



PONTIFICIA UNIVERSIDAD CATÓLICA DE CHILE
Doctorado en Neurociencias

**ATTENTIONAL BIAS FOR FOOD CUES AFTER SLEEVE GASTRECTOMY: A
BEHAVIORAL AND ELECTROPHYSIOLOGICAL STUDY.**

A thesis submitted in partial fulfillment of the requirements for the Doctor of Philosophy
degree in Neuroscience.

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THESIS DEDICATION:

This thesis is dedicated to my wife, Antonieta, and our sons, Alonso and Agustín.

You are the drive of my life, you are my everyday support, you are everything to me.

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ABBREVIATION LIST:

ANCOVA: Analysis of covariance.

ANOVA: Analysis of variance.

AW: Appetizing words.

BG: Bariatric group.

CG: Control group.

CW: Control words.

DW: Diet words.

ICA: Independent Component Analysis

LPP: Late Positive Potential.

SD: Standard deviation.

EEG: Electroencephalography.

ERP: Event-Related Potential.

M: Mean

RT: Reaction Times

SE: Standard error.

VAS: Visual analogue scale.

ABSTRACT:

Obesity has become a global health problem, and evidence suggests that there are important factors promoting overeating behaviour and obesity. This project is mostly based on the "food addiction" hypothesis, which emphasizes the similarities between drug use disorder and obesity. The consumption of high-calorie food, affects the dopaminergic pathway signalling, generating a pathologic response to food-related stimuli, which is the neuropathological basis for the attentional bias for food cues. Attentional bias for food cues could be related to food craving and the inability to lose weight, or a higher probability of weight regain.

The attentional bias towards food stimuli was initially described in patients with eating disorders (ie anorexia nervosa, bulimia nervosa and binge eating disorders). In the last decade, the presence of this bias in patients with obesity has been explored. However, despite the fact that most of the studies support the presence of this bias in patients with obesity, this has been done with very different methodologies, the relevance as a prognostic factor has not been explored in-depth, neither the factors or intervention that could modify this bias in the long term follow-up.

For this study, we selected a group of patients after at least 1 year from sleeve gastrectomy. Our objective was to evaluate the presence of attentional bias towards food and compare it with a control group. To assess the bias for food cues, we generated two tasks: food-modified Stroop task and visual task. The first one with electroencephalographic recording and the second one with eye-tracking recording. The electroencephalographic signal was processed to perform an event-related potentials analysis.

We found that the bariatric group presented a higher variability of reaction times to appetizing words (compared to diet words), which is compatible with the effect of semantic interference. The control group showed a higher amplitude of N1 for the diet stimuli, compared to the bariatric group. The bariatric group showed an increased amplitude of LPP for all the food stimuli (appetizing and diet words), compare to the control group. Both groups presented a greater amplitude of N450 for food stimuli. In eye-tracking data, we did not find differences on direction or duration bias indexes, however, in the bariatric group, we found a lower number of initial fixation on diet foods (competing with faces) and a longer duration of fixation on appetizing food stimuli (competing with diet images). Our data support the idea of an increased attentional bias for appetizing food, a decreased bias for diet food and a prolonged brain processing of food stimuli in the bariatric group. Further studies on the neurobiological bases should be performed, in order to corroborate our findings, and test the clinical relevance of attentional bias in this population.

RESUMEN:

La obesidad se ha convertido en un problema de salud global, y la evidencia sugiere que existen factores importantes que promueven el comportamiento de comer en exceso y obesidad. Este proyecto se basa principalmente en la hipótesis de la "adicción a los alimentos", que enfatiza las similitudes entre el trastorno por consumo de drogas y la obesidad. El consumo de alimentos ricos en calorías, afecta a la señalización de la vía dopaminérgica, generando una respuesta patológica a los estímulos relacionados con la alimentación, siendo la base neuropatológica del sesgo atencional de los estímulos alimentarias. El sesgo atencional hacia estímulos alimentarios podría relacionarse al deseo de comer y la incapacidad de perder peso, o una mayor probabilidad de recuperar el peso.

El sesgo atencional hacia los estímulos alimentarios se describió inicialmente en pacientes con trastornos alimentarios (es decir, anorexia nerviosa, bulimia nerviosa y trastornos del atracón compulsivo). En la última década, se ha explorado la presencia de este sesgo en pacientes con obesidad. Sin embargo, a pesar de que la mayoría de los estudios apoyan la presencia de este sesgo en pacientes con obesidad, esto se ha hecho con metodologías muy diferentes, la relevancia como factor pronóstico no ha sido explorada en profundidad, ni los factores o intervenciones que podrían modificar este sesgo en el seguimiento de largo plazo.

Para este estudio, seleccionamos un grupo de pacientes después de al menos un año de gastrectomía en manga. Nuestro objetivo era evaluar la presencia de sesgo atencional hacia la comida y compararla con un grupo de control. Para evaluar el sesgo de las señales

alimentarias, generamos dos tareas: una tarea de Stroop modificada para estímulos alimentarios y una tarea oculomotora. La primera con registro electroencefalográfico y la segunda con registro de movimientos oculares. La señal electroencefalográfica fue procesada para realizar un análisis de potenciales relacionados a evento.

Se encontró que el grupo bariátrico presentó una mayor variabilidad de los tiempos de reacción a las palabras apetitosas (en comparación con las palabras de dieta), lo cual es compatible con el efecto de la interferencia semántica. El grupo control mostró una mayor amplitud de N1 para los estímulos de la dieta, en comparación con el grupo bariátrico. El grupo bariátrico mostró una mayor amplitud de LPP para todos los estímulos alimentarios (palabras apetitosas y dietéticas), en comparación con el grupo de control. Ambos grupos presentaron una mayor amplitud de N450 para los estímulos alimentarios. En los datos de seguimiento ocular, no se encontraron diferencias en los índices de sesgo de dirección o de duración; sin embargo, en el grupo bariátrico, se encontró un menor número de fijaciones inicial en los alimentos de dieta (al competir con rostros) y una mayor duración de la fijación en los estímulos alimentarios apetitosos (al competir con imágenes de dieta). Nuestros datos apoyan la idea de un mayor sesgo atencional para los estímulos apetitosos, un sesgo disminuido para los estímulo de dieta y un procesamiento cerebral prolongado de los estímulos alimentarios en el grupo bariátrico. Se deben realizar estudios adicionales sobre las bases neurobiológicas para corroborar nuestros hallazgos y probar la relevancia clínica del sesgo atencional en esta población.

INTRODUCTION

Every organism lives in a constantly changing world with a limited capacity for processing the overload of perceptual information (Posner, 1980; Desimone & Duncan, 1995). This flow of external and internal information, includes every stimulus perceived by the sensory systems, signals related to interoceptive and internal states; but also, the presence of thought, emotions, among other subjective experiences that can be included in this great amount of data, competing for been processed by a brain with limited capacity. Because of that constraint, our brain needs to filter relevant and irrelevant information; and in this filtering process, the role of attention is crucial, allowing to focus only in part of the perceived stimuli (Pessoa et al., 2002). This selective attention increases neural resources for processing attended stimuli, by neglecting the rest of the perception (Pessoa et al., 2002).

The factors behind this selection can be classified into three main categories: stimulus characteristics (bottom-up sensory-driven mechanisms or “exogenous attention”), voluntary control of attention (attentional top-down feedback or “endogenous attention”), and emotional content of the stimulus (affective-driven modulation of attention, “emotional attention” or “motivated attention”) (Pool et al., 2016).

Exogenous attention and endogenous attention, have been classically described, and widely studied, as the two central factors in the process of stimulus selection (Corbetta & Shulman, 2002; Posner et al., 1980). Exogenous attention generates a fast an involuntary modification of attentional focus, and is related to stimulus characteristics, for example, colour, size, contrast,

and frequency of appearance, among others. (Theeuwes, 1994). Endogenous attention refers to voluntary control of attention; it is goal-directed, less rapid than the exogenous attention and the selective process is related to personal predisposition and stimulus relevance for a task (Folk et al., 1992). These factors explain the relevance of the stimulus characteristics and the voluntary control of the subject, but a third factor has been described, emotional attention (Vuilleumier, 2005) or motivated attention (Lang, 1995).

Motivated attention is not related to stimulus characteristics or subject disposition, it is based on a special relationship established between the subject and the stimulus. Motivated attention is a fast and involuntary response to a particular stimulus (like exogenous attention); but also, depends on the internal states of the observer (a core characteristic of endogenous attention) (Pool et al., 2016). Motivated attention implies the activation of different brain areas, like the amygdala, which differs from the structures involved in exogenous and endogenous attention (Vuilleumier, 2005). Motivated attention is present in everyday experience, and interacts with exogenous and endogenous attention in the selection of attended stimulus. Motivated attention can be part of normal experience, but can also, be linked to the pathological allocation of attention (attentional bias), especially if stimulus generates a high emotional reaction, that can increase avoiding (eg. phobias) or approaching behaviours (eg. substance use disorder).

In cognitive models, pathological behaviours are the consequence of maladaptive knowledge structures that determine the disturbed allocation of attention (Attentional Bias), pathologically-modified memory process (Memory Bias) and misinterpretation of information (Judgment Bias) (Williamson, 2004). Motivated attention is the base for attentional bias, which refers to a predominant sensitivity for specific environmental stimuli (Williamson et al.,

1999). This predominant sensitivity can be observed as initial orienting attention (before 150 ms) or as difficulty in disengaging attention from the stimulus (after 200-250 ms) (Pool et al, 2016). Attentional bias has been described in mental disorders, playing a central role in causation and maintenance of the pathology (Williams et al., 1996). This attentional biases have been described in a wide variety of mental pathologies; some examples are anxiety disorders (Cisler et al., 2010), depression (Peckham et al., 2010), substance use disorders (Field et al., 2013), and eating behaviour disorders (Brooks et al., 2011).

Attentional bias for food cues refers to selective attention for food stimuli, and have been described in a broad range of eating pathologies, including anorexia nervosa, bulimia nervosa, binge eating disorder, and obesity. Despite the common attentional bias toward food stimuli, these pathologies have different presentations and symptoms, making a unified theory about attentional bias for food a difficult task.

Anorexia nervosa, bulimia nervosa and binge eating, are now part of the feeding and eating disorders chapter in DSM-5 (American Psychiatric Association, 2013). During the preparation of the DSM-5 a debate was generated about the obesity inclusion in the eating disorder spectrum, however, despite its epidemiological relevance, and the great comorbidity with psychiatric pathologies, it was finally excluded. This determination has important foundations, such as the wide range of factors linked to obesity, which is not limited to psychological aspects. However, this exclusion should not discourage research interest in the psychological and neurobiological aspects of this phenomenon, called obesity.

Obesity is rising in our modern society and has become one of the ten global health problems (Li et Al., 2005). Since 1980 the prevalence of obesity in the United States of America has

doubled (Flegal et Al., 2010). Surprisingly, some evidence suggests that the major increases in the body mass indexes occurred in the already obese group (Flegal and Troiano, 2000), so there must be something different in this particular population, that makes them become obese. The “thrifty” genotype hypothesis (Neel, 1962) proposes that our genome is adapted to a past environment with a small quantity of food. In this context our genome was selected to maximize energy input, by eating the highest amount of food available and preferring the food with higher caloric value; and also, to minimize energy output, by avoiding excessive physical activity (Heitmann et Al., 2012). Indeed, about one half of the body mass variation in a population is related to inherited factors (Lyon and Hirschhorn, 2005), but how this genetic disposition translates into energy balance is poorly understood (Knecht et Al, 2008).

In addition to the abundant amount of food and low physical activity, some researchers have argued that there are other “obesogenic” changes in our modern life. The “new modern” food could generate addictive behaviours (Fortuna, 2012; Volkow et Al, 2013), unhealthy food advertisements may have a significant impact on food selection (Gearhardt et Al, 2011) and the reduction of sleep hours have been linked to excessive weight gain (Garaulet et Al, 2010).

In neuroscience, most of the studies about food intake regulation have focused on metabolic regulation and the central role of the hypothalamus in energy balance (Knecht et Al, 2008).

But all the information generated about this "homeostatic" system that regulates food intake, has not been able to explain the full phenomenon of obesity. In recent decades, researchers have moved from the hypothalamus to other brain areas that are related to the hedonic experience of eating, motivational states, behavioural control, among others. Part of these researchers has focused on the common aspects of obesity and drug dependence. Fortuna

(2012) described craving and loss of inhibitory control as “two unmistakable clinical similarities” between these pathologies. Volkow et al. (2013) emphasize the relevance of a common neuropathological feature: the disruption of dopamine pathways, and the subsequent altered responses to environmental stimuli. These modifications can make food-related stimuli more relevant than other stimuli, and affect eating behaviour in pathological ways (Berridge, 2009).

In substance users, the drug-related stimuli are associated with higher amplitude of P300 and LPP, (Littel et Al, 2012); and these ERPs are presents even after a long abstinence period. Furthermore, in substance use disorders, the presence of attentional bias to drug-related cues has been linkage to drug craving, relapse risk and poor treatment outcome (Littel et Al, 2012). Nijs and colleagues developed a series of studies about obesity and attentional bias for food stimuli (Nijs et al., 2008; Nijs et al., 2009; Nijs et al., 2010; Nijs et al., 2011), and part of their theoretical foundations implied the conceptualization of obesity as an addiction to food. Nijs also highlighted the incentive sensitization theory Robinson & Berridge, (1993), Which implies the sensitization of the dopaminergic reward system, after which a greater salience of the stimuli would be generated, and the attentional engagement would be propitiated. This sensitization was originally described in drugs-related disorders, however, highly caloric foods, with high levels of sugars and fat, seem to generate altered dopaminergic responses in the reward system, increasing the risk of an attentional bias towards these stimuli, the risk of food craving and food intake (Hendrikse et al., 2015); and therefore, affecting the possibility of losing weight (Nijs et al, 2010).

Attentional bias for food has been widely explored through a modified Stroop task in patients with eating disorders (ED), mostly in anorexia nervosa and bulimia nervosa. The original Stroop task was developed for studying general aspects of human attention and cognitive competition. Over the years, the task has suffered some methodological variation from the original publication, but Stroop tasks are basically a set of different combinations of words (colour or neutral word) presented in different ink colours (Williams et al, 1996). Modifications of the original Stroop task have been developed, creating tasks usually called emotionally-modified Stroop tasks. In these tasks, the colour words are replaced by disorder-relevant words, for example, for an arachnophobic individual the word “spider” can generate an interference effect. These emotional Stroop tasks can be used for exploring cognitive processes related to emotional disturbance or psychopathology (Williams et al, 1996). According to this idea, the food-modified Stroop task uses food-related words as interference stimuli, and have been useful exploring interference effect of food cues in subjects with pathologic eating behaviours.

