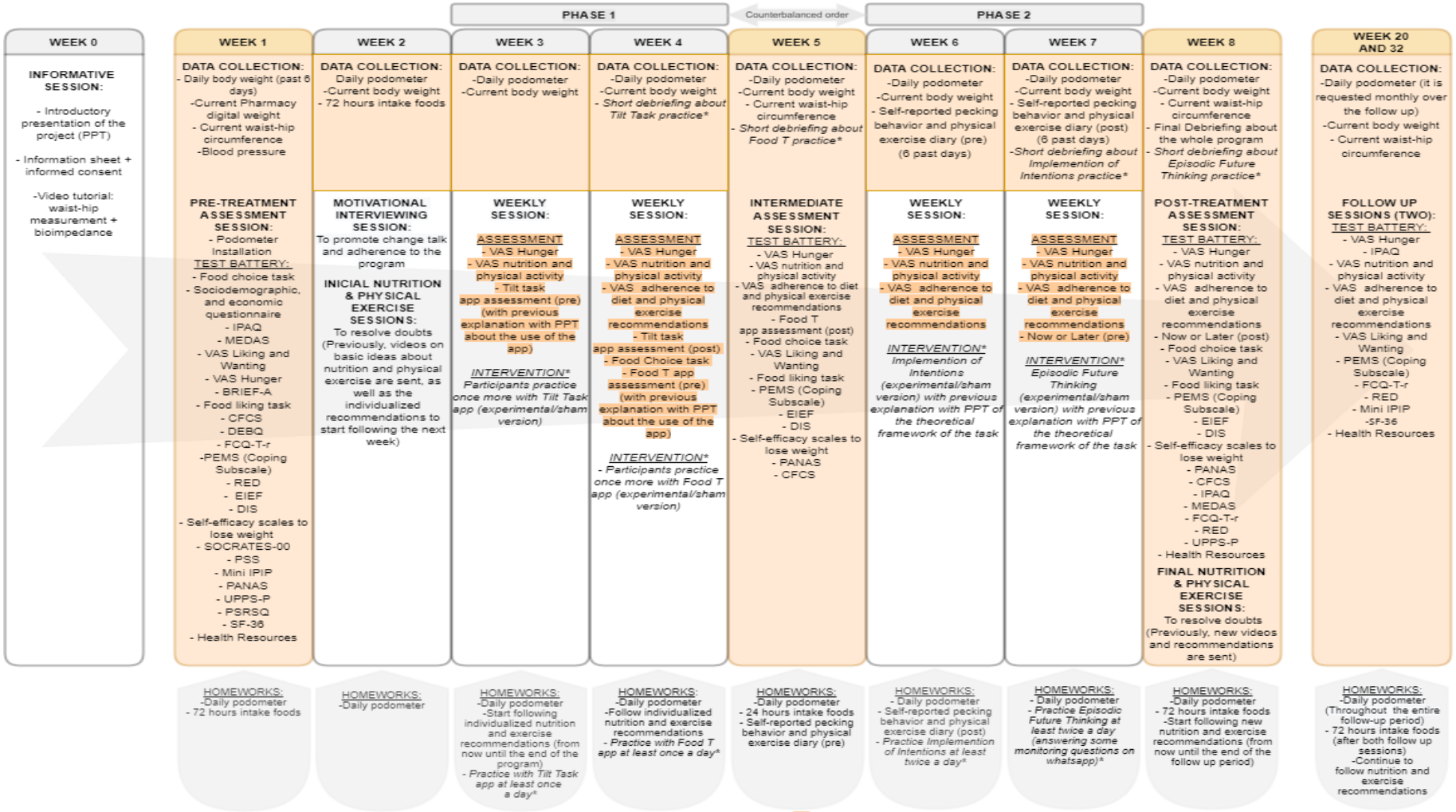

Figure 1: Procedure of the program.