UNIVERSITY OF BERGAMO

Department of Human and Social Sciences

Ph.D. Program in Human Capital Formation and Labour Market Relations; Doctoral Cycle XXXI

Academic Discipline: M-PSI/02, M-PSI/08

NEUROCOGNITIVE ALTERATIONS IN OBESE CANDIDATES FOR BARIATRIC SURGERY AND PSYCHOLOGICAL PREDICTORS OF SUCCESSFUL WEIGHT LOSS

Supervisor:

Prof.ssa Maria Luisa Rusconi

Ph.D. Candidate

GIULIA TESTA

Registration number.

007824

Academic year 2017/2018

ABSTRACT

Background: Neurocognitive alterations have been related to severe obesity, especially in terms of reduced cognitive control and enhanced attention toward food-related stimuli. Laparoscopic Sleeve Gastrectomy (LSG) is a bariatric surgery promoting weight-loss via physiological, metabolic and behavioral changes. Initial evidence for cognitive improvement after surgery exist, suggesting a resolution of obesity-induced changes in reward functions and cognitive control. However, neurophysiological correlates of these processes are poorly investigated and longitudinal studies are needed in this direction. Despite the positive outcomes of LSG, some patients fail to reach successful post-surgery excessive weight loss (EWL). Possible psychological predictors of post-surgery outcomes have been suggested, although contrasting findings are present and studies investigating multiple psychological predictors are warranted.

Aims: This thesis aims at investigating neurophysiological and behavioral correlates of the alteration in cognitive control and food-related attention in obese candidates for LSG and the possible improvement at 12 months post-surgery. Another aim was to identify multiple psychological predictors of successful weight loss at 12 months post-LSG.

Methods: Cognitive control in presence of food-related stimuli was measured using a modified version of the Simon task, during EEG registration. In the first study, 24 obese candidates for LSG were compared with 28 normal-weight individuals, while in the second study patients were followed up at 12 months post-LSG, with the same measures of food-related cognitive control. In the third study, multiple preoperative psychological predictors of successful EWL % at 12 months post-LSG were assessed in 69 patients. Predictive variables included in the model were psychopathological symptoms, dysfunctional eating attitudes, and impulsivity trait.

Results: In the first study, food-related images interfered with cognitive control in obese individuals as assessed with RTs; ERPs measures showed a prefrontal N1 component higher for food in both groups, indexing early attentional capture of food images. Longer P2 latency and smaller N2 amplitude were present in obese individuals. In the second study, a reduction of food-related interference was found in both RTs and P3 amplitude toward food. ERPs indices of general attention (P2 amplitude) and cognitive control (N2

amplitude) were enhanced after LSG. In the third study, a logistic regression showed that age and attentional impulsivity trait positively predicted successful EWL while anxiety symptoms negatively predicted successful EWL.

Discussion: Attentional bias toward food-stimuli interferes with cognitive control in obese candidates for bariatric surgery. This food-related interference on cognitive control is reduced post-LSG. Neurophysiological indices suggested a reduced cognitive control in obese seeking LSG, which can be enhanced post-surgery. Specifically, enhancement of N2 amplitude in frontal electrodes after surgery may suggest higher recruitment of frontal areas during conflict detection processes post-LSG. In a larger sample of obese seeking LSG, elevated preoperative anxiety symptoms negatively predict successful EWL, possibly suggesting the importance of clinical interventions targeting anxiety in bariatric surgery candidates to possibly avoid post-surgery failures. Moreover, the present results on impulsivity trait suggest that restrictive BS procedure such as LSG may be suitable even in patients with moderate impulsivity traits, possibly helping them to avoid risky eating behaviors such as binge eating.

Keywords: obesity; cognitive control; food-related attentional bias; ERPs, bariatric surgery

LIST OF ABBREVIATIONS

BED Binge Eating Disorder

BMI: Body Mass Index

BS: Bariatric Surgery

D2: Dopamine 2 Receptors

DLPFC: Dorsolateral Prefrontal Cortex

EEG: Electroencephalography

ERPs: Event-Related Potentials

EWL: Excessive Weight Loss

fMRI: Functional Magnetic Resonance Imaging

FTO: Fat Mass and Obesity Associated Gene

GLP-1: Glucagon-Like Peptide-1 Receptor

HPA: Hypothalamic-pituitary-adrenal

LABS: Longitudinal Assessment of Bariatric Surgery

LSG: Laparoscopic Sleeve Gastrectomy

LV: Latent Variable

MEG Magneto Encephalography

NAc: Nucleus Accumbens

OFC: Orbitofrontal Cortex

PET: Positron Emission Tomography

PFC: Prefrontal Cortex

PLS: Partial Least Square Analysis

RYGB: Rout-en-Y Gastric Bypass

RTs: reactions times

SST: Stop-Signal Task

SVD: Single Value Decomposition

VTA: Ventral Tegmental Area

ACKNOWLEDGMENTS

I would like to express my sincere gratitude to my supervisor, Professor Maria Luisa Rusconi. She always believed in my capacities, guiding me and inspiring me throughout my Ph.D. She has encouraged my growth as a researcher and motivated me.

I am also very grateful to all the collaborators from the Padua University Hospital where the patients were recruited and the studies were conducted. I would express a special thank to Dr. Sami Schiff which introduce me to the research hospital environment. He gave me important inspirations, guiding me through the completion of the present work, stimulating my critical thinking and inspiring me as a researcher.

I also would express my gratitude to Professor Fernando Fernández-Aranda, Professor Roser Granero-Pérez and all the collaborators from the Bellvitge University Hospital in Barcelona, that I had the opportunity to attend during part of my Ph.D.

I would also like to acknowledge my family and friends for all the support and love that they always gave to me through this important stage of my career and my life.

TABLE OF CONTENTS

EXPERIMENTAL SESSION:

Chapter 2: NEUROPHYSIOLOGICAL CORRELATES OF FOOD-RELATED PROCESSING DURING A COGNITIVE CONTROL TASK: AN ERPs STUDY IN NORMAL WEIGHT AND SEVERELY OBESE CANDIDATES FOR LSG

INTRODUCTION

Neurocognitive alterations have been linked to severe obesity, suggesting an imbalance between brain circuits related to reward and motivation and those related to cognitive control. In particular reduced cognitive control functions and enhanced attention toward food are mechanisms which may contribute to overconsumption of certain foods, ultimately leading to weight gain and obesity.

Bariatric surgery (BS) is the most effective treatment for severe obesity, with Laparoscopic Sleeve Gastrectomy (LSG) being one of the most adopted restrictive surgical procedure for weight loss. Beside the well known physiological and metabolic changes induced by BS, there is emerging evidence for an improvement in neurocognition. However, not all the patients benefit from BS outcomes, with a significant minority who fail to achieve successful weight loss, usually considered as *excessive weight loss* (EWL) higher than 50 %.

In the first chapter, a general introduction of the effects of obesity and bariatric surgery on neurocognition is provided, with a special focus on attentional and cognitive control processes. Moreover, an overview of the literature investigating psychological and neurocognitive predictors of successful post-surgery weight loss is summarized here.

The second chapter presents the first study in severely obese individuals seeking LSG and normal weight participants, which aimed at assessing neurophysiological and behavioral correlates of cognitive control in the presence of food-related distracting stimuli, using a novel experimental paradigm. Neurophysiological indices of these processes were assessed trough EEG acquisition during task execution and subsequent extraction of event-related potentials (ERPs).

The third chapter presents results from a second longitudinal study, assessing post-LSG changes in cognitive control in the presence of food-related stimuli. The differences from pre-LSG to 12 months post-surgery were evaluated with the same cognitive control paradigm and measures as in study 1.

The fourth chapter presents the third study conducted in a larger sample of LSG candidates, aimed at identifying possible psychological predictors of successful EWL at 12 months post-surgery. Given the contrasting findings in the literature and in order to have a

more comprehensive view, multiple preoperative predictors were included in the model such as demographic variables, anxiety and depressive symptoms, dysfunctional eating attitudes and behaviors, and impulsivity trait.

Finally, the fifth chapter summarizes the results from these studies and the general conclusions of these results are discussed.

CHAPTER 1

NEUROCOGNITIVE EFFECTS OF OBESITY AND BARIATRIC SURGERY

1.1 Classification, epidemiology and consequences of obesity

Obesity is a common health problem which has reached epidemic proportions worldwide. The World Health Organization (WHO, 2015) suggested that the prevalence of obesity tripled between 1975 and 2015, indicating that the 39% of the adult world population were overweight and 13% were obese. Moreover, the prevalence of overweight and obesity among children and adolescents (aged between 5 and 19 years old) has risen dramatically from 4% in 1975 to 18% in 2015. In the last few years, obesity rates in Italy have undergone a rapid increase, with national health data reporting 35.3% of the adult population as overweight and 9.8 % obese in 2015. Therefore, there is evidence showing that obesity rates have been rising over the past few decades and that obesity is associated with an increasingly high cost for the healthcare system worldwide.

Obesity is described as an excess in body weight and fat, usually measured via Body mass index (BMI), which is calculated by dividing individual's weight by their height squared (kg/m^2). According to the WHO, a BMI score ranging from 25 kg/m^2 to 29.9 kg/m^2 is considered overweight and 30 kg/m^2 or above is obesity (See table 1.1 for Obesity Classification).

Physical consequences of obesity have been largely reported in the literature. Obesity is associated with increased risk of atherosclerotic cerebrovascular disease, coronary heart disease, hypertension, diabetes Mellitus, dyslipidemia, and obstructive sleep apnea syndrome (OSAS) (Ogden, Yanovski, Carroll, & Flegal, 2007; Pi-Sunyer, 2009). Furthermore, obese individuals have been shown to have a higher risk for certain forms of cancer such as cancers of the colon, breast, kidney, pancreas, liver, and higher mortality rate; epidemiological studies in the United States showed that approximately 15-20% of all

cancer deaths in the United States are linked to overweight or obesity (Adams et al., 2006; Calle, Rodriguez, Walker-Thurmond, & Thun, 2003).

Table 1.1 Obesity Classification adapted from the World Health Organization Consultation of Obesity (1997)

Classification	**BMI** kg/m^2
Underweight	<18.5
normal weight	18.5-24.9
Overweight	25-29-9
obesity class I°	30-34.9
obesity class II°	35-39.9
obesity class III°	>40

1.2. Multifactorial causes of obesity

Obesity is a complex medical condition associated with multifactorial causes including physical inactivity, genetic susceptibility, increased availability of high-density energy foods, nutritional factors, psychological and social factors. In some cases, genetic mutations, endocrine disorders, medication or psychiatric illness may be underlying causes of obesity.

Studies in twins consistently showed that genetic factors strongly contribute to the development of obesity. In a classic study, Stunkard and colleagues (Stunkard, Harris, Pedersen, & McClearn, 1990) showed in 362 couples of monozygotic and dizygotic twins strong weight correlations across a lifetime even when growing in different environments. Furthermore, studies on adoptive families showed stronger correlations between BMI of biological children and their biological fathers compared to correlations between children and adoptive parents (Stunkard, Foch, & Hrubec, 1986). More recent studies estimated that BMI heritability range from 25 to 40 % in large samples (Bouchard, 1994, 1996). While the specific genes involved in common obesity are still unclear, there is evidence that the fat

mass and obesity associated gene (FTO) is related to higher risk of obesity in humans (Fredriksson et al., 2008; Zabena et al., 2009).

Another factor that potentially contributes to overweight and obesity is the so-called "obesogenic environment", which refers to the high availability of affordable high-fat foods (e.g., fast-food, snacking, and sugar-sweetened beverages) (Swinburn et al., 2011). These environment promotes overconsumption of certain foods beyond physiological needs, and paired with increasingly sedentary lifestyles has been shown to substantially contributes to weight gain. Furthermore, overconsumption of high-fat food has been associated with a sedentary lifestyle, suggesting that sedentary activities such as watching television promote increase food intake (Chaput, Klingenberg, Astrup, & Sjödin, 2011). Sedentariness and high availability of certain foods in the family environment have been strongly suggested to facilitate obesity in children and adolescents (Wardle, Guthrie, Sanderson, Birch, & Plomin, 2001). However, it should be considered that not all the individuals who experience the obesogenic environment become obese or overweight, suggesting that the interaction between genes and environment play a crucial role. Hence, vulnerable individuals are more at risk of developing obesity in a particular environment (Loos & Bouchard, 2003).

An alternative approach to understanding the causes of obesity is to examine factors which are contributing to eating behavior beyond physiological needs. Different psychological theories have been implemented to explain possible reasons for overeating and weight gain. Repeated chronic attempts to weight loss through caloric restriction or dieting are frequently observed in overweight and obese individuals, often leading to weight regain.

It has been suggested that food restriction attempts can influence food thought and beliefs, with unhealthy foods used as rewards and restricted in a way that made forbidden food even more desirable (e.g., restrained eating theory; Herman & Polivy, 1980).

Other psychological theories suggested that obese are more vulnerable to the availability of food cues in the environment (e.g., externality theory; Schachter, 1968) or that obese

tend to eat more in response to emotions such as anxiety, fear, boredom, and depression (e.g., emotional eating theory; Schachter & Rodin, 1974).

1.3 Neurocognitive Alterations in obesity

More recently, cognitive and neurobiological models have been adopted to study overeating and body weight regulation. Jansen and colleagues recently explored cognitive mechanisms contributing to overeating and unhealthy eating habits, suggesting a "cognitive profile related to obesity" (Jansen, Houben, & Roefs, 2015). Neuroimaging research showed that different brain circuits and neurotransmitters are implicated in the regulation of food intake and appetitive food-cue processing, suggesting possible obesity-related functional and structural brain alterations.

1.3.1 Independent effect of obesity on the brain

A growing literature showed that obesity is associated with neurological changes and consequently cognitive dysfunctions. On one hand, obesity-related medical comorbidities such as hypertension, diabetes and some psychiatric disorders (e.g., depression) are well recognized to affect cognitive functions (Weisenbach, Boore, & Kales, 2012). Furthermore, obesity has been often associated with an increased risk of dementia (e.g., Alzheimer disease) and stroke (Hassing et al., 2009; Strazzullo et al., 2010). However, there is evidence suggesting that the dementia risk in obese individuals may be independent of medical comorbidities (e.g., vascular diseases) (Whitmer, Gunderson, Barrett-Connor, Quesenberry, & Yaffe, 2005). Other studies which support that obesity-related cognitive deficit are at least partially independent from medical comorbidities are those in obese children, who showed impaired cognitive functions compared to their normal-weight peers (Blanco-Gómez et al., 2015); or other studies in healthy samples showing a relationship between BMI and cognitive impairment (Gunstad et al., 2007).

Therefore, there is an increasing recognition of the independent effects of adiposity on the brain and a growing interest in identifying potential pathophysiological mechanisms underpinning these effects, including impaired cerebral metabolism, metabolic

dysregulation and inflammatory processes (Gunstad, Spitznagel, et al., 2008; Harvey, 2007; Smith, Hay, Campbell, & Trollor, 2011; Volkow et al., 2009).

Accumulating evidence suggested that obesity is not only related to a chronic low-grade systemic inflammation of peripheral tissues (Gregor & Hotamisligil, 2011) but also to inflammation within the central nervous system, particularly in the hypothalamus (Miller & Spencer, 2014). Indeed, studies in animals and humans showed that high-fat diet leads to increased levels of proinflammatory cytokines which can cause hypothalamic inflammation (De Souza et al., 2005; Zhang et al., 2008). Since the hypothalamus regulates a range of physiological and metabolic functions, as well as stress-related response, a dysregulation at this level may also affect inter-related cognitive functions. For instance, studies in humans linked obesity to a dysfunction in the hypothalamic-pituitary-adrenal (HPA) axis (Koessler, Engler, Riether, & Kissler, 2009) and stress-related mood disorders like depression are highly prevalent in obese population (Abilés et al., 2010; Doyle, Le Grange, Goldschmidt, & Wilfley, 2007; Scott, McGee, Wells, & Browne, 2008). Despite the well-documented effect of stress on the brain, hypothalamic dysfunctions are expected to affect other inter-connected brain systems such as the frontal lobe, the hippocampus and the mesocorticolimbic dopamine system (Shin, Zheng, & Berthoud, 2009).

1.3.2 Frontal lobe and cognitive control

The anterior portion of the frontal lobes, the prefrontal cortex (PFC), is conventionally divided into different subregions: dorsolateral prefrontal cortex (DLPFC), ventrolateral PFC and orbital PFC.

Structural and functional changes within the PFC have been reported in obese individuals or in relation to BMI. As for structural changes, high BMI correlates with reduced gray matter volume in different regions within the frontal lobe (Gunstad, Paul, et al., 2008; Kurth et al., 2013; Pannacciulli et al., 2006; Ward, Carlsson, Trivedi, Sager, & Johnson, 2005). In a Positron emission tomography (PET) study, Volkow and co-workers (Volkow et al., 2009) showed lower striatal dopamine (D2) receptor availability in obese compared to normal weight, and in obese that was positively correlated with prefrontal metabolism (e.g., DLPFC, medial orbitofrontal, anterior cingulate gyrus).

The PFC is thought to be involved in a group of high-level cognitive functions variously described as executive functions, a set of cognitive processes which allow the individual to achieve goals or goal-directed behaviors and responding adaptatively in novelty situations (Miyake et al., 2000; Norman & Shallice, 1986). An extensive literature highlighted frontal mediated executive function deficits in obese populations in both adults and children or adolescents (for a systematic review of the literature: Barkin, 2013; Prickett, Brennan, & Stolwyk, 2015), or in relation to BMI in healthy samples (Gunstad et al., 2007).

Among executive functions, cognitive controls abilities are particularly relevant when the individuals have to resist temptations (e.g., refrain from eating high caloric foods) in order to achieve long-term goals (e.g., successful weight loss or weight maintenance); thus, these processes are critical in the regulation of food consumption. Cognitive control has been defined as the ability to control thoughts and to orchestrate goal direct-behaviors in a flexible and adaptive manner (Botvinick, Braver, Barch, Carter, & Cohen, 2001). Cognitive control comprises subsets of processes such as the ability to inhibit an inappropriate response (i.e., response inhibition) or the ability to select the proper response among possible competing responses (i.e., interference control). Response inhibition is experimentally assessed with standardized tests such as the go/no-go task and the stop-signal task (SST) (Donders, 1969; Logan & Cowan, 1984), whereas cognitive tasks which allow measuring interference control are for instance the Stroop task (MacLeod, 1991) or the Simon task (Simon & Rudell, 1967).

Neurophysiological mechanisms of cognitive control can be studied using event-related potentials (ERPs) during the execution of cognitive tasks. ERPs component are scalp-recorded changes in the electroencephalographic signal (EEG) time-locked to sensory, motor and cognitive events that provide a safe noninvasive approach to study psychophysiological correlates of mental processes (Blackwood & Muir, 1990). Specific ERPs components such as the N2 and the P3 (typically from frontocentral electrodes) are elicited during cognitive control tasks, representing the neurophysiological substrate of cognitive control processes.

Cognitive control in obese individuals has been assessed using cognitive control tasks, suggesting an impairment in cognitive control abilities, although contrasting findings are

present in the literature (Lavagnino, Arnone, Cao, Soares, & Selvaraj, 2016). This can be related to the multidimensional nature of cognitive control processes, and to different tasks and methodologies adopted to measure this complex construct. A recent meta-analysis was conducted only with nine studies assessing inhibitory control with the SST task, showing a significant impairment in response inhibition in obese individuals compared to controls (Lavagnino et al., 2016).

Neural correlates of cognitive control processes assessed with functional magnetic resonance imaging (fMRI) showed that BMI inversely correlated with the activation of parietal cortex, insula, cuneus and supplementary motor area, regions which are considered part of an extended "inhibitory control network" (Hendrick, Luo, Zhang, & Li, 2012); whereas two studies in obese individuals with binge eating disorder (BED) showed reduced activation of the PFC during the execution of inhibitory control tasks (Balodis et al., 2013; Hege et al., 2015).

For the studies using ERPs measures, Tarantino and colleagues investigated cognitive control in a group of ex-obese patients which successfully lose weight subsequently to bariatric surgery compared to normal weight individuals (Tarantino, Vindigni, Bassetto, Pavan, & Vallesi, 2017); differences in neurophysiological indices of anticipatory control mechanisms and conflict monitoring were reported in that study. In another study conducted in children while performing a go/no-go task, obese showed lower response accuracy and larger N2 amplitude relative to healthy weight children in no-go trials (Kamijo et al., 2012). However, to date, the few ERPs studies conducted in current obese adults specifically assessed cognitive control processes in presence of food-related stimuli rather than general cognitive control abilities; therefore, these findings will be discussed in the next sessions of this thesis.

1.3.3 Mesocorticolimbic dopamine system and food reward

Beyond the homeostatic regulation of food intake, eating is inseparably associated with reward, especially when is driven by pleasure instead of metabolic needs (i.e., hedonic eating). Reward processing depends on mesocorticolimbic dopamine systems, comprising

dopamine neurons in the ventral tegmental area (VTA) and their projections to nucleus accumbens (NAc), amygdala, prefrontal cortex (PFC), and other forebrain regions.

Dopamine is a key neurotransmitter in reward-saliency and motivation for feeding behaviors. *Incentive-sensitization models* suggested that mesocorticolimbic dopamine systems mediate the incentive salience attributed to neural representations of rewards and cues, causing them to become perceived as "wanted" (Berridge & Robinson, 1998); specifically, the repeated pairing of a salient food-related stimulus with its rewarding proprieties leads to a hypersensitization of the dopaminergic brain reward system, through appetitive conditioning mechanisms.

In line with this model, the hypersensitization of the system due to a repetitive consumption of high-fat foods with rewarding proprieties has been proposed as one of the dysfunctional processes implicated in the developing and maintenance of obesity (Appelhans, 2009).

In particular, similarly to drug-addicted individuals, obese showed a reduced availability of dopamine 2 (D2) receptors in the striatum, as suggested by a PET study from Volkow and co-workers (Volkow, Wang, Fowler, & Telang, 2008). In another study in healthy control participants, lower D2 receptors have been associated with an increased tendency to eat in emotionally stressful situations (Bassareo & Di Chiara, 1999)

In addition to dopamine alterations, abnormalities within the brain regions of the reward network during the presentation of food-related images have been reported in obese individuals. Overall, neuroimaging studies showed an enhanced or abnormal neural response to energy-dense food-related images in obese compared to normal weight (see for a review Burger & Berner, 2014; Carnell, Gibson, Benson, Ochner, & Geliebter, 2012).

Specifically, an exaggerate brain response to food has been shown in the striatum, insula, orbitofrontal cortex (OFC) and amygdala, regions which are part of the brain reward and motivational network and are thought to encode the reward value of stimuli (Burger & Berner, 2014). Despite of the higher striatal response to food-related cues observed in obese, an inverse pattern has been shown during food consumption, with reduced striatal response in obese compared to normal-weight (Babbs et al., 2013; Green, Jacobson, Haase, & Murphy, 2011; Stice, Spoor, Bohon, Veldhuizen, & Small, 2008). Furthermore,

enhanced brain reactivity toward food-related cues in obese individuals has been detected in brain areas involved in visual processing, attention and cognitive control, especially when tested in a fasted state (Carnell et al., 2012).

The cognitive counterpart of enhanced food-cue sensitivity is increased attention (initial orientation or maintenance) toward food-related cues, often referred to as "food-related attentional bias" (i.e., food-related AB). Initial attentional orientation or attentional maintenance toward food-related images have been studied in experimental psychology using different methodologies. ERPs have been adopted as objective measures to study neurophysiological correlates of attentional processes of food cues, in both normal and abnormal eating (Wolz, Fagundo, Treasure, & Fernández-Aranda, 2015).

In the metabolic state of hunger, food-stimuli are salient for the individuals, as suggested by studies which showed a food-related AB in normal weight subjects when tested in food deprivation (Stockburger, Schmälzle, Flaisch, Bublatzky, & Schupp, 2009).

The first hypothesis which highlighted the potential role of food-related AB in obesity, dates back to 70', when Schachter suggested that although all people were responsive to environmental food stimuli (e.g., sight, taste, and smell of food), eating regulation in normal weight is related to internal cues (e.g., hunger, satiety); whereas the obese individuals tend to experience highly and sometimes uncontrollably responsivity to external food cues, despite lower responsiveness to their internal cues (Schachter & Rodin, 1974).

Subsequent studies investigating food-related AB were conducted in overweight and obese participants, or in relation to BMI. A recent systematic review of the literature on this topic compared findings from 19 papers in overweight and obese samples (Hendrikse et al., 2015). Overall, food-related AB has been investigated using a broad range of experimental paradigms and outcome measures including reaction times (RTs), eye movements, electrophysiological indices of attentional processing or brain activations. Most of these studies adopted visual dot probe tasks with food-related stimuli and object-related stimuli as neutral condition, showing differences in food-related AB between obese and normal-weight individuals (Castellanos et al., 2009; Kemps, Tiggemann, & Hollitt, 2014; Loeber et al., 2012; Nijs & Franken, 2012; Nijs, Muris, Euser, & Franken, 2010; Werthmann et al., 2012). Other studies consisted in passing viewing of food and non-food images, while in

others, specific paradigm were implemented adopting food-related stimuli as the case one-back visual recognition task (Stephanie Kullmann et al., 2012), or food-modified Stroop task (Braet & Crombez, 2003; Nijs, Franken, & Muris, 2010).

In spite of the measure adopted to asses attentional bias, results from the majorities of these studies supported differences in food-related AB between normal weight and obese individuals especially at psychophysiological (e.g., ERPs) and neural levels (e.g., fMRI) (Hendrikse et al., 2015).

1.3.4 Imbalance between cognitive control and reward sensitivity

Dual-model processes theories proposed that an override of the hedonic appetitive system over the cognitive control system may lead to difficulties in refraining from overeating in tempting situations (Appelhans, 2009; Houben, Nederkoorn, & Jansen, 2014). This suggests that both attentional bias toward food and cognitive control processes interacts in promoting overconsumption of foods, thus contributing to weight gain and obesity.

From a neurobiological perspective, obesity results in an imbalance between brain circuits related to reward and motivation and those related to cognitive control (Volkow, Wang, & Baler, 2011; Volkow et al., 2008). A meta-analysis of the fMRI studies assessing food-cue processing reported that obese individuals consistently showed enhanced activity of frontal areas associated with stimulus and reward evaluation, such as the OFC, in response to food images (Brooks, Cedernaes, & Schiöth, 2013); by contrast, a reduced activation was shown in brain regions related to cognitive control and interoceptive awareness.

Given this, there is a growing interest in developing experimental tasks with food-related stimuli in order to isolate specific mechanisms and potentially more pronounced neurocognitive deficits in obese individuals or in patients with eating-related problems.

Accordingly, recent studies adopted food-specific tasks to assess cognitive control in overweight and obese participants. Depending on the study, food images were used as a task-irrelevant food-distracter (e.g., Stroop with distracting food-related images) or as a task-related target (e.g., go/no-go with food stimuli as go trials). To have an overview of the current literature, Table 1.2 summarizes tasks, measures and results from studies investigating cognitive control toward food in overweight-obese population (with or

without binge eating disorders). Among these studies, only two were conducted with ERPs measures one adopting a Stroop task with food-related words (i.e., food as task-relevant stimulus) and the other using a Stroop task with distracter food images (i.e., food as task-irrelevant stimulus) (Hume, Howells, Rauch, Kroff, & Lambert, 2015). Taken together, ERPs results from these studies seem to suggest enhanced early food-attentional processes and more efficient maintained food-attentional processing in obese/overweight individuals.

Table 1.2 Studies investigating food-related cognitive control in obese and overweight individuals.

Paper	Task	Subjects	Measures	Results
Nijs et al., 2010	Food-related Stroop	20 OB, 20 NW	RTs, ERPs	RTs for food longer than non-food for all subjects ERPs: P2 amplitude larger for food in OB OB = NW
Mobbs et al., 2011	Food-specific go/no-go	16 OB-BED, 16 OB, 16 NW	errors	OB-BED > NW OB > NW OB-BED > OB
Loeber et al., 2012	Food-specific go/no-go	20 OB, 20 NW	RTs	Faster RTs for food in all participants
Svaldi 2014	Food-Specific Stop-signal task	31 OB-BED; 29 OB	RTs, errors	OB-BED>OB in both SSRT and errors
Hume et al., 2015	Food-specific Stroop	41 NW, 21 OW, 19 OB	RTs, ERPs	RTs NW=OB ERPs right parietal P2 amplitude larger for food in OW vs NW; right parietal P3 latency shorter for food in OB vs NW
Price et al., 2016	Food-specific go/no-go	83 NW; 32 OW/OB	RTs, errors	More errors for food trials in obese with low dietary restraint eating

Notes: OB=obese subjects; OB-BED =obese with binge eating disorders; OW= overweight subjects; NW=normal weight subjects

1.4 Obesity and bariatric surgery

Bariatric surgery (BS) is considered one of the most effective long-term weight loss treatment for severe obesity. Traditional weight-loss treatments such as pharmacological, behavioral therapy, low-caloric diets or physical exercise have shown good results for obesity I or II; however, they seem to be less effective as long-term treatments for severe obesity compared to BS (Mun, Blackburn, & Matthews, 2001; Wing & Phelan, 2005). Moreover, BS has been shown to improve health-related quality of life, with the reduction of medical comorbidities in type 2 diabetes, metabolic syndrome and cardiovascular diseases associated with severe obesity (Buchwald et al., 2004; Buchwald et al., 2009; Colquitt, Pickett, Loveman, & Frampton, 2014; Kwok et al., 2014).

According to international guidelines, potentially eligible patients for surgery are severely obese with BMI $\geq$40, or BMI $\geq$ 35 with comorbid medical conditions (National Institutes of Health 2006). Generally, obese individuals seeking BS come from previous unsuccessful attempts to achieve weight loss through other non-surgical treatments.

Given the limited post-operative complications related to BS (e.g., gastric dumping syndrome; infections), this is considered a treatment of choice for severe obesity, potentially inducing a weight loss around 80% of the excess body weight, depending on the type of surgery.

Multiple different BS techniques are available nowadays, which are frequently divided into three categories:

1) *Restrictive techniques* reduce food intake trough gastric intake restriction or volume reduction. The most adopted is laparoscopic sleeve gastrectomy (LSG), which divides the stomach vertically to reduce its size to about 25%. It leaves the pyloric valve at the bottom of the stomach intact which means that the stomach function and digestion are unaltered (see figure 1.1). Other restrictive procedures include adjustable gastric banding, laparoscopic gastric plication, and vertical banded gastroplasty.
2) *Malabsorptive techniques* reduce malabsorption of nutrients such as the biliopancreatic diversion and the duodenal switch.

3) *Mixed techniques* that combine both restriction and malabsorption. The most used is the Roux-en-Y gastric bypass (RYGB) in which first the top of the stomach is divided from the rest of the stomach and the small intestine is divided, then the bottom end of the divided small intestine is brought up and connected to the newly created small stomach pouch.

The most common types of surgery adopted worldwide are the RYGB and the LSG. Even though the RYGB allows to loss of high amount of weight (60-80 % of the excessive weight loss - EWL) is a complex surgical procedure which could result in greater complication rates and long hospital stay. By contrast, LSG is a less complicated procedure and requires less post-surgery hospitalization; LSG induces rapid weight loss which can reach 50% of the EWL within the first 12 months.

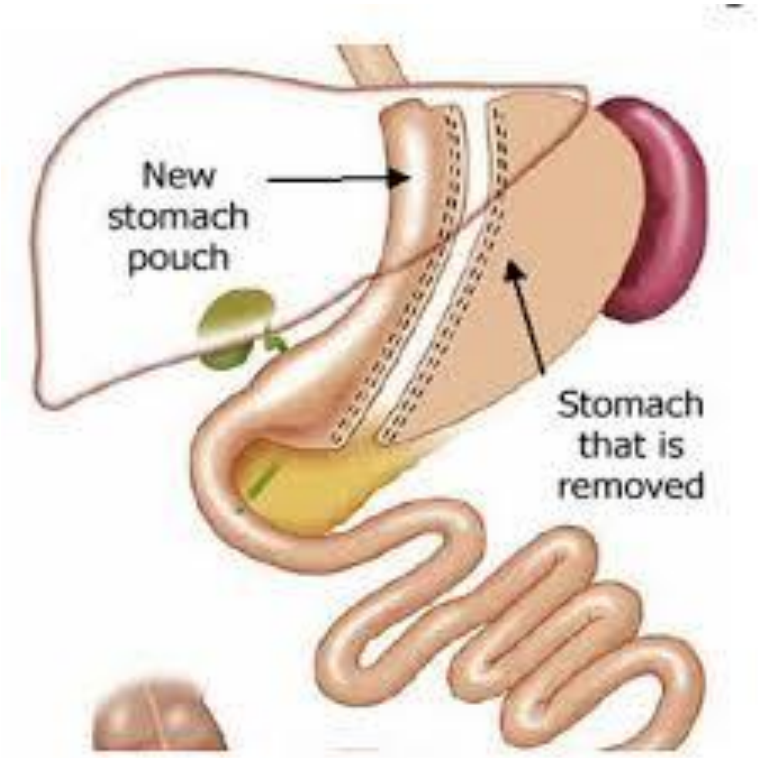

Figure 1.1 laparoscopic sleeve gastrectomy (LSG)

1.4.1 Metabolic effects of bariatric surgery

It is well known that bariatric surgeries lead to significant and potentially long-term weight loss, by limiting the amount of food intake or the absorption of nutrients. Moreover, some types of BS such as RYGB and LSG, induce substantive metabolic changes beyond weight loss alone (Dimitriadis, Randeva, & Miras, 2017). The gastrointestinal tract interacts with the brain through the secretion of hormones which are implicated in appetite regulation and the metabolic effects of LSG or RYGB have been related to changes in the secretion of these peptides. Some of the gut hormones influenced by BS are produced by the stomach (e.g., ghrelin, gastrin), the ilenium (i.e., glucagon-like peptide-1 receptor - GLP-1), the pancreas (insulin, glucagon) and other organs.

Ghrelin is one of these hormones, functioning as a neuropeptide in the central nervous system (Dickson et al., 2011) and regulating appetite. Ghrelin levels usually drop after ingestion and rise with prolonged fasting. LSG has been associated with reduced ghrelin levels, probably due to the removal of that part of the stomach with a high concentration of ghrelin secreting cells (Yousseif et al., 2014).

Since weight loss can itself modify hormones secretion, it is controversial whether the metabolic benefits of BS are secondary to weight loss, regardless of the specific effect of BS. However, it is clear that post-surgery caloric restriction coupled with hormonal adaptations promote weight loss. Overall, physiological and molecular signaling changes in the gastrointestinal tract and other organs observed after BS result in weight loss and improved insulin homeostasis.

1.4.2 Neurocognitive effects of Bariatric surgery

1.4.2.1 Proposed mechanisms

Despite the progress in the understanding of the neural mechanisms related to overeating, it is still unknown if obesity-related neural alterations are consequences or causes of obesity condition. Therefore, longitudinal studies in obese individuals before and after bariatric surgery may allow to a more comprehensive understanding of the effect of obesity and weight loss over cognition.