Despite similarities in stimuli and task instructions, Stroop task and emotional Stroop task explore different phenomena (Algom et al, 2004). Basically, the emotional Stroop task does not use incongruent stimuli, only words with emotional value; based on that, the effect cannot be interpreted as a Stroop effect, only as an “emotional delay” (Algom et al, 2004). This “emotional delay” had been usually interpreted as an attentional bias equivalent, but some researchers argued that this interference effect could be the result of an attentional avoidance (Field & Cox, 2008).

The food-modified Stroop task evaluates differences in reaction times between food-related and control words when the subjects have to respond to the font colour of the word (Brooks et Al, 2011). Food Stroop has been widely used in eating disorders studies, and at this point, we have meta-analytic data (Brooks et Al, 2011) about the relevance of these task as an objective approach for exploring attentional bias for food. For some reason, this particular task has been scarcely used in studies of patients with obesity. In a review article, Hendrikse et Al. (2015) found 19 studies exploring the relationship between obesity and attentional bias for food cues. Most of these studies (fifteen articles with heterogeneous methodologies), support the hypothesis of an attentional bias for food in obese and overweight subjects.

At this point, we already have evidence that supports the presence of attentional bias for food stimuli in patients with obesity, however, little is known about the relevance of this bias in craving, food selection, and the difficulties in controlling food intake. In addition, the development of interventions that modified attentional bias (Hakamata et al., 2010), even with mobile applications (Zhang et al., 2018), make this area a promising field to explore.

The growing rates of overweight and obese individuals have also led to an increase in available therapies to control weight. Bariatric surgery is one of the most gained ground, given its significant weight drop in the first months, and improvement of metabolic parameters (Shauer et al., 2017). However, a percentage of patients after 1 year of the surgery, regain weight, and there are no therapeutic alternatives available with evidence of proven effectiveness (Maleckas et al, 2016). This group of patients is an interesting group of study, given that despite the significant initial weight loss, the improvement of metabolic parameters

and frequent medical visits, they resume pathological alimentary behaviours, generating an important weight regain.

This thesis focuses on the mental processing of food stimuli in patients who underwent bariatric surgery, in order to find elements that guide the presence of an attentional bias towards food, as an indicator of pathological processing of these stimuli.

STUDY AIMS AND HYPOTHESIS

Preparation and pilot study:

- General Aim:
 - Generate specific task to evaluate attentional bias for food, compatible with our national context.
- Specific Aims:
 - Generate a food-modified Stroop task, including 3 subsets of words: Appetizing, Diet and Control words.
 - Programming a digital version of the food-modified Stroop task, compatible with EEG recording.
 - Generate a set of images, including food (appetizing and diet images), and faces.
 - Programming a digital version of an oculomotor task, compatible with Eye Tracking recording.
 - Record and analyze the behavioral and electrophysiological results from the pilot study, in order to adjust the variables and prepare the experimental study.

Thesis study: Attentional bias for food cues in subjects after sleeve gastrectomy (at least one year).

- General aim:
 - Evaluate the attentional bias for food-related cues in individuals after bariatric surgery.
- Specific Study Aims:

- Use a food-modified Stroop task and an oculomotor task, in order to address objectively the attentional bias for food.

- Hypothesis:

General: Individuals after sleeve gastrectomy present a higher attentional bias for food-related cues compared to a control group.

Food-modified Stroop task with EEG recording: Individuals after sleeve gastrectomy present prolonged RT for appetizing words, compared to diet and control words, and also compared to the control group. On ERP analysis, appetizing cues correlates with an increased amplitude in P300 and LPP in individuals after sleeve gastrectomy.

Oculomotor task and eye tracking recording: Individuals after sleeve gastrectomy present higher directional and duration bias to appetizing images, compared to a control group.

MATERIALS

Surveys:

- Edinburgh Handedness Inventory” (Oldfield, 1971): Spanish version.
- Dutch eating behaviour questionnaire. (Tatjana van Strien, 1986). Spanish version (Cebolla et al., 2014)
- Mini International Neuropsychiatric Interview (Lecrubier & Sheehan, 1998). Spanish version 5.0.0 (Bobes et al., 1998)

EEG recording:

- NeuroScan® Digital Electroencephalography from Compumedics Neuroscan was used for EEG recording.
- Quick-Cap Electrode System® from Compumedics Neuroscan: small, medium, and large size were used for electrode placement.

Eye-tracking recording:

- Eyelink® 1000 from SR-Research, was used for eye movement recording.
- Chin rest was used to minimize head movements during the tasks.

Stimuli:

- From the NimStim Set (Tottenham et Al., 2009), a total of 20 faces (10 women and 10 men) from the calm and neutral subset were selected. The rest of stimuli were produced, as part of doctoral thesis, and are described in the methodology section.

Standard-calorie food:

- Glucerna®: every participant received a Glucerna® bottle (237 ml equivalent to 220 kcal), as a standard-calorie food.

Data process and analysis:

- EEGLab 14.1.1 and ERPLab 6.1.4 for MATLAB R2015a®
- ExGUtils 3.0, Numpy 1.15.4 for Python(x,y) version 2.7.10.0
- SPSS® 15.0.1
- LibreOffice Calc from LibreOffice 6.1.1.2 (x64)

METHODOLOGY

RESEARCH DESIGN:

Given the lack of experimental data about the presence of attentional bias for food cues in patients after bariatric surgery, the first steps must focus on the generation of valid tasks, and the characterization of the attentional bias. In order to fulfill that aim, this thesis is a quantitative study, with a descriptive approach.

WORDS OF FOOD-MODIFIED STROOP TASK (in Supplements: S1 and S2):

In preparation for the food-modified Stroop task, a list of appetizing and diet food words was generated. A search of these words was carried out in the Frequency List of Words of the Spanish of Chile (LIFCACH) version 1.0 and then 2.0 (Sadowsky et al., 2004). The appetizing words and the diet words were paired according to the frequency of use, length of the word (letters and syllables), presence of plural and singular words. In this way, a preliminary set of food words were generated and the words that could not be paired were discarded. Following the same criteria, a list of twenty control words was generated, presenting the same frequency of use, length of the word, presence of singular and plural words, in order to have a set with three types of words: appetizing food words, diet words and control words.

To confirm that the three types of words belonged to semantically recognizable subsets, an online survey was conducted. In this survey, participants were asked to respond if the word

generated appetite if they associated it with a low-calorie diet, both or none of the above. We analyzed 87 surveys, 46 women, 41 men, age $M=23.64$ years, $SD=5.3$. The words that managed to come together in clearly distinguishable groups were selected (Figure S1, and Table S2).

FOOD-MODIFIED STROOP TASK:

The food-modified Stroop task was programmed in Presentation® version 14.4, by Neurobehavioral Systems® (<http://www.neurobs.com>). Presentation® software was used for stimuli presentation, response recording (from a gamepad) and sending marking codes through a parallel port to the EEG recording PC.

For the food modified Stroop task, each word was presented in colour at the centre of a black screen, and the participants were asked to respond, as quickly as possible, the colour in which the words appeared, by using gamepad buttons. In order to facilitate the use of the gamepad, each participant made 2 training blocks, the first with coloured circles and the second with a series of signs. To overcome the second training block, the participants had to correctly answer at least 90% of the training trials.

After the training trials, the food-modified Stroop task started. The word Set consisted of 60 words (20 appetizing words, 20 dietary words and 20 control words), and all the words were shown in the 4 possible colours (green, red, blue and yellow), the total number of trails for the food-modified Stroop task was 240 trials. Every trial consisted, of a word appearing at the centre of a black screen, the word was shown until a response is recorded, after that, the word disappears and an intertrial screen was shown for a random time between 300ms and 1000ms.

These 240 trials were presented in 3 blocks of 80 trials each, allowing rest between blocks (Fig.1).

To avoid the subsequent appearance of words in the same colour, or from the same subset, a pseudo-randomized sequence was generated, which would fulfil those conditions. This pseudo-randomized sequence was segmented into 3 files, one for each block of the recording. For each participant, at the beginning of the task, both the list and the initial trial were chosen randomly. All the participants, therefore, responded to the 240 trials, but in a different order.

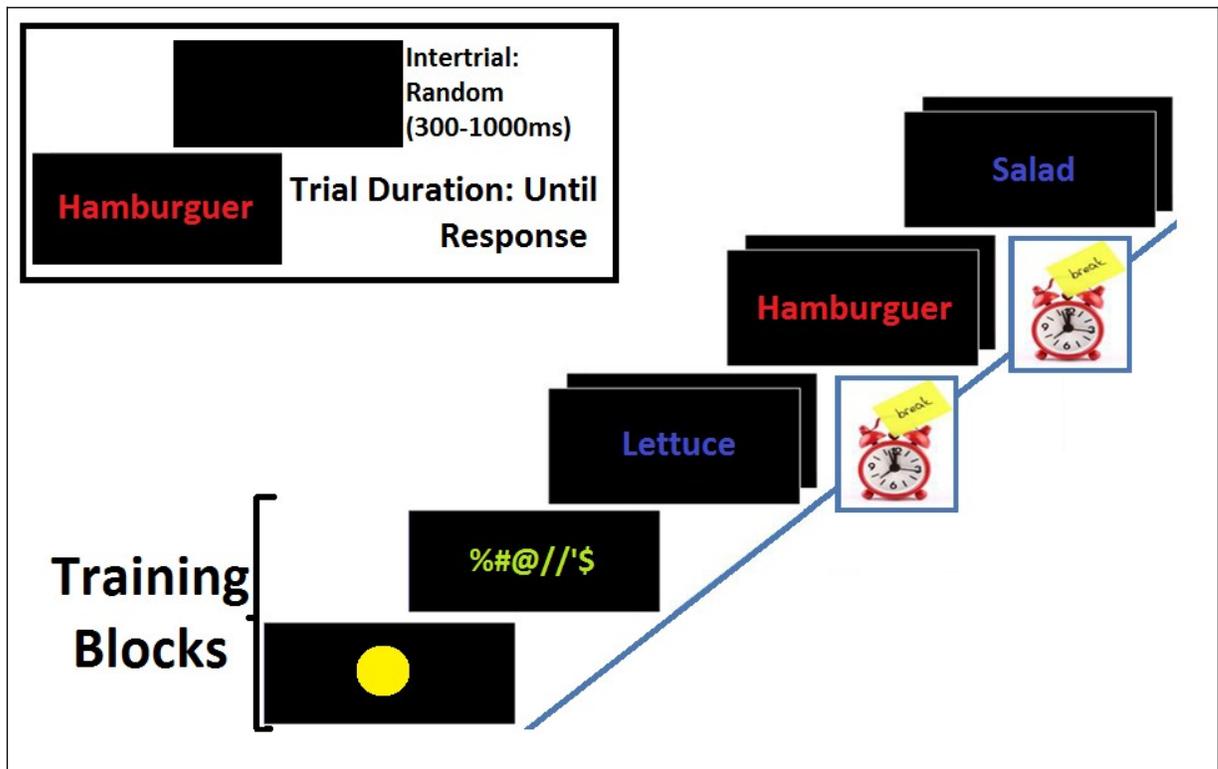


Figure 1: Food-modified Stroop task sequence. The task included two training blocks (dots and signs), and three experimental blocks, with 80 trials per block, with a total of 240 trials. Each trial consisted in a black screen and a word presented at the center in one of four colours (blue, green, red and yellow). The word was presented until response, followed by an intertrial with random duration (300-1000ms).

IMAGES FOR THE VISUAL TASK (in Supplements: S3, S4 and S5):

Twenty images of food available online were chosen, ten of them with appetizing foods (5 salty and 5 sweet) and the other ten with food associated with diet (5 salty and 5 sweet). An online survey was conducted to estimate whether the selected stimuli corresponded to the assigned food groups. The participants were asked to respond if the images seemed attractive if they were associated with a low-calorie diet, both or none of the previous ones. We analyzed 100 surveys, 63 women and 37 men, age $M=23.5$, $SD=6.3$. So that all the images presented similar lighting conditions and the same level of resolution, once the stimuli were selected, the images were reproduced with a Fujifilm FinePix F750EXR digital camera, in the same scenario and conditions.

As mentioned in the materials section, 20 faces of the NimStim Set were used (Tottenham et Al, 2009). From the NimStim Set, faces of 10 men and 10 women were selected in a calm or neutral condition, in order to avoid the emotional component of facial expressions. In addition, faces that could be frequent to see in the national context were chosen, to avoid the salience of an infrequent face.

To control the factors that could generate differences in the physical characteristics of the visual stimuli, a digital edition of every image was performed, in order to balance the number of pixels and the relative luminance. For this purpose, the images were edited using the GNU Image Manipulation Program 2.8.8, in conjunction with the Python Imaging Library 1.1.7 module used in Python (x,y) version 2.7.5.2. The relative luminance was calculated according to the formula: $Y = 0,2126 * R + 0,7152 * G + 0,0722 * B$. In this formula Y represents the relative luminance; and R, G and B, represents values for red, green and blue, in the additive

RGB colour model. This formula allows to calculate the relative luminance of every pixel in the digital image, and after that, estimate the relative luminance of the whole image.

With these stimuli, we generate pairs of images for the visual task: appetizing food versus faces, diet meals versus faces and appetizing food versus diet food. The food images used are shown in S4 and the selected faces from the NimStim set are shown in S5 (due to author's restrictions, only part of the faces can be shown in publications).

VISUAL TASK:

This task was generated, in order to record eye-tracking data for stimuli that usually compete for our visual attention during the periods of food intake, that is, the food stimuli and the faces of the people with whom we eat.

The visual task was programmed using Presentation® software version 14.4, from Neurobehavioral Systems® (<http://www.neurobs.com>). Presentation® was used to control the presentation of the stimuli, responses recording (from a gamepad) and sending trigger and marking signals through an optic fiber interface with the computer in charge of eye-tracking signal recording.

The visual task consists of 120 trials, presented in 2 blocks of 60 trials, with a break between blocks. Each trial consists of the initial presentation of a fixation cross (random duration 500-1000ms), the appearance of a pair of images of food and faces (random duration 1500-2000ms), and finally the appearance of 1 square, accompanied by 5 distractors (Fig.2). The instruction given to the participants consisted in looking at the cross of initial fixation, while the images (food and faces) could be seen freely, and when the last screen appeared, they had

to visually search the square and respond (through the gamepad) if the square had been presented to the right or left of the screen. The data used for analysis, is obtain exclusively from the free viewing part, the target screen was added in order to maintain the participant engaged in the task.