An emerging literature has shown an improvement in neurocognition following BS, suggesting that post-surgery weight loss, along with physiological and metabolic changes and resolution of obesity-related comorbidities may result in the amelioration of neurocognitive functions. Accumulating evidence suggested that neurocognitive deficits associated with severe obesity can be partially reversed after BS, due to multifactorial mechanisms which still have to be completely understood. First, the post-surgery reduction of obesity-related medical comorbidities is one of the factors which can be expected to affect cognitive functions. However, findings from the Longitudinal Assessment of Bariatric Surgery (LABS) project, did not consistently support these expectations (Alosco et al., 2014), suggesting that other mechanisms interact in post-surgery cognitive gain.

Since obesity is related to systemic and central inflammatory processes (Miller & Spencer, 2014) which in turn lead to cognitive deficits, reduced inflammation post-BS could be another mechanism underlying neurocognitive improvement (Hawkins et al., 2014). However, more research is needed in order to corroborate this hypothesis.

Other factors potentially implicated in post-operative neurocognitive gains are the metabolic effect and the normalization in neurohormones related to appetite induced by LSG and RYGB. Specifically, leptin and ghrelin are dysregulated in obesity (Vendrell et al., 2004), and these neurohormones have been implicated in cognitive functioning or in neurodegenerative diseases. In line with this hypothesis, Alosco and co-workers showed that changes in leptin and ghrelin predict better attention and executive function one-year post-BS (Alosco et al., 2015). In addition, there are other factors of interest which are poorly investigated in BS population, such as fitness level (Galioto et al., 2014) and improved cerebral blow flow (Toda, Ayajiki, & Okamura, 2014).

Overall, different factors seem to potentially contribute to the improvement in cognitive functions observed post-BS; however, more investigation is needed to disentangle the complex mechanism implicated in these changes.

1.4.2.2 Neurocognitive improvement after Bariatric Surgery

Nearly 25% of severely obese candidates for BS showed neurocognitive impairment (> 1.5 standard deviation less than normative population) and 40 % showed more subtle cognitive

impairment (> 1 standard deviation) in different cognitive functions such as learning, memory, attention and executive functions (Handley, Williams, Caplin, Stephens, & Barry, 2016; Spitznagel et al., 2015; Thiara et al., 2017).

Improvement in neurocognition has been also suggested by a source of neuroimaging studies conducted in the bariatric population. In a transversal fMRI study, obese women not submitted to BS showed stronger functional connectivity in the default mode network during resting state, whereas patients underwent RYGB did not differs from normal weight controls (Frank et al., 2014). These results suggest that BS-related weight loss may resolve neural alterations showed in obese individuals, even though the cross-sectional design did not allow to directly infer the effect of surgery over cognition. In a subsequent longitudinal PET study, patients underwent RYGB were compared from pre to 6-months post-surgery and with a matched group of normal weight individuals (Marques et al., 2014). Higher cerebral metabolism in some brain regions (e.g., right posterior cingulate gyrus; right posterior lobe of the cerebellum) were present in obese women when tested pre-BS compared to normal weight. By contrast, no differences were observed in brain metabolism when patients tested post-BS were compared to controls.

As suggested in the first part of this thesis, executive dysfunctions are more consistently linked to obesity (Prickett et al., 2015; Spitznagel et al., 2015). Some of the previous studies showed an improvement in executive functioning after weight loss in bariatric surgery patients (Handley et al., 2016; Thiara et al., 2017), which has been shown to persist for 3 years after surgery (Alosco et al., 2014). By contrast, other transversal studies did not find differences in executive functions when comparing obese candidates for BS with post-surgery patients (Georgiadou, Gruner-Labitzke, Köhler, de Zwaan, & Müller, 2014; Sousa, Ribeiro, Horácio, & Faísca, 2012). Despite these discrepancies, it is important to consider that executive function is an "umbrella" term comprising a set of cognitive functions including problem-solving, planning, decision making, cognitive control, working memory, and cognitive flexibilities. Therefore, different abilities have been studied in bariatric surgery patients, making difficult to compare results from different studies.

Among these functions, poor cognitive control abilities - which in turn refers to a subset of processing such as response inhibition and interference control - have been associated with obesity. In a recent study, Tarantino and co-workers assessed cognitive control abilities in ex-obese patients who underwent BS with normal weight controls, by means of cognitive task and ERPs measures (Tarantino et al., 2017). Specifically: interference control was measured with a verbal version and a spatial version of the Stroop task; cognitive flexibility with a switching task; response inhibition adopting a go/no-go paradigm. Cognitive measures showed that ex-obese patients compared to controls were more susceptible to task-irrelevant stimulus dimension (i.e., larger verbal Stroop effect) and were less flexible (i.e., larger switch cost). Neurophysiological measures showed that ex-obese have an alteration in anticipatory control mechanism before switching trials (i.e., switch positivity) and a more pronounced conflict monitoring response in no-go trials (i.e., N2 amplitude). These results are intriguing even though the transversal design of the study and the fact that a pre-surgery obese group was not included can limit the conclusion on the effect of BS on cognitive control abilities. Overall, longitudinal designs with long-term observations are preferred to cross-sectional studies when studying changes related to BS.

On the other hand, obesity has been associated with hypersensitivity of the brain reward system to appetizing foods (Volkow et al., 2011; Wang et al., 2001) and enhanced attention toward food-related stimuli (Hendrikse et al., 2015). It has been suggested that BS may reverse obesity-induced changes in reward functions promoting changes in appetitive responses toward certain food cues and in food preferences (Berthoud, Zheng, & Shin, 2012; Shin & Berthoud, 2011). More specifically, it is supposed that metabolic and endocrinal effects induced by BS, in terms of nutritional adaptation and gut hormones regulation, can result in altered food-cue processing; thus, changes in motivational and cognitive response to food stimuli are expected after BS (Miras et al., 2012). In line with this hypothesis, post-surgery changes in food preferences are frequently observed post-BS (Hansen et al., 2016), which have been related to possible alterations in taste perception and in food-reward evaluation. Accordingly, neuroimaging studies showed a post-surgery reduction in the activation of the mesocorticolimbic reward network in response to food images (Behary & Miras, 2015; Ochner et al., 2011; Scholtz et al., 2013). Interestingly, a

positive correlation has been shown between the decreased desire to eat high-energy foods and the neural activation of reward-related brain areas during passing viewing of food images (Behary & Miras, 2015; Hansen et al., 2016; Ochner et al., 2012). Dopamine, is known to play a crucial role in motivating appetite behavior and in the reinforcement of food stimuli; Wang and colleagues previously showed reduced dopamine D2 receptor availability in obese individuals (Wang et al., 2001), whereas an increase in the availability of D2 has been detected 6 weeks after bariatric surgery (Steele et al., 2010). The changes in dopamine receptor binding could be implicated in appetite suppression and consequently weight loss, although further studies in larger samples are needed.

Obesity has been associated with enhanced sensitivity toward food-related cues which results in enhanced attention toward food (i.e., food-related attentional bias) at a cognitive level (Hendrikse et al., 2015). Along with changes in food preferences and appetitive motivation toward food, a reduction of food-related attentional bias may be also expected after surgery. To date, only one longitudinal study assessed attentional processing of food-related images from pre to post-LSG using eye tracking (Giel et al., 2014). Results from this study suggested lower attention toward food images, less interest in food cues assessed by pleasantness rating and lower subjective food craving post-LSG.

1.5 Factors implicated in weight-regain after Bariatric Surgery

Overall BS has been associated with positive outcomes including weight loss, reduction of obesity-related comorbidities and improvement in the quality of life. Most of the BS patients achieve a successful degree of weight loss, which is defined as >50% excess weight loss (EWL) (Brethauer et al., 2015). Despite this, there is still a significant minority of BS patients, around 15-20%, who did not achieve this expected weight loss (Maggard et al., 2005). This failure is likely to be related to multifactorial causes, which are supposed to influence positive post-operative outcomes.

Previous studies examined possible pre-surgical psychosocial predictors of successful weight loss following BS or those potentially implicated in weight regain. Although mixed findings are present, the growing literature in this filed highlighted potential pre-surgery factors related to post-surgery EWL that will be exposed here.

1.5.1 Demographic variables

Age, gender and socio-economic status have been correlated with successful weight loss post-BS, suggesting that younger patients may have more positive weight outcomes post-surgery, and this may at least in part be related to fewer comorbidities and higher mobility in younger (Busetto et al., 2002; Capella & Capella, 2003; Rowe, Downey, Faust, & Horn, 2000). As for gender, less conclusive results are present since only some studies found females to lose a little more weight than males whereas others did not (Dixon & O'Brien, 2002; Korenkov, Kneist, Heintz, & Junginger, 2004). Lower socioeconomic status has also been related to worst outcomes such as higher post-surgery complications (Renquist et al., 1996), possibly because of the reduced access to healthy foods or physical exercise; although other studies did not confirm the predictive value of socio-economic status over post-surgery EWL (Korenkov et al., 2004; Rowe et al., 2000).

More interestingly, most of the studies reported a negative association between pre-surgery BMI and weight loss post-BS, showing that higher BMI was related to lower EWL, and lower resolution of obesity-related medical comorbidities (Livhits et al., 2012; Van Hout, Verschure, & Van Heck, 2005). However, there are also evidences reporting a positive association, especially in patients underwent RYGB, or no associations (Livhits et al., 2012). Moreover, history of childhood obesity and BMI changes during lifetime (e.g., maximum and minimum weight) are factors which could affect post-surgery weight loss. The few studies which investigated previous weight loss attempts such as frequent diets did not show an effect over post-surgery EWL (Jantz, Larson, Mathiason, Kallies, & Kothari, 2009; Ray, Nickels, Sayeed, & Sax, 2003). Interestingly, mandatory pre-operative weight loss (i.e., in the weeks preceding surgery), although varying across studies, has been associated more consistently with postoperative weight loss (Livhits et al., 2012).

1.5.2 Psychopathology

Obesity has been associated with different psychopathological conditions, with high prevalence psychiatric disorders among bariatric surgery candidates (Herpertz, Kielmann, Wolf, Hebebrand, & Senf, 2004; Herpertz et al., 2003). According to current literature,

there is a high prevalence of axis I psychiatric disorders in BS candidates, with depressive, anxiety and binge eating disorder being the most prevalent (Kalarchian et al., 2007; Mauri et al., 2008; Mühlhans, Horbach, & de Zwaan, 2009).

The literature exploring psychopathological predictor of post-BS outcomes is broad but controversial. A source of studies showed lower weight loss among BS patients with preoperative psychiatric symptoms, especially depressive and anxiety disorders (Legenbauer et al., 2009; Legenbauer, Petrak, de Zwaan, & Herpertz, 2011). In another study by Kinzl and colleagues (2006) a combination of two or more psychiatric disorders and adverse childhood experiences were associated with negative post-surgery weight loss.

The fact that multiple psychiatric conditions are more likely to predict EWL has been reported by other studies (Lanyon & Maxwell, 2007), with a recent study showing that a combination of anxiety and depressive disorders predict less significant post-surgery weight loss (de Zwaan et al., 2011).

By contrast, some of the previous studies did not show preoperative anxiety or depression as having a significant impact on post-surgery outcomes (Dixon, Dixon, & O'brien, 2001, 2003; Dubovsky, Haddenhorst, Murphy, Liechty, & CoyLe, 1986). Although results are somewhat inconsistent, it has been suggested that the severity rather than the specificity of the disorder appears to be more relevant for weight outcome post-BS (Herpertz et al., 2004).

1.5.3 Eating disorders and maladaptive eating habits

Eating disorders and dysfunctional eating-related behaviors and thought have been linked to obesity. Binge eating disorder (BED) is one of the most common eating disorders often associated with obesity, which is characterized by binge eating without subsequent purging episodes (Hudson, Hiripi, Pope Jr, & Kessler, 2007). BED has been frequently reported in obese candidates for BS bariatric population, with a prevalence ranging from 10 to 50 % (Burgmer et al., 2005; Green, Dymek-Valentine, Pytluk, Le Grange, & Alverdy, 2004). The prevalence of sub-clinical binge eating behavior (i.e., overeating with subjective loss of control and psychological distress) is even higher in BS patients (80% ; Sallet et al., 2007). It has been hypothesized that preoperative binge status may directly predict weight

loss, or indirectly by the mediation of post-operative eating behaviors (Wimmelmann, Dela, & Mortensen, 2014). Concerning the direct effect, inconsistent findings are present in the literature, mostly suggesting the absence of a relation between the two factors. In particular, previous studies which adopted self-report measures to assess binge eating, showed that it does not predict weight loss after BS (White, Kalarchian, Masheb, Marcus, & Grilo, 2010; White, Masheb, Rothschild, Burke-Martindale, & Grilo, 2006), whereas in another study using clinical interview based on DSM criteria current or past binge eating behaviors were negatively associated with post-surgery weight loss (Sallet et al., 2007).

Dysfunctional eating-related behaviors other than binge eating have been related to obesity and are common among bariatric surgery patients, even though it is unclear if these behaviors affect post-surgical outcomes. Emotional eating refers to the tendency to eat in response to emotions (e.g., anger, sadness), possibly resulting in overconsumption of certain foods when facing with both positive and negative emotions. Two questionnaires have been implemented to measure emotional eating: the Emotional Eating Scale (EES; Arnow, Kenardy, & Agras, 1995); the Dutch Eating Behavior Questionnaire (DEBQ; Van Strien, Frijters, Bergers, & Defares, 1986). The DEBQ also measures other two maladaptive eating-related attitudes: restrained eating (i.e., attempt to restrain food intake) and external eating (i.e., eating in response to external food-related cues). To date, only a few studies investigated the effect of preoperative emotional eating in BS candidates, with two showing a negative relationship between emotional eating and weight loss 12 months post-surgery (Canetti, Berry, & Elizur, 2009; Miller-Matero et al., 2018), while the others did not find this relation (Kinzl et al., 2006; Wedin et al., 2014).

Another maladaptive eating-related behavior which can contribute to overeating and weight gain is the so-called "food addiction", which refers to the idea that people can become "addicted" to certain types of foods (i.e., sweets, fats, carbohydrates). This concept comes from studies which showed similarities between psychoactive substances use and excessive food consumption, at both behavioral and neural level. In line with this, emerging evidence showed that food and drugs of abuse exploit similar pathways within the brain reward system (Volkow et al., 2008; Volkow, Wang, Tomasi, & Baler, 2013), with dopamine as the principal neurotransmitter implicated (Colantuoni et al., 2001).

Furthermore, a subjective urgency to consume the substance of abuse (e.g., certain foods rich in sugar and fat) namely "craving", is experienced in both behavioral and drugs addiction. Although the "food addiction" concept is still controversial, there is growing interest in assessing this construct in the clinical population which experience problems with food, such as in obese individuals pursuing bariatric surgery. Food addiction prevalence among BS patients has been reported as higher than in obese seeking non-bariatric treatments, ranging from 14 to 58% (Miller-Matero et al., 2014). However, the possible effect of food addiction over BS outcome is still unclear, due to the relatively low number of studies (Koball et al., 2016; Miller-Matero et al., 2018; Sevinçer, Konuk, Bozkurt, & Coşkun, 2016), thus further research evaluating the effect of food addiction over post-surgery weight loss is mandatory.

1.5.4 Personality traits

Although there are no specific personality traits that have been consistently associated with obesity, it has been shown that some personality factors affect health-related behaviors (Wimmelmann et al., 2014). Some of the studies which investigated personality traits as possible predictors of post-surgery outcomes adopted the Minnesota Multiphasic Personality Inventory (MMPI) without showing significant predictors (see for a review: Herpertz et al., 2004). However, the MMPI definition of personality may be too broad, compared with different models of personality which have been more consistently related to health outcomes. For example, "neuroticism" based on the Big Five personality dimensions has related to weight gain and inappropriate eating behaviours (Elfhag & Morey, 2008; Rubinstein, 2006); one study in 44 patients underwent BS reported a negative association between neuroticism and weight grain that was mediated by post-operative eating behaviors (Canetti et al., 2009).

Impulsivity is another personality trait that has been associated with overeating and it tough to contribute to the development and maintenance of obesity. Impulsivity is a multifaceted construct including traits (i.e., personality) and states aspects (i.e., inhibitory control, reward sensitivity) (Guerrieri et al., 2007). The Barratt Impulsiveness scale (BIS-11; Barratt, 1993; Patton, Stanford, & Barratt, 1995) is a multifaced personality measure of

impulsivity which has been adopted in research and in the clinical setting, allowing to separate attentional impulsivity (i.e., inability to focus attention and to concentrate), motor impulsivity (i.e., acting without thinking) and nonplanning impulsivity (i.e., lack of future orientation or forethought). Previous studies suggested a link between attentional and overweight (Murphy, Stojek, & MacKillop, 2014) or binge eating behaviors in clinical samples with eating disorders (Claes, Nederkoorn, Vandereycken, Guerrieri, & Vertommen, 2006). In obese individuals seeking BS, high attentional impulsivity paired with the presence of food-addiction have been suggested (Meule, 2013; Meule, Heckel, Jurowich, Vögele, & Kübler, 2014). However, impulsivity trait as a possible predictor of post-BS weight loss has been poorly investigated. A recent study assessing different facet of impulsivity in BS patients showed that larger post-surgery reduction in inhibitory control was a predictor of good EWL, while impulsivity trait did not significantly predict postoperative weight loss (Kulendran, Borovoi, Purkayastha, Darzi, & Vlaev, 2017). However, in a recent study, trait impulsivity showed an indirect effect on EWL%, which was moderated by post-surgery eating behaviors (Shang et al., 2016). Thus, state impulsivity can be expected to affect post-surgery weight loss possibly because of its effect on post-surgery eating attitudes. However, studies in the literature are limited to draw this conclusion.

1.5.5 Neurocognitive functions

Cognitive dysfunctions have been reported in a large proportion of bariatric surgery patients, especially regarding executive functions (Handley et al., 2016; Thiara et al., 2017); however, preoperative cognitive functions have been poorly investigated as potential predictors of post-surgery outcomes. Executive functions are crucial to maintaining long-term goals, including long weight-loss and weight management, thus preoperative executive functioning is expected to affect post-surgery outcome.

To date, only one study in a large sample of BS showed that specific baseline cognitive functions (e.g., attention, verbal memory, and executive functions) predict successful weight loss 12 months after surgery (Spitznagel et al., 2013). In another study in smaller sample size, response inhibition was assessed form pre to post-BS using a stop-signal task,

showing that the reduction in response inhibition was a significant predictor of lower BMI 6 months post-surgery (Kulendran et al., 2017).

From a neurobiological perspective, one factor that may be associated with unsuccessfully post-surgery weight loss is lower activation in brain areas related to cognitive control, especially in presence of appetitive cues. Previous studies showed higher activation of the dorsolateral prefrontal cortex (DLPFC) in presence of food-related cues in successful dieters (DelParigi et al., 2007). On the other hand, stronger pre-surgery striatal activation can be expected to predict lower EWL post-BS.

Only a few neuroimaging studies assessed how brain activity in cognitive control and reward circuits predict successful weight loss. In the first fMRI study, patients who underwent BS were instructed to "crave" or to "resist craving" while viewing food and neutral images (Goldman et al., 2013). Interestingly, participants who reached a good post-surgery weight loss (EWL >50%) showed increased activation in the DLPFC when instructed to "resist craving". Thus, these results suggested that higher recruitment of cognitive control brain circuits post-surgery may be related with successful weight loss. In another study adopting a similar paradigm, patients were scanned one month prior to LSG and twelve months post, in order to assess brain activation toward food images while "enhancing" or "regulating" their craving (Holsen et al., 2018). On one hand, results showed an increase in post-surgery DLPFC activity during craving regulation coupled with an increase in mesolimbic cortical areas during craving enhancement. Furthermore, the preoperative activity in the nucleus accumbens and the hypothalamus predicted unsuccessful total weight loss 12 months post-surgery.

1.6 Aims of the thesis

Obesity has been related to neurocognitive alterations, suggesting reduced top-down cognitive control and enhanced attention toward food stimuli in obese individuals. Initial evidence for neurocognitive improvement following bariatric surgery has been reported in the literature, probably due to the post-surgery resolution of obesity.

This thesis aims at investigating alterations in cognitive control and attentional mechanisms related to food in severely obese candidates for laparoscopic sleeve gastrectomy (LSG) and the possible improvement at 12 months post-surgery. Second, the thesis aims at assessing neurophysiological correlates of neurocognitive deficits linked to obesity and changes in these indices 12-months post-surgery. In order to investigate behavioral and neurophysiological correlates of these processes, a novel cognitive control task with food-related distracting images was adopted during acquisition of EEG signal.

In the first study, severely obese candidates for LSG were compared with normal weight participants. Enhanced attention toward food images is expected to interfere with cognitive control over motor responses in obese individuals; furthermore, obesity is expected to be associated with general neurocognitive deficits measured by neruophysiological indices.

In the second study, changes in neurocognition were assessed from pre-LSG to 12-months post-LSG. An improvement in cognitive control and a reduction in attentional bias toward food-related stimuli are expected as post-LSG outcomes; second, an improvement in neurophysiological parameters related to neurocognition is expected after surgery.

According to the literature, not all the patients undergoing BS achieve the expected weight loss; however, clear predictors of successful or unsuccessful weight loss are far from being elucidated. Another aim of the thesis was to assess multiple psychological predictors of successful weight loss at 12 months post-LSG. Specifically, preoperative anxiety and depression symptoms and maladaptive eating and impulsivity trait are expected to possibly affect post-surgery outcomes.

EXPERIMENTAL SESSION:

CHAPTER 2

NEUROPHYSIOLOGICAL CORRELATES OF FOOD-RELATED PROCESSING DURING A COGNITIVE CONTROL TASK: AN ERPs STUDY IN NORMAL WEIGHT AND SEVERELY OBESE CANDIDATES FOR LSG

2.1 Introduction

The obesity epidemic is spreading worldwide and represents a serious challenge to the health care system given the related risk for numerous medical conditions, such as arterial hypertension, type 2 diabetes, obstructive sleep apnea syndrome, non-alcoholic fatty liver, and steatohepatitis (Ogden et al., 2007). Beyond that, there is a growing recognition of the adverse effect of adiposity on the brain in terms of functional and structural changes (García-García et al., 2015; Gustafson, Lissner, Bengtsson, Björkelund, & Skoog, 2004; S Kullmann, Schweizer, Veit, Fritsche, & Preissl, 2015; Kurth et al., 2013; Marqués-Iturria et al., 2013; Stanek et al., 2011).

A recent line of evidence has suggested cognitive alterations in severely obese individuals, showing reduced attention and executive dysfunction, such as poor decision-making and poor cognitive control (for reviews, Fagundo et al., 2012; Fitzpatrick, Gilbert, & Serpell, 2013; Prickett et al., 2015; Spitznagel et al., 2015). Among executive functions, cognitive control –the ability to orchestrate thought and action in accordance with internal goals – is critical to regulating food consumption and achieving long-term goals (i.e., successful weight loss). It refers to a subset of processes (Braver, 2012) involving: a) response inhibition (i.e., the suppression of actions no longer required or inappropriate) and b) interference control (i.e., the ability to select the proper response in the face of other, possibly competing responses). Studies comparing obese and normal weight individuals by means of behavioral measures of cognitive control have conflicting results: some showed a reduced inhibitory control (Calvo, Galioto, Gunstad, & Spitznagel, 2014; Chamberlain, Derbyshire, Leppink, & Grant, 2015; Grant, Derbyshire, Leppink, & Chamberlain, 2015;

Mole et al., 2015) and interference control in obese (Cohen, Yates, Duong, & Convit, 2011; Fagundo et al., 2012), or in relation with BMI in healthy individuals (Sellaro & Colzato, 2017), while others did not confirm the presence of altered cognitive control in obese individuals (Bongers et al., 2015; Hendrick et al., 2012).

From the other hand, neuroimaging literature suggested an enhanced reward sensitivity in obese individuals, in terms of hypersensitization within the dopaminergic brain reward system, specifically toward food with high rewarding properties (see for a review Kenny, 2011). These results indicate that certain foods (i.e., saturated in sugar and/or fat) drive the so-called "hedonic" feeding (i.e., feeding in response to pleasure instead of hunger; Appelhans, 2009), increasing the risk of overeating and weight gain. It was suggested that repeated pairing of palatable food with rewarding outcomes allows the formation of new stimulus-response (S-R) associations between food and certain behavioral responses, promoting a hypersensitization of the striatal dopaminergic reward system to food-related stimuli. In line with this, reduced availability of dopamine D2 receptors in the striatum has been reported in obese individuals (Wang et al., 2001), showing similarities with changes in the brain reward system observed in drug and behavioral addiction (Volkow et al., 2008; Volkow et al., 2013).

As a consequence of the sensitization of S-R associations, food stimuli become particularly salient, driving automatic capture of attention and affecting response selection and cognitive control. Enhanced attentional salience toward food (i.e., food-related attentional bias) has been shown in obese and overweight individuals using different experimental paradigms and methodologies (see for a review Hendrikse et al., 2015). An imbalance between cognitive control and reward sensitivity has been suggested to characterize obese individuals, probably leading to impulsive food-related decisions (Schiff et al., 2016; Ziauddeen, Alonso-Alonso, Hill, Kelley, & Khan, 2015).

From a theoretical perspective, dual-process models have been proposed to explain addictive-related behaviors such as overeating (Bechara, 2005; Evans & Coventry, 2006; Wiers, Gladwin, Hofmann, Salemink, & Ridderinkhof, 2013; Wiers & Stacy, 2006), suggesting that healthy/unhealthy actions may depend on the interaction between reflective and impulsive processes, throughout two separate pathways (Hofmann, Friese, & Wiers,

2008). Within the reflective system, behaviors are related to subjective goals and elicited as a consequence of voluntary decision processes, including executive functions. In contrast, the impulsive system activates overlearned behavioral schemata through spreading activation, which may originate from S-R associative clusters in long-term memory in close interaction with perceptual stimulus input. If cognitive resources are wakened, individuals may fail to inhibit or override impulsive influences on response selection. Thus, it may be assumed that in obese individuals enhanced attention toward food-related stimuli may result in impulsive eating behaviors, driven by hedonic characteristics of palatable unhealthy food throughout the impulsive system, especially when cognitive control processes within the reflective pathway are weakened. In line with this, recent behavioral studies showed correlations between body mass index (BMI) and difficulty in response inhibition specifically toward food-related stimuli (Houben et al., 2014), as well as reduced inhibitory control in the presence of food images in obese individuals with low restrained eating compared to normal weight individuals (Price et al., 2016).

Neuroimaging studies investigating brain response to food in different hunger conditions in normal weight and obese individuals highlighted that the activation of the reward system and the lateral prefrontal cortex predicts individual differences in the regulation of eating behaviors, successful weight loss and weight-loss maintenance in dieters (Murdaugh, Cox, Cook, & Weller, 2012; Tuulari et al., 2015). Recent studies in obese individuals have observed higher reactivity to food-related stimuli in the striatum, amygdala and orbitofrontal cortex–which are part of the brain reward system –and lower activity in the lateral prefrontal cortex (Brooks et al., 2013; Nummenmaa et al., 2012); other studies have shown that BMI inversely correlates with activation of frontal regions linked to inhibitory control during the execution of a go/no-go task with food-related stimuli (Batterink, Yokum, & Stice, 2010; He et al., 2014). Thus, impulsive behaviors toward food reward seem to be related to lower executive control and higher sensitivity of the reward system to food (Schiff et al., 2016; Ziauddeen et al., 2015).

Event-related potentials (ERPs) have been used to measure neural indices of cognitive control and selective attention toward food. ERPs have excellent time resolution, which may allow for distinguishing between fast automatic/impulsive processes on the one hand,

probably occurring early after stimulus onset and related to the subjective value of food-related stimuli, and reflective/deliberate processes on the other, probably occurring at later stages of processing and related to goal-directed behaviors. The majority of ERP studies in obese individuals assessed attentional processing of food-related stimuli (Nijs & Franken, 2012; Wolz et al., 2015) whereas only a few studies investigated both cognitive control and higher sensitivity of the reward system toward food in this population (Carbine et al., 2018; Hume et al., 2015; Nijs, Franken, et al., 2010). These studies were mainly conducted in participants ranging from overweight to Grade I obesity; however, the results are difficult to compare given the methodological differences (e.g., tasks adopted to assess cognitive control; metabolic conditions of participants; food as task-relevant information or as distracter).

Since studies of ERPs in obese populations specifically assessed with interference control in the presence of food-related stimuli are limited, we decided to measure interference control adopting a modified version of the classic visual Simon task, which includes task-irrelevant food and object images, with the simultaneous acquisition of EEG signals. The Simon task has been shown to be a suitable method for studying the spatial S-R interference effect on response selection. In the task, participants respond with spatially arranged keys to a non-spatial stimulus attribute (i.e., color or shape) of lateralized targets. Besides the fact that the spatial position of stimuli is irrelevant for the task, reaction times (RTs) are faster when target and response positions correspond spatially than when they do not – the so-called Simon effect. In this task, S-R conflict arises because irrelevant spatial information competes for response selection with task-relevant information (Lu & Proctor, 1995; Simon & Rudell, 1967; Umiltá & Nicoletti, 1990). Similarly to the dual-system models used to explain healthy/unhealthy behaviors (Wiers et al., 2013), in the Simon task, a conflict between a fast, direct automatic pathway and a slow, indirect controlled pathway appears to affect response selection processes (Ridderinkhof, 2002). Specifically, stimulus location activates the spatially corresponding response that arises from long-term associations between perceptual and motor processes and relies on genetic factors or on the synaptic consolidation of S-R associations widely overlearned during the lifespan (Cohen, Dunbar, & McClelland, 1990; Tagliabue, Zorzi, Umiltà, & Bassignani, 2000). On the other

hand, a slower indirect (controlled) route controls goal-directed behavior and activates the appropriate response according to task demands. The use of a dual-route theoretical framework seems useful to study the influence of irrelevant food stimuli on the control of interference during response selection; furthermore, the use of ERPs may help to shed light on the relationship between behavioral and neural markers of food-related processing in obese individuals.

In this study, a population of severely obese candidates for bariatric surgery was evaluated and compared to a control sample of normal weight matched individuals, after six hours of fasting. Given the novelty of the task and the lack of literature on the ERP correlates of interference control in the presence of food-related stimuli in obese individuals, a spatio-temporal multivariate Partial least square analysis (PLS) was performed (Lobaugh, West, & McIntosh, 2001). This data-driven approach allows for first exploring ERPs without a priori assumptions of the expected results. In a second step, a traditional ERPs analysis based on a priori assumption on specific ERPs components was performed. In line with previous studies on cognitive control or food-cue processing, we analyzed: 1) food-related attention trough P2 and P3 ERPs components, that have been shown to be modulated by food-cues in obese individuals (Hume et al., 2015; Nijs, Franken, et al., 2010); 2) cognitive control during interference control task, by analysis on N2 and P3 components. The neural generator of N2 can be localized to the ACC, that is involved in conflict detection and cognitive control (Folstein & Van Petten, 2008; Kok, Ramautar, De Ruiter, Band, & Ridderinkhof, 2004; Nieuwenhuis, Yeung, Van Den Wildenberg, & Ridderinkhof, 2003; Roche, Garavan, Foxe, & O'Mara, 2005), whereas the P3 component arises from more a widespread cortical generator and is related to stimulus categorization, selective attention and working memory updating (Polich, 2007). In particular, P3 component has been shown to be modulated by S-R interference effect in the Simon task (Donchin & Coles, 1988; Leuthold, 2011; Leuthold & Sommer, 1999; Ragot & Renault, 1981; Schiff et al., 2014; Smulders, 1993) ; 3) additional relevant ERPs components highlighted by the PLS analysis.

Overall, we predict that food-distracting images may interfere with goal-directed behaviors during the execution of the modified Simon task, especially in obese individuals,

and these should be detectable at both behavioral and neurophysiological levels. Furthermore, differences in neurocognitive functioning between severely obese and normal weight individuals are expected, in line with studies suggesting obesity-related cognitive dysfunction (Spitznagel et al., 2015).

2.2 Materials and methods

2.2.1 Participants

Twenty-four severely obese and twenty-six normal weight individuals matched for age and education level were enrolled in the study (See Table 2.1). Obese individuals were recruited from the Bariatric Surgery Unit of Padua University Hospital since they were candidates for laparoscopic sleeve gastrectomy. Exclusion criteria were neurological diseases, psychiatric disorders, and age <18 or >60 years. Obese participants presented other medical conditions: type 2 Diabetes (8.3%); OSAS (33.3%); hypertension (37%); dyslipidemia (33.3%). Participants were informed about the experimental procedure and gave their written consent. The study was performed in accordance with the Helsinki Declaration (Editors, 2004) and approved by the local Ethical Committee.

2.2.2 Modified Simon task (Figure 2.1)

Participants performed the task in a dimly lighted room seated in front of a 15-inch CRT computer screen at a distance of 58 cm. The task consisted of 600 experimental trials presented in five blocks of 120 trials. Each trial started with a central black fixation cross subtending 0.5° of visual angle, displayed on a light gray background. The fixation cross was surrounded by a black square perimeter with the side subtending 3° of visual angle. After a variable interval, ranging from 2000 to 3500 ms, target stimuli were presented,4.5° of visual angle on the left or right of the fixation cross for 147 ms. The target stimuli were 4x4 red-and-black or green-and-black checkerboards subtending 1.48° of visual angle. A 4x4 black-and-white checkerboard was presented together with the target as contralateral filler. At the same time, a central distracter was displayed with target onset inside the square that surrounds the fixation cross for 2000 ms. Distracters consisted of food and object images displayed on a white background or an empty square with a white

background. Intertrial intervals ranged from 1000 to 2000 ms. Ten food and 10 object images were selected from a validated dataset (Blechert, Meule, Busch, & Ohla, 2014).

Participants were invited to maintain central fixation and to respond to the lateral target as fast and accurately as possible. Half of the participants were instructed to press the left button (the letter 'Z' of the keyboard) with their left index finger if the target was the red-and-black checkerboard, and the right button (the letter 'M') with their right index finger if it was the green-and-black one, independently of its spatial position. The association between response hands and the target color was inverted for the remaining participants. In half the trials, response position corresponded with the spatial location of the target (corresponding condition – C) whereas in the other half response position did not correspond with the spatial location of the target (non-corresponding condition – NC).

Corresponding and non-corresponding conditions were divided according to the three types of distracter: food, object, and neutral condition (i.e., the white square). Mean RTs and response accuracy were calculated separately for each corresponding condition and type of distracters. Differences in RTs between non-corresponding and corresponding trials were analyzed for each condition (i.e., food, object, neutral) as a measure of interference control over task-irrelevant spatial information (i.e., Simon effect or S-R interference effect).