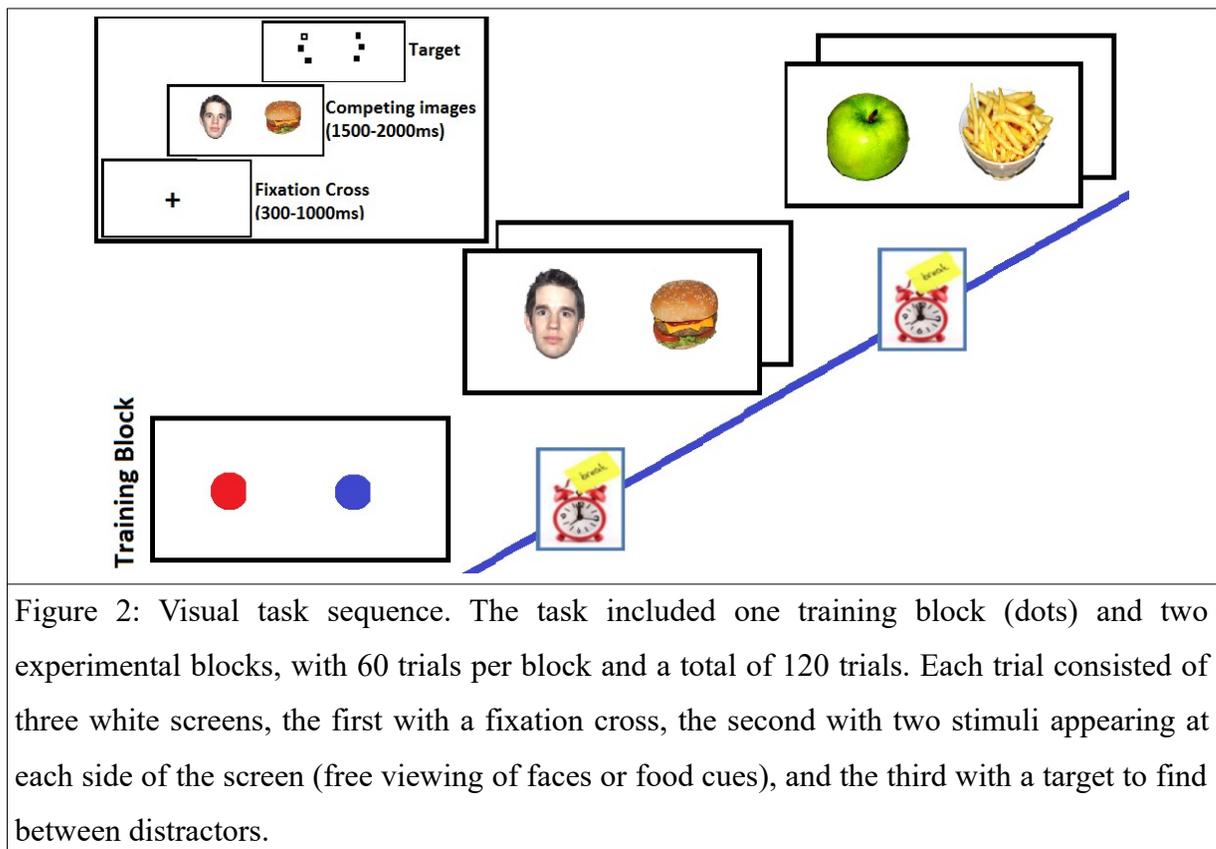


Figure 2: Visual task sequence. The task included one training block (dots) and two experimental blocks, with 60 trials per block and a total of 120 trials. Each trial consisted of three white screens, the first with a fixation cross, the second with two stimuli appearing at each side of the screen (free viewing of faces or food cues), and the third with a target to find between distractors.

PARTICIPANTS SELECTION AND RECORDING CONDITIONS:

Thirty volunteers were selected, all of them, Chilean women, native Spanish speakers, right-handed, without relevant medical or mental illnesses. Fifteen of them underwent sleeve gastrectomy, at least 1 year before their participation in the study, and they will be mentioned

as the bariatric group. The rest of the participants correspond to volunteers selected to match the age range and body mass index of the bariatric group.

Each of the participants was contacted by telephone to explain the purpose of the research, the risks and benefits of the study. If they were willing to participate, the exclusion criteria were evaluated, which included: being left-handed, presence of uncorrected visual pathology, dyschromatopsia, severe mental pathology, uncompensated medical illness, history of dermatological disease. All participants have at least twelve years of education.

Participants who voluntarily accepted to participate in the study and who did not present exclusion criteria were cited to the Cognitive Neuroscience Laboratory, Department of Psychiatry, of the Pontificia Universidad Católica de Chile. In a single day, the informed consent was read, reviewed and signed, the surveys were administered, and the study tasks were carried out. For this day they were asked to come with at least 4 hours of fasting, without makeup, with hair washed with shampoo, without the use of balm or conditioner.

To control the level of appetite as an affecting factor of attentional bias, all participants received a standard food before registration (described in the materials section). In order to facilitate the collection of data, the surveys were answered digitally in a computer arranged in the laboratory.

VISUAL ANALOGUE SCALE:

In order to evaluate some factors that could alter the answers, 6 subjective aspects were explored: level of fatigue, drowsiness, appetite, satiety, anxiety and mood. To do this, the participants were asked to respond on a Visual Analogue Scale. This evaluation was done

before and after the task of food-modified Stroop task. The same scale was used to answer the level of craving for different food, before and after the food-modified Stroop task.

EEG PROCEDURES:

EEG signal acquisition: Before EEG recording, the contact areas of the electrodes were prepared, in order to lower the local impedance. Mechanical local cleaning with alcohol and Nuprep® was carried out in specific areas. A Quik-Cap® was used for the 40 electrodes placement, according to the 10-20 system. Electro-Gel® was used in the contact area of each electrode, in order to lower the impedance. In order to minimize the electromagnetic noise, EEG recording was performed inside a Faraday cage. EEG signals were recorded using a NeuroScan® digital electroencephalograph with high-resolution NuAmps® amplifiers. During EEG recording the impedance was kept below 5 k Ω . The sampling rate during acquisition was 1000Hz. All electrodes were referenced to CPz during acquisition but for off-line analysis were re-referenced the averages mastoids. Additional electrodes were placed for electro-oculogram recording.

EEG pre-processing: For offline processing of EEG signals, ERPLAB 6.1.4 and EEGLAB 14.1.1 were used for Matlab R2015a®. All electrodes were re-referenced to the average mastoids, and the sampling rate was modified to 500Hz. A Butterworth IIR pass-high filter was used, 0.1Hz and low-pass 30Hz. Subsequently, the EEG record was divided into epochs, including the 200ms prior to the occurrence of the stimulus, up to the following 1000ms. An Independent Component Analysis (ICA) was performed to eliminate blinking, eye movements, muscle activity or another signal that did not correspond to neuronal activity. An artefact

detection was performed through a Moving Window Peak-to-Peak Function (ERPLAB), to eliminate the Trials that presented variations greater than 100mV. The average of rejected trials for the bariatric group was 1 (SD=1.36) and for the control group 0.8 (SD=1.25).

ERP processing: Only trials with correct answers were selected, and trials with artefacts were ruled out. The selected trials were grouped by type of stimulus and the signals were averaged for the generation of an ERP signal. This procedure was performed for each subject, and then the ERP signals of bariatric group and control group were averaged to generate a Grand ERP for each group. For ERP categorization, a visual inspection was used, analyzing the positive and negative deflections of the ERP signal. Our hypothesis included a P3 analysis, however, no P3 could be characterized in the visual inspection; and in order to expand the analysis other ERPs were added. For the subsequent statistical analysis, the individual latency and amplitude data of the following ERPs were extracted: N1 (local peak 100-140 ms on F3, Fz, F4, FC3, FCz, FC4, C3, Cz and C4), P1 (local peak 130-180 ms), N400 (mean voltage value 390-410ms on CP3, CPz, CP4, P3, Pz and P4), N450 (local peak 500-560 ms on CP3, CPz, CP4, P3, Pz and P4) and LPP (mean voltage value 800-1000 ms on Pz, PO1, Oz and PO2).

EYE-TRACKING RECORDING AND PROCEDURES:

For eye-tracking recording EyeLink 1000 was used, for recognition and recording of saccades, fixations, and pupillary area. Details about EyeLink 1000 can be found in http://www.sr-research.com/EL_1000.html

Following a similar approach used by Castellanos et al. (2009), 2 visual indexes were generated: a) Direction bias and b) Duration bias. For Direction bias, we select the first

fixation, and for Duration bias, we select every fixation and calculate the time spent on each image.

STATISTIC METHODS:

Most of the statistical analyses were performed on SPSS® version 15.0.1. Depending on the type of analysis, different statistical methods were used, including t-test for independent samples, factorial ANOVA, repeated measure ANOVA, and ANCOVA. For post hoc analysis the Bonferroni correction was implemented. If a significant interaction was found in the ANOVA or ANCOVA test, we performed a Simple Effect test, in order to characterize the interactions (<https://www.ibm.com/support/pages/significant-interaction-anova-how-obtain-simple-effects-test>).

RESULTS

PARTICIPANTS CHARACTERISTICS:

The bariatric group included 15 women, with an average age of 34 years (SD=6.84), with a current BMI of 25.34 kg/m² (SD=3.3), and a mean time since sleeve gastrectomy of 2.1 years (SD=1). The control group consists of 15 women, with an average age of 31.47 years (SD=7.75), and a current BMI of 23.99kg/m² (SD=2.66). The t-test for independent samples showed no significant difference between groups on age, $t(28)=.950$, $p=.35$, and current BMI, $t(28)=1.275$, $p=.213$.

The data of higher and lower BMI in life showed that the bariatric group had a maximum BMI of 36.9kg/m² (SD=6.42), a minimum BMI of 23.27kg/m² (SD=3.57) and a delta of BMI (higher-lower) of 13.63kg/m² (SD=5.). The control group had a maximum BMI of 25.57kg/m² (SD=3.34), a minimum BMI of 20.88kg/m² (SD=2.21) and a delta of IMC (higher-lower) of 4.34kg/m² (SD=2.24). The t-test for independent samples showed significant differences between groups, for higher BMI in life, $t(28)=6.068$, $p <.001$, lower BMI in life, $t(28) =2.206$, $p=.036$, and delta BMI, $t(19.42) =6.561$, $p <.001$; all these variables were higher in the bariatric group.

The manual dominance inventory of Edinburgh showed that the participants of both groups could be considered right-handed, with a laterality index for the bariatric group of 83.3 (SD=16.22) and for the control group of 75.6 (SD=10.33). The t-test for independent samples showed no significant differences between the groups, $t(28)=1.54$, $p=.134$.

The data obtained with the DEBQ did not show significant differences between the groups in the values obtained for the emotional eating subscale (bariatric group: $M = 2.3$, $SD = 1.$, control group: $M = 2.05$, $SD = .68$; $t(28)=.80$, $p=.43$), external eating subscale (bariatric group: $M = 2.7$, $SD = .75$, control group: $M = 2.8$, $SD = .76$; $t(28) = - .483$, $p=.63$), or restrictive eating subscale (bariatric group: $M=2.7$, $SD=.90$, control group: $M = 2.67$, $SD = .83$; $t(28)=.105$, $p=. 917$).

In order to analyze the percentage of medications used by each group, a t-test for independent samples was performed. The use of medication is statistically higher in the bariatric group, compared to the control group (bariatric group: $M=2.53$, $SD=2.3$, control group: $M=.93$, $SD=.799$; $t(17.17)=2.49$, $p=.023$). However, after dismissing vitamin and mineral supplements, there was no difference between groups in the number of medications used (bariatric group: $M=1.27$, $SD=1.3$, control group: $M=.93$, $SD=.799$; $t(22.89)=.83$, $p=.415$). To explore the difference in vitamin use between groups, a t-test for independent samples was performed, showing significant difference in the use of vitamins between groups (bariatric group: $M=1.27$, $SD=1.49$, control group: $M=0$, $SD=0$; $t(14)=3.3$, $p=.005$).

	Bariatric Group	Control Group
N (Sex)	15 (Women)	15 (Women)
Mean Age (in years)	M=34, SD=6.8	M=31.5, SD=7.7
Years after Sleeve Gastrectomy	M=2.1, SD=1	-
Current BMI	M=25.3, SD=3.3	M=23.9, SD=2.7
Higher BMI in lifetime **	M=36.9, SD=6,4	M=25.6, SD=3.3
Lower BMI in lifetime *	M=23.3, SD=3,6	M=20.9, SD=2.2
Delta of BMI (Higher-Lower) **	M=13.63, SD=5	M=4.34, SD = 2.2
Laterality Index	M=83.3, SD=16.2	M=75.7, SD=10.3
DEBQ Emotional Eating Subscale	M=2.3, SD=1	M=2.1, SD=0.7
DEBQ External Eating Subscale	M=2.7, SD=0.7	M=2.8, SD=0.8
DEBQ Restrained Eating Subscale	M=2.7, SD=0.9	M=2.7, SD=0.8
Total medication *	M=2.53, SD=2.3	M=.93, SD=.799
Non-vitamin medication	M=1.27, SD=1.3	M=.93, SD=.799
Vitamin medication *	M=1.27, SD=1.49	M=0, SD=0
* p< .05; **p< .001		

FOOD-MODIFIED STROOP TASK:

Accuracy rate:

The accuracy rate of all participants was above 90%, and the t-test analysis for independent samples, showed no significant difference between groups in total accuracy rate (bariatric group: M=97.33, SD=2.58, control group: M=98.08, SD=1.27; $t(28)=-1.01$, $p=.32$). A 2 (group) x 3 (word type) ANOVA was performed in order to explore the effect of different cues on accuracy rates for each group. The interaction between word type and group was not significant ($F(1,28)=1.59$, $p=.22$), and there was no significant effect of word type on accuracy rates ($F(1,28)=.032$, $p=.86$).

Error rate:

The error rate of all participants was below 10%, and the t-test for independent samples showed no significant difference between groups in total error rates (bariatric group: $M=2.67$, $SD=2.58$, control group: $M= 1.92$, $SD=1.27$, $t(28)=1.01$, $p=.75$). A 2 (group) x 3 (word type) ANOVA was performed in order to explore the effect of different cues on error rates. The interaction between word type and group was not significant ($F(1, 28)=1.59$, $p=.22$), and there was no significant effect of word type on error rates ($F(1,28)=.032$, $p=.86$).

In order to analyze the effect of previous word on error rate, a 2 (group) x 3 (word type of previous trial) ANOVA was performed. We found no significant interaction between previous word type and group ($F(1,28)=.51$, $p=.48$), and no significant word type effect ($F(1,28)=.23$, $p=.64$).