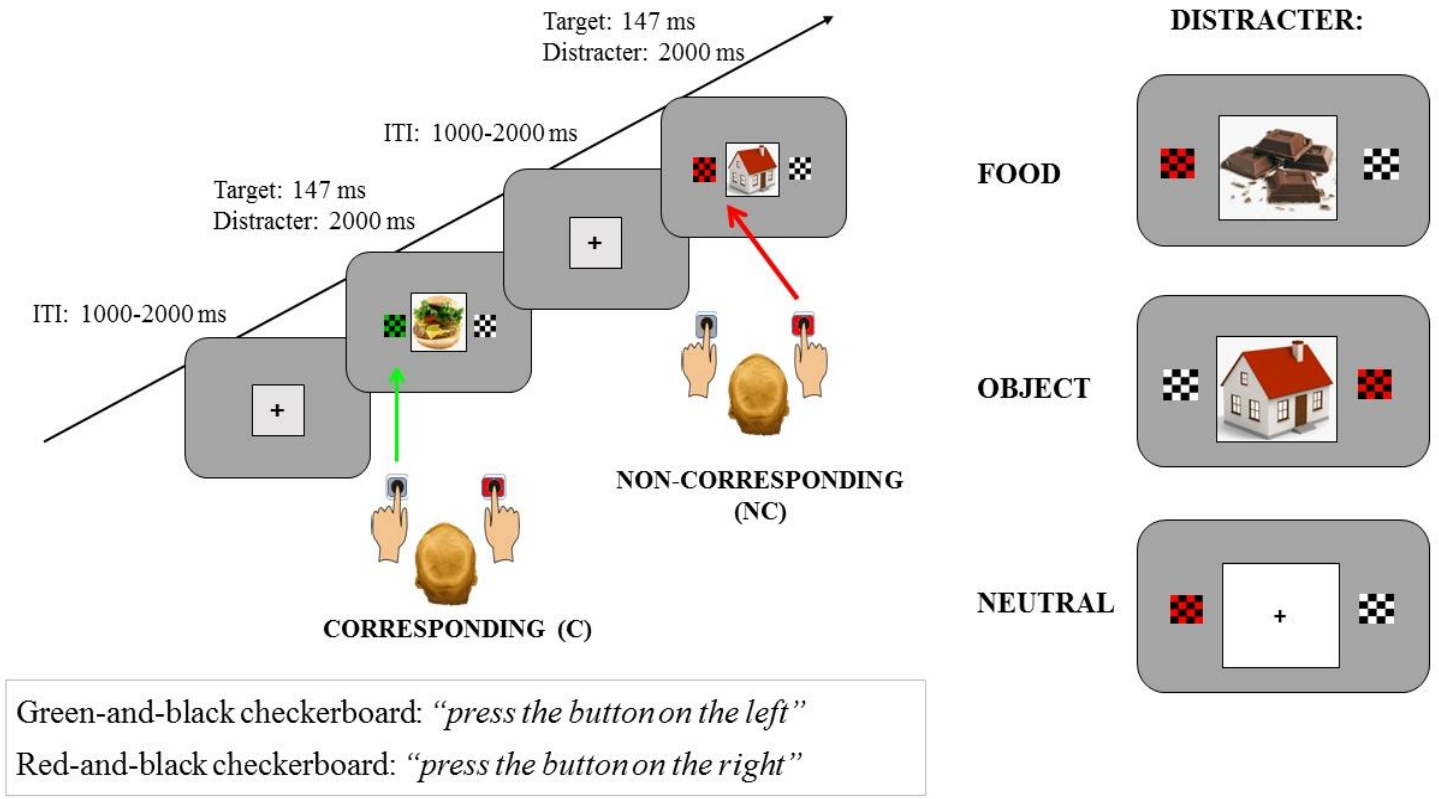

Figure 2.1 Schematic representation of the trials timeline of the Simon task with corresponding (C) and non-corresponding (NC) conditions (on the left); types of distracter presented during the task: food, object, and neutral (on the right).

2.2.3 EEG recording/preprocessing

Electroencephalographic signal (EEG) was continuously acquired with Micromed BQ3200S equipment (Mogliano, Veneto, Italy) from 29Ag/AgCl electrodes pre-cabled on an elastic cap according to the 10–20 international EEG system. The two mastoid electrodes sorted together and Fpz were used as reference and ground, respectively. Signals from all channels were digitized with a sampling rate of 512 Hz and 8 bit/channel resolution. Each signal was filtered online in the 0.03–30Hz range. Impedance was kept lower than 5 KΩ. Offline EEG analyses were performed with EEGlab (MATLAB® toolbox) applying the following: band-pass filter (0.1–30 Hz); segmentation in 3000 ms epochs (1500 ms pre-stimulus, 2000 ms post-stimulus); eye-blink and artifacts correction using independent component analysis (ICA); rejection of trials with an amplitude exciding ± 100 μV; and baseline correction was applied adopting the pre-stimulus interval between -200 and 0 ms. Averaging of segments between -200 and 1000 ms was applied separately according to distracters (i.e., food, object, neutral) and correspondence (i.e., C, NC). The number of valid segments for each condition was as follow: Neutral C (90± 9); Neutral NC (90± 13); Food C (93±10); Food NC (89±11); Object C (90±9); Object NC (87±11); there were no significant differences across conditions or groups (all ps > .05).

2.2.4 Self-report measures

Questionnaires were used to assess dysfunctional eating behaviors and attitudes toward food: binge eating (BES, Gormally, Black, Daston, & Rardin, 1982); food addiction (YFAS, Innamorati et al., 2015); emotional, restrained, and external eating (PFS, Lowe et al., 2009; DEBQ, Van Strien et al., 1986). Furthermore, trait impulsivity was investigated by administering the Barratt Impulsiveness Scale (BIS- 11, Fossati, Di Ceglie, Acquarini, & Barratt, 2001). Subjective levels of hunger, satiety, and desire to eat were rated with Likert scales ranging from -5 (max) to 5 (min).

2.2.5 Procedure

Participants performed the modified Simon task to assess interference control and attentional bias toward task-irrelevant food and object images during EEG recording. Prior

to the experimental session, self-report measures to assess eating behavior and trait impulsivity were collected. All participants were instructed to fast six hours before the experimental session that took place at the same time of the day (12–14 p.m.). Hunger ratings were collected at baseline (T0) and after the Simon task (T1).

2.3 Data analysis

2.3.1Self-report measures

Between-group differences in hunger/satiety/desire-to-eat scales were measured with mixed analysis of variance (ANOVA) using the group (obese, normal weight) as between-subject factor and time (T0, T1) as within-subject factor. Questionnaire scores were compared between obese and normal weight participants, by independent samples t-tests.

2.3.2 Modified Simon task

The differences in the Simon effect between obese and normal weight individuals across distracters (food, object, neutral) was analyzed with 2 x 3 x 2 mixed ANOVA with the group (obese, normal weight) as between-subject factor, and the distracter (food, object, neutral) and correspondence (C, NC) as within-subject factors. Bonferroni post-hoc correction for multiple comparisons followed significant effects.

2.3.4 ERP analysis

Partial least squares (PLS) analysis (Kovacevic & McIntosh, 2007; Lobaugh et al., 2001) is a multivariate data analysis technique that describes the spatio-temporal relationship between a set of independent variables of the experimental design (group and/or conditions) and a set of dependent measures (scalp ERPs). PLS enables detection of where the strongest experimental effects are expressed over the scalp and when these occur in time, without prior assumptions on the expected results. Specifically, PLS consists of the computation of the optimal least squares fit to part of the correlation or covariance matrix of data (Lobaugh et al., 2001). The ERPs data matrix contained subjects and conditions as rows and ERPs amplitude at subsequent time points and electrodes as columns. The data

matrix was transformed by mean centering the columns of the ERP data with respect to the grand mean. As the second step, the data matrix underwent singular value decomposition (SVD) to obtain a set of latent variables (LVs), each describing how strongly a certain pattern of experimental conditions (design scores) is expressed by each electrode at each time point (electrode salience). Statistical significance of each LV was calculated using 2000 permutation tests (Edgington, 1980; McIntosh, Bookstein, Haxby, & Grady, 1996). This consist of sampling without replacement to reassign the order of each condition for each subject. PLS is recalculated for each new permuted sample, and the number of times the permuted singular values exceeded the observed singular value in each LV is calculated as a probability (significant at $p < .05$). A subsequent bootstrap resampling was performed to estimate the stability of the maximal electrode saliencies identified on the LVs; thus, the standard errors of the saliencies were estimated through 1000 bootstrap samples (Efron & Tibshirani, 1986; Fabiani, Gratton, Corballis, Cheng, & Friedman, 1998).

This procedure allows for determining those portions of the ERP waveforms that show reliable experimental effects across subjects. The PLS analysis included 12 conditions: 2 groups (obese, normal weight) x3 distracters (food, object, neutral) x2 correspondences (C, NC).

Traditional ERP analyses were then conducted based on both visual inspection of the ERPs' grand average and PLS results. In agreement with previous studies (Bar-Haim, Lamy, & Glickman, 2005; Folstein & Van Petten, 2008; Mapelli, Di Rosa, Cavalletti, Schiff, & Tamburin, 2014; Polich & Kok, 1995; Thai, Taber-Thomas, & Pérez-Edgar, 2016), adaptative mean amplitudes (μV) and peak latencies (ms) were extracted for P2 (120-250 ms) and N2 (150–300 ms) in fronto-central midline electrodes (Cz, Fz), and for P3 (250–500 ms) in centro-parietal midline electrodes (Cz, Pz), in accordance with the usual topographical distribution of these components. In addition, PLS analysis allowed to detect a significant latent variable (i.e., LV3; see below in PLS results for details) sensitive to the type of distracter within an early time window (around 100 ms after stimulus presentation) topographically distributed in prefrontal electrodes, which we further explored with traditional ERP analyses. These analyses were performed by extraction of adaptative mean amplitude (μV) and peak latency (ms) of this prefrontal N1 component

(PF-N1) in the time window between 50 and 150 ms in frontal electrodes (Fp1, Fp2, F3, F4, Fz, Cz).

Adaptative mean amplitudes and latencies of ERP differences between obese and normal weight individuals were investigated applying a 2 x 3 x 2 mixed ANOVA with the group (obese, normal weight) as between-group factor and the distracter (food, object, neutral) and correspondence (C, NC) as within-group factors. Bonferroni post-hoc correction for multiple comparisons followed significant effects.

2.3.5 Correlations

Pearson correlations were calculated between the Simon effect for food distracters (RTs) and subjective hunger/satiety/desire to eat. Furthermore, correlations with hunger were performed with those ERPs components which showed to be modulated by food-related stimuli.

2.4 Results

2.4.1 Self-report measures

Questionnaires showed that obese individuals had higher scores in BES ($t_{47} = 4.71$, $p < .0001$), Y-FAS ($t_{47} = 3.67$, $p < .0001$), EAT-26 ($t_{47} = 3.04$, $p < .01$), DEBQ-emotional ($t_{47} = 4.61$, $p < .0001$), and PFS ($t_{47} = 2.72$, $p < .01$) compared to normal weight individuals. No significant differences were observed for DEBQ-external, DEBQ-restrained or self-reported impulsivity (all p's > .05; see Table 2.1 for details).

Analysis on subjective hunger/satiety/desire to eat showed a significant effect of group for hunger ratings ($F_{1, 46} = 7.33$, $p < .009$, $\eta_p^2 = .138$), satiety ($F_{1, 46} = 10.7$, $p < .002$, $\eta_p^2 = .189$), and desire to eat ($F_{1, 46} = 6.57$, $p < .001$, $\eta_p^2 = .125$). Specifically, obese individuals perceived lower levels of hunger and desire to eat, and higher level of satiety compared to the normal weight group (Table 2.2).

Table 2.1. Mean (SD) demographics variables and self-report measures

	Normal weight	**Obese**
Gender (F/M)	22/4	19/5
Age (years)	32.8 (9.79)	37.6 (10.1)
Education (years)	11.9 (3.45)	13.6 (3.69)
Weight (kg)	60.4 (6.37)	123 (19.1) **
Height (m)	1.66 (.70)	1.66 (.89)
BMI (kg/m2)	21.7 (1.75)	44.71 (6.44) **
BES	4.58 (4.31)	14.3 (9.26) **
YFAS	1.04 (.916)	3.26 (1.98) **
EAT-26	4.73 (5.43)	10 (6.78) **
DEBQ-restrained	2.44 (.78)	2.68 (.71)
DEBQ-emotional	1.82 (.70)	3.16 (1.28) **
DEBQ-external	2.66 (.45)	3.01 (8.14)
PFS-available	1.44 (0.55)	2.06 (.81) *
PFS-present	1.69 (0.63)	2.55 (1.27) **
PFS-tasted	2.06(0.51)	2.38(1.05)
PFS-total	1.68 (.471)	2.31 (1.06) **
BIS-11 attentional	14.11 (2.12)	15.54 (3.47)
BIS-11 motor	18.7(4.75)	20.45(5.70)
BIS-11 non-planning	24.3 (4.71)	26.9 (5.22)
BIS-11-total	57.2 (9.77)	60.4 (15.1)

Notes: SD = standard deviation; F = female; M = male; m = meter; kg = kilogram; BMI = Body Mass Index; BES = Binge Eating Scale; YFAS = Yale Food Addiction Scale (total score); EAT-26 = Eating Attitude Test; DEBQ = Dutch Eating Behavior Questionnaire (subscales: restrained, emotional, external); PFS = Power of Food Scale; BIS-11 = Behavioral Inhibition Scale (total score). * $p < .05$; ** $p < .001$

Table 2.2. Mean (SD) Likert scales hunger/satiety/desire to eat

	Normal weight	**Obese**
Hunger	-1.87 (.392)	-.375 (-392) *
Satiety	-3.08 (.441)	-1.04 (.441) *
Desire to eat	-2.29 (.497)	-.488 (.497) **

Negative values indicate higher hunger, satiety, and desire to eat; Notes: SD = standard deviation; * $p < .05$; ** $p < .001$.

2.4.2 Modified Simon task

The ANOVA on the RTs showed that distracter had a main effect: $F_{2, 96} = 27.7$, $p < .00001$, $\eta_p^2 = .367$, with faster RTs for the neutral condition compared to both food and object conditions (Bonferroni $p < .05$ neutral vs. food; neutral vs. object), and a main effect of correspondence: $F_{1, 48} = 107$, $p < .000001$, $\eta_p^2 = .691$, with faster RTs in C compared to NC. A significant distracter x correspondence interaction was found: $F_{2, 96} = 8.52$, $p = .0003$, $\eta_p^2 = .151$, with faster RTs in NC trials in the neutral condition compared to both food and object conditions. Interestingly, a significant distracter x correspondence x group interaction was found: $F_{2, 96} = 3.73$, $p = .027$, $\eta_p^2 = .07$, highlighting that in C trials neither group showed differences across distracters, whereas in NC trials both obese and normal weight groups showed slower RTs in the presence of food and object distracters compared to the neutral condition.

The ANOVA on the accuracy showed a main effect of distracter: $F_{2, 96} = 3.97$, $p = .022$, $\eta_p^2 = .076$, with higher accuracy in the neutral condition compared to object but not compared to food. The analysis also indicated a main effect of correspondence: $F_{1, 48} = 53.2$, $p < .000001$, $\eta_p^2 = .526$, with higher accuracy in C compared to NC trials as well as a significant distracter x correspondence interaction: $F_{2, 96} = 12.8$, $p < .000001$, $\eta_p^2 = .210$, showing higher accuracy in the neutral condition compared to object one, but only in the NC trials.

The ANOVA on the Simon effect (i.e., the difference in RTs between NC and C trials) separated for the three distracting conditions, showed a main effect of distracter: $F_{2, 96} = 8.52$, $p = .0003$, $\eta_p^2 = .151$, highlighting a larger interference effect for both food and object compared to neutral conditions. More relevant, a significant distracter x group interaction was found: $F_{2, 96} = 3.73$, $p = .027$, $\eta_p^2 = .07$ (see Figure 2.3), showing that in the obese group the interference effect is larger in the presence of food images compared to the neutral condition, whereas there is no difference between the neutral and object conditions (Bonferroni correction: food vs. neutral $p = .0001$; neutral vs. object and food vs. object all p's $> .12$). In contrast, in the normal weight group, no differences were present across

distracters (all p's > 1). Means and standard deviations of RTs and accuracy in different task conditions are reported in Table 2.3.

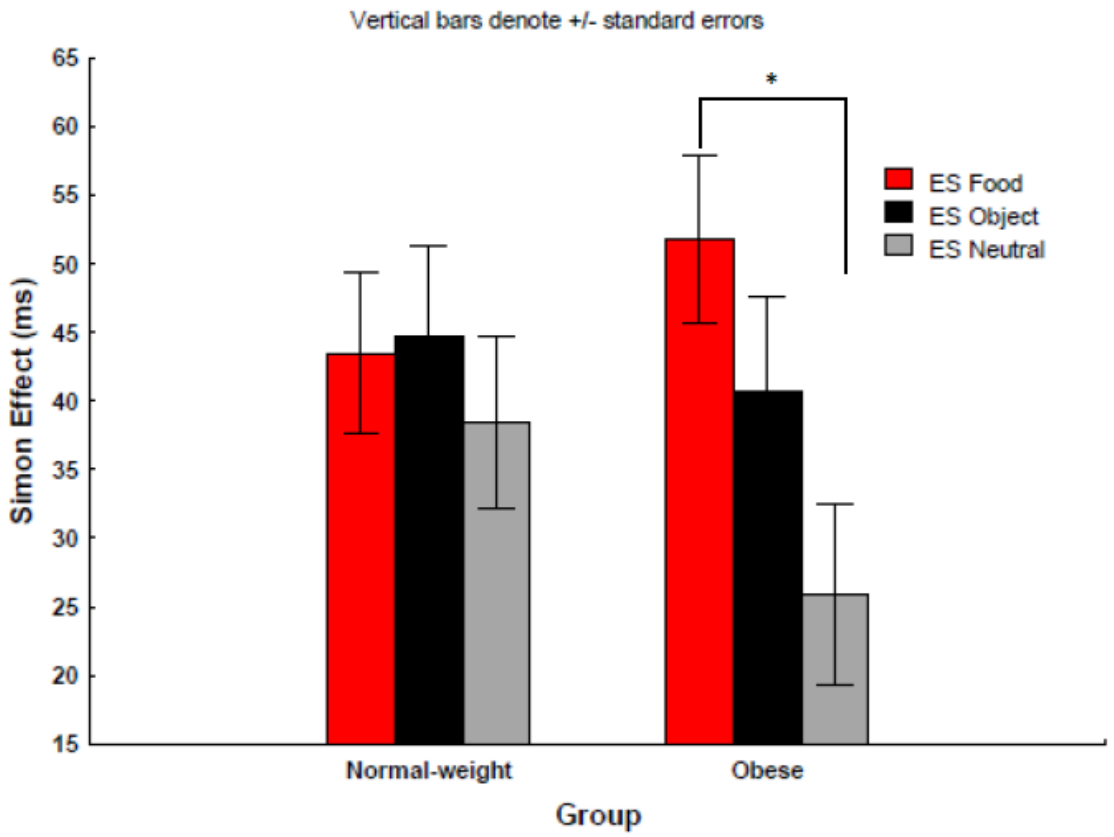

Figure 2.3. Simon effect (ms) in obese and normal weight subjects, in trials with different distracters: food (red), object (black), neutral (gray). Vertical bars denotes standard errors.

Table 2.3 Mean (SD) in the Simon task

	Normal weight	**Obese**
RTs (ms)		
Food C	567 (96)	567 (79)
Food NC	611 (96)	619 (84)
Object C	566 (93)	569 (78)
Object NC	611 (106)	610 (68)
Neutral C	558 (90)	563 (83)
Neutral NC	596 (99)	589 (75)
Accuracy (%)		
Food C	.98 (.02)	.97 (.02)
Food NC	.93 (.05)	.92 (.05)
Object C	.98 (.02)	.97 (.02)
Object NC	.93 (.05)	.92 (.05)
Neutral C	.97 (.03)	.97 (.02)
Neutral NC	.95 (.03)	.94 (.04)
SE (ms)		
Food	43.4 (33)	51.7 (25)
Object	44.6 (43)	40.7 (16)
Neutral	38.4 (39)	25.8 (21)

Notes: SD = standard deviation; C= corresponding trials; NC = non-corresponding trials; SE= Simon effect (NC – C).

2.4.3 ERP results

Multivariate PLS analysis revealed three significant latent variables (LV1: $p < 0.0001$; LV2: $p < 0.0001$; LV3 $p < .01$) that accounted for 82.2%, 6.73%, and 3.31% of the cross-block covariance, respectively. LV1 distinguished between ERPs elicited in the neutral condition compared to both food or object distracters in obese and normal weight groups. The electrode salience for LV1 highlighted a difference between neutral conditions and food and object distracters in frontal and central sites, with greater negativity in the time window between 150 and 300 ms (i.e., the typical time window and distribution of the N2 ERP component), as well as greater positivity between 350 and 500 ms (i.e., the typical time window and distribution of the P3 ERP component). LV2 distinguished between ERPs elicited in C compared to NC trials. The electrode salience for LV2 highlighted a difference between C and NC trials in central and parietal sites in time windows of 300–400 ms and 400–600 ms. Interestingly, LV3 distinguishes trials with food images from those with objects as distracters. This later LV describes an early negative component (time window between 50 and 150 ms) mainly distributed in frontal sites; thus, we call this component prefrontal-N1 (PF-N1). LV3 also describes a later positive peak in the time window between 120 and 250 ms corresponding to the P2 ERP component. Design scores and electrode salience of each latent variable are depicted in Figure 2.3.

After PLS analysis, traditional ERP analysis of amplitudes and latencies was applied (see Figure 2.4). The ANOVA for the PF-N1 amplitude showed a main effect of distracter: $F_{2, 96} = 10.7$, $p = .00006$, $\eta_p^2 = .182$, with higher PF-N1 for food compared with both objects and neutral conditions (Bonferroni correction: food vs. neutral $p < .00001$; food vs. object $p = .01$).

The ANOVA for PF-N1 latency showed a significant effect of distracter: $F_{2, 96} = 29.5$, $p = .0000001$, $\eta_p^2 = .381$, with longer latency for the neutral compared to both food and object conditions. Mean and standard deviations of the PF-N1 amplitude and latency are depicted in Table 2.4.

The ANOVA for P2 amplitude showed a main effect of distracter: $F_{2, 96} = 4.64$, $p = .01$, $\eta_p^2 = .088$, showing greater P2 amplitude for the object condition compared to food, but not

to the neutral condition. No other main effects or interaction, including the groups, were found for P2 amplitude.

The ANOVA for P2 latency highlighted a significant effect of distracter: $F_{2, 96} = 40.3$, $p = .00001$, $\eta_p^2 = .457$, showing longer P2 latency in the neutral condition compared to both food and object conditions. A significant main effect of group was also found: $F_{1, 48} = 4.64$, $p = .036$, $\eta_p^2 = .457$, with obese showing longer latencies compared to normal-weight. A significant interaction between group and distracter was found: $F_{2, 96} = 3.07$, $p = .05$, $\eta_p^2 = .060$; suggesting a larger difference between P2 latencies for distracters compared to the neutral condition only in normal-weight. In order to explore in deep this interaction, the effects of food or object distracters were isolated by subtracting the latency of these two conditions from the latency of the neutral one. However, the ANOVA on this differential score (Food-Neutral; Object-Neutral) did not show a significant effect of the group or interaction between group and distracter. Mean and standard deviations of the P2 amplitude and latency are depicted in Table 2.5.

The ANOVA for N2 amplitude showed a main effect of distracter: $F_{2, 96} = 124$, $p < .00001$, $\eta_p^2 = .722$, with smaller amplitude for the neutral condition compared to both food and object. A significant distracter x group interaction: $F_{2, 96} = 3.77$, $p = .026$, $\eta_p^2 = .073$. However, post-hoc analysis showed smaller amplitude for neutral conditions compared to food and object distracters in both groups. To further explore this interaction, we isolate the effect of distracters form the neutral condition by calculating a differential score (Food-Neutral; Object-Neutral) as for the P2 latency. The ANOVA on this differential score measure showed a main effect of group: $F_{1, 48} = 4.06$, $p = .049$, $\eta_p^2 = .078$, with a smaller amplitude of the N2 for obese compared to normal weight.

The ANOVA for N2 latency showed a significant effect distracter: $F_{1, 48} = 5.37$, $p = .006$, $\eta_p^2 = .101$, suggesting longer latency for the neutral condition compared to both food and object conditions (Bonferroni correction: food vs. neutral $p < .001$; object vs neutral $p < .05$). Mean and standard deviations of the N2 amplitude and latency are depicted in Table 2.6.

The ANOVA for P3 amplitude highlighted a main effect of distracter: $F_{2, 96} = 52.9$, $p = .000001$, $\eta_p^2 = .524$, showing greater amplitudes for both food and object conditions

compared to the neutral one, as well as a main effect of correspondence: $F_{1, 48} = 28.2$, $p = .000001$, $\eta_p^2 = .371$, showing greater P3 amplitude for C compared to NC trials. No others main effects or interactions were found.

The ANOVA for P3 latency highlighted a main effect of distracter: $F_{2, 96} = 6.94$, $p = .002$, $\eta_p^2 = .126$, with shorter latency for the neutral compared to both food and object conditions; a main effect of correspondence: $F_{1, 48} = 8.61$, $p = .005$, $\eta_p^2 = .152$, with shorter latency in C compared to NC trials; The main effect of group did not reach statistical significance: $F_{1, 48} = 3.86$, $p = .055$, $\eta_p^2 = .075$, even if normal weight individuals seems to point out shorter P3 latency compared to the severe obese individuals. Mean and standard deviations of the P3 amplitude and latency are depicted in Table 2.7.

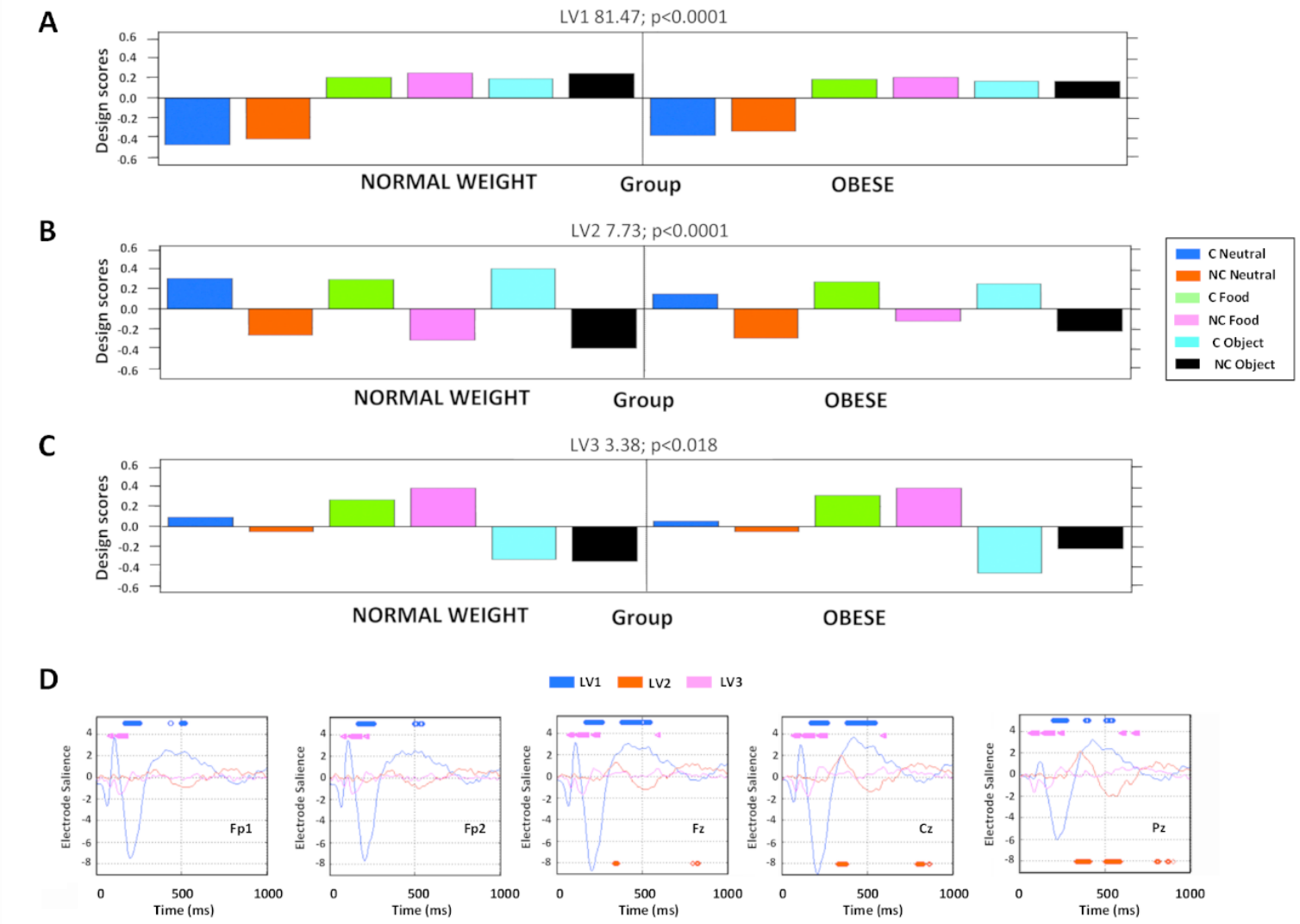

Figure 2.3. (A–C) Design scores of the latent variables LV1, LV2, LV3; (D) Electrode salience for the LVs in Fp1, Fp2, Fz, Cz, Pz.

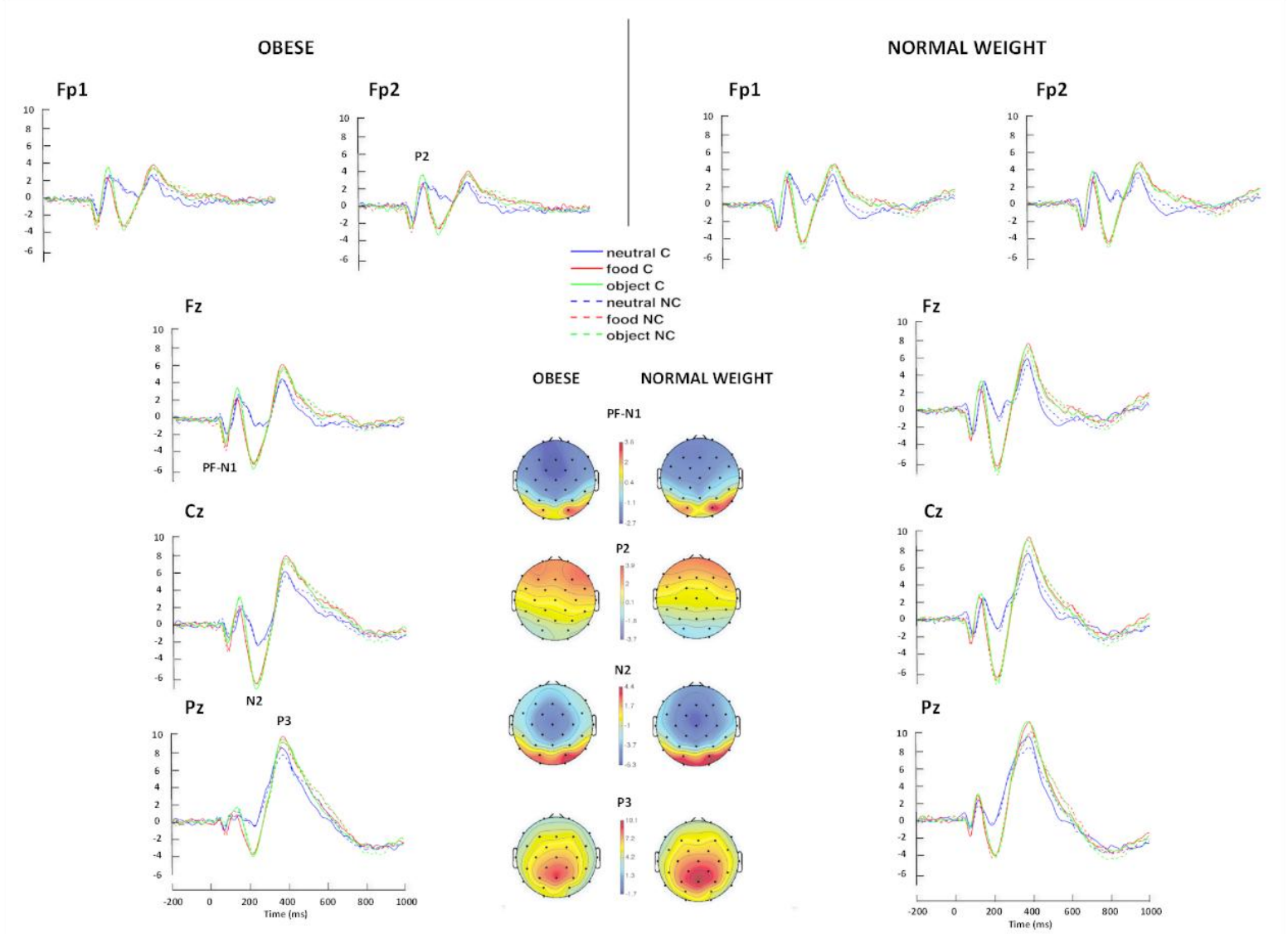

Figure 2.4. Grand mean and topographical distribution of PF-N1, P2, N2, and P3 ERP components, for both obese and normal-weight participants

Table 2.4. Mean (SD) PF-N1 amplitude (μV) and latency (ms)

	Normal weight	**Obese**
PF-N1 Amplitude		
Food C	-3.11 (2.40)	- 3.01 (2.15)
Food NC	-3.22 (2.10)	- 3.42 (2.23)
Object C	-2.62 (2.19)	- 2.68 (1.67)
Object NC	-2.73 (2.29)	- 2.31 (2.51)
Neutral C	-2.42 (1.67)	- 1.98 (1.21)
Neutral NC	- 2.70 (1.57)	- 1.76 (1.14)
PF-N1 Latency		
Food C	81 (10)	84 (14)
Food NC	79 (9)	81 (8)
Object C	78 (10)	81 (10)
Object NC	80 (9)	81 (14)
Neutral C	93 (10)	90 (12)
Neutral NC	91 (12)	88 (10)

Notes: SD = standard deviation; C= corresponding trials; NC = non-corresponding trials

Table 2.5 Mean (SD) P2 amplitude (μV) and latency (ms)

	Normal weight	Obese
P2 Amplitude		
Food C	3.26 (2.99)	2.94 (3.39)
Food NC	3.25 (3.29)	3.06 (2.95)
Object C	3.87 (3.09)	4.02 (2.93)
Object NC	3.97 (3.33)	4.12 (2.98)
Neutral C	3.91 (3.15)	3.17 (2.63)
Neutral NC	3.64 (3.06)	3.47 (2.51)
P2 Latency		
Food C	127 (19)	144 (27)
Food NC	127 (13)	138 (12)
Object C	127 (13)	143 (14)
Object NC	130 (13)	139 (13)
Neutral C	158 (26)	159 (26)
Neutral NC	154 (25)	155 (28)

Notes: SD = standard deviation; C= corresponding trials; NC = non-corresponding trials

Table 2.6 Mean (SD) N2 amplitude (μV) and latency (ms)

	Normal weight	Obese
N2 Amplitude		
Food C	-6.85 (3.92)	-6.67 (4.27)
Food NC	-7.18 (4.47)	- 6.61 (4.33)
Object C	-7.11 (3.66)	-6.98 (4.39)
Object NC	-7.45 (3.72)	-6.47 (3.89)
Neutral C	-2.20 (3.01)	-3.03 (4.27)
Neutral NC	-2.24 (3.06)	-3.39 (4.04)
N2 Latency		
Food C	232 (43)	239 (37)
Food NC	227 (38)	234 (43)
Object C	221 (20)	237 (34)
Object NC	221 (29)	234 (28)
Neutral C	223 (43)	304 (25)
Neutral NC	226 (38)	238 (31)

Notes: SD = standard deviation; C= corresponding trials; NC = non-corresponding trials

Table 2.7 Mean (SD) P3 amplitude (μV) and latency (ms)

	Normal weight	Obese
P3 Amplitude		
Food C	11.4 (4.45)	10.1 (4.58)
Food NC	10.3 (4.41)	9.18 (4.03)
Object C	11.1 (4.67)	9.96 (4.20)
Object NC	9.93 (4.08)	9.19 (3.89)
Neutral C	9.49 (4.09)	8.63 (3.72)
Neutral NC	8.50 (3.61)	8.22 (3.61)
P3 Latency		
Food C	383 (28)	410 (70)
Food NC	387 (24)	421 (74)
Object C	388 (44)	410 (72)
Object NC	392 (41)	422 (87)
Neutral C	360 (38)	407 (72)
Neutral NC	379 (55)	406 (78)

Notes: SD = standard deviation; C= corresponding trials; NC = non-corresponding trials

2.4.4 Correlations

Desire to eat at T0 correlated with both RTs in NC trials with food distracters (r = -.310, p = .028) and with the magnitude of the Simon effect in the food condition (r = -3.08, p = .029; see Figure 2.6), showing slower RTs and a higher Simon effect in those individuals who experienced greater desire to eat at baseline. In contrast, ERPs component which showed a food-related modulation (i.e., N1 amplitude; P2 latencies) did not correlate with hunger/satiety or desire to eat.

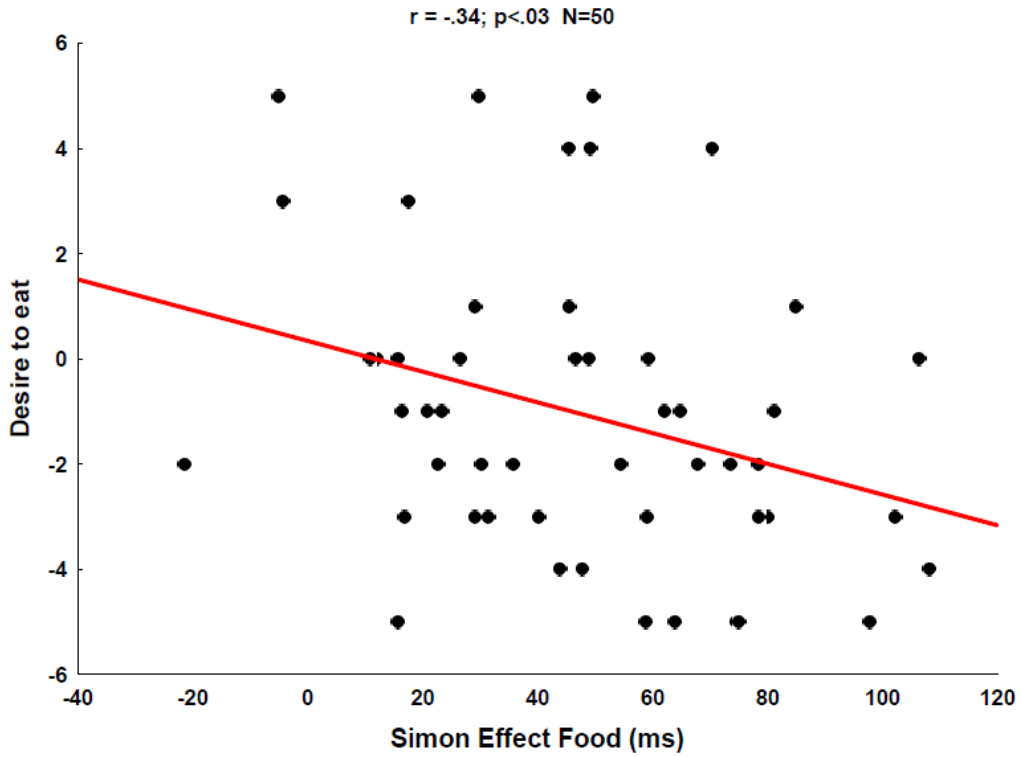

Figure 2.6. Pearson's correlations between "desire to eat" and the magnitude of the Simon effect (ms).

2.5 Discussion

In the present study, cognitive control in the presence of food-related and non-food related stimuli was investigated in severely obese individuals compared to normal weight controls, by means of behavioral and ERP measures. Specifically, interference control was assessed with a modified version of the Simon task, which includes task-irrelevant images of food or objects as distracters and a neutral condition without distracters. Likert scales were adopted to assess levels of subjective hunger, satiety, and desire to eat. Furthermore, questionnaires were administered to evaluate eating-related behaviors and attitudes and traits of impulsivity.

Although all participants were tested in a fasting state (i.e., 6 hours), lower levels of subjective hunger and desire to eat, as well as higher satiety, were observed at baseline in obese compared to normal weight individuals. These results are in line with evidence showing reduced sensibility to body signals such as hunger (i.e., interoceptive sensitivity) in obese individuals (Herbert & Pollatos, 2014). Alternatively, obese individuals may have underreported their sensation of hunger, satiety and desire to eat in order to give more acceptable responses.

Compared to normal weight individuals, obese subjects scored higher in binge eating, food addiction, emotional eating (i.e., DBEQ-Emotional), and external eating (i.e., PFS-total, PFS-present, and PFS-available), suggesting that, in our sample, the obese were more prone to dysfunctional eating-related behaviors, in line with current literature (Miller-Matero et al., 2014; Pedram et al., 2013; Schultes, Ernst, Wilms, Thurnheer, & Hallschmid, 2010). By contrast, the two groups did not differ in trait impulsivity as assessed by self-report measures (i.e., BIS-11).

In the Simon task, slower RTs were observed for non-corresponding conditions and for trials with distracting images (i.e., food and object). More interestingly, the interaction between correspondence, distracter, and group highlighted that, only in obese individuals, the correspondence effect (i.e., the Simon effect) is larger for food images compared to the neutral condition. This result shows that task-irrelevant food images interfere with cognitive control in obese individuals, as a sort of "food-related interference effect". This is

in line with the suggestion that obese subjects specifically failed in cognitive control toward food but not so much toward other stimuli (Price et al., 2016), as a result of the hypersensitization of the reward system to food stimuli. Moreover, another study in normal weight and overweight individuals showed that BMI was related to reduced cognitive control toward food, measured with a stop-signal task in the presence of food images (Houben et al., 2014).

Regarding the Likert scales that measure subjective experience of hunger, positive correlations were found between 'desire to eat' and the magnitude of the Simon effect for food and RTs in the NC trials with food distracters. Thus, at a behavioral level, food-related stimuli slowed down response selection and reduced interference control, especially in those individuals that experienced higher desire to consume food.

For neurophysiological results, PLS analysis revealed a first latent variable (LV1) that distinguished between neutral conditions and distracters (both food and object) in a time window and electrode sites typically associated with the N2 and P3 ERP components. Traditional analysis of these ERP components showed longer latencies and higher amplitudes for distracters compared to the neutral condition, suggesting that the presence of distracting images modulates ERPs at middle/late stages of information processing in both obese and normal weight individuals.

The N2 ERP component is considered a neural marker on the engagement of selective attention toward relevant and irrelevant information and is usually enhanced when different sources of information compete during the recruitment of attention resources toward task-relevant perceptual information (Folstein & Van Petten, 2008).

The P3 is a positive deflection, reaching its maximum amplitude over the parietal sites of the scalp. The peak latency of the P3 occurs at roughly 300–400 ms after stimulus onset. P3 is the best known ERP correlates of updating information in the working memory and of information processing speed (Polich, 2007; Sur & Sinha, 2009). The effect of distracting images on this component may be regarded as a neurophysiological correlate of the conscious evaluation of stimulus categorization and orienting attention toward task-related information.

The second latent variable (LV2), derived by PLS analysis, confirmed the effect of correspondence in the time window and topography of P3, and, as expected, traditional ERP analysis highlighted shorter P3 latency and higher amplitude in corresponding compared to non-corresponding conditions. Substantial evidence reported shorter latency and higher amplitude of P3 in the corresponding compared to the non-corresponding condition (Donchin & Coles, 1988; Leuthold, 2011; Leuthold & Sommer, 1999; Ragot, 1984; Ragot & Renault, 1981; Smulders, 1993). In the literature, a distinction between different sources of conflict was proposed to explain interference during cognitive control tasks (Hommel, 1997; Kornblum, Hasbroucq, & Osman, 1990). For example, in the Stroop and Flanker tasks, a conflict occurs between different stimulus dimensions (i.e., stimulus-stimulus conflict, S-S), whereas in the Simon task a conflict occurs between stimulus and response spatial location (i.e., stimulus-response conflict, S-R). Recent EPR studies suggested that these two types of conflicts affect different ERP components: N2 is mainly modulated by S-S conflict, whereas P3 seems to be more sensitive to S-R conflict (Frühholz, Godde, Finke, & Herrmann, 2011; K. Wang, Li, Zheng, Wang, & Liu, 2014). This is in line with our results showing the effect of S-R correspondence on the P3 but not on the N2 component.

Interestingly, the analysis of the N2 amplitude differential score (Food-Neutral; Object-Neutral), showed a significant effect of group, with a smaller amplitude of the N2 in obese compared to normal weight. The N2 ERP component has been related to conflict detection and cognitive control, with its neural generator probably localized in the anterior cingulate cortex (ACC), which is known to play a key role in conflict detection and cognitive control processes (Folstein & Van Petten, 2008). In a previous study, the N2 amplitude during response inhibition tasks (i.e., go/no-go) has been shown to be reduced for no-go trials in smokers (Buzzell, Fedota, Roberts, & McDonald, 2014), and this has been interpreted as an index of lower cognitive control. In line with this, the fact that we showed reduced N2 amplitude during the Simon task in obese compared to normal weight, may be interpreted as an index of reduced cognitive control in severely obese. In particular, we suggest that this effect is meanly related to the S-S conflict between task-relevant information (i.e., target position) and task-irrelevant ones (i.e., food and object images). In a recent study,

Tarantino and colleagues showed an enhanced fronto-central N2 in response to no-go stimuli in ex-obese which underwent bariatric surgery to lose weight, compared to normal weight individuals (Tarantino et al., 2017). Although the design of that study is different from our work, it is worth noting that they found a modulation of the N2 in ex-obese patients during a cognitive control task. This suggests that it would be of interest to explore possible changes observed from pre to post-bariatric surgery trough this neurophysiological marker of cognitive control.

From the other hand, the analysis of P3 latency showed a numerical trend for longer latency in obese compared to normal weight individuals, independently to the type of distracters, suggesting a slowing down in information processing speed and working memory updating in obese that is in line with cognitive alterations observed in previous studies in obese individuals (Smith et al., 2011; Spitznagel et al., 2015).

Overall, we suggest that N2 and P3 may reflect the activity of a frontal-parietal network known to be involved in deliberate cognitive processes and should be considered neural markers of processing within the reflective indirect pathway during stimulus categorization, working memory updating and deliberate response selection (Polich, 2007). Given the link between N2 and P3 components, the fronto-parietal network, and the reflective indirect pathway, the fact that the obese showed smaller o reduced N2 amplitude may further support the hypothesis of weakened deliberative cognitive control ability in the severely obese.

The third latent variable (LV3) distinguished between ERPs in trials with food as distracter from those with object as distracter, showing an early negative peak in the time window between 50 and 150 ms, maximal in frontal electrodes (PF-N1), and a positive peak in the time window between 120 and 250 ms corresponding to the P2 ERP component.

ERPs analysis on the PF-N1 showed higher amplitude for the food distracter compared to both object and neutral conditions. In a recent study in normal weight individuals, the visualization of food images was associated with a similar PF-N1 ERP component which was modulated by hunger and dieting history (Feig et al., 2017). Although a correlation between the PF-N1 and subjective hunger may be expected, as for the magnitude of the

Simon effect for food, that was not the case. However, the present study was not designed to compare metabolic conditions of hunger and satiety like the study of Feig et al. (2017); furthermore, differently to this previous work, in our study food information were irrelevant for the task.

It is possible to speculate that our PF-N1 reflects an early facilitation in object recognition of environmental stimuli with a behavioral relevant value. Indeed, in a previous study with magneto encephalography (MEG), a cortical network including regions of the orbitofrontal cortex (OFC) was suggested to mediate object recognition at an early stage of information processing, around 50 ms after stimulus onset (Bar et al., 2001). Interestingly, the OFC is part of the dopaminergic reward system and is known to be involved in processing food value, in reinforcement learning, and in the formation of long-term consolidation of S-R associative clusters (Rolls et al., 2010). Thus, we suggest that the PF-N1 detected here should be considered an early neural marker of discriminative and evaluative processes of sensorial information, probably associated with the fast/indirect impulsive pathway, which in some condition may interfere with response selection and cognitive control. In our data, this early prefrontal enhanced response to food-stimuli may be related to the greater magnitude of the Simon task in the food compared to object condition detected in obese but not in normal weight individuals.

In a recent work, Harris and co-workers (2013) showed a reduced N1 response during successful self-control, associated with the activity of prefrontal regions that can reflect anticipatory suppression in presence of potentially tempting foods. We found higher prefrontal activity in presence of food-related stimuli, that only in obese is associated with larger food-related interference effect at behavioral level. In this view, our results can be interpreted in terms of reduced attentional filtering toward food-related stimuli, which in turn is related to the reduce interference control toward response selection at behavioral level.

The analysis of P2 amplitude showed a difference between food and object distracters, as suggested both by PLS and traditional ERPs analysis. On the other hand, the analysis of P2 latency revealed a difference between food and object distracters compared to the neutral condition in both groups, and shorter P2 latency in obese compared to normal

weight, independently from the type of distracter. The P2 ERP component is held to index mechanisms of selective attention and feature detection (Hillyard, Teder-Sälejärvi, & Münte, 1998; Luck & Hillyard, 1994), reflecting the distribution of attentional resources. Longer P2 latency for images of food and objects compared to neutral condition suggests faster capture of attentional resources due to distracting stimuli. The fact that obese individuals showed longer overall P2 latency compared to normal-weight, could reflect slower engagement of attentional processing due to the presence of distracting stimuli, which can be explained in terms of alteration in the control of selective attention and/or in the suppression of distracting information in severely obese individuals (Prickett et al., 2015).

Overall, the present findings can be interpreted within the framework of the dual-process model of healthy/unhealthy behaviors (i.e., overeating; Wiers et al., 2013). Since obese individuals fail to inhibit prepotent responses in the presence of food distracters when cognitive control is required, it can be suggested that attentional bias toward food showed at a neurophysiological level (i.e., larger PF-N1 and smaller P2 amplitudes for food compared to object distracters) results in impulsive actions toward food only in severe obese individuals (i.e., larger Simon effect for food distracters in RTs). Given these early neural markers of food-related interference, it can be hypothesized that this effect relies on processes within the impulsive system, which overrides the reflective system in the presence of appetizing foods, especially when deliberate cognitive processes are altered.

Specifically, it can be supposed that the repeated exposure to and consumption of high palatable and rewarding foods may enhance the incentive salience of food-related stimuli, especially in hunger condition. This early food-related prefrontal neural enhancement (i.e., PF-N1 amplitude) may affect attentional filtering of irrelevant food information both in normal weight and obese individuals (i.e., P2 amplitude). On the other hand, deliberative processes associated with the reflective system seem to be altered in obese individuals, as revealed by the smaller N2 amplitude and longer P2 latency, indicating an imbalance between the impulsive and reflective systems, which may disentangle impulsive responses toward food only in obese individuals.

2.6 Limitations

The current study presents some limitations. First, the sample of obese individuals seeking bariatric treatment presents some medical comorbidities such as diabetes, cardiovascular diseases, and OSAS; thus, future studies in larger samples should address this issue. Second, the clinical sample was composed of a specific type of severely obese individuals seeking bariatric surgery, which have been passed through the history of repetitive unsuccessfully dieting attempts. Thus, our results should be replicated taking into account current present and past dietary status of both obese and normal weight controls. Another limitation to consider is that participants were tested in the metabolic state of hunger (6 h fasting), and differences in neurophysiological and cognitive outcomes can be expected in satiety, thus this issue should be further explored.

2.7 Conclusions

In conclusion, the present results show an early neural marker of sensorial evaluation of relevant food-related information in the prefrontal areas (i.e., PF-N1), both in obese and normal weight individuals when tested in a metabolic state of hunger (i.e., 6 hours of fasting), which seems to interfere with cognitive control only in obese individuals at a behavioral level. This result may suggest that in presence of food-related images, the impulsive system overrides the reflective one when cognitive control functioning is reduced (i.e., smaller N2 amplitude) and attentional resources are limited (i.e., longer P2).

Extending our results to treatment, we can suggest the development of personalized procedures to enhance cognitive control abilities or to target automatic processes associated with unhealthy behaviors, in order to influence the relative balance between impulsive and reflective systems (Wiers et al., 2013). Thus, implementing usable tools to reduce food-related bias and/or to enhance cognitive control mechanisms in obese individuals is a fascinating perspective. However, further studies are needed to support the present results or to extend the limitations of dual-route models.

CHAPTER 3:

NEUROCOGNITIVE EFFECT OF BARIATRIC SURGERY: AN ERPs STUDY ON COGNITIVE CONTROL AND FOOD-RELATED ATTENTION IN OBESE PATIENTS UNDERWENT LSG

3.1 Introduction

Bariatric surgery is considered one of the most effective long-term weight loss treatment for severe obesity, promoting higher and stable weight loss compared to pharmacological or behavioral treatments for obesity (Ayyad & Andersen, 2000; Wadden & Osei, 2002). Rout-en-Y gastric bypass (RYGB) and Laparoscopic Sleeve Gastrectomy (LSG), are two of the most effective and performed types of BS. LSG is a restrictive procedure which consists in the reduction of the volume of the stomach by approximately 80% leading to an impressive weight loss and a relatively low rate of post-surgical complications (Magouliotis et al., 2017). Besides weight loss, resolution of obesity-related comorbidities (i.e., type 2 diabetes; hypertension, obstructive sleep apnea) is frequently observed post-LSG (Buchwald et al., 2009; Colquitt et al., 2014; Kwok et al., 2014).

Profound metabolic and physiological changes are induced by BS (Papailiou et al., 2010); specifically, LSG has been shown to influence the secretion of gastrointestinal hormones which regulate appetite, such as ghrelin (Yousseif et al., 2014), substantially contributing to weight loss. Furthermore, behavioral changes have been described following LSG, in terms of reduced caloric intake both in terms of quantity and quality of the food that can be consumed at one time (Coluzzi et al., 2016).

Beyond physiological and behavioral changes, the possible positive effects of BS on neurocognition have been suggested by a source of studies (Spitznagel et al., 2015). Multiple factors have been proposed as possible causes of cognitive improvement after BS, including the resolution of comorbid medical diseases (i.e., diabetes type2, hypertension); the reduction of the inflammatory processes within the central nervous system associated with adiposity and high-fat diet; the normalization of metabolic dysregulation and neurohormones related to appetite (see for a review: Spitznagel et al., 2015). Thus, studying

the population of bariatric surgery patients provides a unique method to study the cognitive effect of severe obesity and the beneficial effect of weight loss on cognition.

Neuroimaging studies in bariatric surgery patients, even though limited, showed post-surgery changes in brain metabolism in specific regions (i.e., posterior cingulate gyrus) (Marques et al., 2014), restored functional connectivity in the default mode network (Frank et al., 2014) and altered resting-state activity in different brain regions including the thalamus and frontal regions (Wiemerslage et al., 2017).

Despite the general neurocognitive improvement, more consistent findings regard post-surgery improvement in executive functions (for recent reviews see: Handley et al., 2016; Thiara et al., 2017). Among executive functions, cognitive control abilities refer to a set of processes which regulate lower level processes toward adaptative goal-directed behaviors (Braver, 2012; Shallice, 1994). A source of studies reported deficits in obese compared to normal weight individuals in subset of functions related to cognitive control such as response inhibition (i.e., the suppression of actions no longer required or inappropriate) (Calvo et al., 2014; Chamberlain et al., 2015; Grant et al., 2015; Mole et al., 2015) and control of interference (i.e., the ability to select the proper response in the face of other, possibly competing responses) (Cohen et al., 2011; Fagundo et al., 2012).

Cognitive control processes are crucial to achieving long-term weight loss and weight management; accordingly, a neuroimaging study showed that higher activation of frontal areas devoted to cognitive control (e.g., DLPFC) predicts successful weight loss post-BS (Goldman et al., 2013). Furthermore, a recent resting-state fMRI study showed that the decreased activity of the prefrontal cortex in obese individuals recovered to normal level post-LSG (Li et al., 2018). In another study, event-related potentials (ERPs) during the execution of a Stroop interference control task were measured in ex-obese patients underwent BS compared to normal weight controls (Tarantino et al., 2017). At a behavioral level post-bariatric patient showed to be more susceptible to task-irrelevant dimension, with larger Stroop effect compared to controls, whereas at neurophysiological level, ex-obese showed in exaggerate amplitude of anterior N2 component in no-go trials. N2 is a negative wave detected around 200 ms after stimulus onset, which has been related to conflict

detection and cognitive control processes with its neural generator probably localized in the anterior cingulate cortex (ACC) (Folstein & Van Petten, 2008).

On the other hand, changes in food preferences have been reported after bariatric surgery, showing that both animals and humans switch their preference from high to low-fat food after RGYB or LSG (Wilson-Perez et al., 2013; for a review see Shin and Berthoud 2011). These changes are at least in part related to possible changes in food-reward sensitivity post-BS. Obesity has been associated with hypersensitivity of the reward system to appetizing food and higher attention toward food-related cues (i.e., food-related attentional bias); it has been suggested that bariatric surgery may reverse obesity-induced changes in reward functions (Shin and Berthoud 2013).

In line with this, neuroimaging studies showed a blunted brain activation in regions of the reward network while passing viewing food images (Behary & Miras, 2015; Ochner et al., 2011; Ochner et al., 2012; Scholtz et al., 2013), and changes in dopamine D2 receptor availability following bariatric surgery (Dunn et al., 2012, Steele et al., 2010). At a cognitive level, changes in food-related processing can be investigated assessing attention toward food-related cues after bariatric surgery. First evidence for reduced food-related attention following BS comes from a longitudinal study in patients who underwent LSG, showing a post-surgery decrease in attention toward food images, as assessed by eye tracking (Giel et al., 2014).

Overall, preliminary evidence suggested that enhanced cognitive control and reduced food-related processing may occur after surgery, possibly affecting long-term weight-loss maintenance. However, longitudinal studies are limited and further works addressing this issue with objective measures are warranted. Given the excellent temporal resolution of ERPs, previous studies in obese individuals adopted this methodology to assess food-related attention and cognitive control (Carbine et al., 2018; Hume, Howells, Rauch, Kroff, & Lambert, 2015; Nijs, Franken, & Muris, 2010).

Here, we aimed at investigating possible changes in cognitive control in the presence of food-related and non-food related stimuli assessed prior to LSG and twelve months post-surgery, by means of behavioral and ERPs measures. Based on previous literature, even if limited, blunted sensitivity to food-related cues and higher cognitive control can be

expected post-LSG; specifically: 1) food-related images are expected to interfere less with cognitive control after surgery; 2) ERP indices of cognitive control (i.e., N2) are expected to increase post-surgery 3) a general improvement in neurophysiological parameter related to cognition is expected post-LSG.

3.2 Material and Methods

3.2.1 Participants

Twenty-three severely obese individuals who participated in the study 1, were followed-up 12 months after LSG. Patients were recruited from the Bariatric Surgery Unit of Padua University Hospital. They were 19 females and 4 males, with a mean age of 37.6 years (±10.1) and education level of 11.9 (±3.53). Exclusion criteria were neurological diseases, psychiatric disorders, and age <18 or > 60 years. Participants were informed about the experimental procedure and gave their written consent. The study was performed in accordance with the Helsinki Declaration (Editors, 2004) and approved by the local Ethical committee.

3.2.2 Modified Simon Task

Participants performed the task in a dimly light room sited in front of a 15 inches CRT computer screen at a distance of 58 cm. The task consisted of 600 experimental trials presented in 5 blocks of 120 trials. Each trial started with a central black fixation cross subtending 0.5° of visual angle, displayed on a light gray background. The fixation cross was surrounded by a black square perimeter with the side subtending 3° of visual angle.

After a variable interval, ranging from 2000 to 3500 ms, target stimuli were presented, 4.5° of visual angle on the left or right of the fixation cross for 147 ms. The target stimuli were 4x4 red-and-black or green-and-black checkerboards subtending 1.48° of visual angle. A 4x4 black-and-white checkerboard was presented together with the target as controlateral filler. At the same time, a central distracter was displayed with target onset inside the square that surrounds the fixation cross for 2000 ms. Distracters consisted of food and object images displayed on a white background or a white filled square displayed without

any image. Inter-trial interval ranged from 1000 to 2000 ms. Ten food and 10 object images were selected from a validated dataset (Blechert et al., 2014).

Participants were invited to maintain central fixation and to respond to the lateral target as fast and accurately as possible. Half of the participants were instructed to press the left button (the letter 'Z' of the keyboard) with their left index finger if the target was the red-and-black checkerboard, and the right button (the letter 'M') with their right index finger if it was the green-and-black one, independently of its spatial position. The association between response hands and the target color was inverted for the remaining participants. In half of the trial, response position corresponded with the spatial location of the target (corresponding condition - C) whereas in the other half response position did not correspond with the spatial location of the target (non-corresponding condition - NC). Corresponding and non-corresponding conditions were divided according to the three types of distracter: food, object and neutral condition (i.e., the white square). Mean reaction times (RTs) and response accuracy were calculated separately for each corresponding condition and type of distracters. Differences in RTs between non-corresponding and corresponding trials were analyzed in each condition (i.e., food, object, neutral) as a measure of interference control over task-irrelevant spatial information (i.e., Simon effect or S-R interference effect).

3.2.3 EEG recording/preprocessing

The electroencephalogram (EEG) was continuously acquired with Micromed BQ3200S equipment (Mogliano, Veneto, Italy) from 29 Ag/AgCl electrodes pre-cabled on an elastic cap according to the 10-20 international EEG system. The two mastoids electrodes sorted together and Fpz were used as reference and ground respectively. Signals from all channels were digitized with a sampling rate of 512 Hz and 8 bit/channel resolution. Signal was filtered online in the 0.03-30 Hz range. Impedance was kept lower than 5 KΩ. Offline EEG analyses were performed with EEGlab (MATLAB toolbox) applying: band-pass filter (0.1-30 Hz); eye-blink correction using independent component analysis (ICA); segmentation in 3000 ms epochs (1500 ms pre-stimulus, 2000 ms post-stimulus); baseline correction was applied with a pre-stimulus interval between -200 to 0 ms. Averaging of segments between

-200 and 1000 ms was applied separately according to distracters (i.e., food, object, neutral) and correspondence (i.e., C, NC).

3.2.4 Self-report measures

Subjective levels of hunger, satiety, and desire to eat were rated with Likert scales ranging from -5 (max) to 5 (min). Questionnaires were used to assess maladaptive eating-related attitudes and behaviors: binge eating (BES, Gormally et al., 1982), food addiction (YFAS, Innamorati et al., 2015), emotional eating, restrained eating and external eating (PFS, Lowe et al., 2009; DEBQ, Van Strien et al., 1986).

3.2.5 Procedure

Questionnaires were collected at baseline (T0), between one and two months before LSG, to measure eating-related attitudes and behaviors. Then participants underwent experimental session consisting in 1) assessment of subjective levels of hunger/satiety/desire to eat; 2) modified Simon task to measure interference control and attentional bias toward task-irrelevant food and object images during EEG recording. the experimental session took place at the same time of the day (between 12-14 p.m.) and participants were instructed to fast six hours prior to this session.

Participants were followed-up 12 months Post-LSG (T1), after significant weight loss. Changes in eating-related attitudes and behaviors were assessed with questionnaires and participants underwent the same experimental session adopted at T0.

3.3 Data Analysis

3.3.1 Self-report measures

Differences from pre to post-LSG in hunger/satiety/desire-to-eat and eating-related attitudes were observed from pre to post-sleeve with paired sample t-tests.

3.3.2 Modified Simon task

The differences in the Simon effect between Pre-Sleeve and Post-Sleeve was analyzed with 2 x 3 x 2 repeated measures ANOVA with time (pre-Sleeve, post-Sleeve), distracter (food,

object, neutral) and correspondence (C, NC) as within-subject factors. Bonferroni post-hoc correction for multiple comparisons followed significant effects.

3.3.3 ERP analysis

ERPs analyses were conducted based on visual inspection of the ERPs grand-average. Adaptative mean amplitudes (μV) and peak latencies (ms) were extracted for the prefrontal N1 (PF-N1) in the time-window between 50-150 ms in frontal-central electrodes (Fp1, Fp2, F3, F4, Fz, Cz); P2 in the time-window between 120-250 ms in fronto-central midline electrodes (Fz, Cz); N2 (150-300 ms) time-window between 150-300 in Fz; P3 (250-500 ms) in centro-parietal midline electrodes (Cz, Pz).

Adaptative mean amplitudes and peak latencies of ERPs components were investigated applying a 2 x 3 x 2 mixed-ANOVA with time (pre-Sleeve, post-Sleeve), distracter (food, object, neutral) and correspondence (C, NC) as within-group factors. Bonferroni post-hoc correction for multiple comparisons followed significant effects.

3.4 Results

3.4.1 Self-report measures

A significant effect of time was present only for hunger ratings: $F_{1,46}$= 7.33, p < .009, η_p^2 = .138, with lower subjective hunger experienced Post-LSG. No differences between pre and post-sleeve were present for satiety or desire to eat.

For eating-related attitudes and behaviors: lower scores in BES (t_{21}=4.83, p<.00001), Y-FAS (t_{21} = 3.48, p = -002), DEBQ-Emotional (t_{21} = 4.46, p < .00001), DEBQ-External (t_{21} = 5.33, p <.00001) and PFS (t_{21} = 3.74, p = .001) were detected Post-LSG. No significant differences between pre and post-sleeve were observed for DEBQ-restrained and EAT-26 (See Table 3.1 for details).

3.4.2 Modified Simon task

The ANOVA on the RTs showed a main effect of distracter: $F_{2,44} = 32.01$, $p < .000001$, $\eta_p^2 = .593$, showing faster RTs in neutral condition compared to both food and object ones (Bonferroni $p<.05$ neutral vs food; neutral vs object), and a main effect of correspondence: $F_{1, 22} = 193$, $p<. 000001$, $\eta_p^2 =.898$, with faster RTs in C compared to NC. A significant distracter x correspondence interaction was found: $F_{2, 44} = 11.8$, $p = .00008$, $\eta_p^2 = .350$, showing only for the NC trials faster RTs in neutral condition compared to both food and object ones. No main effect of time or other significant interactions were present.

The ANOVA on the accuracy showed a main effect of distracter: $F_{2,44} = 7.59$, $p = .001$, $\eta_p^2 = .257$, with higher accuracy in neutral condition compared to object but not compared to food; a main effect of correspondence: $F_{1,22} = 40.63$, $p < .000001$, $\eta_p^2 = .526$, with higher accuracy in C compared to NC trials and a significant distracter x correspondence interaction: $F_{2,44} = 11.4$, $p < .0001$, $\eta_p^2 = .341$, showing, only in the NC trials, higher accuracy in the neutral condition compared to both object and food.

The ANOVA on the Simon effect (SE) separated for the three distracting conditions, showed a main effect of distracter: $F_{2, 44} = 11.84$, $p = .000007$, $\eta_p^2 = .350$, highlighting a larger interference effect for both food and object compared to the neutral condition. Time x distracter interaction was not significant ($F_{2, 44} = 2.75$, $p = .07$, $\eta_p^2 = .18$), although showing a trend for the reduction of the Simon effect toward food distracters from pre to post-sleeve.

In order to better elucidate the effect of distracters on cognitive control from that observed without distracters, differential scores were calculated by subtracting the SE in the neutral condition from the SE in presence of food (SE_Food – SE_Neutral) or object distracters (SE_Food – SE Neutral). The ANOVA using these differential scores showed an interaction between time and distracter: $F_{2, 44} = 11.84$, $p = .000007$, $\eta_p^2 = .210$, with a significant reduction of the SE toward food distracters from pre to post-Sleeve, that was not present for objects distracters (See Figure 3.1).

Table 3.1 Mean (SD) Weight, BMI and eating-related attitudes

	Pre-LSG	**Post-LSG**
Weight (kg)	123 (19.5)	80 (12.39)**
BMI (kg/m2)	44.6 (6.58)	29.5 (4.99)**
BES	14.5 (9.26)	5.95 (6.11)**
YFAS	3.19 (1.96)	1.71 (1.01)*
EAT-26	10.4 (6.59)	11.05 (10.5)
DEBQ-restrained	2.68 (.754)	2.83 (.863)
DEBQ-emotional	3.24 (1.25)	2.03 (1.04)**
DEBQ-external	3.08 (.818)	2.28 (.623)**
PFS-available	2.17 (1.08)	1.51 (.603)*
PFS-present	2.65 (1.26)	1.70 (.709)**
PFS-tasted	2.41 (1.09)	1.90 (.662)*
PFS-total	2.38 (1.07)	1.69 (.589)*

Notes: SD = standard deviation; m = meter; kg = kilogram; BMI = Body Mass Index; BES = Binge Eating Scale; YFAS = Yale Food Addiction Scale (total score); EAT-26 = Eating Attitude Test; DEBQ = Dutch Eating Behavior Questionnaire (subscales: restrain, emotional, external); PFS = Power of Food Scale (subscales: food available, food present, food tasted); Pre-LSG = prior to laparoscopic sleeve gastrectomy; Post-LSG = 12 months post laparoscopic sleeve gastrectomy .* $p < .05$; ** $p < .001$

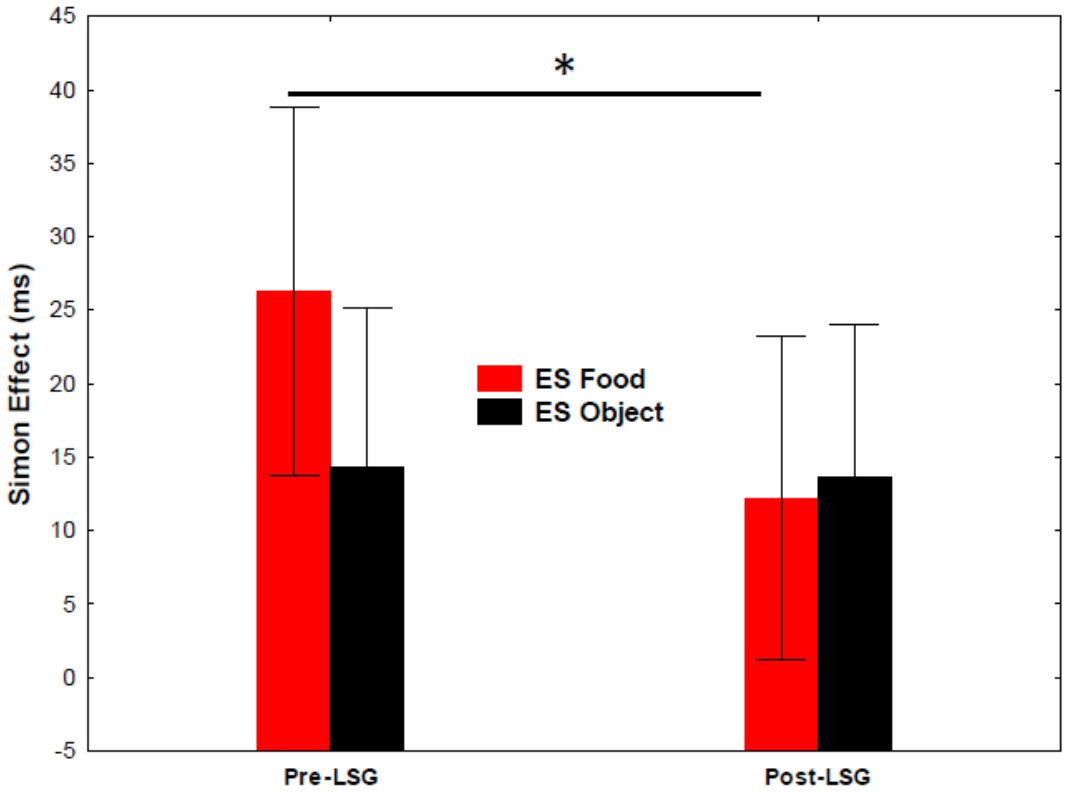

Figure 3.1 Simon effect for food (SE_Food – SE_Neutral) and for object distracters (SE_Food – SE Neutral). Vertical bars denote standard errors.