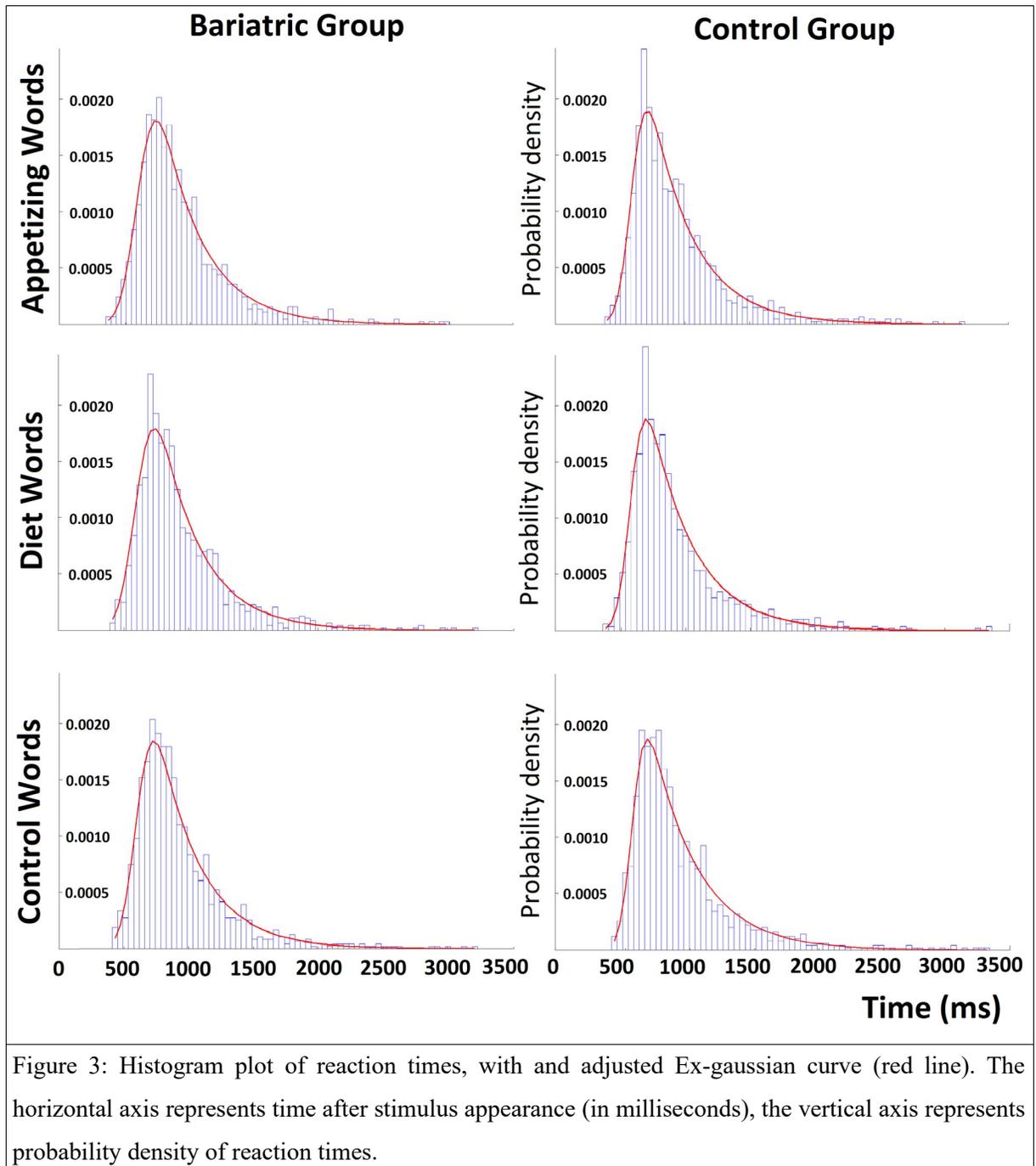
Reaction Times:

In order to test significant effects or interaction on RT, a mixed 2 (group) x 3 (word type) factorial ANOVA was used. This analysis showed no significant interactions between groups and reaction times for trials with appetizing words (bariatric group $M = 893.91$, $SE = 169.79$, control group $M = 891.6$, $SD = 208.88$), diet words (bariatric group $M = 884.78$, $SD = 181.04$, control group $M = 873.31$, $SD = 205.37$), or control words (bariatric group $M = 885.87$, $SD = 173.68$, control group $M = 884.60$, $SD = 219.29$).

Ex-gaussian:

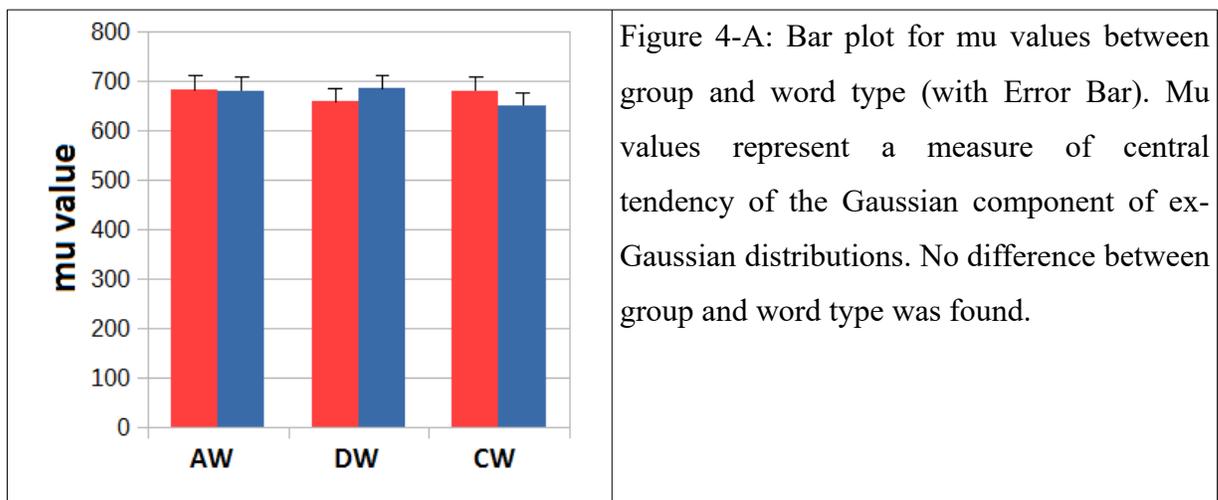
The analyzes usually performed at the reaction times have focused on the mean comparisons, assuming that they have a normal or Gaussian distribution. However, late responses end up generating a tail to the right, which resembles a distribution called exponential modified Gaussian or ex-Gaussian. Usually, to avoid the effect of these extreme values, the extreme reaction times are usually eliminated, thus approaching, even more, the normal distribution, however, the late responses may also reflect relevant information that could be analyzed. As an example, the normalized histograms of the response times from the bariatric group and the control group are shown in figure 3.

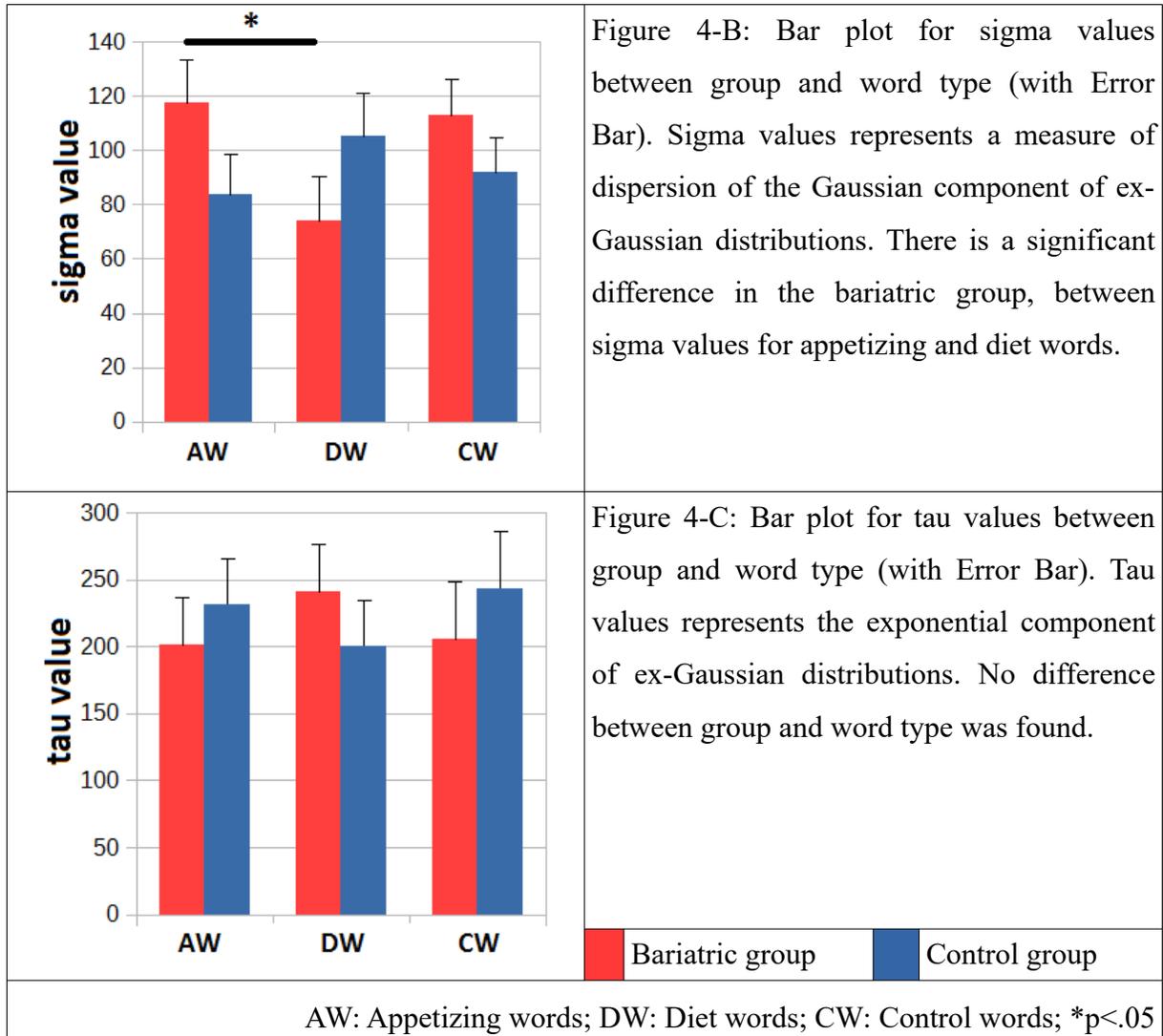
If we assume that the distribution of response times are better suited to the ex-Gaussian distribution, it is not absolutely necessary to eliminate these extreme data, and we can perform alternative analyzes. In fact, the analysis of the response time as an ex-Gaussian allows obtaining 3 values: μ , σ and τ . These values represent the components of this distribution, that is, the mean of the normal distribution (μ), the standard deviation of the normal distribution (σ) and the exponential component (τ).



Using the ExGUtils 3.0 tool for Python (x,y) the mu, sigma and tau data were extracted for each participant. These data were analyzed statistically using SPSS 15.0.1. In a 2 (group) x3

(word type) factorial ANOVA for mu values no interaction was found between groups and stimulus type, $F(2,27) = 2.75$, $p = .073$ (Fig.4-A). In a 2 (group) x 3 (word type) factorial ANOVA for the sigma data, the multivariate contrast showed near to significant interaction between group and stimulus type $F(2,26) = 3.31$, $p = .052$, $\eta^2 = .2$, and the intra-subject analyzes showed a significant interaction between groups and stimulus type, $F(2,27) = 3.49$, $p = .037$, $\eta^2 = .12$. The simple effect analysis showed a significant difference in sigma values, comparing appetizing and diet stimuli, but only in the bariatric group, $F(2,26) = 2.995$, $p = .024$ (Fig.4-B). The 2 (group) x3 (word type) factorial ANOVA for the tau data, showed no significant differences in the interaction group with type of stimulus, $F(2,27) = 2.472$, $p = .094$ (Fig.4-C).





ERP RESULTS:

N1: for N1 amplitude analysis a 2x3x3x3 factorial ANOVA was performed, including group (2), type of stimulus (3), location of electrodes from anterior to posterior (3) and locations from left to right (3). No interaction was statistically significant, however, the effect of laterality was significant, $F(2,27) = 5.27, p = .008$. The post hoc analysis with the Bonferroni correction showed a significant difference of the left electrodes, compared with the midline electrodes ($F(2,27) = 4.79, p = .033$), and with the right electrodes ($F(2,27) = 4.79, p = .027$).

The simple effect analysis showed a significant difference between the bariatric group and the control group, only for the diet stimuli, with higher amplitude of N1 for the control group in the electrodes F3 ($F(1,28) = 5.73, p=.024$), Fz ($F(1, 28) = 4.7, p=.039$), F4 ($F(1,28) = 6.61, p=.016$), FC3 ($F(1,28) = 6.65, p=.04$), FCz ($F(1,28) = 6.45, p=.017$), FC4 ($F(1,28) = 5.98, p=.021$), Cz ($F(1,28) = 5.91, p=.02$), and C4 ($F(1,28) = 6.77, p=.015$, Fig.5)

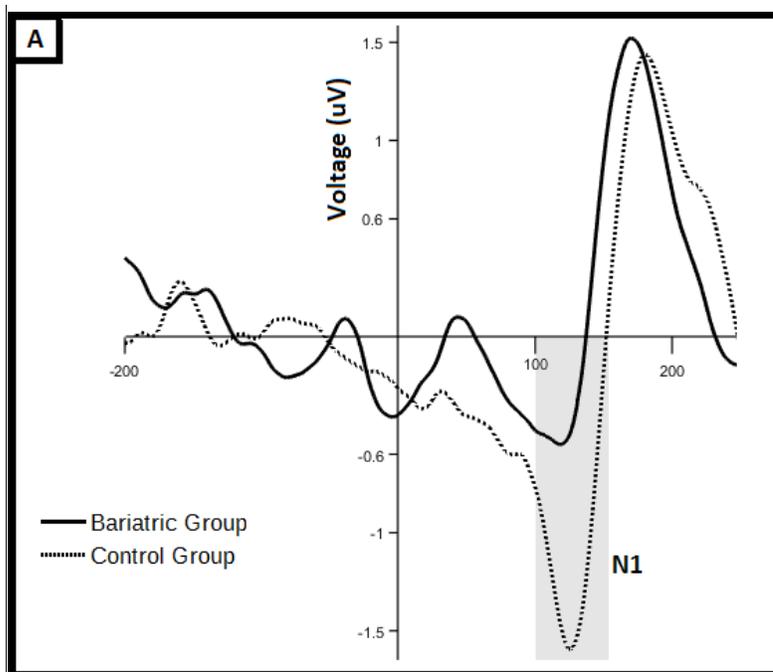


Figure 5-A: N1 for diet words in C4 electrode, between bariatric group (continuous line) and control (dashed line). The gray area represents the time window between 100-140ms after stimulus presentation.

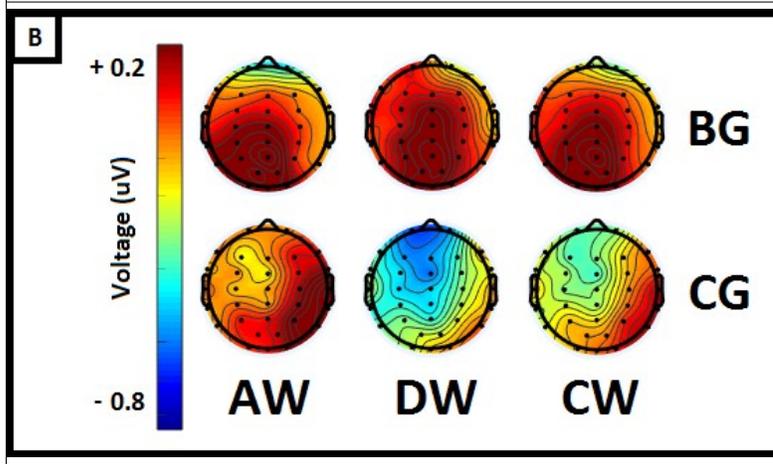


Figure 5-B: Scalp map of N1 between group and word type (mean voltage value for each electrode in a time window between 100 and 140ms). The control group showed a frontal negativity after diet word presentation.

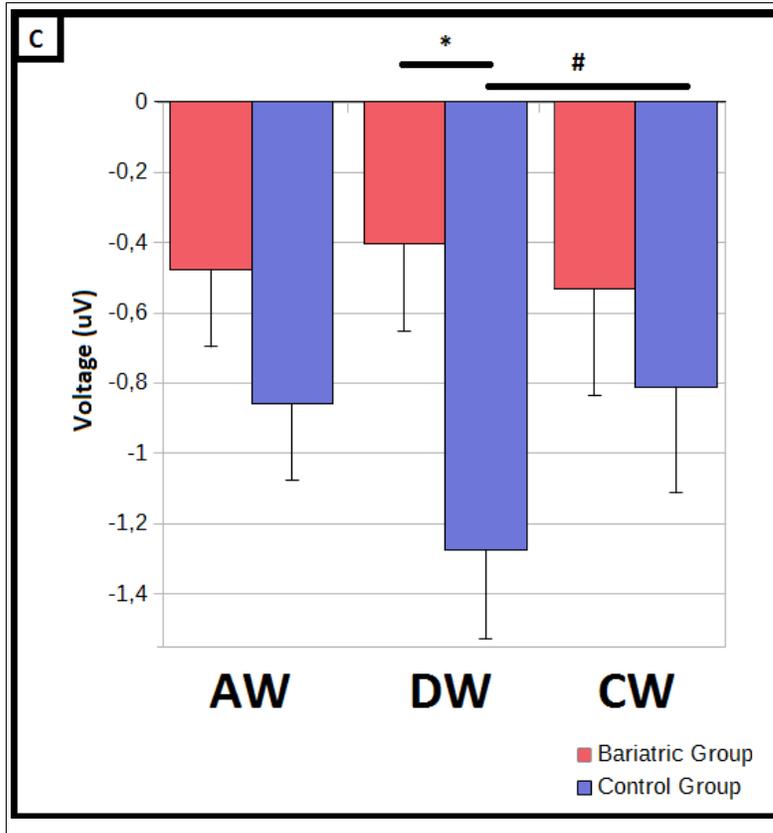


Figure 5-C: Bar plot of mean amplitude of N1 for each group and stimulus type (local peak value in the time window 100-140ms). The control group have an increased amplitude in N1 for diet words, compared to control words (#). A significant between group difference is shown (*), with increased amplitude of N1 for control group, compared to bariatric group.

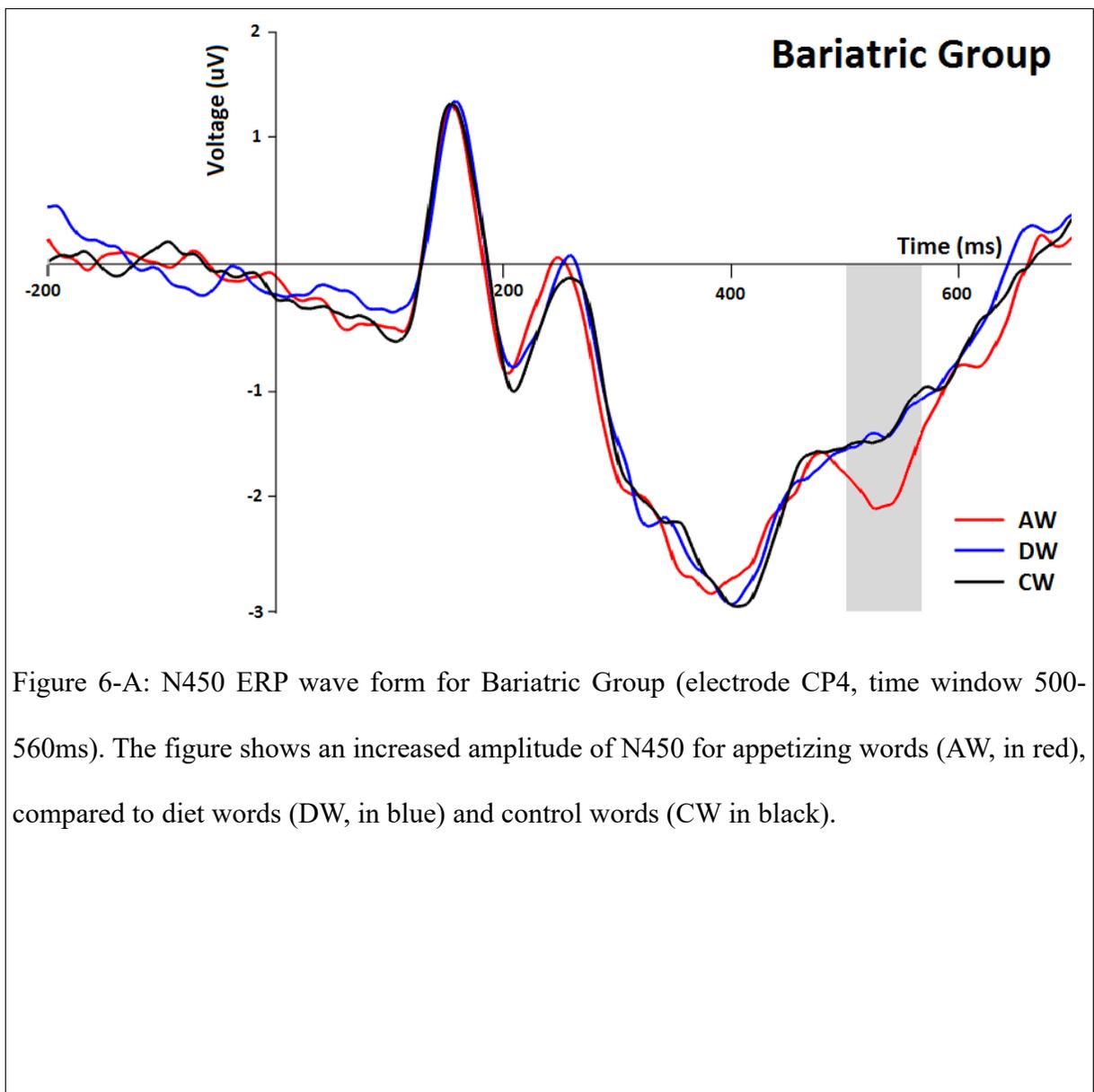
P1: the analysis for the P1 latency was made through a 2x3x2x2 factorial ANOVA, including the groups (2), the type of stimulus (3), anterior vs posterior location (2) lateral electrode location (2). The analysis did not show an interaction of the factors, however, the post hoc analysis with the Bonferroni correction showed a significant difference between groups, $F(1,28) = 5.35, p = .028$. In the simple effect analysis, a significant difference was found between groups, but only in control words, $F(1,28) = 7.96, p = .009$. The electrodes that showed significant differences for groups in the P1 latency were: PO1 ($F(1,28) = 6.053, p = .02$) and PO2 ($F(1,28) = 5.77, p = .023$). In the simple effect analysis a significant difference in the latency of P1 between the appetizing stimuli and the control words in the electrode O1 ($F(2,27) = 2.84, p = .038$), and O2 ($F(2,27) = 2.88, p = .043$), in addition to a significant

difference between diet and controls words in the electrode O2 ($F(2,27) = 2.88, p=.035$). For P1 amplitude analysis a $2 \times 3 \times 4$ ANOVA was performed, for the group (2), type of stimulus (3), and electrodes (4). The analysis showed a significant interaction between group and stimulus, $F(2,27) = 6.14, p=.038$. The post hoc analysis showed no significant differences between groups or between stimuli.

N400: the amplitude of N4 was analyzed with a $2 \times 3 \times 6$ factorial ANOVA, for the group (2), stimulus (3) and electrode (6). In this analysis, a significant interaction between group, stimulus and electrode was observed, $F(1,28)=1.953, p=.039$. The post hoc analysis using the Bonferroni correction, showed no difference in group or stimulus type.

N450: the N450 amplitude was analyzed by a $2 \times 3 \times 2 \times 3$ factorial ANOVA, for the group (2), stimulus (3), antero-posterior distribution (2), and lateral distribution of the electrodes (3). The analysis showed an interaction between the group and the antero-posterior location of the electrodes, $F(2,28) = 4.6, p=.041$. The post hoc analysis, with the Bonferroni correction, showed a significant difference between the appetizing stimuli and the control words, $F(2,27) = 6.423, p=.005$. The simple effect analysis showed a significant difference in the control group, between appetizing and controls words ($F(2,27) = 7.58, p=.003$), as well as between the words of diet and controls ($F(2,27)=7.58, p=.005$). The bariatric group presented a significant difference between the appetizing stimuli and control words in the electrode P4 ($F(2,27) = 2.93, p=.021$). The control group presented a significant difference between the appetizing and control words in the CP3 electrode ($F(2,27)= 7.403, p=.004$), CPz ($F(2,27) = 6.66, p=.006$),

CP4 ($F(2,27) = 5.44, p=.008$), P3 ($F(2,27)=7.36, p=.006$), Pz ($F(2,27) = 8.23, p=.004$), P4 ($F(2,27) = 6.86, p=.004$), as well as for diet versus control words on CP3 ($F(2,27) = 7.403, p=.003$), CPz ($F(2,27)=6.66, p=.005$), CP4 ($F(2,27)=5.44, p=.018$), P3 ($F(2,27) = 7.36, p=.004$), Pz ($F(2,27)= 8.23, p=.0024$), P4 ($F(2,27)= 6.86, p=.015$). (Fig.6)



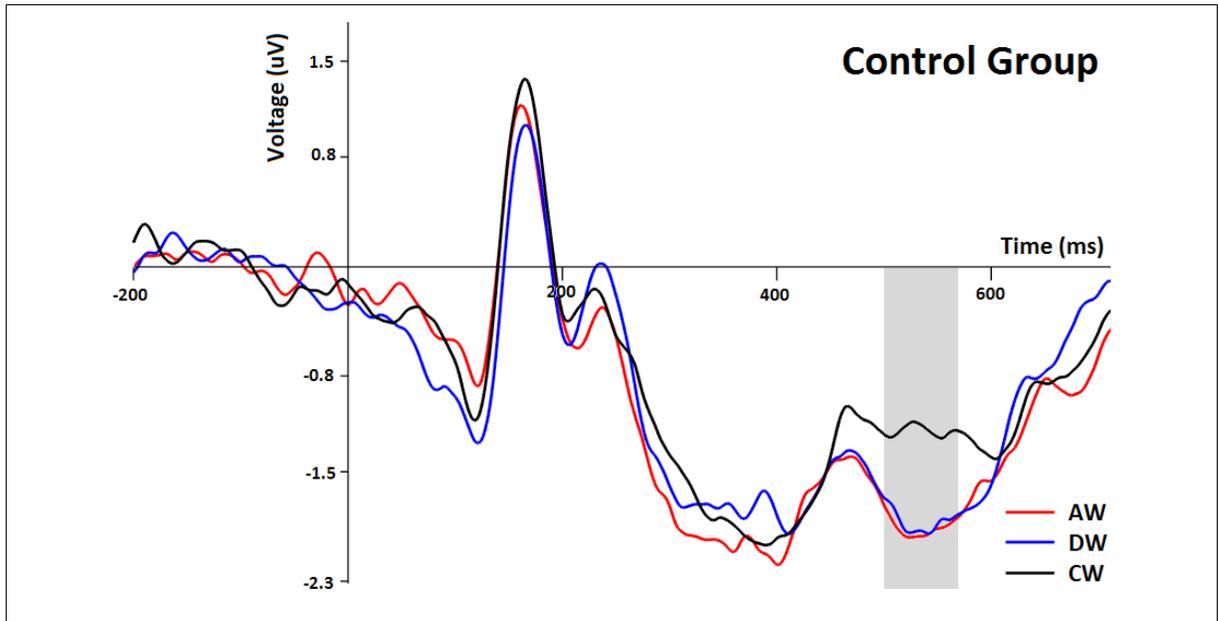


Figure 6-B: N450 ERP waveform for Control Group (electrode CP4, time window 500-560ms). The figure shows an increased amplitude of N450 for appetizing (AW, in red) and diet words (DW, in blue), compared to control words (CW in black).