Table 3.2 Mean (SD) Simon task

	Pre-LSG	**Post-LSG**
RTs (ms)		
Food C	567 (80)	573 (87)
Food NC	619 (86)	613 (85)
Object C	570 (80)	566 (87)
Object NC	610 (82)	607 (82)
Neutral C	564 (85)	560 (82)
Neutral NC	589 (77)	587 (84)
Accuracy (%)		
Food C	.97 (.02)	.98 (.02)
Food NC	.92 (.05)	.92 (.06)
Object C	.98 (.21)	.99 (.01)
Object NC	.92 (.05)	.91 (.07)
Neutral C	.97 (.02)	.99 (.01)
Neutral NC	.94 (.04)	.95 (.04)
SE (ms)		
Food	51.8 (26)	39.8 (19)
Object	39.8 (15)	41.2 (26)
Neutral	25.5 (21)	27.6 (22)

Notes: SD = standard deviation; C= corresponding trials; NC = non-corresponding trials; SE= Simon effect (NC – C); Pre-LSG = prior to laparoscopic sleeve gastrectomy; Post-LSG = 12 months post laparoscopic sleeve gastrectomy.

3.4.3 ERPs results

The ANOVA for the PF-N1 amplitude showed a main effect of distracter: $F_{2, 44} = 12.4$, $p = .00001$, $\eta_p^2 = .361$, showing significant differences in PF-N1 amplitude across distracters with food > object > neutral (Bonferroni correction: food vs neutral $p < .00001$; food vs object $p = .03$; object vs neutral $p = .008$).

The ANOVA for PF-N1 latency showed a significant effect of distracter: $F_{2,44} = 7.14$, $p = .002$, $\eta_p^2 = .245$, with longer latency for neutral compared to both food and object conditions. No other main effect or interactions were found.

The ANOVA for P2 amplitude showed a main effect of distracter: $F_{2, 44} = 3.44$, $p = .041$, $\eta_p^2 = .135$; however, post-hoc Bonferroni did not highlight significant differences across conditions. A main effect of time was present: $F_{1, 22} = 5.77$, $p = .025$, $\eta_p^2 = .208$, showing higher amplitude post-sleeve compared to pre.

The ANOVA for P2 latency highlighted a significant effect of distracter: $F_{2, 44} = 28.5$, $p = .00001$, $\eta_p^2 = .565$, showing longer P2 latency in neutral condition compared to both food and object. No other main effect or interactions were present.

The ANOVA for N2 amplitude showed a main effect of distracter: $F_{2, 44} = 40.1$, $p = .00001$, $\eta_p^2 = .646$, with smaller amplitude for neutral condition compared to both food and object. A significant effect of time: $F_{1, 22} = 4.62$, $p = .042$, $\eta_p^2 = .174$, showing higher N2 amplitude post-sleeve (See Figure 3.3). A significant interaction between time and type of distracter: $F_{2, 44} = 3.64$, $p = .034$, $\eta_p^2 = .042$ showing a significant increase in N2 amplitude post-sleeve for food and object distracters.

The ANOVA for N2 latency showed a significant interaction between time and type of distracter: $F_{2, 44} = 3.41$, $p = .042$, $\eta_p^2 = .034$, showing longer latency for neutral compared to food and object pre-sleeve, that was not significant post-sleeve.

The ANOVA for P3 amplitude showed a main effect of distracter: $F_{2, 44} = 18.4$, $p = .000001$, $\eta_p^2 = .455$, with greater amplitudes for both food and object compared to neutral condition; a main effect of correspondence: $F_{1, 22} = 20.8$, $p = .0001$, $\eta_p^2 = .486$, showing higher P3 amplitude for C compared to NC trials. An interaction between time and type of distracter was also present: $F_{2, 44} = 6.12$, $p = .004$, $\eta_p^2 = .218$, specifically the amplitude of the P3 in neutral condition was significantly enhanced post-sleeve. Even though not

significant, mean amplitudes for food distracter seem to reduce post-sleeve, whereas object distracter enhanced post-sleeve, similarly to the neutral condition. To better explore the effect of time on different types of distracters, we further calculate a differential score between pre and post measures for each type of distracter and corresponding condition. The ANOVA on this differential score (Post – Pre) highlighted the main effect of type of distracter, $F_{1, 44} = 6.12$, $p = .004$, $\eta_p^2 = .218$, post hoc showed a significant reduction in P3 amplitude for food distracter compared to neutral (Figure 3.4).

The ANOVA for P3 latency highlighted a main effect of correspondence: $F_{1, 22} = 7.81$, $p = .01$, $\eta_p^2 = .262$, with shorter latency in C compared to NC trials. No other main effects of interaction were observed for P3 latency.

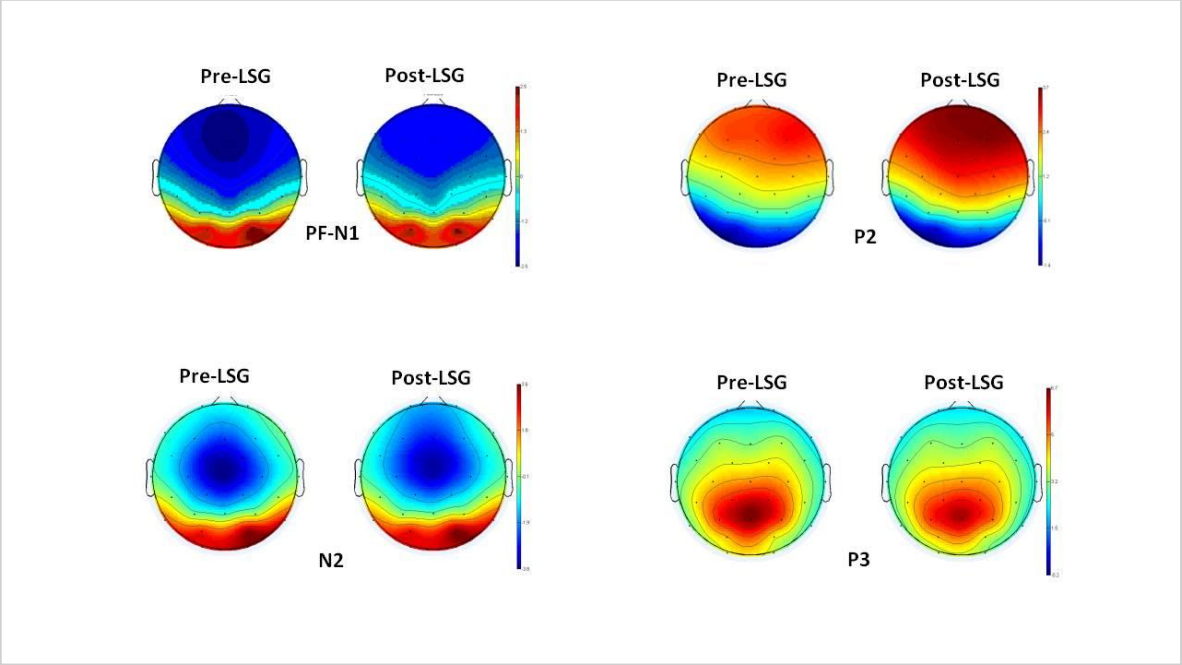

Figure 3.2 Scalp maps showing the topography of ERPs components

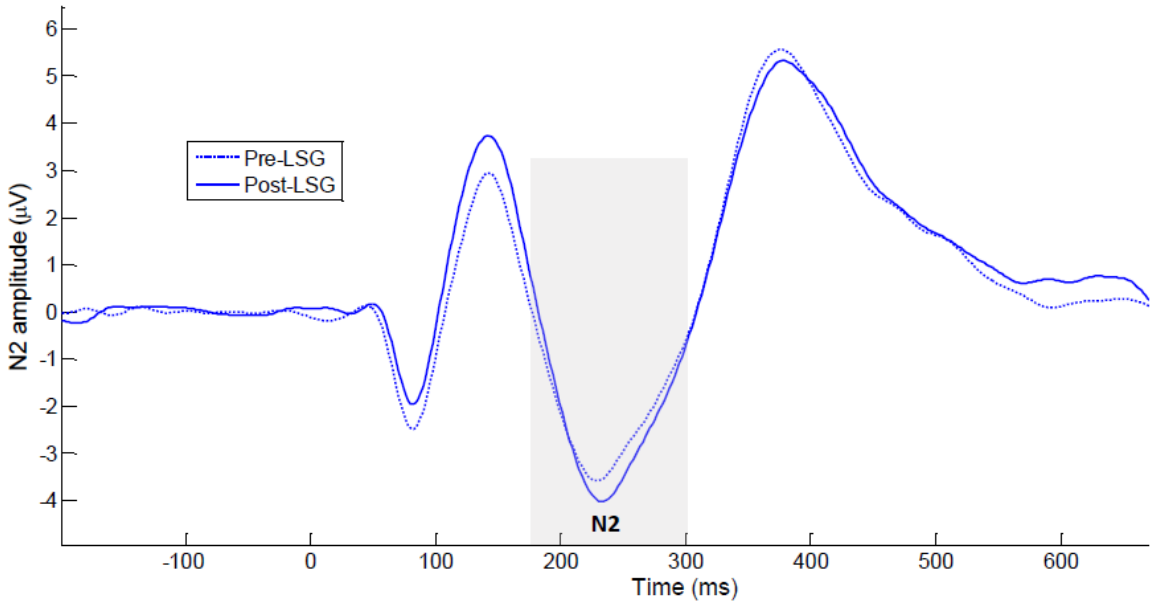

Figure 3.3 ERPs waveforms in Fz depicting N2 amplitude (μV) Pre-LSG (dashed line) and post-LSG (solid line).

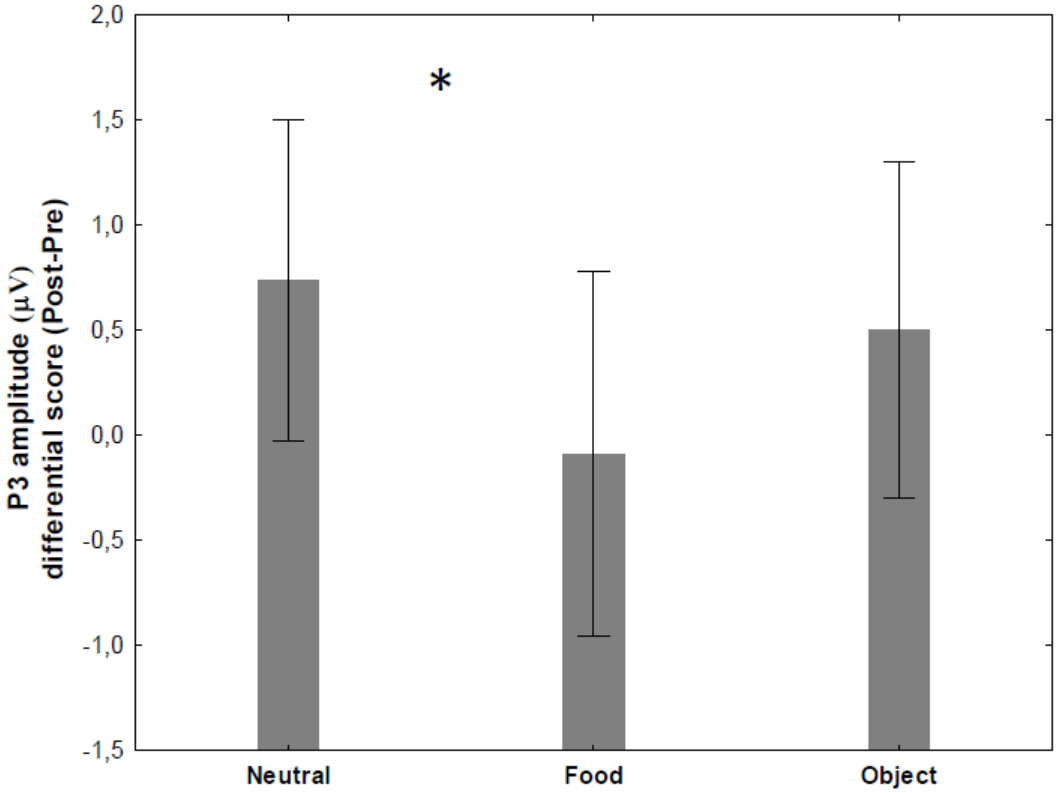

Figure 3.4 P3 amplitude (μV) differential score (Post-LSG minus Pre-LSG) for each type of distracter (neutral, food, object).

Table 3.3 Mean (SD) PF-N1 amplitude (μV) and latency (ms)

	Pre-LSG	**Post-LSG**
PF-N1 Amplitude		
Food C	-3.08 (2.08)	- 2.89 (1.90)
Food NC	-3.51 (2.09)	- 2.73 (1.95)
Object C	-2.73 (1.63)	- 2.32 (1.52)
Object NC	-2.65 (2.08)	- 2.15 (1.62)
Neutral C	-2.05 (1.17)	- 1.72 (1.21)
Neutral NC	- 1.78 (1.15)	- 1.88 (1.26)
PF-N1 Latency		
Food C	81 (18)	80 (12)
Food NC	78 (14)	77(16)
Object C	78 (13)	77 (12)
Object NC	75 (21)	78 (16)
Neutral C	86 (12)	87 (12)
Neutral NC	91 (12)	84 (15)

Notes: SD = standard deviation; C= corresponding trials; NC = non-corresponding trials; Pre-LSG = prior to laparoscopic sleeve gastrectomy; Post-LSG = 12 months post laparoscopic sleeve gastrectomy

Table 3.4 Mean (SD) P2 amplitude (μV) and latency (ms)

	Pre-LSG	Post-LSG
P2 Amplitude		
Food C	2.89 (3.46)	3.75 (4.01)
Food NC	3.04 (3.01)	3.78 (3.72)
Object C	3.92 (2.96)	3.92 (2.96)
Object NC	3.88 (2.80)	3.88 (2.81)
Neutral C	3.29 (2.61)	3.58 (2.45)
Neutral NC	3.50 (2.56)	3.31(2.65)
P2 Latency		
Food C	144 (28)	141 (18)
Food NC	138 (13)	139 (19)
Object C	143 (15)	143 (17)
Object NC	139 (14)	143 (17)
Neutral C	160 (26)	160 (24)
Neutral NC	156 (28)	160 (24)

Notes: SD = standard deviation; C= corresponding trials; NC = non-corresponding trials; Pre-LSG = prior to laparoscopic sleeve gastrectomy; Post-LSG = 12 months post laparoscopic sleeve gastrectomy

Table 3.5 Mean (SD) N2 amplitude (μV) and latency (ms)

	Pre-LSG	Post-LSG
N2 Amplitude		
Food C	-5.45 (3.70)	-6.45 (4.29)
Food NC	-5.43 (3.63)	-6.11 (4.43)
Object C	-5.61 (3.80)	-6.33 (4.52)
Object NC	-5.23 (3.52)	-5.97 (4.66)
Neutral C	-2.06 (4.06)	-2.48 (4.27)
Neutral NC	-2.44 (3.75)	-2.51 (4.06)
N2 Latency		
Food C	236 (35)	243 (32)
Food NC	235 (33)	246 (37)
Object C	231 (28)	242 (30)
Object NC	237 (35)	241 (35)
Neutral C	254 (41)	250 (42)
Neutral NC	249 (45)	245 (47)

Notes: SD = standard deviation; C= corresponding trials; NC = non-corresponding trials; Pre-LSG = prior to laparoscopic sleeve gastrectomy; Post-LSG = 12 months post laparoscopic sleeve gastrectomy

Table 3.6 Mean (SD) P3 amplitude (μV) and latency (ms)

	Pre-LSG	Post-LSG
P3 Amplitude		
Food C	9.95 (4.75)	9.91 (3.94)
Food NC	9.11 (4-18)	8.96 (3.68)
Object C	9.54 (4.33)	9-68 (3.82)
Object NC	8.83 (3.93)	9.91 (3.94)
Neutral C	8.01 (3.83)	8.88 (3.48)
Neutral NC	7.54 (3.70)	8.15 (3.22)
P3 Latency		
Food C	404 (55)	415 (62)
Food NC	413 (53)	418 (67)
Object C	405 (59)	406 (64)
Object NC	414 (64)	428 (103)
Neutral C	400 (54)	403 (92)
Neutral NC	404 (71)	403 (92)

Notes: SD = standard deviation; C= corresponding trials; NC = non-corresponding trials; Pre-LSG = prior to laparoscopic sleeve gastrectomy; Post-LSG = 12 months post laparoscopic sleeve gastrectomy

3.5 Discussion

In the present longitudinal study, changes in cognitive control in the presence of food-related and non-food-related stimuli were assessed in severely obese individuals prior to undergoing LSG and twelve months post-surgery, by means of behavioral and ERP measures. Interference control was assessed with a modified version of the Simon task, which includes task-irrelevant images of food or objects as distracters and a neutral condition without distracters. Furthermore, differences from pre to post-LSG in subjective hunger, satiety, and desire to eat were assessed using Likert scales and possible reduction of dysfunctional eating-related behaviors was measured administering specific questionnaires.

Participants were evaluated under a metabolic state of hunger since they have to refrain from eating at least 6 hours prior to the experimental session. Although controlling for metabolic state, Likert scales suggested that hunger was experienced as less intense in the post-surgery assessment. This effect can be related to physiological and metabolic changes induced by bariatric surgery, which may affect appetite regulation leading patients to experience a lower level of hunger post-LSG (Dimitriadis et al., 2017). Accordingly, in a previous study, a decrease in hunger levels has been shown following BS (Schultes et al., 2010).

Results from questionnaires showed a reduction in some dysfunctional eating-related behaviors post-LSG. Specifically, reduced symptoms related to binge eating (i.e., BES), emotional eating (i.e., DEBQ-emotional) and external eating (i.e., DEBQ-external and PSF) were detected post-surgery. These results corroborated previous findings which showed a post-BS reduction in binge eating (Boan, Kolotkin, Westman, McMahon, & Grant, 2004; Kalarchian, Wilson, Brolin, & Bradley, 1999) and in emotional eating (Dymek, le Grange, Neven, & Alverdy, 2001). External eating has been less investigated in the bariatric surgery population, although it can be supposed that external food-related cues are perceived as less attracting after surgery. This can be related to changes in appetitive responses toward food and reduced preferences for high-fat food frequently observed after BS (Shin & Berthoud, 2011), even though food preferences were not directly assessed in the present study.

In the Simon task, slower RTs and lower accuracy were observed for non-corresponding conditions and for trials with distracting images (i.e., food and objects). Interestingly, a

smaller Simon effect in presence of food-related images was detected post-sleeve, possibly suggesting reduced interference of food with cognitive control after surgery. Previous studies showed a reduced cognitive control toward food-related stimuli in obese compared to normal-weight individuals (Price et al., 2016), which may be related to attentional bias toward food paired with reduced cognitive control abilities in the obese population. The fact that we found lower interference effect for food post-LSG, could be due to reduced attention toward food stimuli which are possibly perceived as less salient post-LSG because of changes in motivational and cognitive response toward food. More specifically, it has been suggested that BS may reverse obesity-induced alterations in reward functions (Berthoud et al., 2012), and this would affect post-surgery food-cue processing.

Accordingly, a previous longitudinal study showed reduced attention toward food stimuli following LSG, as measured by eye-tracking (Giel et al., 2014). Specifically, participants did allocate their visual attention longer (i.e., gaze duration) on non-food-related pictures 6 months post-LSG.

For ERPs results, an early prefrontal N1 (PF-N1) component showed higher amplitude in presence of food-related stimuli, both pre and post-LSG. In the first study of this thesis, PF-N1 were higher for food compared to other stimuli in both obese and normal-weight, suggesting early attentional processing of food stimuli possibly related to hunger (i.e., 6 hours fasting). The same PF-N1 component has been shown to be modulated by hunger in a previous study (Feig et al., 2017). Thus, the present results seem to suggest that food distracters capture automatic attention an early stage of information processing, which does not change after LSG.

More interestingly, differences from pre to post-LSG were detected in P2 and N2 amplitudes. The P2 component has been related to mechanisms of selective attention and feature detection, reflecting the distribution of attentional resources (Hillyard et al., 1998; Luck & Hillyard, 1994). In line with this, P2 latency was longer for distracting images (both food and objects) compared to the neutral condition, reflecting faster capture of attentional resources due to distracting stimuli. On the other hand, the overall increase in P2 amplitude post-surgery may be related to improvement in selective attention subsequently to LSG. Previous studies in larger samples of patients who underwent different types of BS

showed significant post-surgery improvement in attentional domain tested with neuropsychological assessment (Lavender et al., 2014).

Analysis of the N2 component showed enhanced amplitude post-LSG, and this increase seems to be more evident in presence of task-irrelevant distracting stimuli (both foods and objects). In addition, differences in N2 latencies between distracters and neutral condition were reduced post-sleeve. According to an extensive literature, the N2 component with frontal topographical distribution underlies processes of conflict detection and cognitive control (see for a review: Folstein & Van Petten, 2008). To date, only one previous study investigated cognitive control in ex-obese patients which underwent bariatric surgery compared to normal-weight controls (Tarantino et al., 2017), showing exaggerate N2 amplitude in ex-obese patients during a go/no-go task. Despite the methodological difference from the present work (e.g., transversal study; a different subset of cognitive control), our results are in line with the ones from the authors, suggesting N2 as a possible neurophysiological marker of improvement in cognitive control following BS.

Interestingly, a recent fMRI study assessing neural changes from pre to post-LSG showed that post-surgery, the DLPFC activity was increased when participants had to exert top-down control (e.g., "reduce your desire for food") (Holsen et al., 2018).

Finally, analysis on P3 component showed that amplitude and latency were modulated by the correspondence, as expected from previous studies using conflict interference tasks (Donchin & Coles, 1988; Leuthold, 2011; Leuthold & Sommer, 1999; Ragot, 1984; Ragot & Renault, 1981; Smulders, 1993). More interestingly, additional analysis showed a decrease in P3 amplitude for food distracters post-LSG. The P3 amplitude reflects electrophysiological activity related to motivated and conscious allocation of attention (Cuthbert, Schupp, Bradley, Birbaumer, & Lang, 2000). Affective picture processing literature reported higher P3 amplitude for motivationally relevant stimuli, with both positive or negative valence compared to the neutral ones (Olofsson, Nordin, Sequeira, & Polich, 2008). Food-related stimuli are perceived as salient in the metabolic state of hunger, as suggested by previous ERPs studies in normal weight individuals showing increased P3 amplitude for food-related stimuli in fast condition (Feig et al., 2017; Nijs, Muris, et al., 2010; Stockburger et al., 2009). Despite hunger, certain foods rich in fat and sugar are

perceived as more appealing because of their rewarding proprieties; ERPs studies on food-cue processing in normal weight individuals generally found increased P3 and late positive component (LPP) to more palatable food compared to low palatable food or neutral stimuli, suggesting increased allocation of motivated attention toward these stimuli (see for a recent review: Carbine et al., 2018). The present results on P3 amplitude may, therefore, suggest that patients reduced their attentional allocation to food-related cues post-LSG, possibly because of the decreased motivational saliency of food post-surgery.

3.6 Limitations:

The present work presents some limitations, including the relatively small sample size which does not allow to assess if post-surgery reduced medical comorbidities (i.e., Type 2 diabetes; hypertension, OSAS) may modulate the effect of LSG over cognition. Another limitation is related to the fact that participants were tested only in the metabolic state of hunger (i.e., six hours fasting); thus, future studies should further assess patients in fed condition, in order to give a more comprehensive overview of food-related processing in different metabolic conditions. Moreover, it would be interesting to investigate possible neurocognitive predictors of weight-loss trajectories at longer terms follow up when some patients are more at risk to regain weight.

3.7 Conclusions:

Overall, food-related distracting stimuli interfered less with cognitive control post-LSG at a behavioral level; this results may suggest both a reduction of the attentional bias toward food stimuli and an enhancement in cognitive control abilities. These are possible consequences of surgery-induced changes in motivational salience for food and higher prefrontal mediated ability to exert top-down cognitive control.

Accordingly, neurophysiological results indicate an overall increase of N2 amplitude in prefrontal electrodes, which may reflect higher recruitment of cognitive resources to control interference, possibly affecting reaction times when distracting food stimuli are presented and higher cognitive control abilities are needed (i.e., reduced Simon Effect in RTs for food distracters).

On the other hand, results from the present work did not highlight post-LSG changes in early food processing, which is still perceived as attentional capturing compared to non-food stimuli, possibly because of hunger. However, at later stages of information processing, P3 amplitude selectively decrease in presence of food distracters post-LSG. This can be related to a possible reduction in motivated attention toward food which is perceived as less salient. As a behavioral effect of the reduced motivational saliency and enhanced cognitive control, food distracters interfered less with motor responses of the Simon task post-LSG. In addition to food-specific attention, overall improvement in attentional mechanisms following LSG may be hypothesized, as indexed by increase P2 amplitude from pre to post-sleeve.

To date, this is the first longitudinal study investigating attentional and cognitive changes in food-cue processing following LSG, using behavioral and neurophysiological measures. Future studies in larger samples are warranted in order to replicate and extend the present findings to different BS procedures.

CHAPTER 4

PSYCHOLOGICAL PREDICTORS OF SUCCESSFUL WEIGHT LOSS AFTER LSG

4.1 Introduction

Obesity is a common health problem worldwide, which has reached epidemic proportions. Prevalence data reported 13 % of the adult population being obese in 2016 (WHO, 2016), with a marked increase of severe obesity (class III, body mass index - BMI≥40, or a BMI ≥ 35 with comorbid conditions. Severely obese individuals are at higher risk of mortality (Adams et al., 2006), often because of medical co-morbidities such as type 2 diabetes mellitus, arterial hypertension obstructive sleep apnea syndrome, cardiovascular diseases and cancer (Bray, 2004; Residori, García-Lorda, Flancbaum, Pi-Sunyer, & Laferrère, 2003). Bariatric surgery (BS) is considered one of the most effective long-term weight loss treatment for severe obesity, inducing a greater amount of weight loss compared to pharmacological or behavioral treatments (Ayyad & Andersen, 2000; Wadden & Osei, 2002). In addition, BS has been associated with improvement in health status, with post-surgery reduction of obesity-related comorbidities (Buchwald et al., 2009; Kwok et al., 2014).

Different types of BS are available for the treatment of severe obesity, ranging from techniques based on gastric intake restriction (i.e., restrictive procedures) or reduced absorption of nutrients in the gastric tract (i.e., malabsorptive procedures). Among restrictive techniques, one of the most adopted is Laparoscopic Sleeve Gastrectomy (LSG) which consists in the removal of the 80% of the stomach along the greater curvature, limiting the amount of food that can be eaten at one time. Furthermore, LSG has been shown to induce changes in gut hormones which influence glucose homeostasis and appetite (Sandoval, 2011).

Most of the patients undergoing BS reach a successful weight loss after surgery, typically defined as achieving at least the 50% of excess weight loss (EWL %) (Buchwald et al., 2004). Despite this, not all the patient's benefits from long-term surgery outcomes, with a significant minority (15-20%) not achieving a successful EWL% or regaining weight

(Himpens, Dobbeleir, & Peeters, 2010; Maggard et al., 2005; Magro et al., 2008). The causes of this failure are complex and multi-factorial, and there is a growing interest in elucidating possible non-surgical factors implicated in positive or negative post-surgery outcomes.

Psychosocial factors have been studies as possible preoperative predictors of good EWL %; however, results are contrasting and far from being conclusive (Courcoulas et al., 2015; Herpertz et al., 2004; Van Hout et al., 2005). Pre-surgical BMI has been investigated as possible predictive factor in several studies, with the majority suggesting a negative relationship between BMI and weight loss, although findings for a positive or a no relationship are also present in the literature (see for a review Livhits et al., 2012; Wimmelmann et al., 2014). Rather than baseline BMI, higher preoperative weight loss has been more consistently reported as a positive predictor of EWL (S. Alger-Mayer, Polimeni, & Malone, 2008; Livhits et al., 2009; Still et al., 2007). Others sociodemographic factors such as age, gender or socioeconomic status have been reported as predictors of good weight loss by some studies (Van Hout et al., 2005). Despite these factors that cannot be modified (i.e., age, gender), there is an increasing interest in investigating behavioral predictors of good post-surgery weight loss, such as psychiatric conditions, dysfunctional eating attitudes and some personality traits associated with obesity, such as impulsivity.

Psychiatric symptomatology has been reported in severe obese patient's candidates for BS, showing a high prevalence of clinically significant levels of depression, anxiety, personality disorders and substance abuse in this population (Kalarchian et al., 2007; Rosik, 2005; Sarwer et al., 2004). Psychiatric disorders are often considered as contraindications for BS, even though it is still controversial if the presence of psychopathology affects post-surgery outcomes. A negative relationship between preoperative psychiatric symptoms, especially depressive and anxiety disorders, and post-surgery weight loss has been suggested (de Zwaan et al., 2011; Legenbauer et al., 2009; Legenbauer et al., 2011). However, not all the studies confirmed preoperative anxiety or depression as having a negative effect on post-surgery outcomes, with some showing no effect (Dixon et al., 2001, 2003; Dubovsky et al., 1986) and others reporting a positive effect (Livhits et al., 2012). Given the contrasting findings in the literature, the predictive role of preoperative

psychiatric symptoms over post-surgery EWL is still unclear although it has been suggested that a combination of multiple psychiatric disorders is more likely to predict EWL outcomes (de Zwaan et al., 2011; Kinzl et al., 2006).

On the other hand, dysfunctional eating-related attitudes and behaviors are frequently associated with obesity. In particular, the presence of binge eating disorder (BED) or sub-clinical binge eating behavior is high in bariatric population (Burgmer et al., 2005; Green et al., 2004; Sallet et al., 2007), thus binge status can be expected to affect post-surgery weight loss. By contrast, the majorities of the studies reported no association with preoperative BED and post-surgery EWL (see for a review: Livhits et al., 2012; Wimmelmann et al., 2014), although a few studies reported that binge eating diagnosis was associated with higher BMI at long-term follow-up (i.e., 5 years) (Marek, Ben-Porath, van Dulmen, Ashton, & Heinberg, 2017) and with poorer dietary adherence (Adler et al., 2018). Dysfunctional eating attitudes and behaviors other than binge eating have been linked to obesity and overeating, such as food addiction (i.e., addiction to certain types of foods), restrained eating (i.e., attempt to restrain food intake) emotional eating (i.e., eating in response to emotions) and external eating (i.e., eating in response to external food-related cues). Among the bariatric population, the prevalence of food addiction and emotional eating has been shown to be even higher than in the obese nonbariatric population (Fischer et al., 2007; Miller-Matero et al., 2014). However, the impact of these factors on post-surgery weight loss has been explored only by a few studies which showed contrasting findings: some suggested a negative association between EWL and emotional eating or food addiction (Canetti et al., 2009; Miller-Matero et al., 2018), while others found no relationship (Kinzl et al., 2006; Koball et al., 2016; Sevinçer et al., 2016; Wedin et al., 2014).

With regard to personality traits, impulsivity is one factor that has been linked to obesity (Gerlach, Herpertz, & Loeber, 2015; Giel, Teufel, Junne, Zipfel, & Schag, 2017; K. Schag, Schönleber, Teufel, Zipfel, & Giel, 2013) and may be expected to influence post-surgery outcomes. Impulsivity is a complex and multifaceted factor, which includes personality traits, inhibitory control and reward sensitivity (Guerrieri et al., 2007). A widely used questionnaire to assess impulsivity as a multidimensional personality trait is the Barratt

Impulsiveness Scales (BIS-11; Patton et al., 1995), which assess the tendency to act without thinking (i.e., motor impulsiveness), fail to plan ahead (i.e., non-motor impulsiveness), and difficulties to focus attention (i.e., attentional impulsiveness). The theoretical substrates of the BIS-11 derived from the integration of cognitive and behavioral tasks and brain-behavioral research in animals (Barratt, 1993). Among the subscales of the BIS-11, attentional impulsiveness has been more consistently related to overeating (Murphy et al., 2014); other studies suggested a high relation between attentional impulsivity and food-addiction in the obese population seeking bariatric surgery (Meule, 2013; Meule et al., 2014). To date, only a previous study assessed different facets of impulsivity as possible predictors, showing that changes in inhibitory control but not preoperative impulsivity traits, was associated with EWL % six months post-LSG (Kulendran et al., 2017).

Given the existing literature, clear predictors of post-BS outcomes are far from being elucidated, and further studies including multiple psychological factors are warranted. In this direction, the present work aimed at investigating different psychosocial factors as possible predictors of successful EWL % in patients underwent LSG. Specifically, psychopathological symptoms, dysfunctional eating behaviors, and trait impulsivity were assessed in severely obese candidates for LSG, to develop a predictive model of good weight loss at 12 months follow-up.

4.2 Materials and methods

4.2.1 Participants

Sixty-nine severely obese individuals underwent LSG between September 2013 and June 2017 were recruited from the Bariatric Surgery Unit of Padua University Hospital. Participants ages were 18 to 67 years, with a mean age of 42.5 (±11.6) and 87% of the sample being female. The mean BMI at recruitment was 43.6 (±6.25) and the mean body weight was 117 (±19.6).

The inclusion criteria for the study were as follows: 1) BMI $\geq$ 40 kg/m^2 or > 35 kg/m^2 with obesity-related comorbidities such as type 2 diabetes Mellitus, arterial hypertension,

dyslipidemia, obstructive sleep apnea (OSA) or severe osteoarthritis; 2) aged between 18 and 70 years old; 3) the capacity to understand and desire to complete the BS procedure and protocol; 5) motivation for surgery. The exclusion criteria were the presence of relevant psychiatric disorders (i.e., bipolar disorder, schizophrenia, among other psychotic disorders; active alcohol or substance abuse) or the presence of any unstable medical condition, or neurological disorders.

Participants were informed about the experimental procedure and gave their written consent. The study was performed in accordance with the Helsinki Declaration (Editors, 2004) and approved by the local Ethical Committee of the Padova University Hospital.

4.2.2 Assessment

Symptom Checklist-90 Items Revised (SCL-90-R; Derogatis, 1979)

The SCL-90-R is a 90-item questionnaire widely used to assess psychopathological symptoms along nine primary dimensions (somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism). However, in the present study, only the subscales assessing anxiety, depression and a total score indicating a global severity index (GSI) were considered as a predictor in the model. Responses are on a 5-point Likert scales which measures the frequency of the symptoms (0=never; 5 = always).

Barratt Impulsiveness Scale-11 (BIS-11; Fossati et al., 2001)

This is a 30-item questionnaire which assesses different dimensions of impulsivity as a personality trait; the items are on a 4-point Likert scales ranging from 1 (rarely/never) to 4 (very often). There are three subscales: attentional impulsiveness (i.e., tendency to rapid shift in attention); motor impulsiveness (i.e., tendency to rush, immediate actions); non-planning impulsiveness (i.e., a tendency to not plan ahead and to ignore long-term consequences of one's actions) and a total score ranging from 30 to 120, with higher scores indicating higher impulsiveness.

Binge Eating Scale (BES, Gormally et al., 1982)

The BES is a 16-item questionnaire assessing behavioral characteristics (e.g., amount of food consumed) emotional and cognitive response (e.g., guilt or shame) related to binge eating. For each item, participants have to choose between 3 or 4 response statement which corresponds to different symptoms severity. Scores range from 0 to 46, with scores lower than 17 indicating the absence of binge eating; scores from 18 to 26 indicating the possible presence of moderate binge eating and scores higher than 27 indicating a clinically relevant binge eating.

Dutch Eating Behavior Questionnaire (DEBQ, Van Strien et al., 1986)

This 33-items questionnaire assess eating-related attitudes in three different dimensions: 1) "emotional eating", defined as the tendency to eat in response to emotions (DEBQ-Emotional); 2) "restrained eating", which refers to frequent attempts to restrain food intake; 3) "external eating", defined as the tendency to eat in response to external food-related cues which are present in the environment. For each subscale, the items are on a 4-point Likers scales to assess how often each dimension is experienced (1 = never; 5 = very often).

Yale Food Addiction Questionnaire (Gearhardt, Corbin, & Brownell, 2009)

The YFAS is a 25-item self-report measure to assess food addiction based on specific criteria that resemble the symptoms for substance dependence of the DSM-IV-TR (American Psychiatric Association, 2000). The questionnaire includes mixed response categories (dichotomic and Likert type format). It is possible to calculate two measures: 1) a continuous symptom count score that reflects the number of fulfilled diagnostic criteria (ranging from 0 to 11); and 2) a food addiction threshold based on the number of symptoms (at least 2) and self-reported clinically significant impairment or distress. Here, only the continuous version of the scale was adopted as a predictor in the model.

4.2.3 Procedure

All participants completed the assessment between one and two months prior to undergoing LSG. Following the protocol for BS candidates, participants underwent medical assessment prior to surgery to explore the history of obesity and medical history. Demographic information (i.e., sex, age) were collected, along with the assessment of pre-surgery metabolic diseases: hypertension, Type-2 diabetes, dyslipidemia, obstructive sleep apnea (OSA) and hypothyroidism. Anthropometric measures (i.e., height, weight, BMI) were collected prior to surgery and 12 months after LSG. According to standardized outcome measures (Brethauer et al., 2015), post-surgery weight loss was calculated in term of excess weight loss (EWL) % derived from the formula: %EWL = (weight loss / excess weight) x 100, with excess weight being the total preoperative weight minus the ideal weight. Successful weight loss was defined as losing at least the 50% of the EWL.

4.3 Data analysis

The statistical analysis was done with SPSS22 for Windows. Comparisons between the groups (bad versus good weight loss) were based on chi-square tests for categorical variables (χ^2) and analysis of variance (ANOVA) for quantitative variables. All the comparisons for psychological variables were adjusted by the covariates patients' age and the presence of metabolic diseases at baseline. Cohen's-*d* coefficient measured effect size for pairwise comparisons ($|d|>0.20$ was considered low effect size, $|d|>0.50$ mild-moderate effect size and $|d|>0.80$ large-good effect size; (Kelley & Preacher, 2012). Increase in Type-I error due to multiple statistical comparisons was controlled with Simes' correction method, a familywise error rate stepwise procedure which offers a more powerful test than the classical Bonferroni correction (Simes, 1986).

Finally, logistic binary regression in two blocks was used to obtain predictive models of good weight loss at 12 months follow up after bariatric surgery (criterion: 0=loss lower than 50% versus 1=loss 50% or higher). The first block added and fixed the covariates patients' sex, age and the presence of metabolic diseases at baseline. In the second block, a stepwise procedure automatically selected the significant predictors of successful weight loss across preoperative psychological measures (baseline BMI, SCL-90R anxiety

symptoms; SCL-90R depression symptoms; SCL-90R GSI; BIS-11 attentional, BIS-11 nonplanning; BIS-11 motor, YFAS, BES, and DEBQ subscales).

4.4 Results

4.4.1 Group comparisons at baseline

Patients were divided in two groups based on EWL % 12 months LSG: 1) *successful weight loss* (n = 52) showing EWL % > 50; 2) *unsuccessful weight loss* (n = 17), showing EWL% < 50. The successful weight loss group was characterized by younger age and lower baseline BMI compared to the unsuccessful weight loss group.

Regarding preoperative metabolic diseases, unsuccessful weight loss patients showed the higher presence of hypertension, dyslipidemia, and OSAS, compared to the successful weight loss group. Table 4.1 resume demographic characteristics of the sample and psychological profile at baseline (pre-LSG).

4.4.2 Predictive model

Table contains the final predictive logistic regression of achieving a good percent of the excess of weight loss (EWL%) (binary criterion: 0=low than 50% versus 1= 50% or higher) considering the psychopathological measures at baseline and adjusting by age and the presence of metabolic diseases pre-surgery.

Successful EWL was found to increase for younger ages, lower anxiety symptoms (SCL-90 Anxiety) and higher attentional impulsivity (BIS-11 attentional). No others psychological or demographic variables significantly predicted a good percent of EWL 12 months post-LSG.

Table 4.1 Comparison between the groups at baseline

	EWL<50%; *n=17*		EWL≥50%; *n=52*				
Metabolic disease	*N*	*%*	*N*	*%*	χ^2*(df=1)*	p	|*d*|
Any metabolic disease	11	64.7%	25	48.1%	1.42	.233	0.34
Hypertension	10	58.8%	17	32.7%	3.97	**.045***	**0.54**†
Type-2 diabetes	4	23.5%	8	15.4%	0.59	.442	0.21
Dyslipidemia	3	17.6%	0	0.0%	9.59	**.002***	**0.65**†
Apnea-obstructive	6	35.3%	8	15.4%	3.94	**.046***	**0.53**†
Hypothyroidism	1	5.9%	4	7.7%	0.06	.803	0.07
Sex *Female*	15	88.2%	45	86.5%	0.03	.857	0.05
Male	2	11.8%	7	13.5%			
Age and BMI (kg/m²)	*Mean*	*SD*	*Mean*	*SD*	F*(df=1/67)*	p	|*d*|
Age (years-old)	49.00	11.97	40.44	10.82	7.61	**.007***	**0.75**†
BMI-Baseline	47.28	6.75	42.40	5.66	8.65	**.004***	**0.78**†
[1]*Psychological profile*	*Mean*	*SD*	*Mean*	*SD*	F*(df=1/64)*	p	|*d*|
SCL-90R Depression	1.82	1.73	1.68	1.79	0.07	.800	0.08
SCL-90R Anxiety	1.57	2.07	1.21	1.63	0.47	.495	0.19
SCL-90R GSI	1.95	1.95	1.73	1.97	0.14	.711	0.11
BIS-11 Motor	21.90	6.79	21.67	5.34	.02	.893	0.04
BIS-11 Non planning	24.34	3.83	26.91	5.52	2.77	.101	**0.54**†
BIS-11 Attentional	15.42	2.57	16.63	3.74	1.40	.240	0.38
BIS-11 Total score	61.66	10.28	65.21	12.76	.979	.326	0.31
YFAS-total score	2.93	1.78	3.04	1.80	.047	.830	0.06
DEBQ restrain	3.03	.631	2.82	.866	0.69	.409	0.27
DEBQ emotional	2.58	1.04	2.94	1.21	1.04	.312	0.31
DEBQ external	2.75	.514	2.77	.833	0.01	.928	0.03
BES total score	14.77	9.23	14.42	9.21	0.02	.900	0.04

Note. EWL: excess weight loss. SD: standard deviation. BMI: body mass index (kg/m^2).

[1]Results adjusted by age and metabolic state at baseline.[†]Bold: effect size into the mild/moderate (|*d*|>0.50) to large/good range (|*d*|>0.80).

Table 3.2 Predictive models of excess of weight loss at 12 months follow up after bariatric surgery

[1]Criterion: EWL≥50%	*B*	*SE*	*P*	OR	95% CI (OR)		ΔNR^2
First block							.161
Sex (0=female; 1=male)	-0.088	0.960	.927	0.916	0.139	6.012	
Age (years-old)	-0.079	0.033	**.016***	0.924	0.867	0.985	
Any metabolic disease	-0.072	0.666	.914	0.931	0.252	3.432	
Second block							.081
SCL-90R Anxiety	-0.359	0.222	**.049***	0.698	0.452	0.998	
BIS-11 Attentional	0.235	0.130	**.045***	1.265	1.02	1.632	

Note. [1]Logistic regression. EWL: excess of weight loss.

OR: odds ratio. ΔNR^2: increase/change in Nagelkerke's R^2. ΔR^2: increase/change in R^2.

*Bold: significant coefficient.

4.5 Discussion

The present study aimed at investigating psychological predictors of successful EWL % at 12 months post-LSG. Preoperative demographic variables were collected, and self-report measures were adopted to quantify symptoms of anxiety and depression, dysfunctional eating-related attitudes and behaviors (i.e., emotional eating, binge eating, food addiction, external eating, restrained eating) and trait impulsivity.

First, successful EWL % was associated with younger age of the BS candidates. Accordingly, most of the previous studies suggested age as a significant predictor of weight loss after BS, with younger patients showing to lose more weight post-surgery (Herpertz et al., 2004; Livingston & Langert, 2006; Wimmelmann et al., 2014). It has been suggested that young patients may benefit more from surgery because of the better resolution of medical comorbidities and greater mobility (Averbukh et al., 2003; Busetto et al., 2002; Rowe et al., 2000), with some authors highlighting the advantages of performing BS in adolescent patients to minimize physical and psychological comorbidities (Capella & Capella, 2003).

Baseline BMI of the patients who successfully lost weight was lower than the BMI of those who lost less than 50 % of EWL. However, preoperative BMI did not significantly predict post-surgery EWL in the regression model. This is in contrast with some previous studies which showed baseline BMI to be negatively correlated with post-surgery EWL (Livhits et al., 2012; Van Hout et al., 2005). However, discrepancies are present in the literature, with some studies that did not show an effect of presurgery BMI on EWL, and others even reporting the opposite effect (Kinzl et al., 2006; Larsen et al., 2004). Overall, it has been suggested that the amount of pre-surgery weight loss (i.e., in the weeks preceding surgery) rather than baseline BMI positively predict post-surgery EWL (Alger-Mayer, Rosati, Polimeni, & Malone, 2009; Livhits et al., 2009; Still et al., 2007).

Second, when considering pre-surgical psychopathology, our results showed that baseline anxiety symptoms negatively predict successful EWL. This finding corroborates some of the previous studies showing that higher levels of anxiety predict lower post-surgery weight loss (de Zwaan et al., 2011; Legenbauer et al., 2009), although other studies

found a positive relationship between anxiety and post-surgery outcomes (Herpertz et al., 2004). In our sample, patients who did not reach successful EWL (<50%) presented elevated anxiety symptoms scores, whereas patients who showed a successful EWL (>50%) had moderated anxiety symptoms. Since anxiety levels negatively predict EWL, it could be suggested that elevated symptoms of anxiety, distress, and worry may have a negative impact on post-surgery weight loss. By contrast, milder symptoms of anxiety may still guarantee a good EWL achievement. This interpretation of the current results would be coherent with a previous study showing that mild levels of anxiety measured with the SCL-90R subscale positively predict post-surgery EWL% (Agüera et al., 2015).

Despite elevated depressive symptoms and global psychopathological index in our sample, nor of the two variables significantly predicted successful EWL. Likewise, a relationship between preoperative depression or psychopathology and post-surgery EWL was not found in some of the previous studies (Dixon et al., 2001, 2003; Dubovsky et al., 1986). By contrast, other studies reported a negative effect of depression over post-surgery weight loss (Kinzl et al., 2006; Legenbauer et al., 2011). Thus, contrasting findings are present in the literature. However, psychopathological conditions which persist post-surgery have been associated more consistently with poor weight loss outcomes rather than preoperative psychopathology per se (de Zwaan et al., 2011; Kinzl et al., 2006; Legenbauer et al., 2009). Furthermore, discrepancies across studies may be related to different methods to assess psychopathology (e.g., self-report measures or clinical interviews) (Alger-Mayer et al., 2009; Dixon et al., 2003) For instance, in a retrospective study in 145 patients, preoperative depression measured with the Beck Depression Inventory was found to be positively related post-surgery EWL, which is quite unexpected (Averbukh et al., 2003).

Third, nor of the preoperative eating-related attitudes and behaviors seem to predict EWL outcomes. As for binge eating, our results are in line with those showing no relationship between the preoperative BED or sub-clinical binge eating behaviors and post-surgery EWL. The impact of preoperative binge eating on weight loss remains disputed, whereas evidence for an association between post-surgery eating behaviors and weight loss are more consistent in the literature. Hence, the presence of binge eating post-surgery has been shown to negatively predict post-surgery weight loss (Colles, Dixon, & O'brien, 2008;

Odom et al., 2010; White et al., 2010). Furthermore, binge eating scores in our sample were within the normal range, thus it could be suggested that higher presence of binge eating symptoms even preoperatively would be more likely to impact post-surgical eating behaviors and weight loss.

As for other maladaptive eating-related attitudes, emerging evidence highlighted the possible effect of emotional eating and food addiction on successful weight loss and post-surgery outcomes (Miller-Matero et al., 2018); however, studies which include these variables are limited and future studies in larger samples could help to clarify the relationship between pre-surgery dysfunctional eating and weight loss. To date, this is the first study evaluating preoperative restrain and external eating as possible predictors of BS outcome; our results did not show the effect of these variables over successful EWL at 12 months following LSG.

Finally, patients with a higher pre-surgical level of attentional impulsivity showed a higher probability to obtain EWL > 50 %, 12 months post-LSG. However, even patients with higher scores of BIS-11, total impulsivity levels were within the normal range (Fossati et al., 2001), suggesting that obese patients who experienced mild difficulties in focus attention and cognitive instability pre-surgery (i.e., higher attentional impulsivity) are those who benefit more from LSG in terms of weight loss, possibly because of the strong restriction in food-intake imposed by the reduction of the stomach. Thus, restrictive BS procedures may be suitable even in patients with higher trait impulsivity, helping them to carry out nutritional and lifestyle recommended guidelines and achieving successful weight loss, at least in a short-term follow-up. Overall, impulsivity should be considered a complex and multifaced construct, which not only includes personality traits but also state impulsivity (e.g., inhibitory control, reward sensitivity) (Guerrieri et al., 2007), and different facets of impulsivity can be expected to predict BS outcomes in different ways. For instance, in a previous study, the post-surgery improvement in response inhibition has been related with good EWL, while preoperative impulsivity traits (i.e., a total score of the BIS-11) did not significantly predict weight loss (Kulendran et al., 2017). Interestingly, in a recent study, impulsivity trait affects post-surgery eating behaviors, which in turn predict EWL % four years after BS (Schag et al., 2016). Therefore, impulsivity may be tough to

affect weight indirectly by modulating post-surgical dysfunctional eating behaviors such as binge eating. This can also be expected given the relationship between impulsivity traits and eating behaviors (Meule, 2013). Despite this interesting speculation, the design of the present study does not allow to test this hypothesis, since eating attitudes and behaviors were not measured post-LSG.

4.6 Limitations

The principal limitation of the present study is the lack of a post-surgical assessment of psychopathological symptoms and eating-related maladaptive behaviors, which could give a more comprehensive view of LSG outcomes. Indeed, post-surgical reduction in psychopathological conditions has been reported as well as possible effects of post-surgical predictors over EWL (Hindle, de la Piedad Garcia, & Brennan, 2017). For instance, it has been suggested that reduction in binge eating affect EWL, and its effect on weight loss is mediated by presurgical levels of impulsivity (Schag et al., 2016). Therefore, future studies in larger samples should examine both pre and post-surgical psychological variable at multiple levels (e.g., eating behaviors, psychopathology) in order to define possible interactions between these variables and their effect on weight loss.

A second limitation of the study is the relatively short follow up post-LSG. Some studies suggested that patients may successfully lose weight 12 months post-surgery, which has been called the "honeymoon", while higher risks of regaining weight may be expected at later follow up (e.g., 24 months) (Magro et al., 2008). Thus, the psychopathological symptoms, eating-related attitudes or personality traits considered here, could be expected to differently predict EWL later than 12 months.

Finally, only EWL% was evaluated as post-surgery successful outcome. However, BS has been suggested to improve general health status and to reduce dysfunctional eating-related symptoms. Therefore, investigating possible predictors of these factors could give a more comprehensive view of the benefits related to BS.

4.7 Conclusions

In conclusion, the present study investigated multiple predictors of successful EWL % at 12 months post-LSG, including preoperative assessment of psychosocial variables, psychopathological symptoms, dysfunctional eating attitudes, and trait impulsivity. Younger age positively predicts successful EWL as suggested in previous studies (Livhits et al., 2012). Among presurgical psychopathological conditions, anxiety but not depression, predicts successful EWL%, showing that patients with elevated anxiety symptoms fail to reach a good weight loss 12 months post-LSG. Nore of the dysfunctional eating attitudes assessed here showed to predict EWL, although remission of some of these conditions such as binge eating, may be expected to follow restrictive BS procedures. Finally, individuals with moderate attentional impulsivity trait were more prone to reach a successful EWL 12 months post-surgery. Although these later results are somewhat unexpected, it can be hypothesized that a restrictive procedure such as LSG may help impulsive patients in reducing their attitudes to binge eating, since the reduction of the stomach does not allow them to incur in risky eating-related behaviors such as binge eating.

Overall, the present work is the first including a comprehensive assessment of preoperative predictors of weight loss in patients which underwent LSG. The majority of the previous studies investigated only some of these predictors (e.g., psychopathology or eating-related behaviors) of good weight loss following different types of BS. Therefore, the present findings contribute to disentangle multiple factors associated with good EWL at 12 months following LSG.

GENERAL DISCUSSION AND CONCLUSIONS

One of the primary aims of the thesis was to assess cognitive control in presence of food-related stimuli in severely obese individuals compared with normal-weight, by means of neurophysiological and behavioral measures. Evidence for poor cognitive control in the obese sample is suggested by the reduced amplitude of the N2, an ERP component linked to cognitive control mechanisms (Folstein & Van Petten, 2008). On the other hand, enhanced attention toward food seems to be present in both obese and normal weight participants, given the enhanced amplitude of the PF-N1 component in presence of food-related stimuli. This may suggest an attentional bias toward food which occurs at early stages of attentional processing, possibly related to the metabolic state of hunger which has been shown to modulate food-attentional bias (Feig et al., 2017; Stockburger et al., 2009). According to the hypothesis of reduced cognitive control in presence of food stimuli in obese individuals, results on RTs showed that food-distracters interfere with cognitive control only in the obese group. It can be speculated that in obese, enhanced early attentional processing of food-related stimuli may contribute to the lower cognitive control detected at a behavioral level; along with this, poor cognitive control abilities in obese are further suggested by altered neurophysiological indices of cognitive control (i.e., N2) and selective attention (i.e., P2).

Another main objective of the thesis was to assess improvement neurocognitive functions following bariatric surgery; specifically, changes in cognitive control in presence of food-related stimuli were assessed from pre to 12 months post laparoscopic sleeve gastrectomy (LSG). Post-surgical improvement in cognitive control is suggested by an enhanced frontal N2 component post-LSG, which may reflect a higher recruitment of cognitive resources to control interference. On the other hand, food-related stimuli capture attention at early stages of information processing, as suggested by the higher PF-N1 in presence of food distracters. This does not change form pre to post-LSG and is possibly related to hunger state of the participants. By contrast, the P3 amplitude selectively decreases in presence of food distracters post-LSG, suggesting a possible reduction in motivated attention toward food subsequently to bariatric surgery. As a possible

consequence of lower attention toward food and higher cognitive control post-LSG, behavioral results showed a reduction in food-related interference during the execution of a cognitive control task. This corroborates results from a study which showed lower attentional processing of food post-LSG using eye-tracking measures (Giel et al., 2014) In addition to food-specific attention, overall improvement in attentional mechanisms following LSG may be suggested by the increase in P2 amplitude from pre to post-sleeve.

Overall, results from these two studies seem to confirm the hypothesis of lower cognitive control toward food in severely obese individuals extending previous behavioral findings which suggested lower food-related cognitive control in relation with BMI (Hendrick et al., 2012; Price et al., 2016). Second, as expected, cognitive control abilities increase after LSG, putting evidence for N2 component as a possible neurophysiological marker of enhanced cognitive control post-bariatric surgery (Tarantino et al., 2017). In addition, evidence for a reduced motivated attention toward food-related stimuli is suggested here, in line with the emerging literature that showed a resolution of obesity-related alterations after surgery.

Finally, the third study of this dissertation highlighted multiple preoperative factors which predict successful excessive weight loss (EWL % >50) at least 12 months post-LSG. Among others factors, younger patients were more prone to achieve successful weight loss, in line with consistent findings from the previous literature (Herpertz et al., 2004; Livingston & Langert, 2006; Wimmelmann et al., 2014). More interestingly, elevated anxiety symtoms pre-surgery negatively predict weight loss, suggesting that preoperative anxiety negatively impacts LSG outcomes, in line with previous studies (de Zwaan et al., 2011; Legenbauer et al., 2009). Clinical implications of this latter result are related to the developement of psychological interventions to manage and reduce anxiety that should be considered in obese candidates for bariatric surgery. Finally, patients with moderate impulsivity traits, in particular, attentional impulsivity as assessed by the BIS-11 subscale, seems to positively predict weight loss post-LSG. even though it could be expected that impulsivity would interfere with the ability to control food-related temptations and follow nutritional guidelines, it can be supposed that restrictive BS (e.g., LSG) may be suitable in helping impulsive individuals to restrict food intake, possibly because of the reduction of

the stomach and the associated behavioral changes. In addition, a reduction in motivational salience attributed to foods along with improved cognitive control abilities, may also play a role in the regulation of food intake, helping even impulsive patients to lose weight. This latter conclusion is only speculative, based on the results from our second study. However, future studies in larger samples which specifically assess relationship between trait impulsivity and neurocognitive amelioration post-LSG are needed to test this hypothesis.

In conclusion, the present thesis elucidated some of the cognitive alterations related to obesity and their improvement after LSG, and highlighted possible psychological predictors of positive LSG outcomes, which can be informative to develop specific clinical interventions in bariatric surgery population.

List of References

Abilés, V., Rodríguez-Ruiz, S., Abilés, J., Mellado, C., García, A., De La Cruz, A. P., & Fernández-Santaella, M. C. (2010). Psychological characteristics of morbidly obese candidates for bariatric surgery. *Obesity surgery, 20*(2), 161-167.

Adams, K. F., Schatzkin, A., Harris, T. B., Kipnis, V., Mouw, T., Ballard-Barbash, R., . . . Leitzmann, M. F. (2006). Overweight, obesity, and mortality in a large prospective cohort of persons 50 to 71 years old. *New England Journal of Medicine, 355*(8), 763-778.

Adler, S., Fowler, N., Robinson, A. H., Salcido, L., Darcy, A., Toyama, H., & Safer, D. L. (2018). Correlates of dietary adherence and maladaptive eating patterns following Roux-en-Y bariatric surgery. *Obesity surgery, 28*(4), 1130-1135.

Agüera, Z., García-Ruiz-de-Gordejuela, A., Vilarrasa, N., Sanchez, I., Baño, M., Camacho, L., . . . Lopez-Urdiales, R. (2015). Psychological and personality predictors of weight loss and comorbid metabolic changes after bariatric surgery. *European Eating Disorders Review, 23*(6), 509-516.

Alger-Mayer, S., Rosati, C., Polimeni, J., & Malone, M. (2009). Preoperative binge eating status and gastric bypass surgery: a long-term outcome study. *Obesity surgery, 19*(2), 139-145.

Alger-Mayer, S., Polimeni, J. M., & Malone, M. (2008). Preoperative weight loss as a predictor of long-term success following Roux-en-Y gastric bypass. *Obesity surgery, 18*(7), 772-775.

Alosco, M. L., Galioto, R., Spitznagel, M. B., Strain, G., Devlin, M., Cohen, R., . . . Gunstad, J. (2014). Cognitive function after bariatric surgery: evidence for improvement 3 years after surgery. *The American Journal of Surgery, 207*(6), 870-876.

Alosco, M. L., Spitznagel, M. B., Strain, G., Devlin, M., Cohen, R., Crosby, R. D., . . . Gunstad, J. (2015). Improved serum leptin and ghrelin following bariatric surgery predict better postoperative cognitive function. *Journal of clinical neurology, 11*(1), 48-56.

Appelhans, B. M. (2009). Neurobehavioral inhibition of reward-driven feeding: Implications for dieting and obesity. *Obesity, 17*(4), 640-647.

Arnow, B., Kenardy, J., & Agras, W. S. (1995). The Emotional Eating Scale: The development of a measure to assess coping with negative affect by eating. *International Journal of Eating Disorders, 18*(1), 79-90.

Averbukh, Y., Heshka, S., El-Shoreya, H., Flancbaum, L., Geliebter, A., Kamel, S., . . . Laferrère, B. (2003). Depression score predicts weight loss following Roux-en-Y gastric bypass. *Obesity surgery, 13*(6), 833-836.

Ayyad, C., & Andersen, T. (2000). Long-term efficacy of dietary treatment of obesity: a systematic review of studies published between 1931 and 1999. *Obesity Reviews, 1*(2), 113-119.

Babbs, R. K., Sun, X., Felsted, J., Chouinard-Decorte, F., Veldhuizen, M. G., & Small, D. M. (2013). Decreased caudate response to milkshake is associated with higher body mass index and greater impulsivity. *Physiology & behavior, 121*, 103-111.

Balodis, I. M., Molina, N. D., Kober, H., Worhunsky, P. D., White, M. A., Sinha, R., . . . Potenza, M. N. (2013). Divergent neural substrates of inhibitory control in binge eating disorder relative to other manifestations of obesity. *Obesity, 21*(2), 367-377.

Bar-Haim, Y., Lamy, D., & Glickman, S. (2005). Attentional bias in anxiety: A behavioral and ERP study. *Brain and cognition, 59*(1), 11-22.

Bar, M., Tootell, R. B., Schacter, D. L., Greve, D. N., Fischl, B., Mendola, J. D., . . . Dale, A. M. (2001). Cortical mechanisms specific to explicit visual object recognition. *Neuron, 29*(2), 529-535.

Barkin, S. L. (2013). The relationship between executive function and obesity in children and adolescents: a systematic literature review. *Journal of obesity, 2013*.

Barratt, E. S. (1993). Impulsivity: Integrating cognitive, behavioral, biological, and environmental data.

Bassareo, V., & Di Chiara, G. (1999). Modulation of feeding-induced activation of mesolimbic dopamine transmission by appetitive stimuli and its relation to motivational state. *European Journal of Neuroscience, 11*(12), 4389-4397.

Batterink, L., Yokum, S., & Stice, E. (2010). Body mass correlates inversely with inhibitory control in response to food among adolescent girls: an fMRI study. *Neuroimage, 52*(4), 1696-1703.

Bechara, A. (2005). Decision making, impulse control and loss of willpower to resist drugs: a neurocognitive perspective. *Nature neuroscience, 8*(11), 1458.

Behary, P., & Miras, A. D. (2015). Food preferences and underlying mechanisms after bariatric surgery. *Proceedings of the Nutrition Society, 74*(4), 419-425.

Berridge, K. C., & Robinson, T. E. (1998). What is the role of dopamine in reward: hedonic impact, reward learning, or incentive salience? *Brain research reviews, 28*(3), 309-369.

Berthoud, H. R., Zheng, H., & Shin, A. C. (2012). Food reward in the obese and after weight loss induced by calorie restriction and bariatric surgery. *Annals of the New York Academy of Sciences, 1264*(1), 36-48.

Blackwood, D., & Muir, W. (1990). Cognitive brain potentials and their application. *The British Journal of Psychiatry*.

Blanco-Gómez, A., Ferré, N., Luque, V., Cardona, M., Gispert-Llauradó, M., Escribano, J., . . . Canals-Sans, J. (2015). Being overweight or obese is associated with inhibition control in children from six to ten years of age. *Acta paediatrica, 104*(6), 619-625.

Blechert, J., Meule, A., Busch, N. A., & Ohla, K. (2014). Food-pics: an image database for experimental research on eating and appetite. *Frontiers in Psychology, 5*.

Boan, J., Kolotkin, R. L., Westman, E. C., McMahon, R. L., & Grant, J. P. (2004). Binge eating, quality of life and physical activity improve after Roux-en-Y gastric bypass for morbid obesity. *Obesity surgery, 14*(3), 341-348.

Bongers, P., van de Giessen, E., Roefs, A., Nederkoorn, C., Booij, J., van den Brink, W., & Jansen, A. (2015). Being impulsive and obese increases susceptibility to speeded detection of high-calorie foods. *Health Psychology, 34*(6), 677.

Botvinick, M. M., Braver, T. S., Barch, D. M., Carter, C. S., & Cohen, J. D. (2001). Conflict monitoring and cognitive control. *Psychological review, 108*(3), 624.

Bouchard, C. (1994). Genetics of Obesity: Overview and Research. *The genetics of obesity*, 223.

Bouchard, C. (1996). Genetics of obesity in humans: current issues. *The Origins and consequences of obesity*, 108-117.

Braet, C., & Crombez, G. (2003). Cognitive interference due to food cues in childhood obesity. *Journal of clinical child and adolescent psychology, 32*(1), 32-39.

Braver, T. S. (2012). The variable nature of cognitive control: a dual mechanisms framework. *Trends in cognitive sciences, 16*(2), 106-113.

Bray, G. (2004). Obesity is a chronic, relapsing neurochemical disease. *International Journal of Obesity, 28*(1), 34.

Brethauer, S. A., Kim, J., El Chaar, M., Papasavas, P., Eisenberg, D., Rogers, A., . . . Committee, A. C. I. (2015). Standardized outcomes reporting in metabolic and bariatric surgery. *Obesity surgery, 25*(4), 587-606.

Brooks, S. J., Cedernaes, J., & Schiöth, H. B. (2013). Increased prefrontal and parahippocampal activation with reduced dorsolateral prefrontal and insular cortex activation to food images in obesity: a meta-analysis of fMRI studies. *PloS one, 8*(4), e60393.

Buchwald, H., Avidor, Y., Braunwald, E., Jensen, M. D., Pories, W., Fahrbach, K., & Schoelles, K. (2004). Bariatric surgery: a systematic review and meta-analysis. *Jama, 292*(14), 1724-1737.

Buchwald, H., Estok, R., Fahrbach, K., Banel, D., Jensen, M. D., Pories, W. J., . . . Sledge, I. (2009). Weight and type 2 diabetes after bariatric surgery: systematic review and meta-analysis. *The American journal of medicine, 122*(3), 248-256. e245.

Burger, K. S., & Berner, L. A. (2014). A functional neuroimaging review of obesity, appetitive hormones and ingestive behavior. *Physiology & behavior, 136*, 121-127.

Burgmer, R., Grigutsch, K., Zipfel, S., Wolf, A. M., de Zwaan, M., Husemann, B., . . . Herpertz, S. (2005). The influence of eating behavior and eating pathology on weight loss after gastric restriction operations. *Obesity surgery, 15*(5), 684-691.

Busetto, L., Segato, G., De Marchi, F., Foletto, M., De Luca, M., Caniato, D., . . . Enzi, G. (2002). Outcome predictors in morbidly obese recipients of an adjustable gastric band. *Obesity surgery, 12*(1), 83-92.

Buzzell, G. A., Fedota, J. R., Roberts, D. M., & McDonald, C. G. (2014). The N2 ERP component as an index of impaired cognitive control in smokers. *Neuroscience letters*, *563*, 61-65.

Calle, E. E., Rodriguez, C., Walker-Thurmond, K., & Thun, M. J. (2003). Overweight, obesity, and mortality from cancer in a prospectively studied cohort of US adults. *New England Journal of Medicine*, *348*(17), 1625-1638.

Calvo, D., Galioto, R., Gunstad, J., & Spitznagel, M. (2014). Uncontrolled eating is associated with reduced executive functioning. *Clinical obesity*, *4*(3), 172-179.

Canetti, L., Berry, E. M., & Elizur, Y. (2009). Psychosocial predictors of weight loss and psychological adjustment following bariatric surgery and a weight-loss program: The mediating role of emotional eating. *International Journal of Eating Disorders*, *42*(2), 109-117.

Capella, J. F., & Capella, R. F. (2003). Bariatric surgery in adolescence. is this the best age to operate? *Obesity surgery*, *13*(6), 826-832.

Carbine, K. A., Duraccio, K. M., Kirwan, C. B., Muncy, N. M., LeCheminant, J. D., & Larson, M. J. (2018). A direct comparison between ERP and fMRI measurements of food-related inhibitory control: Implications for BMI status and dietary intake. *Neuroimage*, *166*, 335-348.

Carnell, S., Gibson, C., Benson, L., Ochner, C., & Geliebter, A. (2012). Neuroimaging and obesity: current knowledge and future directions. *Obesity Reviews*, *13*(1), 43-56.

Castellanos, E. H., Charboneau, E., Dietrich, M. S., Park, S., Bradley, B. P., Mogg, K., & Cowan, R. L. (2009). Obese adults have visual attention bias for food cue images: evidence for altered reward system function. *International Journal of Obesity*, *33*(9), 1063-1073.

Chamberlain, S. R., Derbyshire, K. L., Leppink, E., & Grant, J. E. (2015). Obesity and dissociable forms of impulsivity in young adults. *CNS spectrums*, *20*(5), 500-507.

Chaput, J. P., Klingenberg, L., Astrup, A., & Sjödin, A. M. (2011). Modern sedentary activities promote overconsumption of food in our current obesogenic environment. *Obesity Reviews*, *12*(5), e12-e20.

Claes, L., Nederkoorn, C., Vandereycken, W., Guerrieri, R., & Vertommen, H. (2006). Impulsiveness and lack of inhibitory control in eating disorders. *Eating behaviors*, *7*(3), 196-203.

Cohen, J. D., Dunbar, K., & McClelland, J. L. (1990). On the control of automatic processes: a parallel distributed processing account of the Stroop effect. *Psychological review*, *97*(3), 332.

Cohen, J. I., Yates, K. F., Duong, M., & Convit, A. (2011). Obesity, orbitofrontal structure and function are associated with food choice: a cross-sectional study. *BMJ open*, *1*(2), e000175.

Colantuoni, C., Schwenker, J., McCarthy, J., Rada, P., Ladenheim, B., Cadet, J.-L., . . . Hoebel, B. (2001). Excessive sugar intake alters binding to dopamine and mu-opioid receptors in the brain. *Neuroreport*, *12*(16), 3549-3552.