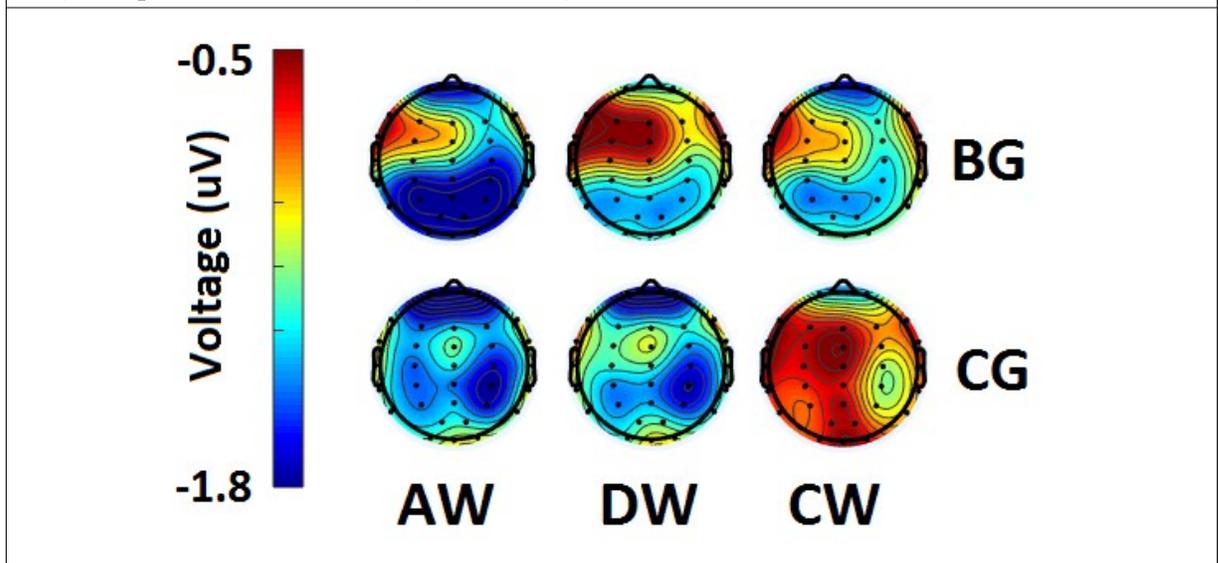
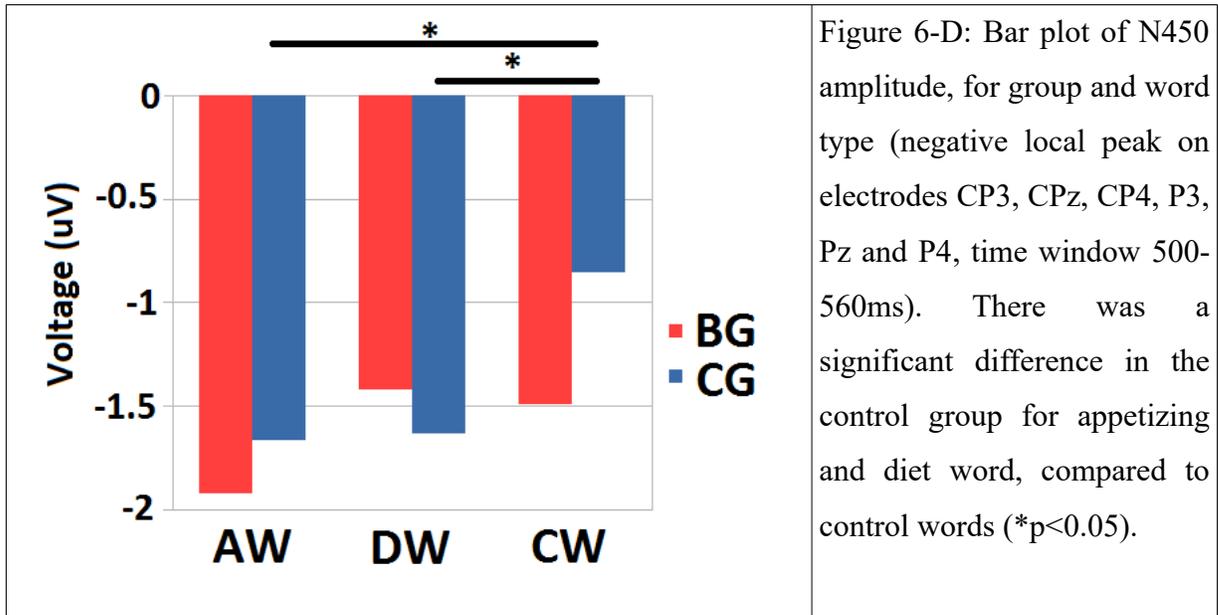


Figure 6-C: N450 Scalp map for group and word type (mean voltage in time window 500-560ms). In our data, N450 is seen as a posterior negativity, predominant on right electrodes, and in trials related to food.



LPP: the amplitude of LPP was analyzed using a 2x3x4 factorial ANOVA, including group (2), stimulus (3) and electrodes (4), showing a near to significant interaction between group and stimulus type, $F(2,27)=3.32$, $p=.051$. In the simple effect analysis, a significant difference between appetizing and control words was shown only in the bariatric group, $F(2,27)=5.227$, $p=.02$, as well as between diet words and control words, $F(2,27) = 5.227$, $p=.01$. Also in the simple effect analysis, showed a significant difference between groups on diet words, $F(1,28) = 4.92$, $p=.035$. On electrode PO2, there was a difference between bariatric group and control group on LPP amplitude for appetizing words ($F(1,28)=4.52, p=.043$), diet words ($F(1,28)=6.09$, $p=.02$), but not for control words ($F(2,28)=2.27, p=.143$). On the same electrode, we found a significant difference on LPP amplitude between appetizing words and control words ($F(2,27)=6.53$, $p=.011$), diet words and control words ($F(2,27)=6.53$, $p=.006$), only for the bariatric group. (Fig. 7)

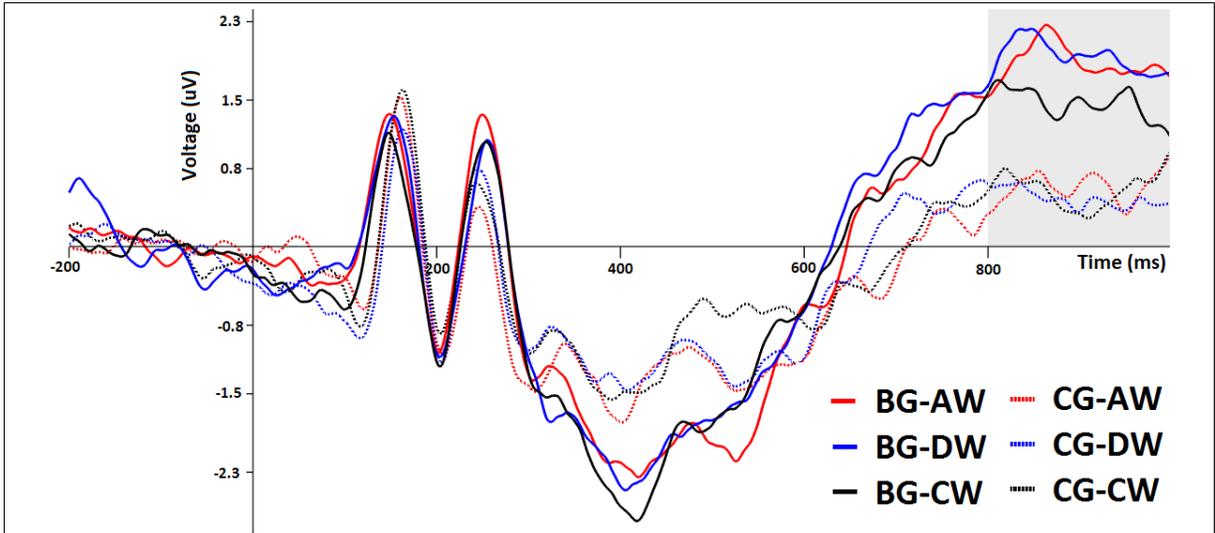


Figure 7-A: LPP ERP waveform for group and stimulus type (PO2 electrode). Bariatric group is shown in continuous line, and Control group in dashed line. Appetizing words is shown in red, Diet words in blue and control words in light black. LPP is seen as a positive deflection in the time window from 800-1000ms (grey rectangle), and our data showed an increased amplitude for bariatric group compared to control group, especially for appetizing and diet words.

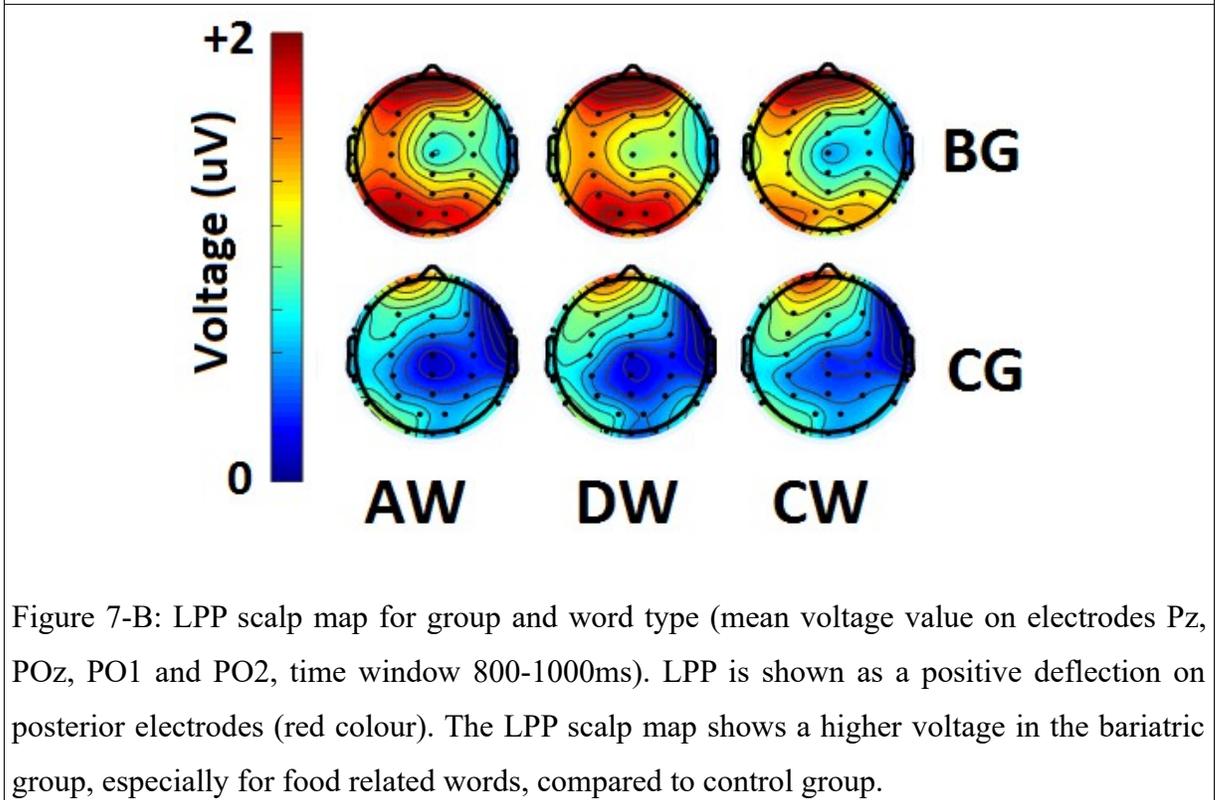


Figure 7-B: LPP scalp map for group and word type (mean voltage value on electrodes Pz, POz, PO1 and PO2, time window 800-1000ms). LPP is shown as a positive deflection on posterior electrodes (red colour). The LPP scalp map shows a higher voltage in the bariatric group, especially for food related words, compared to control group.

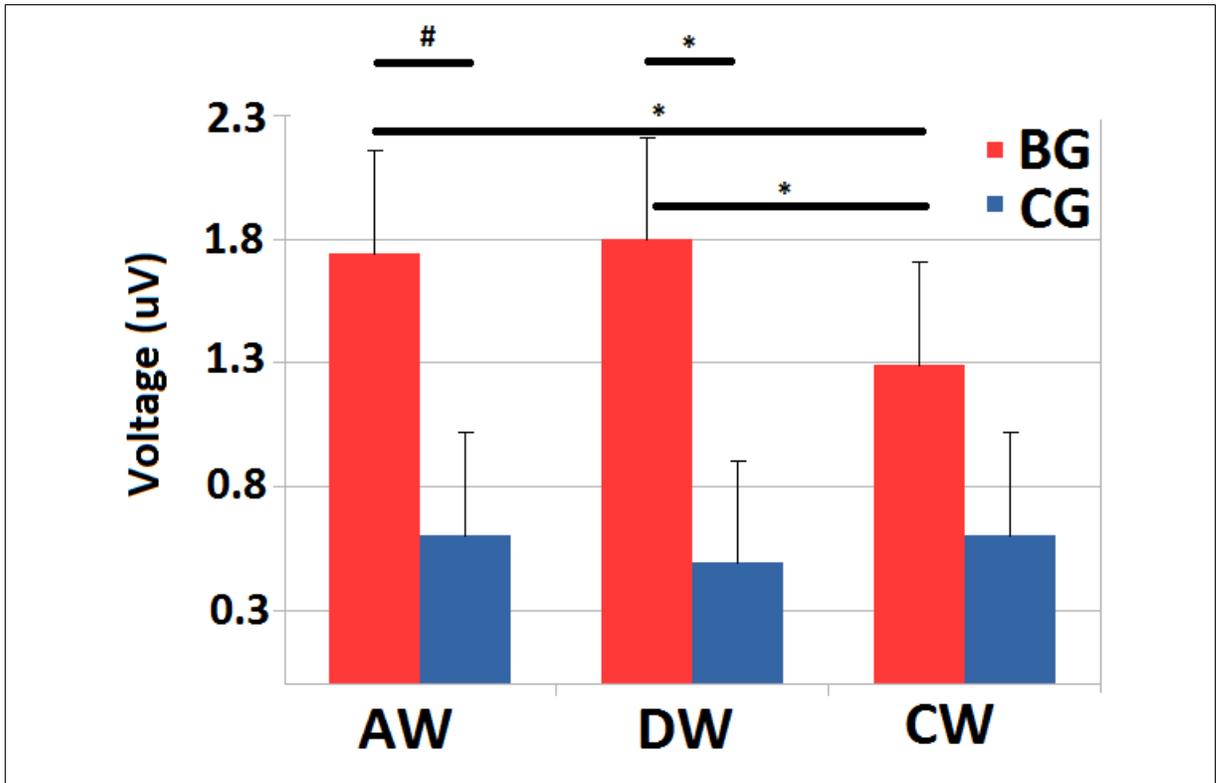


Figure 7-C: Bar plot of LPP amplitude (mean voltage value on electrodes Pz, POz, PO1 and PO2, time window 800-1000ms). Our data showed a significant increase in amplitude of LPP related to appetizing and diet words, compared to control words; and also a significant difference between groups only in diet words (* $p < .05$). A between group difference on appetizing words was only present on electrode PO2 (# $p < .05$).

	Bariatric Group		Control Group	AW: Appetizing words; DW: Diet words; CW: Control words
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In summary, appetizing words generates an increased N450 amplitude in both groups, compared with control words. Appetizing words, compared to the control words, produce increased N400 and LPP amplitude only in the BG. Diet words, compared to control words, produce higher LPP amplitude only in the BG, and increase N450 amplitude only in the CG. The main differences between groups are in N1 and LPP amplitudes. N1 amplitude for diet

words is increased in the CG, compared with the BG. Appetizing and diet words generate a higher LPP in the BG, compared to the CG.

Oculomotor task:

Direction and duration bias: The t-test analysis for direction and duration bias did not show any significant difference.

First Fixation: We performed a 2 (group) x 2 (stimulus type) ANCOVA on first fixations, using the number of trials per subject as a covariance factor. With this approach, in the post hoc analysis with the Bonferroni correction, we observed a significant difference in stimulus type, for diet images versus faces, $F(1,25)=17.16, p<.001$. In the simple effect analysis, we observed that this difference is only present in the BG ($F(1,25)=3.29, p=.001$), with predominant first fixations on faces (Fig.8-B). On trials with appetizing images versus faces, there was a significant difference in post hoc analysis with the Bonferroni correction for stimulus type ($F(1,25)=6.88, p=.015$). In the simple effect analysis, this difference was present only in the CG ($F(1,25)=4.37, p=.047$), with more fixation on faces (Fig.8-A).

Total Fixations: A 2 (group) x 3 (stimulus type) ANOVA was performed for the total number of fixations per trial. In the trials of appetizing versus diet images, we found a significant effect of stimulus type ($F(1,26)=33.34, p<.001$). In the post hoc analysis, using the Bonferroni correction, we found a significant difference between the type of stimulus, $F(1,26) = 33.34, p<.001$. The simple effect analysis showed that this significant difference is present in both groups (BG: $F(1,26)=11.49, p=.002$; CG: $F(1, 26)=22.81, p<.001$), with more fixations on diet images (Fig.8-F). In trials with appetizing images versus faces we found a significant effect of stimulus type, $F(1,26)=28.63, p<.001$. The post hoc analysis with the Bonferroni correction, showed a significant difference between stimulus type ($F(1,26)=28,63, p<.001$). The simple effect analysis showed that this difference was significant in both groups (BG: $F(1,26)=12.01, p=.002$; CG: $F(1,26)=16.83, p<.001$), with more fixations on faces (Fig.8-C).

Duration of fixation: A 2 (group) x 2 (stimulus type) factorial ANCOVA was performed including group and stimulus type, with the number of trials per subject as a covariance factor. In trials of appetizing versus diet images, there was a significant interaction between group and stimulus type, $F(1,25)=5.2, p=.031$. In the simple effect analysis, we found a significant difference between groups in the duration of fixation on appetizing images ($F(1,25)=6.64, p=.016$), with longer fixations in the BG (Fig.8-I). In trials with appetizing

images versus faces, the post hoc analysis showed a significant difference between stimulus type ($F(1,25)=7.04, p=.014$). The simple effect analysis showed that this difference is only significant in the BG ($F(1,25)=8.1, p=.009$), with longer fixations on faces (Fig.8-G). In trials with diet images versus faces, we found a significant effect of the stimulus type ($F(1,25)=8.9, p=.006$). The simple effect analysis showed a significant difference between groups only in the fixation on faces ($F(1,25)=4.99, p=.035$), with longer fixations in the BG (Fig.8-H).

In summary, first fixation data showed that diet images tend to be less attention engaging for BG, and appetizing images are less appealing for the CG, when a face is present. During the rest of the task, both groups tend to have less number of fixations on appetizing images, but there are differences in the duration of eye fixation. A significant difference between groups was found in trials of appetizing versus diet images, with the BG presenting higher duration of fixation on appetizing images, which is related to difficulties in disengaging attention.

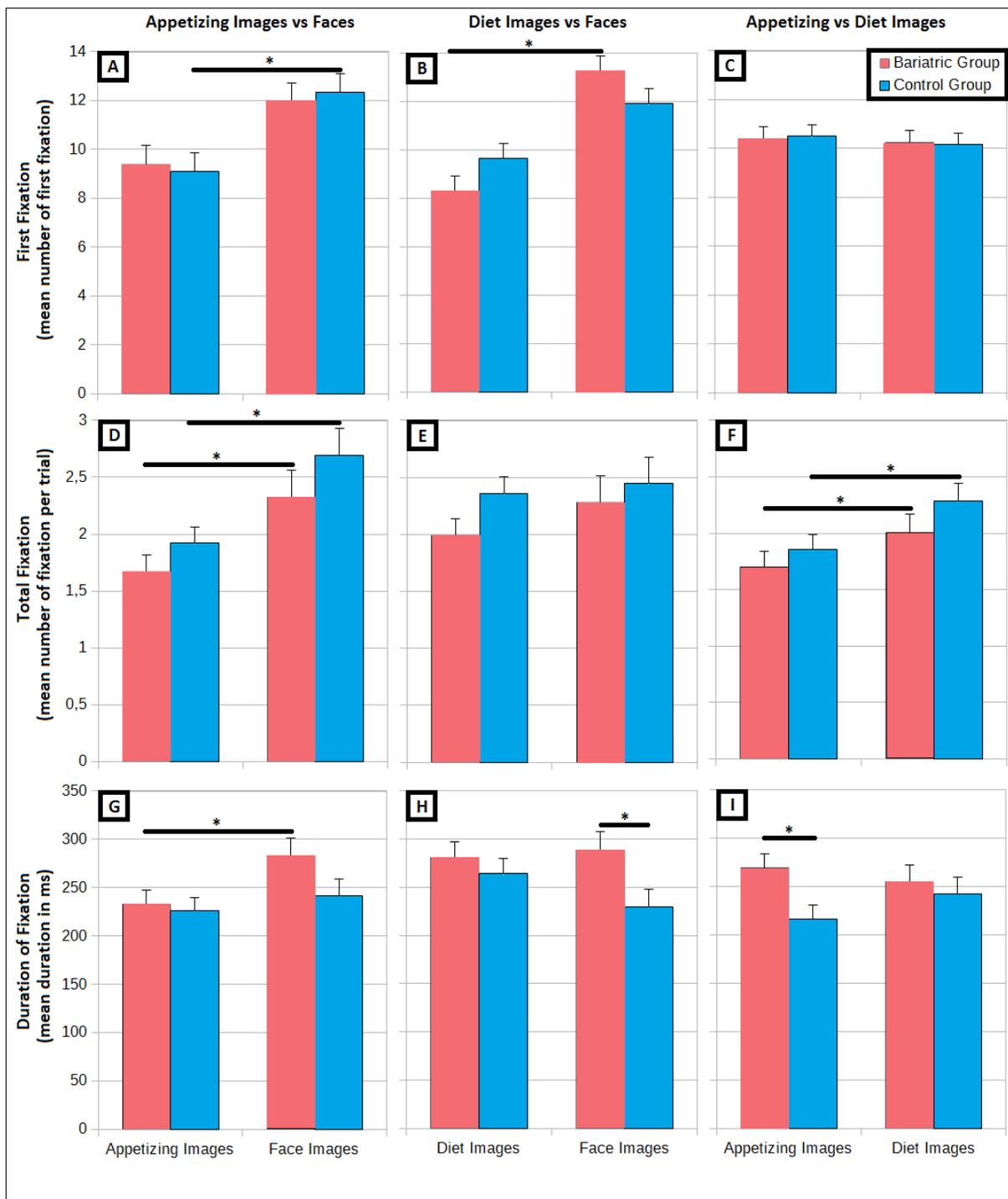
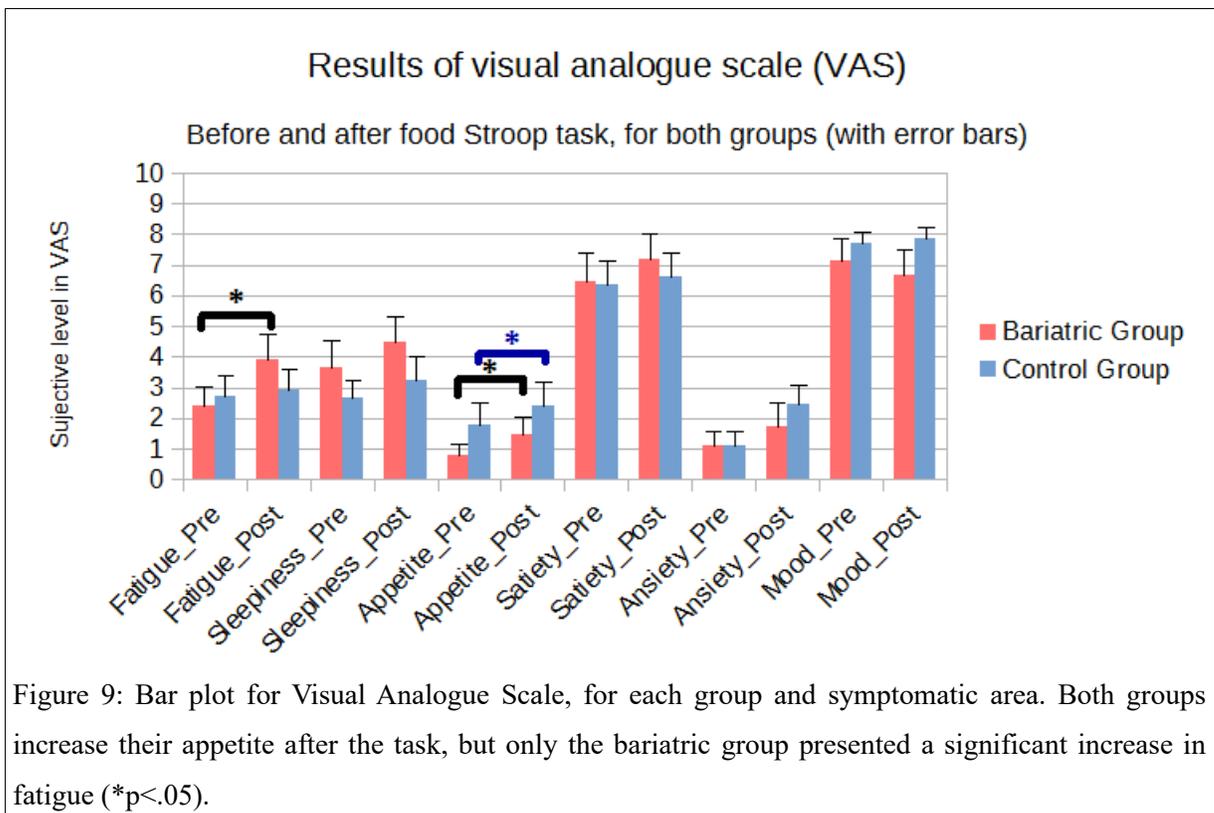


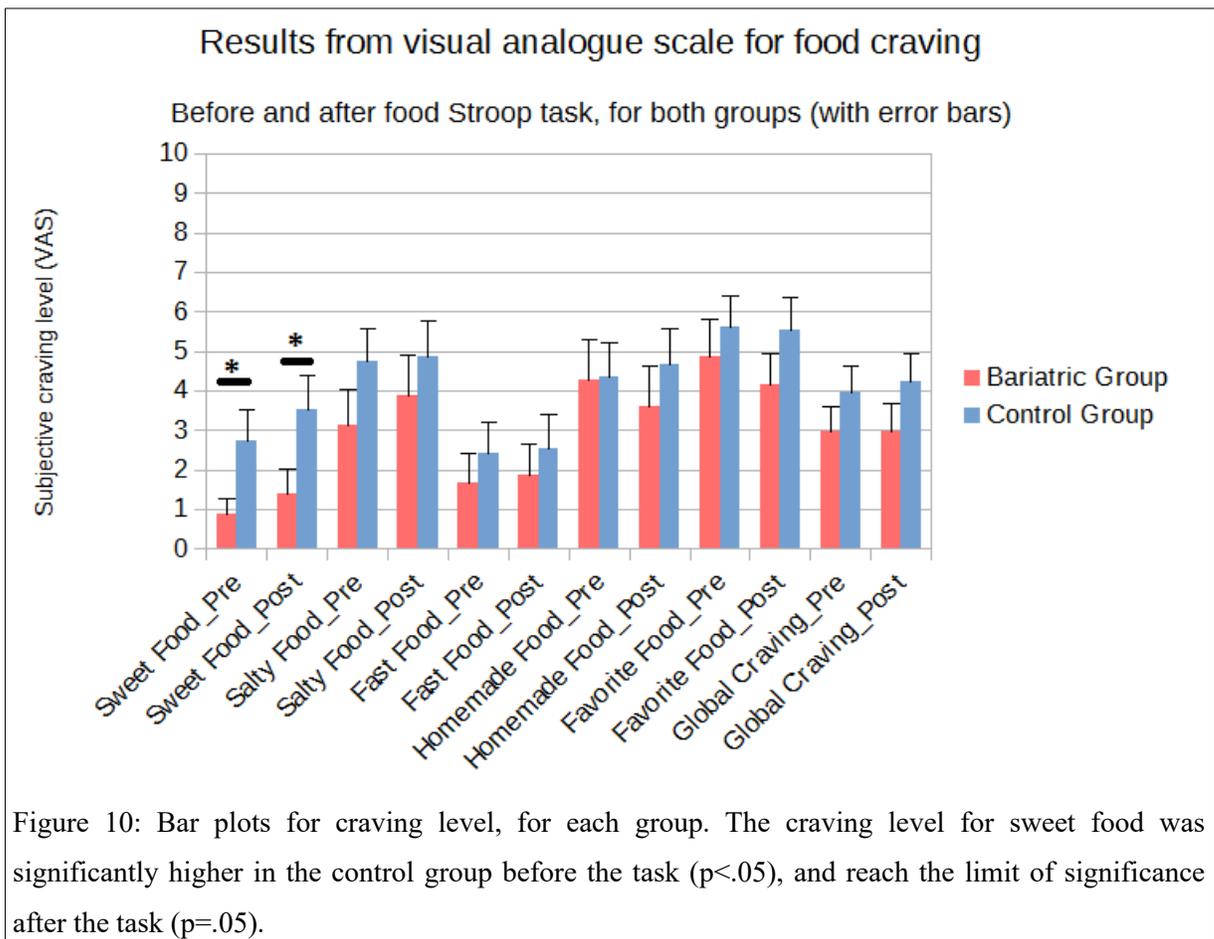
Figure 8: Bar plots for Eye Tracker results, for first fixation (A, B and C), total fixation (D, E and F) and duration of fixation (G, H and I), for each trial type, including appetizing images versus faces (A, D and G), diet images versus faces (B, E and H), and appetizing versus diet images (C, F and I). Bariatric group in red and control group in blue. * $p < .05$

VISUAL ANALOGUE SCALE:

In order to analyze the visual analogue scale results, a 2 (group) x 6 (symptom) x 2 (time) mixed factorial ANOVA was performed. This analysis showed that there was not group interaction with any symptomatic area, however, there was a significant effect of time, $F(1,28) = 6,52, p=.016$. The post hoc analysis using the Bonferroni correction showed a significant difference between time of application, $F(1,28) = 6,523, p=.016$. The simple effect analysis showed a significant difference in the fatigue level reported before and after the task, $F(1,28) = 6.58, p=.016$, being significantly higher after the task but only in the bariatric group. In addition, the appetite level increased in both groups (bariatric group: $F(1,28) = 6,45, p=.017$; control group: $F(1,28) = 5.23, p=.03$) (Fig.9).