Colles, S. L., Dixon, J. B., & O'brien, P. E. (2008). Grazing and loss of control related to eating: two high-risk factors following bariatric surgery. *Obesity*, *16*(3), 615-622.

Colquitt, J. L., Pickett, K., Loveman, E., & Frampton, G. K. (2014). Surgery for weight loss in adults. *The Cochrane Library*.

Coluzzi, I., Raparelli, L., Guarnacci, L., Paone, E., Del Genio, G., Le Roux, C. W., & Silecchia, G. (2016). Food intake and changes in eating behavior after laparoscopic sleeve gastrectomy. *Obesity surgery*, *26*(9), 2059-2067.

Courcoulas, A. P., Christian, N. J., O'Rourke, R. W., Dakin, G., Dellinger, E. P., Flum, D. R., . . . Pomp, A. (2015). Preoperative factors and 3-year weight change in the Longitudinal Assessment of Bariatric Surgery (LABS) consortium. *Surgery for Obesity and Related Diseases*, *11*(5), 1109-1118.

Cuthbert, B. N., Schupp, H. T., Bradley, M. M., Birbaumer, N., & Lang, P. J. (2000). Brain potentials in affective picture processing: covariation with autonomic arousal and affective report. *Biological Psychology*, *52*(2), 95-111.

De Souza, C. T., Araujo, E. P., Bordin, S., Ashimine, R., Zollner, R. L., Boschero, A. C., . . . Velloso, L. c. A. (2005). Consumption of a fat-rich diet activates a proinflammatory response and induces insulin resistance in the hypothalamus. *Endocrinology*, *146*(10), 4192-4199.

de Zwaan, M., Enderle, J., Wagner, S., Mühlhans, B., Ditzen, B., Gefeller, O., . . . Müller, A. (2011). Anxiety and depression in bariatric surgery patients: a prospective, follow-up study using structured clinical interviews. *Journal of affective disorders, 133*(1-2), 61-68.

DelParigi, A., Chen, K., Salbe, A., Hill, J., Wing, R., Reiman, E., & Tataranni, P. (2007). Successful dieters have increased neural activity in cortical areas involved in the control of behavior. *International Journal of Obesity, 31*(3), 440.

Derogatis, L. R. (1979). Symptom Checklist-90-Revised (SCL-90-R). *Lyndhurst, NJ: NCS Pearson*.

Dickson, S. L., Egecioglu, E., Landgren, S., Skibicka, K. P., Engel, J. A., & Jerlhag, E. (2011). The role of the central ghrelin system in reward from food and chemical drugs. *Molecular and cellular endocrinology, 340*(1), 80-87.

Dimitriadis, G. K., Randeva, M. S., & Miras, A. D. (2017). Potential hormone mechanisms of bariatric surgery. *Current obesity reports, 6*(3), 253-265.

Dixon, J. B., Dixon, M. E., & O'brien, P. E. (2001). Pre-operative predictors of weight loss at 1-year after Lap-Band® surgery. *Obesity surgery, 11*(2), 200-207.

Dixon, J. B., Dixon, M. E., & O'Brien, P. E. (2003). Depression in association with severe obesity: changes with weight loss. *Archives of internal medicine, 163*(17), 2058-2065.

Dixon, J. B., & O'Brien, P. E. (2002). Selecting the optimal patient for LAP-BAND placement. *The American Journal of Surgery, 184*(6), S17-S20.

Donchin, E., & Coles, M. G. (1988). Is the P300 component a manifestation of context updating? *Behavioral and brain sciences, 11*(3), 357-374.

Donders, F. C. (1969). On the speed of mental processes. *Acta psychologica, 30*, 412-431.

Doyle, A. C., Le Grange, D., Goldschmidt, A., & Wilfley, D. E. (2007). Psychosocial and physical impairment in overweight adolescents at high risk for eating disorders. *Obesity, 15*(1), 145-154.

Dubovsky, S. L., Haddenhorst, A., Murphy, J., Liechty, R. D., & CoyLe, D. A. (1986). A preliminary study of the relationship between preoperative depression and weight

loss following surgery for morbid obesity. *The International Journal of Psychiatry in Medicine, 15*(2), 185-196.

Dymek, M. P., le Grange, D., Neven, K., & Alverdy, J. (2001). Quality of life and psychosocial adjustment in patients after Roux-en-y gastric report bypass: a brief report. *Obesity surgery, 11*(1), 32-39.

Edgington, E. (1980). Randomization Tests. Marcel Dekker. *Inc.: New York*.

Editors, I. C. o. M. J. (2004). International Committee of Medical Journal Editors (ICMJE): Uniform Requirements for Manuscripts Submitted to Biomedical Journals: writing and editing for biomedical publication. *Haematologica, 89*(3), 264.

Efron, B., & Tibshirani, R. (1986). Bootstrap methods for standard errors, confidence intervals, and other measures of statistical accuracy. *Statistical science*, 54-75.

Elfhag, K., & Morey, L. C. (2008). Personality traits and eating behavior in the obese: poor self-control in emotional and external eating but personality assets in restrained eating. *Eating behaviors, 9*(3), 285-293.

Evans, J., & Coventry, K. (2006). A dual-process approach to behavioral addiction: the case of gambling. *Handbook of implicit cognition and addiction*, 29-43.

Fabiani, M., Gratton, G., Corballis, P. M., Cheng, J., & Friedman, D. (1998). Bootstrap assessment of the reliability of maxima in surface maps of brain activity of individual subjects derived with electrophysiological and optical methods. *Behavior Research Methods, Instruments, & Computers, 30*(1), 78-86.

Fagundo, A. B., De la Torre, R., Jiménez-Murcia, S., Agüera, Z., Granero, R., Tárrega, S., . . . Rodríguez, R. (2012). Executive functions profile in extreme eating/weight conditions: from anorexia nervosa to obesity. *PloS one, 7*(8), e43382.

Feig, E. H., Winter, S. R., Kounios, J., Erickson, B., Berkowitz, S., & Lowe, M. R. (2017). The role of hunger state and dieting history in neural response to food cues: An event-related potential study. *Physiology & behavior*.

Fischer, S., Chen, E., Katterman, S., Roerhig, M., Bochierri-Ricciardi, L., Munoz, D., . . . Le Grange, D. (2007). Emotional eating in a morbidly obese bariatric surgery-seeking population. *Obesity surgery, 17*(6), 778-784.

Fitzpatrick, S., Gilbert, S., & Serpell, L. (2013). Systematic review: are overweight and obese individuals impaired on behavioural tasks of executive functioning? *Neuropsychology review, 23*(2), 138-156.

Folstein, J. R., & Van Petten, C. (2008). Influence of cognitive control and mismatch on the N2 component of the ERP: a review. *Psychophysiology, 45*(1), 152-170.

Fossati, A., Di Ceglie, A., Acquarini, E., & Barratt, E. S. (2001). Psychometric properties of an Italian version of the Barratt Impulsiveness Scale-11 (BIS-11) in nonclinical subjects. *Journal of clinical psychology, 57*(6), 815-828.

Frank, S., Wilms, B., Veit, R., Ernst, B., Thurnheer, M., Kullmann, S., . . . Schultes, B. (2014). Altered brain activity in severely obese women may recover after Roux-en Y gastric bypass surgery. *International Journal of Obesity, 38*(3), 341.

Fredriksson, R., Hägglund, M., Olszewski, P. K., Stephansson, O., Jacobsson, J. A., Olszewska, A. M., . . . Schiöth, H. B. (2008). The obesity gene, FTO, is of ancient origin, up-regulated during food deprivation and expressed in neurons of feeding-related nuclei of the brain. *Endocrinology, 149*(5), 2062-2071.

Frühholz, S., Godde, B., Finke, M., & Herrmann, M. (2011). Spatio-temporal brain dynamics in a combined stimulus–stimulus and stimulus–response conflict task. *Neuroimage, 54*(1), 622-634.

Galioto, R., King, W. C., Bond, D. S., Spitznagel, M. B., Strain, G., Devlin, M., . . . Gunstad, J. (2014). Physical activity and cognitive function in bariatric surgery candidates. *International Journal of Neuroscience, 124*(12), 912-918.

García-García, I., Jurado, M. Á., Garolera, M., Marqués-Iturria, I., Horstmann, A., Segura, B., . . . Villringer, A. (2015). Functional network centrality in obesity: A resting-state and task fMRI study. *Psychiatry Research: Neuroimaging, 233*(3), 331-338.

Gearhardt, A. N., Corbin, W. R., & Brownell, K. D. (2009). Preliminary validation of the Yale food addiction scale. *Appetite, 52*(2), 430-436.

Georgiadou, E., Gruner-Labitzke, K., Köhler, H., de Zwaan, M., & Müller, A. (2014). Cognitive function and nonfood-related impulsivity in post-bariatric surgery patients. *Frontiers in Psychology, 5*, 1502.

Gerlach, G., Herpertz, S., & Loeber, S. (2015). Personality traits and obesity: a systematic review. *Obesity Reviews, 16*(1), 32-63.

Giel, K. E., Rieber, N., Enck, P., Friederich, H.-C., Meile, T., Zipfel, S., & Teufel, M. (2014). Effects of laparoscopic sleeve gastrectomy on attentional processing of food-related information: evidence from eye-tracking. *Surgery for Obesity and Related Diseases, 10*(2), 277-282.

Giel, K. E., Teufel, M., Junne, F., Zipfel, S., & Schag, K. (2017). Food-related impulsivity in obesity and Binge Eating Disorder—a systematic update of the evidence. *Nutrients, 9*(11), 1170.

Goldman, R. L., Canterberry, M., Borckardt, J. J., Madan, A., Byrne, T. K., George, M. S., . . . Hanlon, C. A. (2013). Executive control circuitry differentiates degree of success in weight loss following gastric-bypass surgery. *Obesity, 21*(11), 2189-2196.

Gormally, J., Black, S., Daston, S., & Rardin, D. (1982). The assessment of binge eating severity among obese persons. *Addictive behaviors, 7*(1), 47-55.

Grant, J. E., Derbyshire, K., Leppink, E., & Chamberlain, S. R. (2015). Obesity and gambling: neurocognitive and clinical associations. *Acta Psychiatrica Scandinavica, 131*(5), 379-386.

Green, A. E. C., Dymek-Valentine, M., Pytluk, S., Le Grange, D., & Alverdy, J. (2004). Psychosocial outcome of gastric bypass surgery for patients with and without binge eating. *Obesity surgery, 14*(7), 975-985.

Green, E., Jacobson, A., Haase, L., & Murphy, C. (2011). Reduced nucleus accumbens and caudate nucleus activation to a pleasant taste is associated with obesity in older adults. *Brain research, 1386*, 109-117.

Gregor, M. F., & Hotamisligil, G. S. (2011). Inflammatory mechanisms in obesity. *Annual review of immunology, 29*, 415-445.

Guerrieri, R., Nederkoorn, C., Stankiewicz, K., Alberts, H., Geschwind, N., Martijn, C., & Jansen, A. (2007). The influence of trait and induced state impulsivity on food intake in normal-weight healthy women. *Appetite, 49*(1), 66-73.

Gunstad, J., Paul, R. H., Cohen, R. A., Tate, D. F., Spitznagel, M. B., & Gordon, E. (2007). Elevated body mass index is associated with executive dysfunction in otherwise healthy adults. *Comprehensive psychiatry, 48*(1), 57-61.

Gunstad, J., Paul, R. H., Cohen, R. A., Tate, D. F., Spitznagel, M. B., Grieve, S., & Gordon, E. (2008). Relationship between body mass index and brain volume in healthy adults. *International Journal of Neuroscience, 118*(11), 1582-1593.

Gunstad, J., Spitznagel, M. B., Keary, T. A., Glickman, E., Alexander, T., Karrer, J., . . . Juvancic-Heltzel, J. (2008). Serum leptin levels are associated with cognitive function in older adults. *Brain research, 1230*, 233-236.

Gustafson, D., Lissner, L., Bengtsson, C., Björkelund, C., & Skoog, I. (2004). A 24-year follow-up of body mass index and cerebral atrophy. *Neurology, 63*(10), 1876-1881.

Handley, J. D., Williams, D. M., Caplin, S., Stephens, J. W., & Barry, J. (2016). Changes in cognitive function following bariatric surgery: a systematic review. *Obesity surgery, 26*(10), 2530-2537.

Hansen, T. T., Jakobsen, T. A., Nielsen, M. S., Sjödin, A., Le Roux, C. W., & Schmidt, J. B. (2016). Hedonic changes in food choices following Roux-en-Y gastric bypass. *Obesity surgery, 26*(8), 1946-1955.

Harris, A., Hare, T., & Rangel, A. (2013). Temporally dissociable mechanisms of self-control: early attentional filtering versus late value modulation. *Journal of Neuroscience, 33*(48), 18917-18931.

Harvey, J. (2007). Leptin regulation of neuronal excitability and cognitive function. *Current opinion in pharmacology, 7*(6), 643-647.

Hassing, L. B., Dahl, A. K., Thorvaldsson, V., Berg, S., Gatz, M., Pedersen, N. L., & Johansson, B. (2009). Overweight in midlife and risk of dementia: a 40-year follow-up study. *International Journal of Obesity, 33*(8), 893-898.

He, Q., Xiao, L., Xue, G., Wong, S., Ames, S. L., Schembre, S. M., & Bechara, A. (2014). Poor ability to resist tempting calorie rich food is linked to altered balance between neural systems involved in urge and self-control. *Nutrition journal, 13*(1), 92.

Health, N. I. o. (2006). Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: the evidence report. National Institutes of

Health; National Heart, Lung, and Blood Institute; September 1998. Publication No. 98-4083.

Hege, M., Stingl, K., Kullmann, S., Schag, K., Giel, K., Zipfel, S., & Preissl, H. (2015). Attentional impulsivity in binge eating disorder modulates response inhibition performance and frontal brain networks. *International Journal of Obesity, 39*(2), 353.

Hendrick, O. M., Luo, X., Zhang, S., & Li, C. S. R. (2012). Saliency processing and obesity: a preliminary imaging study of the stop signal task. *Obesity, 20*(9), 1796-1802.

Hendrikse, J., Cachia, R., Kothe, E., McPhie, S., Skouteris, H., & Hayden, M. (2015). Attentional biases for food cues in overweight and individuals with obesity: a systematic review of the literature. *Obesity Reviews, 16*(5), 424-432.

Herbert, B. M., & Pollatos, O. (2014). Attenuated interoceptive sensitivity in overweight and obese individuals. *Eating behaviors, 15*(3), 445-448.

Herman, C., & Polivy, J. (1980). Restrained eating (In AJ Stunkard (Ed.), Obesity (pp. 208-225). *Philadelphia: WB Saunders*.

Herpertz, S., Kielmann, R., Wolf, A., Hebebrand, J., & Senf, W. (2004). Do psychosocial variables predict weight loss or mental health after obesity surgery? A systematic review. *Obesity research, 12*(10), 1554-1569.

Herpertz, S., Kielmann, R., Wolf, A., Langkafel, M., Senf, W., & Hebebrand, J. (2003). Does obesity surgery improve psychosocial functioning? A systematic review. *International Journal of Obesity, 27*(11), 1300.

Hillyard, S. A., Teder-Sälejärvi, W. A., & Münte, T. F. (1998). Temporal dynamics of early perceptual processing. *Current opinion in neurobiology, 8*(2), 202-210.

Himpens, J., Dobbeleir, J., & Peeters, G. (2010). Long-term results of laparoscopic sleeve gastrectomy for obesity. *Annals of surgery, 252*(2), 319-324.

Hindle, A., de la Piedad Garcia, X., & Brennan, L. (2017). Early post-operative psychosocial and weight predictors of later outcome in bariatric surgery: a systematic literature review. *Obesity Reviews, 18*(3), 317-334.

Hofmann, W., Friese, M., & Wiers, R. W. (2008). Impulsive versus reflective influences on health behavior: A theoretical framework and empirical review. *Health Psychology Review, 2*(2), 111-137.

Holsen, L., Davidson, P., Cerit, H., Hye, T., Moondra, P., Haimovici, F., . . . Evins, A. (2018). Neural predictors of 12-month weight loss outcomes following bariatric surgery. *International Journal of Obesity, 42*(4), 785.

Hommel, B. (1997). Interactions between stimulus-stimulus congruence and stimulus-response compatibility. *Psychological research, 59*(4), 248-260.

Houben, K., Nederkoorn, C., & Jansen, A. (2014). Eating on impulse: The relation between overweight and food-specific inhibitory control. *Obesity, 22*(5).

Hudson, J. I., Hiripi, E., Pope Jr, H. G., & Kessler, R. C. (2007). The prevalence and correlates of eating disorders in the National Comorbidity Survey Replication. *Biological psychiatry, 61*(3), 348-358.

Hume, D. J., Howells, F. M., Rauch, H. L., Kroff, J., & Lambert, E. V. (2015). Electrophysiological indices of visual food cue-reactivity. Differences in obese, overweight and normal weight women. *Appetite, 85*, 126-137.

Innamorati, M., Imperatori, C., Manzoni, G. M., Lamis, D. A., Castelnuovo, G., Tamburello, A., . . . Fabbricatore, M. (2015). Psychometric properties of the Italian Yale Food Addiction Scale in overweight and obese patients. *Eating and Weight Disorders-Studies on Anorexia, Bulimia and Obesity, 20*(1), 119-127.

Jansen, A., Houben, K., & Roefs, A. (2015). A cognitive profile of obesity and its translation into new interventions. *Frontiers in Psychology, 6*, 1807.

Jantz, E. J., Larson, C. J., Mathiason, M. A., Kallies, K. J., & Kothari, S. N. (2009). Number of weight loss attempts and maximum weight loss before Roux-en-Y laparoscopic gastric bypass surgery are not predictive of postoperative weight loss. *Surgery for Obesity and Related Diseases, 5*(2), 208-211.

Kalarchian, M. A., Marcus, M. D., Levine, M. D., Courcoulas, A. P., Pilkonis, P. A., Ringham, R. M., . . . Rofey, D. L. (2007). Psychiatric disorders among bariatric surgery candidates: relationship to obesity and functional health status. *American journal of Psychiatry, 164*(2), 328-334.

Kalarchian, M. A., Wilson, G., Brolin, R., & Bradley, L. (1999). Effects of bariatric surgery on binge eating and related psychopathology. *Eating and Weight Disorders-Studies on Anorexia, Bulimia and Obesity, 4*(1), 1-5.

Kamijo, K., Pontifex, M. B., Khan, N. A., Raine, L. B., Scudder, M. R., Drollette, E. S., . . . Hillman, C. H. (2012). The association of childhood obesity to neuroelectric indices of inhibition. *Psychophysiology, 49*(10), 1361-1371.

Kelley, K., & Preacher, K. J. (2012). On effect size. *Psychological methods, 17*(2), 137.

Kemps, E., Tiggemann, M., & Hollitt, S. (2014). Biased attentional processing of food cues and modification in obese individuals. *Health Psychology, 33*(11), 1391.

Kenny, P. J. (2011). Reward mechanisms in obesity: new insights and future directions. *Neuron, 69*(4), 664-679.

Kinzl, J. F., Schrattenecker, M., Traweger, C., Mattesich, M., Fiala, M., & Biebl, W. (2006). Psychosocial predictors of weight loss after bariatric surgery. *Obesity surgery, 16*(12), 1609-1614.

Koball, A. M., Clark, M. M., Collazo-Clavell, M., Kellogg, T., Ames, G., Ebbert, J., & Grothe, K. B. (2016). The relationship among food addiction, negative mood, and eating-disordered behaviors in patients seeking to have bariatric surgery. *Surgery for Obesity and Related Diseases, 12*(1), 165-170.

Koessler, S., Engler, H., Riether, C., & Kissler, J. (2009). No retrieval-induced forgetting under stress. *Psychological Science, 20*(11), 1356-1363.

Kok, A., Ramautar, J. R., De Ruiter, M. B., Band, G. P., & Ridderinkhof, K. R. (2004). ERP components associated with successful and unsuccessful stopping in a stop-signal task. *Psychophysiology, 41*(1), 9-20.

Korenkov, M., Kneist, W., Heintz, A., & Junginger, T. (2004). Laparoscopic gastric banding as a universal method for the treatment of patients with morbid obesity. *Obesity surgery, 14*(8), 1123-1127.

Kornblum, S., Hasbroucq, T., & Osman, A. (1990). Dimensional overlap: cognitive basis for stimulus-response compatibility--a model and taxonomy. *Psychological review, 97*(2), 253.

Kovacevic, N., & McIntosh, A. R. (2007). Groupwise independent component decomposition of EEG data and partial least square analysis. *Neuroimage, 35*(3), 1103-1112.

Kulendran, M., Borovoi, L., Purkayastha, S., Darzi, A., & Vlaev, I. (2017). Impulsivity predicts weight loss after obesity surgery. *Surgery for Obesity and Related Diseases, 13*(6), 1033-1040.

Kullmann, S., Pape, A.-A., Heni, M., Ketterer, C., Schick, F., Häring, H.-U., . . . Veit, R. (2012). Functional network connectivity underlying food processing: disturbed salience and visual processing in overweight and obese adults. *Cerebral cortex, 23*(5), 1247-1256.

Kullmann, S., Schweizer, F., Veit, R., Fritsche, A., & Preissl, H. (2015). Compromised white matter integrity in obesity. *Obesity Reviews, 16*(4), 273-281.

Kurth, F., Levitt, J. G., Phillips, O. R., Luders, E., Woods, R. P., Mazziotta, J. C., . . . Narr, K. L. (2013). Relationships between gray matter, body mass index, and waist circumference in healthy adults. *Human brain mapping, 34*(7), 1737-1746.

Kwok, C. S., Pradhan, A., Khan, M. A., Anderson, S. G., Keavney, B. D., Myint, P. K., . . . Loke, Y. K. (2014). Bariatric surgery and its impact on cardiovascular disease and mortality: a systematic review and meta-analysis. *International journal of cardiology, 173*(1), 20-28.

Lanyon, R. I., & Maxwell, B. M. (2007). Predictors of outcome after gastric bypass surgery. *Obesity surgery, 17*(3), 321-328.

Larsen, J. K., Geenen, R., Maas, C., De Wit, P., Van Antwerpen, T., Brand, N., & Van Ramshorst, B. (2004). Personality as a predictor of weight loss maintenance after surgery for morbid obesity. *Obesity research, 12*(11), 1828-1834.

Lavagnino, L., Arnone, D., Cao, B., Soares, J. C., & Selvaraj, S. (2016). Inhibitory control in obesity and binge eating disorder: A systematic review and meta-analysis of neurocognitive and neuroimaging studies. *Neuroscience & Biobehavioral Reviews, 68*, 714-726.

Lavender, J. M., Alosco, M. L., Spitznagel, M. B., Strain, G., Devlin, M., Cohen, R., . . . Wonderlich, S. A. (2014). Association between binge eating disorder and changes

in cognitive functioning following bariatric surgery. *Journal of psychiatric research, 59*, 148-154.

Legenbauer, T., De Zwaan, M., Benecke, A., Mühlhans, B., Petrak, F., & Herpertz, S. (2009). Depression and anxiety: their predictive function for weight loss in obese individuals. *Obesity Facts, 2*(4), 227-234.

Legenbauer, T., Petrak, F., de Zwaan, M., & Herpertz, S. (2011). Influence of depressive and eating disorders on short-and long-term course of weight after surgical and nonsurgical weight loss treatment. *Comprehensive psychiatry, 52*(3), 301-311.

Leuthold, H. (2011). The Simon effect in cognitive electrophysiology: a short review. *Acta psychologica, 136*(2), 203-211.

Leuthold, H., & Sommer, W. (1999). ERP correlates of error processing in spatial SR compatibility tasks. *Clinical neurophysiology, 110*(2), 342-357.

Li, P., Shan, H., Liang, S., Nie, B., Liu, H., Duan, S., . . . Guo, Y. (2018). Sleeve Gastrectomy Recovering Disordered Brain Function in Subjects with Obesity: a Longitudinal fMRI Study. *Obesity surgery*, 1-8.

Livhits, M., Mercado, C., Yermilov, I., Parikh, J. A., Dutson, E., Mehran, A., . . . Gibbons, M. M. (2009). Does weight loss immediately before bariatric surgery improve outcomes: a systematic review. *Surgery for Obesity and Related Diseases, 5*(6), 713-721.

Livhits, M., Mercado, C., Yermilov, I., Parikh, J. A., Dutson, E., Mehran, A., . . . Gibbons, M. M. (2012). Preoperative predictors of weight loss following bariatric surgery: systematic review. *Obesity surgery, 22*(1), 70-89.

Livingston, E. H., & Langert, J. (2006). The impact of age and Medicare status on bariatric surgical outcomes. *Archives of Surgery, 141*(11), 1115-1120.

Lobaugh, N. J., West, R., & McIntosh, A. R. (2001). Spatiotemporal analysis of experimental differences in event-related potential data with partial least squares. *Psychophysiology, 38*(3), 517-530.

Loeber, S., Grosshans, M., Korucuoglu, O., Vollmert, C., Vollstädt-Klein, S., Schneider, S., . . . Kiefer, F. (2012). Impairment of inhibitory control in response to food-

associated cues and attentional bias of obese participants and normal-weight controls. *International Journal of Obesity, 36*(10), 1334.

Logan, G. D., & Cowan, W. B. (1984). On the ability to inhibit thought and action: A theory of an act of control. *Psychological review, 91*(3), 295.

Loos, R. J., & Bouchard, C. (2003). Obesity–is it a genetic disorder? *Journal of internal medicine, 254*(5), 401-425.

Lowe, M. R., Butryn, M. L., Didie, E. R., Annunziato, R. A., Thomas, J. G., Crerand, C. E., . . . Wallaert, M. (2009). The Power of Food Scale. A new measure of the psychological influence of the food environment. *Appetite, 53*(1), 114-118.

Lu, C.-H., & Proctor, R. W. (1995). The influence of irrelevant location information on performance: A review of the Simon and spatial Stroop effects. *Psychonomic bulletin & review, 2*(2), 174-207.

Luck, S. J., & Hillyard, S. A. (1994). Electrophysiological correlates of feature analysis during visual search. *Psychophysiology, 31*(3), 291-308.

MacLeod, C. M. (1991). Half a century of research on the Stroop effect: an integrative review. *Psychological bulletin, 109*(2), 163.

Maggard, M. A., Shugarman, L. R., Suttorp, M., Maglione, M., Sugerman, H. J., Livingston, E. H., . . . Hilton, L. (2005). Meta-analysis: surgical treatment of obesity. *Annals of internal medicine, 142*(7), 547-559.

Magouliotis, D. E., Tasiopoulou, V. S., Svokos, A. A., Svokos, K. A., Sioka, E., & Zacharoulis, D. (2017). Roux-en-Y gastric bypass versus sleeve gastrectomy as revisional procedure after adjustable gastric band: a systematic review and meta-analysis. *Obesity surgery, 27*(5), 1365-1373.

Magro, D. O., Geloneze, B., Delfini, R., Pareja, B. C., Callejas, F., & Pareja, J. C. (2008). Long-term weight regain after gastric bypass: a 5-year prospective study. *Obesity surgery, 18*(6), 648-651.

Mapelli, D., Di Rosa, E., Cavalletti, M., Schiff, S., & Tamburin, S. (2014). Decision and dopaminergic system: an ERPs study of Iowa gambling task in Parkinson's disease. *Frontiers in Psychology, 5*, 684.

Marek, R. J., Ben-Porath, Y. S., van Dulmen, M. H., Ashton, K., & Heinberg, L. J. (2017). Using the presurgical psychological evaluation to predict 5-year weight loss outcomes in bariatric surgery patients. *Surgery for Obesity and Related Diseases, 13*(3), 514-521.

Marqués-Iturria, I., Pueyo, R., Garolera, M., Segura, B., Junqué, C., García-García, I., . . . Ariza, M. (2013). Frontal cortical thinning and subcortical volume reductions in early adulthood obesity. *Psychiatry Research: Neuroimaging, 214*(2), 109-115.

Marques, E. L., Halpern, A., Corrêa Mancini, M., de Melo, M. E., Horie, N. C., Buchpiguel, C. A., . . . Santo, M. A. (2014). Changes in neuropsychological tests and brain metabolism after bariatric surgery. *The Journal of Clinical Endocrinology & Metabolism, 99*(11), E2347-E2352.

Mauri, M., Rucci, P., Calderone, A., Santini, F., Oppo, A., Romano, A., . . . Pinchera, A. (2008). Axis I and II disorders and quality of life in bariatric surgery candidates. *The Journal of clinical psychiatry*.

McIntosh, A., Bookstein, F., Haxby, J. V., & Grady, C. (1996). Spatial pattern analysis of functional brain images using partial least squares. *Neuroimage, 3*(3), 143-157.

Meule, A. (2013). Impulsivity and overeating: a closer look at the subscales of the Barratt Impulsiveness Scale. *Frontiers in Psychology, 4*, 177.

Meule, A., Heckel, D., Jurowich, C., Vögele, C., & Kübler, A. (2014). Correlates of food addiction in obese individuals seeking bariatric surgery. *Clinical obesity, 4*(4), 228-236.

Miller-Matero, L.R., Armstrong, R., McCulloch, K., Hyde-Nolan, M., Eshelman, A., & Genaw, J. (2014). To eat or not to eat; is that really the question? An evaluation of problematic eating behaviors and mental health among bariatric surgery candidates. *Eating and Weight Disorders-Studies on Anorexia, Bulimia and Obesity, 19*(3), 377-382.

Miller-Matero, L.R., Bryce, K., Saulino, C. K., Dykhuis, K. E., Genaw, J., & Carlin, A. M. (2018). Problematic Eating Behaviors Predict Outcomes After Bariatric Surgery. *Obesity surgery*, 1-6.

Miller, A. A., & Spencer, S. J. (2014). Obesity and neuroinflammation: a pathway to cognitive impairment. *Brain, behavior, and immunity, 42*, 10-21.

Miras, A. D., Jackson, R. N., Jackson, S. N., Goldstone, A. P., Olbers, T., Hackenberg, T., . . . le Roux, C. W. (2012). Gastric bypass surgery for obesity decreases the reward value of a sweet-fat stimulus as assessed in a progressive ratio task–. *The American journal of clinical nutrition, 96*(3), 467-473.

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: A latent variable analysis. *Cognitive psychology, 41*(1), 49-100.

Mobbs, O., Iglesias, K., Golay, A., & Van der Linden, M. (2011). Cognitive deficits in obese persons with and without binge eating disorder. Investigation using a mental flexibility task. *Appetite, 57*(1), 263-271.

Mole, T. B., Irvine, M. A., Worbe, Y., Collins, P., Mitchell, S. P., Bolton, S., . . . Voon, V. (2015). Impulsivity in disorders of food and drug misuse. *Psychological medicine, 45*(4), 771-782.

Mühlhans, B., Horbach, T., & de Zwaan, M. (2009). Psychiatric disorders in bariatric surgery candidates: a review of the literature and results of a German prebariatric surgery sample. *General Hospital Psychiatry, 31*(5), 414-421.

Mun, E. C., Blackburn, G. L., & Matthews, J. B. (2001). Current status of medical and surgical therapy for obesity. *Gastroenterology, 120*(3), 669-681.

Murdaugh, D. L., Cox, J. E., Cook, E. W., & Weller, R. E. (2012). fMRI reactivity to high-calorie food pictures predicts short-and long-term outcome in a weight-loss program. *Neuroimage, 59*(3), 2709-2721.

Murphy, C. M., Stojek, M. K., & MacKillop, J. (2014). Interrelationships among impulsive personality traits, food addiction, and body mass index. *Appetite, 73*, 45-50.

Nieuwenhuis, S., Yeung, N., Van Den Wildenberg, W., & Ridderinkhof, K. R. (2003). Electrophysiological correlates of anterior cingulate function in a go/no-go task: effects of response conflict and trial type frequency. *Cognitive, affective, & behavioral neuroscience, 3*(1), 17-26.

Nijs, I. M., & Franken, I. H. (2012). Attentional processing of food cues in overweight and obese individuals. *Current obesity reports, 1*(2), 106-113.

Nijs, I. M., Franken, I. H., & Muris, P. (2010). Food-related Stroop interference in obese and normal-weight individuals: Behavioral and electrophysiological indices. *Eating behaviors, 11*(4), 258-265.

Nijs, I. M., Muris, P., Euser, A. S., & Franken, I. H. (2010). Differences in attention to food and food intake between overweight/obese and normal-weight females under conditions of hunger and satiety. *Appetite, 54*(2), 243-254.

Norman, D. A., & Shallice, T. (1986). Attention to action *Consciousness and self-regulation* (pp. 1-18): Springer.

Nummenmaa, L., Hirvonen, J., Hannukainen, J. C., Immonen, H., Lindroos, M. M., Salminen, P., & Nuutila, P. (2012). Dorsal striatum and its limbic connectivity mediate abnormal anticipatory reward processing in obesity. *PloS one, 7*(2), e31089.

Ochner, C. N., Kwok, Y., Conceição, E., Pantazatos, S. P., Puma, L. M., Carnell, S., . . . Geliebter, A. (2011). Selective reduction in neural responses to high calorie foods following gastric bypass surgery. *Annals of surgery, 253*(3), 502.

Ochner, C. N., Stice, E., Hutchins, E., Afifi, L., Geliebter, A., Hirsch, J., & Teixeira, J. (2012). Relation between changes in neural responsivity and reductions in desire to eat high-calorie foods following gastric bypass surgery. *Neuroscience, 209*, 128-135.

Odom, J., Zalesin, K. C., Washington, T. L., Miller, W. W., Hakmeh, B., Zaremba, D. L., . . . Krause, K. R. (2010). Behavioral predictors of weight regain after bariatric surgery. *Obesity surgery, 20*(3), 349-356.

Ogden, C. L., Yanovski, S. Z., Carroll, M. D., & Flegal, K. M. (2007). The epidemiology of obesity. *Gastroenterology, 132*(6), 2087-2102.

Olofsson, J. K., Nordin, S., Sequeira, H., & Polich, J. (2008). Affective picture processing: an integrative review of ERP findings. *Biological Psychology, 77*(3), 247-265.

Organization, W. H. (1997). Obesity: preventing and managing the global epidemic. Report of a WHO Consultation presented at the World Health Organization, June 3–5, 1997, Geneva, Switzerland. *Geneva, Switzerland: WHO*.

Organization, W. H. (2015). Obesity and overweight. Fact sheet no. 311. Updated January 2015. *World Health Organization.[Cited: 2015 November 20] Available from: http://www. who. int/mediacentre/factsheets/fs311/en*.

Organization, W. H. (2016). World Health Organization obesity and overweight fact sheet.

Pannacciulli, N., Del Parigi, A., Chen, K., Le, D. S. N., Reiman, E. M., & Tataranni, P. A. (2006). Brain abnormalities in human obesity: a voxel-based morphometric study. *Neuroimage, 31*(4), 1419-1425.

Papailiou, J., Albanopoulos, K., Toutouzas, K. G., Tsigris, C., Nikiteas, N., & Zografos, G. (2010). Morbid obesity and sleeve gastrectomy: how does it work? *Obesity surgery, 20*(10), 1448-1455.

Patton, J. H., Stanford, M. S., & Barratt, E. S. (1995). Factor structure of the Barratt impulsiveness scale. *Journal of clinical psychology, 51*(6), 768-774.