The visual analogue scale was also used to assess the level of craving for specific foods, before and after the food-modified Stroop task. The data were analyzed with a 2 (group) x 6 (craving type) x 2 (time of application) mixed factorial ANOVA. This analysis showed no interaction between the variables, but a significant effect of craving type, $F(4,25) = 7.42$, $p < .001$. The simple effect analysis showed that the level of craving for sweet foods was significantly higher for the control group, compared to the bariatric group, $F(1,28) = 4.82$, $p = .037$. This difference was present before the experiment ($F(1,28) = 4.55$, $p = .042$), and reached the limit of statistical significance after finishing the task of food-modified Stroop task ($F(1,28) = 4.2$, $p = .05$). (Fig. 10)



DISCUSSION

To our knowledge, there is only one publication about attentional bias for food cues in a bariatric group (Giel et al. 2014). In that study, attentional bias was explored by using an eye-tracking, before and after bariatric surgery, finding a significant reduction of attentional bias for food at 6 months post-surgery, with no posterior follow up. The original design of our study, was prospective, with evaluation before and after bariatric surgery. The prospective design would allow the characterization of the attentional bias prior to surgery, and the evolution after the intervention. However, one of the most relevant difficulties after bariatric surgery is weight regain, and occurs in a long follow up. The weight regain usually starts after 18 to 24 months (Magro et al., 2018) and it has been suggested that the success of surgery should be evaluated at least 5 years after the intervention (Maciejewski et al., 2016). Sleeve gastrectomy have higher rates of weight regain, than other bariatric surgeries, with weight regain rates between 26.3-75.6% at 6 years (Lauti et al., 2016); and there is no effective treatment for weight regain after bariatric surgery (Maleckas et al, 2016). Every member of the bariatric group tested in our study, had 1 to 5 years of evolution after sleeve gastrectomy, which is a time period of high weight regain risk. Basically, this research focused on a high risk group, and explored specific behavioral and electrophysiological aspects that make them different to a control group; with the notion that, this difference could explain, or partially explain, the risk, and guide future studies.

Attentional bias for food cues have been described as a prognostic factor for weight changes. Calitri et al. (2010), in a behavioral study, which included a food-modified Stroop task, found that attentional bias for unhealthy food was related to an increase in BMI at 1 year of follow-up; and on the other hand, attentional bias for healthy food was associated to a decrease in BMI at the same period. Meule and Platte (2016), found that the interaction between a high attentional bias for high-caloric food and a high motor impulsivity predicted an increase in BMI at 6 months. In a fMRI study (Yokum et al., 2011), activation of lateral orbitofrontal cortex, during initial allocation of attention on appetizing food, correlates to an increase in BMI at 1 year of follow-up. Activation of the orbitofrontal cortex, have been linked to reward evaluation, and the lateral orbitofrontal cortex to subjective appetite level (Simon et al., 2017). In addition to the prognostic properties, modification of attentional bias for food have been recently studied. Jones et al. (2017), published a review about cognitive training as a treatment for overweight and obesity, including 32 study, and 10 of them focus exclusively on attentional bias modification. Attentional bias modification implies training the attention to move away from appetizing cues, to other stimulus (Jones et al., 2017). Each study showed a reduction of calories ingested at the laboratory, but the major critic of these studies is the short follow up (Jones et al., 2017), with only 1 open-label study showing reduction of binge eating and BMI at 3 months (Boutelle et al., 2016). Taken together, attentional bias is an interesting aspect to explore in patients with obesity, bariatric surgery candidates, and patients at risk of weight regain, given the possibility of predicting BMI changes and modification therapies. From our data, we could not find the emotional delay expected in the RT of appetizing words. Similarly, Nijs et al. (2010) did not find any difference between groups (overweight/obese

versus control) in the behavioral level, only in the physiological level. To improve our analysis, the implementation of an ex-Gaussian data processing for RT allows a better adjustment to the obtained data and minimizes the eliminated records (Dawson, 1988). In our analysis, we only found a significant difference in the bariatric group for the sigma values from highly caloric stimuli, when compared with diet foods. The implementation of this method could improve interpretations of reaction times data. The significant difference in sigma is coherence with previous reports of other semantic Stroop tasks, in which differences are described in mu and sigma, but not in tau (White et al., 2016). The difference in tau are observed in the classic Stroop task, and it is proposed that tau reflected interference in response preparation, but mu and sigma represent semantic interference (White et al., 2016). The finding that the bariatric group have higher sigma value for appetizing versus diet words, can be interpreted as a semantic effect, generating a higher variability of RT in this group.

It is interesting to mention the findings in early ERPs since we did not expect a group difference at this level. The amplitude of N1 has been associated with selective attention (Hillyard et al., 1998). The higher amplitude of N1 in the control group, specifically for diet words, may imply higher attention to these stimuli, which is lacking in the bariatric group, supporting the idea that these stimuli are unappealing to them. Calitri et al. (2010) evaluated the attentional bias towards healthy and unhealthy foods, and an attentional bias towards healthy food was associated with a decrease in BMI at one year of follow-up. In that sense, a smaller amplitude of N1 for diet stimuli could be related to lower attention to healthy food and therefore decrease the probability of healthy food selection.

On the other side, we analysed the later potentials, like the N450 and the LPP, both associated with emotional Stroop tasks (Imbir et al., 2017). The N450 has been described as negativity with a peak at 350 to 500ms, and fronto-central predominance (Imbir et al., 2017), however, it has also been registered in a more diffuse way (Imbir et al., 2018). The amplitude of N450 seems to increase according to the word valence, as well as in the presence of inconsistencies, or when detecting conflicts (Imbir et al., 2017). In this sense, it is interesting to analyze that, in both groups, we found a higher amplitude of this component for food stimuli.

LPP is a late component, and in the context of the emotional Stroop, it is thought to involve late processing of the words. In this sense, our data showed that only the bariatric group presents an increase in this component, for food stimuli. It is interesting that in drug users, Littel (2012), described that higher amplitudes on P3 and LPP, are associated with attentional bias, craving, risk of relapse and worst outcome. Taking together, it is possible that the bariatric group have extended processing of food words, which can increase the probability of eating in the short term.

As described by Castellanos (2009), we expected to find a direction and duration bias for appetizing stimuli, however, like Nijs et al. (2010), we did not find differences between the groups. With a different approach, we found a lower number of initial fixations on diet images versus faces, only in the bariatric group, which is compatible with the idea that these stimuli are less attentional-grabbing in this group. In the trials with appetizing and diet images, the

BG have a higher duration of fixation on appetizing images, which is compatible with difficulty in disengaging attention from these stimuli, when they compete with diet images. In the BG, the shorter duration of fixations on appetizing images when competing with faces is difficult to interpret, given that it could correspond to a strategy implemented by the subjects (Nijs et al., 2010), an avoiding reaction from appetizing images (Doolan et al., 2014), or a real decrease in attentional bias (Giel et al., 2014).

VAS data showed an increase in appetite in both groups after the task, however, only the bariatric group presented an increase in the level of fatigue. This is a difficult aspect to interpret, given that there are many factors involved, and fatigue is relatively frequent after bariatric surgery, usually associated with vitamin deficiencies (Richardson et al., 2009), and iron deficiencies (Broeke et al., 2013), among other nutritional deficiencies (Al-Jafar et al., 2018). Our study, did not include testing for nutritional deficiencies, and we did not have access to the clinical record of the bariatric group; but future studies must include this aspect, in order to explore nutritional confounding factors.

Taken together, these data support not only the idea of attentional bias for food cues after bariatric surgery but also, whole altered processing of food cues, from an early N1 to an LPP. With an increased attentional bias to appetizing words, a decreased attentional bias to diet words and images, a longer word processing for food words in general (LPP). Further studies, must focus on the specific contribution of these differences and how can be associated with clinically relevant aspects like weight regain risk.

CONCLUSION

Attention bias has been described in a wide variety of psychiatric pathologies, and have been associated with the appearance and maintenance of abnormal behaviour. It is possible to estimate the attentional bias with behavioural tasks, being able to objectively evaluate the presence of this bias, with tasks easily applicable in usual clinical practice. Attention bias has been associated with modifications in the ERPs, which allows studying the brain mechanisms involved. And attentional bias modification techniques are been tested and could be a clinical option in future years.

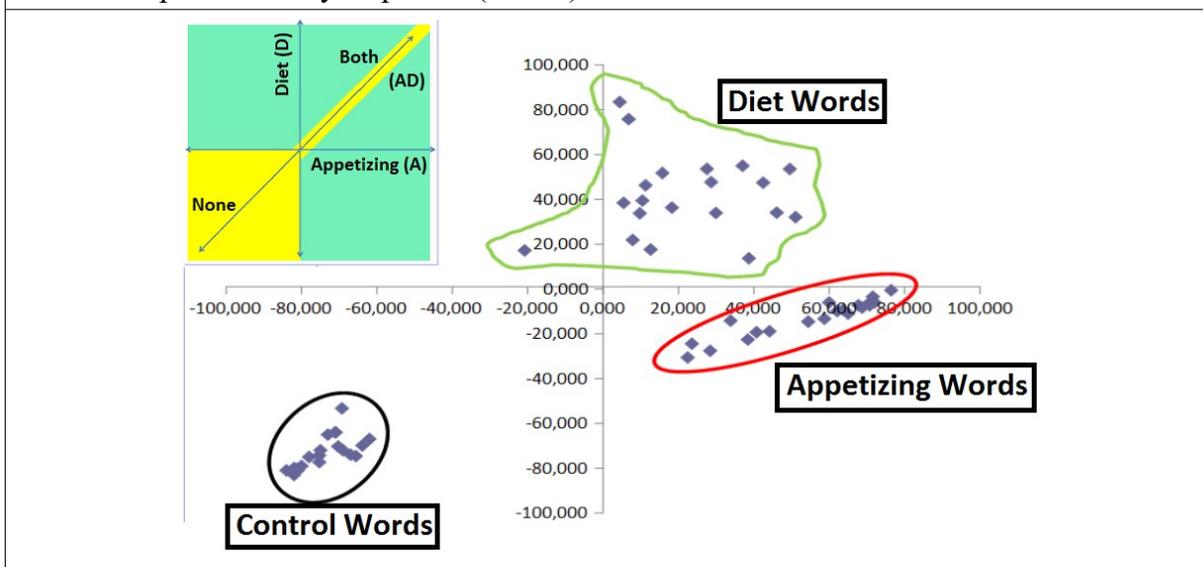
Our results showed that, after at least 1 year of sleeve gastrectomy, there is an increased attention bias towards appetizing stimuli, and a decreased attentional bias for diet stimuli. Given the high risk of weight regain present in this population, and the prognostic properties of attentional bias for food cues on BMI, the difference in attentional bias found in our study, could be a relevant factor behind the weight regain, by increasing the selection of high caloric food and decreased the probability of healthy food eating. In addition, the greater amplitude of LPP in the bariatric group after food stimuli implies prolonged processing of this type of cues and could increase the risk of craving and subsequent intake.

It is expected that in future investigations, the relevance of the attentional bias towards food will be explored, as a prognostic factor to be evaluated before surgery, those effective interventions will be implemented as a real treatment alternative or at least improve surgery outcomes, by decreasing weight regain. From the neurobiological point of view, studies of the

brain mechanisms involved in attentional bias for food are needed, in order to generate a better understanding about the neurobiological bases of the obesity phenomenon, which could support new interventions for weight control treatment.

SUPPLEMENTS

S1: Scatter plot of survey responses (Words).

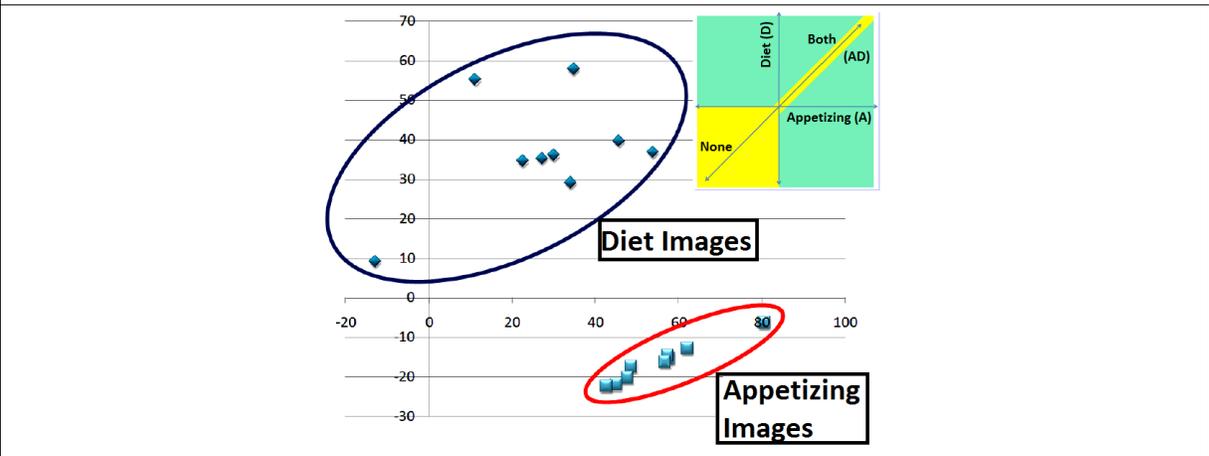


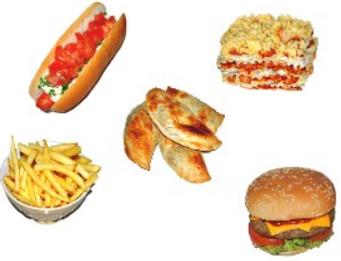
S2: Set of words used in the food-modified Stroop task.

Appetizing Words (Spanish)	Diet Words (Spanish)	Control Words (Spanish)
Bread (pan)	Fruit (fruta)	Train (tren)
Candy (dulce)	Diet (dieta)	Clock (reloj)
Desserts (postres)	Apple (manzana)	Journey (trayecto)
With cream (con crema)	Steamed (al vapor)	Of thread (de hilo)
Chocolate (chocolate)	Vegetables (verduras)	Television (televisor)
Cake (torta)	Light (light)	Pencil (lápiz)
Pastry (pasteles)	Salad (ensalada)	Backpacks (mochilas)
Hamburger (hamburguesa)	Integral (integral)	Scanner (escáner)
Barbecue (parrillada)	Vegetarian (vegetariano)	Futuristic (futurista)
[Milk candy]* (manjar)	Kiwi (kiwi)	Sunset (ocaso)

Whim (antojo)	Cucumber (pepino)	Spin (trompo)
Mashed potatoes (puré)	Celery (apio)	Sofa (sofá)
Cake shop (pastelería)	Carrots (zanahorias)	Dock (banquillo)
Chop (chuleta)	Lettuce (lechuga)	Monolith (monolito)
[Whipped bread]* (marraqueta)	Cabbage (repollos)	Blackboard (pizarrón)
[Chilean pumpkin fritters]* (sopaipilla)	[Natural food]* (naturista)	Locks (cerraduras)
Lasagna (lasaña)	[Fresh cheese]* (quesillo)	Sunshade (quitasol)
Paella (paella)	Grapefruit (pomelo)	Armor (coraza)
Salami (salame)	Arugula (rúcula)	Stay (estancia)
Kuchen (kuchen)	Radish (rábano)	Hammock (hamaca)
[*] not an exact translation		

S3: Scatter plot for survey responses (Images).



S4: Food images, for the visual task.		
	Sweet	Salty
Appetizing		
Diet		

S5: Faces selected for the oculomotor task.				
				
				
(*) Due to the author's restrictions, only part of the faces can be shown in publications				

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