Pedram, P., Wadden, D., Amini, P., Gulliver, W., Randell, E., Cahill, F., . . . Zhai, G. (2013). Food addiction: its prevalence and significant association with obesity in the general population. *PloS one, 8*(9), e74832.

Pi-Sunyer, X. (2009). The medical risks of obesity. *Postgraduate medicine, 121*(6), 21-33.

Polich, J. (2007). Updating P300: an integrative theory of P3a and P3b. *Clinical neurophysiology, 118*(10), 2128-2148.

Polich, J., & Kok, A. (1995). Cognitive and biological determinants of P300: an integrative review. *Biological Psychology, 41*(2), 103-146.

Price, M., Lee, M., & Higgs, S. (2016). Food-specific response inhibition, dietary restraint and snack intake in lean and overweight/obese adults: a moderated-mediation model. *International journal of obesity (2005), 40*(5), 877.

Prickett, C., Brennan, L., & Stolwyk, R. (2015). Examining the relationship between obesity and cognitive function: a systematic literature review. *Obesity research & clinical practice, 9*(2), 93-113.

Ragot, R. (1984). Perceptual and Motor Space Representation: An Event-Related Potential Study. *Psychophysiology, 21*(2), 159-170.

Ragot, R., & Renault, B. (1981). P300, as a function of S—R compatibility and motor programming. *Biological Psychology, 13*, 289-294.

Ray, E. C., Nickels, M. W., Sayeed, S., & Sax, H. C. (2003). Predicting success after gastric bypass: the role of psychosocial and behavioral factors. *Surgery, 134*(4), 555-563.

Renquist, K. E., Mason, E. E., Tang, S., Cullen, J. J., Doherty, C., Maher, J. W., & Contributors, N. (1996). Pay status as a predictor of outcome in surgical treatment of obesity. *Obesity surgery, 6*(3), 224-232.

Residori, L., García-Lorda, P., Flancbaum, L., Pi-Sunyer, F. X., & Laferrère, B. (2003). Prevalence of co-morbidities in obese patients before bariatric surgery: effect of race. *Obesity surgery, 13*(3), 333-340.

Ridderinkhof, R. K. (2002). Micro-and macro-adjustments of task set: activation and suppression in conflict tasks. *Psychological research, 66*(4), 312-323.

Roche, R. A., Garavan, H., Foxe, J. J., & O'Mara, S. M. (2005). Individual differences discriminate event-related potentials but not performance during response inhibition. *Experimental Brain Research, 160*(1), 60-70.

Rosik, C. H. (2005). Psychiatric symptoms among prospective bariatric surgery patients: rates of prevalence and their relation to social desirability, pursuit of surgery, and follow-up attendance. *Obesity surgery, 15*(5), 677-683.

Rowe, J. L., Downey, J. E., Faust, M., & Horn, M. J. (2000). Psychological and demographic predictors of successful weight loss following silastic ring vertical stapled gastroplasty. *Psychological reports, 86*(3), 1028-1036.

Rubinstein, G. (2006). The big five and self-esteem among overweight dieting and non-dieting women. *Eating behaviors, 7*(4), 355-361.

Sallet, P. C., Sallet, J. A., Dixon, J. B., Collis, E., Pisani, C. E., Levy, A., . . . Cordás, T. A. (2007). Eating behavior as a prognostic factor for weight loss after gastric bypass. *Obesity surgery, 17*(4), 445.

Sandoval, D. (2011). Bariatric surgeries: beyond restriction and malabsorption. *International Journal of Obesity, 35*(S3), S45.

Sarwer, D. B., Cohn, N. I., Gibbons, L. M., Magee, L., Crerand, C. E., Raper, S. E., . . . Wadden, T. A. (2004). Psychiatric diagnoses and psychiatric treatment among bariatric surgery candidates. *Obesity surgery, 14*(9), 1148-1156.

Schachter. S. (1968). Obesity and eating. *Science*.

Schachter, S., & Rodin, J. (1974). Obese humans and rats. Potomac, MD: Lawrence Erlbaum Associates, Inc.

Schag, Mack, I., Giel, K. E., Ölschläger, S., Skoda, E.-M., von Feilitzsch, M., . . . Teufel, M. (2016). The impact of impulsivity on weight loss four years after bariatric surgery. *Nutrients, 8*(11), 721.

Schag, K., Schönleber, J., Teufel, M., Zipfel, S., & Giel, K. (2013). Food-related impulsivity in obesity and Binge Eating Disorder–a systematic review. *Obesity Reviews, 14*(6), 477-495.

Schiff, S. Amodio, P., Testa, G., Nardi, M., Montagnese, S., Caregaro, L., . . . Sellitto, M. (2016). Impulsivity toward food reward is related to BMI: Evidence from intertemporal choice in obese and normal-weight individuals. *Brain and cognition, 110*, 112-119.

Schiff, S., D'Avanzo, C., Cona, G., Goljahani, A., Montagnese, S., Volpato, C., . . . Bisiacchi, P. (2014). Insight into the relationship between brain/behavioral speed and variability in patients with minimal hepatic encephalopathy. *Clinical neurophysiology, 125*(2), 287-297.

Scholtz, S., Miras, A. D., Chhina, N., Prechtl, C. G., Sleeth, M. L., Daud, N. M., . . . Olbers, T. (2013). Obese patients after gastric bypass surgery have lower brain-hedonic responses to food than after gastric banding. *Gut*, gutjnl-2013-305008.

Schultes, B., Ernst, B., Wilms, B., Thurnheer, M., & Hallschmid, M. (2010). Hedonic hunger is increased in severely obese patients and is reduced after gastric bypass surgery. *The American journal of clinical nutrition, 92*(2), 277-283.

Scott, K. M., McGee, M. A., Wells, J. E., & Browne, M. A. O. (2008). Obesity and mental disorders in the adult general population. *Journal of psychosomatic research, 64*(1), 97-105.

Sellaro, R., & Colzato, L. S. (2017). High body mass index is associated with impaired cognitive control. *Appetite, 113*, 301-309.

Sevinçer, G. M., Konuk, N., Bozkurt, S., & Coşkun, H. (2016). Food addiction and the outcome of bariatric surgery at 1-year: Prospective observational study. *Psychiatry research, 244*, 159-164.

Shallice, T. (1994). Multiple levels of control processes. *Attention and performance XV*, 395-420.

Shin, A. C., & Berthoud, H. (2011). Food reward functions as affected by obesity and bariatric surgery. *International Journal of Obesity, 35*(S3), S40.

Shin, A. C., Zheng, H., & Berthoud, H.-R. (2009). An expanded view of energy homeostasis: neural integration of metabolic, cognitive, and emotional drives to eat. *Physiology & behavior, 97*(5), 572-580.

Simes, R. J. (1986). An improved Bonferroni procedure for multiple tests of significance. *Biometrika, 73*(3), 751-754.

Simon, J. R., & Rudell, A. P. (1967). Auditory SR compatibility: the effect of an irrelevant cue on information processing. *Journal of applied psychology, 51*(3), 300.

Smith, E., Hay, P., Campbell, L., & Trollor, J. N. (2011). A review of the association between obesity and cognitive function across the lifespan: implications for novel approaches to prevention and treatment. *Obesity Reviews, 12*(9), 740-755.

Smulders, F. T. Y. (1993). *The selectivity of age effects on information processing: Response times and electrophysiology*: Faculteit Psychologie, Universiteit van Amsterdam.

Sousa, S., Ribeiro, O., Horácio, J., & Faísca, L. (2012). Executive functions in patients seeking and undergoing bariatric surgery. *Psic Saúde Doenças, 13*(2), 389-398.

Spitznagel, M. B., Garcia, S., Miller, L. A., Strain, G., Devlin, M., Wing, R., . . . Mitchell, J. E. (2013). Cognitive function predicts weight loss after bariatric surgery. *Surgery for Obesity and Related Diseases, 9*(3), 453-459.

Spitznagel, M. B., Hawkins, M., Alosco, M., Galioto, R., Garcia, S., Miller, L., & Gunstad, J. (2015). Neurocognitive effects of obesity and bariatric surgery. *European Eating Disorders Review, 23*(6), 488-495.

Stanek, K. M., Grieve, S. M., Brickman, A. M., Korgaonkar, M. S., Paul, R. H., Cohen, R. A., & Gunstad, J. J. (2011). Obesity is associated with reduced white matter integrity in otherwise healthy adults. *Obesity, 19*(3), 500-504.

Steele, K. E., Prokopowicz, G. P., Schweitzer, M. A., Magunsuon, T. H., Lidor, A. O., Kuwabawa, H., . . . Wong, D. F. (2010). Alterations of central dopamine receptors before and after gastric bypass surgery. *Obesity surgery, 20*(3), 369-374.

Stice, E., Spoor, S., Bohon, C., Veldhuizen, M. G., & Small, D. M. (2008). Relation of reward from food intake and anticipated food intake to obesity: a functional magnetic resonance imaging study. *Journal of abnormal psychology, 117*(4), 924.

Still, C. D., Benotti, P., Wood, G. C., Gerhard, G. S., Petrick, A., Reed, M., & Strodel, W. (2007). Outcomes of preoperative weight loss in high-risk patients undergoing gastric bypass surgery. *Archives of Surgery, 142*(10), 994-998.

Stockburger, J., Schmälzle, R., Flaisch, T., Bublatzky, F., & Schupp, H. T. (2009). The impact of hunger on food cue processing: an event-related brain potential study. *Neuroimage, 47*(4), 1819-1829.

Strazzullo, P., D'elia, L., Cairella, G., Garbagnati, F., Cappuccio, F. P., & Scalfi, L. (2010). Excess body weight and incidence of stroke: meta-analysis of prospective studies with 2 million participants. *Stroke, 41*(5), e418-e426.

Stunkard, A. J., Foch, T. T., & Hrubec, Z. (1986). A twin study of human obesity. *Jama, 256*(1), 51-54.

Stunkard, A. J., Harris, J. R., Pedersen, N. L., & McClearn, G. E. (1990). The body-mass index of twins who have been reared apart. *New England Journal of Medicine, 322*(21), 1483-1487.

Sur, S., & Sinha, V. (2009). Event-related potential: An overview. *Industrial psychiatry journal, 18*(1), 70.

Swinburn, B. A., Sacks, G., Hall, K. D., McPherson, K., Finegood, D. T., Moodie, M. L., & Gortmaker, S. L. (2011). The global obesity pandemic: shaped by global drivers and local environments. *The Lancet, 378*(9793), 804-814.

Tagliabue, M., Zorzi, M., Umiltà, C., & Bassignani, F. (2000). The role of long-term-memory and short-term-memory links in the Simon effect. *Journal of Experimental Psychology: Human perception and performance, 26*(2), 648.

Tarantino, V., Vindigni, V., Bassetto, F., Pavan, C., & Vallesi, A. (2017). Behavioral and electrophysiological correlates of cognitive control in ex-obese adults. *Biological Psychology, 127*, 198-208.

Thai, N., Taber-Thomas, B. C., & Pérez-Edgar, K. E. (2016). Neural correlates of attention biases, behavioral inhibition, and social anxiety in children: An ERP study. *Developmental cognitive neuroscience, 19*, 200-210.

Thiara, G., Cigliobianco, M., Muravsky, A., Paoli, R. A., Mansur, R., Hawa, R., . . . Sockalingam, S. (2017). Evidence for neurocognitive improvement after bariatric surgery: a systematic review. *Psychosomatics, 58*(3), 217-227.

Toda, N., Ayajiki, K., & Okamura, T. (2014). Obesity-induced cerebral hypoperfusion derived from endothelial dysfunction: one of the risk factors for Alzheimer's disease. *Current Alzheimer Research, 11*(8), 733-744.

Tuulari, J. J., Karlsson, H. K., Hirvonen, J., Salminen, P., Nuutila, P., & Nummenmaa, L. (2015). Neural circuits for cognitive appetite control in healthy and obese individuals: an fMRI study. *PloS one, 10*(2), e0116640.

Umiltá, C., & Nicoletti, R. (1990). Spatial stimulus-response compatibility. *Advances in psychology, 65*, 89-116.

Van Hout, G. C., Verschure, S. K., & Van Heck, G. L. (2005). Psychosocial predictors of success following bariatric surgery. *Obesity surgery, 15*(4), 552-560.

Van Strien, T., Frijters, J. E., Bergers, G., & Defares, P. B. (1986). The Dutch Eating Behavior Questionnaire (DEBQ) for assessment of restrained, emotional, and external eating behavior. *International Journal of Eating Disorders, 5*(2), 295-315.

Vendrell, J., Broch, M., Vilarrasa, N., Molina, A., Gómez, J. M., Gutiérrez, C., . . . Richart, C. (2004). Resistin, adiponectin, ghrelin, leptin, and proinflammatory cytokines: relationships in obesity. *Obesity research, 12*(6), 962-971.

Volkow, N. D., Wang, G.-J., & Baler, R. D. (2011). Reward, dopamine and the control of food intake: implications for obesity. *Trends in cognitive sciences, 15*(1), 37-46.

Volkow, N. D., Wang, G.-J., Fowler, J. S., & Telang, F. (2008). Overlapping neuronal circuits in addiction and obesity: evidence of systems pathology. *Philosophical Transactions of the Royal Society of London B: Biological Sciences, 363*(1507), 3191-3200.

Volkow, N. D., Wang, G. J., Telang, F., Fowler, J. S., Goldstein, R. Z., Alia-Klein, N., . . . Ma, Y. (2009). Inverse association between BMI and prefrontal metabolic activity in healthy adults. *Obesity, 17*(1), 60-65.

Volkow, N. D., Wang, G. J., Tomasi, D., & Baler, R. D. (2013). Obesity and addiction: neurobiological overlaps. *Obesity Reviews, 14*(1), 2-18.

Wadden, T. A., & Osei, S. (2002). The treatment of obesity: an overview. *Handbook of obesity treatment, 2*, 229-248.

Wang, G. T., Volkow, N. D., Logan, J., Pappas, N. R., Wong, C. T., Zhu, W., . . . Fowler, J. S. (2001). Brain dopamine and obesity. *The Lancet, 357*(9253), 354-357.

Wang, K., Li, Q., Zheng, Y., Wang, H., & Liu, X. (2014). Temporal and spectral profiles of stimulus–stimulus and stimulus–response conflict processing. *Neuroimage, 89*, 280-288.

Ward, M. A., Carlsson, C. M., Trivedi, M. A., Sager, M. A., & Johnson, S. C. (2005). The effect of body mass index on global brain volume in middle-aged adults: a cross sectional study. *BMC neurology, 5*(1), 23.

Wardle, J., Guthrie, C., Sanderson, S., Birch, L., & Plomin, R. (2001). Food and activity preferences in children of lean and obese parents. *International Journal of Obesity, 25*(7), 971.

Wedin, S., Madan, A., Correll, J., Crowley, N., Malcolm, R., Byrne, T. K., & Borckardt, J. J. (2014). Emotional eating, marital status and history of physical abuse predict 2-year weight loss in weight loss surgery patients. *Eating behaviors, 15*(4), 619-624.

Weisenbach, S. L., Boore, L. A., & Kales, H. C. (2012). Depression and cognitive impairment in older adults. *Current psychiatry reports, 14*(4), 280-288.

Werthmann, J., Roefs, A., Nederkoorn, C., Mogg, K., Bradley, B., & Jansen, A. (2012). Can (not) take my eyes off food. Attention bias, craving and overeating. *Appetite, 59*(2), 637.

White, M. A., Kalarchian, M. A., Masheb, R. M., Marcus, M. D., & Grilo, C. M. (2010). Loss of control over eating predicts outcomes in bariatric surgery: a prospective 24-month follow-up study. *The Journal of clinical psychiatry, 71*(2), 175.

White, M. A., Masheb, R. M., Rothschild, B. S., Burke-Martindale, C. H., & Grilo, C. M. (2006). The prognostic significance of regular binge eating in extremely obese gastric bypass patients: 12-month postoperative outcomes. *The Journal of clinical psychiatry*.

Whitmer, R. A., Gunderson, E. P., Barrett-Connor, E., Quesenberry, C. P., & Yaffe, K. (2005). Obesity in middle age and future risk of dementia: a 27 year longitudinal population based study. *Bmj, 330*(7504), 1360.

Wiemerslage, L., Zhou, W., Olivo, G., Stark, J., Hogenkamp, P. S., Larsson, E. M., . . . Schiöth, H. B. (2017). A resting-state fMRI study of obese females between pre-and postprandial states before and after bariatric surgery. *European Journal of Neuroscience, 45*(3), 333-341.

Wiers, R. W., Gladwin, T. E., Hofmann, W., Salemink, E., & Ridderinkhof, K. R. (2013). Cognitive bias modification and cognitive control training in addiction and related psychopathology: Mechanisms, clinical perspectives, and ways forward. *Clinical Psychological Science, 1*(2), 192-212.

Wiers, R. W., & Stacy, A. W. (2006). Implicit cognition and addiction. *Current Directions in Psychological Science, 15*(6), 292-296.

Wimmelmann, C. L., Dela, F., & Mortensen, E. L. (2014). Psychological predictors of weight loss after bariatric surgery: a review of the recent research. *Obesity research & clinical practice, 8*(4), e299-e313.

Wing, R. R., & Phelan, S. (2005). Long-term weight loss maintenance–. *The American journal of clinical nutrition, 82*(1), 222S-225S.

Wolz, I., Fagundo, A. B., Treasure, J., & Fernández-Aranda, F. (2015). The processing of food stimuli in abnormal eating: a systematic review of electrophysiology. *European Eating Disorders Review*, *23*(4), 251-261.

Yousseif, A., Emmanuel, J., Karra, E., Millet, Q., Elkalaawy, M., Jenkinson, A. D., . . . Fiennes, A. G. (2014). Differential effects of laparoscopic sleeve gastrectomy and laparoscopic gastric bypass on appetite, circulating acyl-ghrelin, peptide YY3-36 and active GLP-1 levels in non-diabetic humans. *Obesity surgery*, *24*(2), 241-252.

Zabena, C., González-Sánchez, J. L., Martínez-Larrad, M. T., Torres-García, A., Alvarez-Fernández-Represa, J., Corbatón-Anchuelo, A., . . . Serrano-Ríos, M. (2009). The FTO obesity gene. Genotyping and gene expression analysis in morbidly obese patients. *Obesity surgery*, *19*(1), 87-95.

Zhang, X., Zhang, G., Zhang, H., Karin, M., Bai, H., & Cai, D. (2008). Hypothalamic IKKβ/NF-κB and ER stress link overnutrition to energy imbalance and obesity. *Cell*, *135*(1), 61-73.

Ziauddeen, H., Alonso-Alonso, M., Hill, J. O., Kelley, M., & Khan, N. A. (2015). Obesity and the neurocognitive basis of food reward and the control of intake. *Advances in Nutrition: An International Review Journal*, *6*(4), 474-486.

APPENDIX A

Symptom Checklist-90 Items Revised (S.C.L.-90)

In che maniera soffri o hai sofferto di	**0 per niente**	**1 un poco**	**2 modera-tamente**	**3 molto**	**4 moltis-simo**
1- mal di testa					
2- nervosismo o agitazione interna					
3- incapacità a scacciare pensieri, parole o idee indesiderate					
4- sensazione di svenimento o di vertigini					
5- perdita dell'interesse o del piacere sessuale					
6- tendenza a criticare gli altri					
7- convinzione che gli altri possano controllare i tuoi pensieri					
8- convinzione che gli altri siano responsabili dei tuoi disturbi					
9- difficoltà a ricordare le cose					
10- preoccupazioni per la tua negligenza o trascuratezza					
11- sentirsi facilmente infastidito o irritato					
12- dolori al cuore o al petto					
13- paura degli spazi aperti o delle strade					
14- sentirti debole o fiacco					
15- idee di toglierti la vita					
16- udire voci che le altre persone non odono					
17- tremori					
18- mancanza di fiducia negli altri					

In che misura soffri o hai sofferto di ...	**0** **per niente**	**1** **un poco**	**2** **modera-tamente**	**3** **molto**	**4** **moltis-simo**
19- scarso appetito					
20- facili crisi di pianto					
21- sentirsi intimidito nei confronti dell'altro sesso					
22- sensazione di essere preso in trappola					
23- paure improvvise senza ragione					
24- scatti d'ira incontrollabili					
25- paura di uscire da solo					
26- rimproverarti per qualsiasi cosa					
27- dolori alla schiena					
28- senso di incapacità a portare a termine le cose					
29- sentirti solo					
30- sentirti giù di morale					
31- preoccuparsi eccessivamente per qualsiasi cosa					
32- mancanza di interesse					
33- senso di paura					
34- sentirti facilmente ferito o offeso					
35- convinzione che gli altri percepiscano i tuoi pensieri					
36- sensazione di non trovare comprensione o simpatia					
37- sensazione che gli altri non ti siano amici o ti abbiano in antipatia					

In che misura soffri o hai sofferto di ...	**0** **per niente**	**1** **un poco**	**2** **modera-tamente**	**3** **molto**	**4** **moltis-simo**
38- dover fare le cose molto lentamente per essere sicuro di farle bene					
39- palpitazioni o sentirti il cuore in gola					
40- senso di nausea o mal di stomaco					
41- sentimenti di inferiorità					
42- dolori muscolari					
43- sensazione che gli altri ti guardino o parlino di te					
44- difficoltà ad addormentarti					
45- bisogno di controllare ripetutamente ciò che fai					
46- difficoltà a prendere decisioni					
47- paura di viaggiare in autobus, nella metropolitana o in treno					
48- sentirsi senza fiato					
49- vampate di calore o brividi di freddo					
50- necessità di evitare certi oggetti, luoghi o attività perché ti spaventano					
51- senso di vuoto mentale					
52- intorpidimento o formicolio di alcune parti del corpo					
53- nodo alla gola					
54- guardare al futuro senza speranza					
55- difficoltà a concentrarti					
56- senso di debolezza in qualche parte del corpo					
57- sentirti teso o sulle spine					

In che misura soffri o hai sofferto di ...	**0** **per niente**	**1** **un poco**	**2** **modera-tamente**	**3** **molto**	**4** **moltis-simo**
58- senso di pesantezza alle braccia o alle gambe					
59- idee di morte					
60- mangiare troppo					
61- senso di fastidio quando la gente ti guarda o parla di te					
62- avere dei pensieri che non sono tuoi					
63- sentire l'impulso di colpire, ferire o fare male a qualcuno					
64- svegliarsi presto al mattino senza riuscire a riaddormentarsi					
65- avere bisogno di ripetere lo stesso atto come toccare, contare, lavarsi, etc.					
66- sonno inquieto o disturbato					
67- sentire l'impulso di rompere gli oggetti					
68- avere idee o convinzioni che gli altri non condividono					
69- sentirsi penosamente imbarazzato in presenza di altri					
70- sentirsi a disagio tra la folla, come nei negozi, al cinema, etc...					
71- sensazione che tutto richieda uno sforzo					
72- momenti di terrore o di panico					
73- sentirsi a disagio quando mangi o bevi in presenza di altri					
74- ingaggiare frequenti discussioni					
75- sentirti a disagio quando sei solo					

In che misura soffri o hai sofferto di ...	**0** **per niente**	**1** **un poco**	**2** **modera-tamente**	**3** **molto**	**4** **moltis-simo**
76- convinzione che gli altri non apprezzino il tuo lavoro					
77- sentirti solo e triste anche in compagnia					
78- senso di irrequietezza, tanto da non poter stare seduto					
79- sentimenti di inutilità					
80- sensazione che le cose più comuni e familiari siano estranee o irreali					
81- urlare o scagliare oggetti					
82- aver paura di svenire davanti agli altri					
83- impressione che gli altri possano approfittare di te o delle tue azioni					
84- pensieri sul sesso che ti affliggono					
85- idea di dover scontare i propri peccati					
86- sentirti costretto a portare a termine ciò che hai iniziato					
87- pensiero di avere una grave malattia fisica					
88- non sentirti mai vicino alle altre persone					
89- sentirti in colpa					
90- idea che qualche cosa non vada bene nella tua mente					

Barratt Impulsiveness Scale-11 (BIS-11)

	Mai/ Raramente	**Talvolta**	**Spesso**	**Quasi sempre/ Sempre**
1. Pianifico le attività attentamente				
2. Faccio le cose senza pensarci				
3. Decido velocemente				
4. Mi affido alla sorte				
5. Non "focalizzo l'attenzione"				
6. I miei pensieri "vanno a gran velocità"				
7. Pianifico i viaggi con molto anticipo				
8. Ho autocontrollo				
9. Mi concentro facilmente				
10. Risparmio con regolarità				
11. Non riesco a star fermo durante gli spettacoli o le lezioni				
12. Sono un attento pensatore				
13. Faccio progetti per una sicurezza lavorativa				
14. Dico cose senza pensare				
15. Mi piace pensare a problemi complessi				
16. Cambio lavoro				
17. Agisco "d'impulso"				
18. Mi annoio facilmente quando devo risolvere dei problemi concettuali				
19. Agisco sull'impulso del momento				
20. Sono un pensatore assiduo				

	Mai/ Raramente	**Talvolta**	**Spesso**	**Quasi sempre/ Sempre**
21. Cambio residenza				
22. Compro le cose d'impulso				
23. Riesco a pensare ad un solo problema per volta				
24. Cambio hobby				
25. Spendo più di quello che guadagno				
26. Quando penso ho spesso pensieri estranei				
27. Mi interesso più al presente che al futuro				
28. Sono irrequieto a teatro o durante le lezioni				
29. Mi piacciono i rompicapo				
30. Sono orientato verso il futuro				

YALE FOOD ADDICTION SCALE (YFAS)

Negli ultimi 12 mesi:	**Mai**	**1 volta in un mese**	**2 volte in un mese**	**3-4 volte a settimana**	**4 volte o più o ogni giorno**
1. Quando comincio a mangiare certi tipi di cibo, finisco per mangiare molto più di quanto avevo previsto.	0	1	2	3	4
2. Continuo a consumare certi tipi di cibo anche quando non ho più fame.	0	1	2	3	4
3. Mangio fino al punto di sentirmi male fisicamente.	0	1	2	3	4
4. Non mangiare o ridurre certi tipi di cibo è qualcosa che mi preoccupa.	0	1	2	3	4
5. Passo molto tempo a sentirmi fiacco o affaticato per aver mangiato troppo.	0	1	2	3	4
6. Mi ritrovo sempre a mangiare determinati alimenti nel corso della giornata.	0	1	2	3	4
7. Quando alcuni alimenti non sono disponibili, trovo il modo di ottenerli. Per esempio, guidare fino al negozio per l'acquisto di determinati alimenti, anche se ho altre opzioni disponibili per me in casa.	0	1	2	3	4
8. Ci sono stati momenti in cui ho consumato alcuni alimenti così spesso o in quantità talmente grandi da iniziare a mangiare cibo invece di lavorare, passare il tempo con la mia famiglia o con gli amici o intraprendere altre attività importanti o attività ricreative che mi piacciono.	0	1	2	3	4
9. Ci sono stati momenti in cui ho consumato alcuni alimenti così spesso o in quantità talmente grandi da passare il tempo ad affrontare sentimenti negativi verso il cibo, invece di lavorare, passare il tempo con la mia famiglia o con gli amici o intraprendere altre attività importanti o attività ricreative che mi piacciono.	0	1	2	3	4

Negli ultimi 12 mesi:	**Mai**	**1 volta in un mese**	**2 volte in un mese**	**3-4 volte a settimana**	**4 volte o più o ogni giorno**
10. Ci sono stati momenti in cui ho evitato situazioni professionali o sociali in cui erano disponibili alcuni alimenti, perché avevo paura di mangiare troppo.	0	1	2	3	4
11. Ci sono stati momenti in cui ho evitato situazioni professionali o sociali perché non potevo consumare determinati alimenti lì presenti.	0	1	2	3	4
12. Ho avuto sintomi di astinenza quali agitazione, ansia, o altri sintomi fisici quando ho ridotto o smesso di mangiare determinati alimenti. (si prega di NON includere sintomi di astinenza causati da riduzione di bevande contenenti caffeina, come bibite gassate, caffè, tè, bevande energetiche, ecc.).	0	1	2	3	4
13. Ho consumato alcuni alimenti per evitare sentimenti di ansia, agitazione, o altri sintomi fisici che si stavano sviluppando (si prega di NON includere sintomi di astinenza causati da riduzione di bevande contenenti caffeina, come bibite gassate, caffè, tè, bevande energetiche, ecc.).	0	1	2	3	4
14. Provo un forte desiderio o una spinta a consumare determinati alimenti quando riduco o smetto di mangiarli.	0	1	2	3	4
15. Il mio comportamento rispetto al cibo e all'alimentazione causa un disagio significativo.	0	1	2	3	4
16. Ho problemi significativi nella mia capacità di funzionare in modo efficace (routine quotidiana, lavoro / scuola, attività sociali, attività di famiglia, problemi di salute) a causa del cibo e del mangiare.	0	1	2	3	4

Negli Ultimi 12 mesi		
17. Le mie abitudini alimentari hanno causato notevoli problemi psicologici come depressione, ansia, disgusto di sé, o senso di colpa.	NO	SI
18. Le mie abitudini alimentari hanno causato notevoli problemi fisici o aggravato un problema fisico già esistente.	NO	SI
19. Continuo a consumare gli stessi tipi di cibo o la stessa quantità di cibo anche se ho avuto problemi emotivi e / o fisici.	NO	SI
20. Nel corso del tempo, ho scoperto che ho bisogno di mangiare sempre di più per ottenere la sensazione che voglio, come ad esempio ridurre emozioni negative o ottenere un piacere maggiore.	NO	SI
21. Ho scoperto che mangiare la stessa quantità di cibo non riduce le mie emozioni negative o aumenta le mie sensazioni piacevoli come una volta.	NO	SI
22. Voglio ridurre o smettere di mangiare certi tipi di cibo.	NO	SI
23. Ho cercato di ridurre o smettere di mangiare certi tipi di cibo.	NO	SI
24. Ho avuto successo a ridurre o non mangiare un certo alimento.	NO	SI

25. Quante volte nell'ultimo anno hai provato a ridurre o eliminare del tutto certi tipi di cibo?	1 volta o meno	2 volte	3 volte	4 volte	5 volte o più

Binge Eating Scale (BES)

1.

Non penso consciamente al mio peso ed alle dimensioni del mio corpo quando sono con altre persone.	
Mi preoccupo del mio aspetto, ma questo non mi rende normalmente insoddisfatto/a di me stesso/a.	
Sono consapevole del mio aspetto e del mio peso e questo mi rende deluso/a di me stesso/a.	
Sono molto consapevole del mio peso e spesso provo forte vergogna e disgusto per me stesso/a. Perciò cerco di evitare di incontrare altre persone.	

2.

Non ho difficoltà a mangiare lentamente, seduto/a in maniera corretta.	
Mi sembra di trangugiare il cibo. Nonostante ciò, non finisco per sentirmi troppo pieno/a per aver mangiato eccessivamente.	
Talvolta, tendo a mangiare velocemente e dopo mi sento troppo pieno/a.	
Ho l'abitudine di ingollare il cibo quasi senza masticarlo. Quando faccio così, di solito mi sento scoppiare perché ho mangiato troppo.	

3.

Quando voglio, sono capace di controllare i miei impulsi verso il cibo.	
Penso di aver minor controllo sul cibo rispetto alla maggior parte delle persone.	
Mi sento totalmente incapace di controllare i miei impulsi verso il cibo.	
Siccome mi sento totalmente incapace di controllare il mio rapporto con l'alimentazione, sto cercando disperatamente di raggiungere il controllo sul cibo.	

4.

Non ho l'abitudine di mangiare quando sono annoiato.	
Qualche volta mangio quando sono annoiato, ma talvolta riesco a distrarmi e a non pensare al cibo	
Ho una vera abitudine di mangiare quando sono annoiato, ma talvolta riesco a distrarmi e a non pensare al cibo.	
Ho una forte abitudine di mangiare quando sono annoiato. Niente riesce a farmi smettere.	

5.

Quando mangio qualcosa, di solito, è perché ho fame.	
Talvolta mangio qualcosa d'impulso, senza avere veramente fame	
Mangio regolarmente per soddisfare una sensazione di fame, pur non avendo davvero bisogno fisicamente del cibo. In queste occasioni, non riesco neanche a gustare quello che mangio.	
Anche se non ho fisicamente fame, avverto il bisogno di mettere qualcosa in bocca e mi sento soddisfatto/a solo quando riesco a mangiare qualcosa per riempirmi la bocca, come un pezzo di pane. Qualche volta, quando questo succede, risputo il cibo per non ingrassare	

6.

Non mi sento per nulla in colpa, né provo odio per me stesso/a, dopo aver mangiato troppo.	
Talvolta, mi sento in colpa o provo odio per me stesso/a dopo aver mangiato troppo.	
Quasi sempre vivo un forte senso di colpa o provo odio per me stesso/a dopo aver mangiato troppo.	

7.

Quando sono a dieta, non perdo mai del tutto il controllo sul cibo, anche dopo periodi in cui ho mangiato troppo.	
Quando sono a dieta e mangio un cibo "proibito", sento che ormai ho "sgarrato" e mangio ancora di più.	
Quando sono a dieta e mangio troppo spesso mi dico: "Ormai hai sgarrato, perché non vai fino in fondo?". Quando questo succede, mangio ancora di più.	
Mi metto regolarmente a dieta stretta, ma poi interrompo la dieta con un'abbuffata. La mia vita è fatta di abbuffate e digiuni.	

8.

Raramente mangio così tanto da sentirmi sgradevolmente pieno/a.	
Circa una volta al mese, mangio così tanto da sentirmi sgradevolmente pieno/a.	
Ci sono periodi regolari durante il mese in cui mangio grandi quantità di cibo, ai pasti o fuori dai pasti.	
Mangio così tanto che di solito, dopo aver mangiato, mi sento piuttosto male ed ho nausea.	

9.

La quantità di calorie che assumo è abbastanza costante nel tempo.	
Qualche volta, dopo aver mangiato troppo, cerco di ridurre al minimo le calorie, per compensare l'eccesso di calorie che ho mangiato.	
Abitualmente mangio troppo di notte. Solitamente non ho fame la mattina e mangio troppo la sera.	
Da adulto, ho avuto periodi di circa una settimana in cui mi sono imposto diete "da fame", a seguito di periodi in cui avevo mangiato troppo. La mia vita è fatta di abbuffate e digiuni.	

10.

Di solito riesco a smettere di mangiare quando voglio. So quando è ora di dire basta.	
Talvolta avverto un impulso incontrollabile a mangiare.	
Frequentemente avverto forti impulsi a mangiare, che sembro incapace di controllare, mentre altre volte riesco a controllarmi.	
Mi sento incapace di controllare i miei impulsi a mangiare. Ho paura di non riuscire a smettere di mangiare volontariamente.	

11.

Non ho problemi a smettere di mangiare quando mi sento pieno/a.	
Di solito posso smettere di mangiare quando sono pieno/a, ma talvolta mangio così tanto da sentirmi sgradevolmente pieno/a.	
Per me è un problema smettere di mangiare una volta che ho iniziato e di solito mi sento sgradevolmente pieno/a dopo aver finito di mangiare.	
Siccome per me è un problema smettere di mangiare, qualche volta devo provocarmi il vomito per avere sollievo.	

12.

Quando sono con gli altri (incontri familiari, occasioni sociali) mi sembra di mangiare come quando sono solo.	
Talvolta quando sono con gli altri non mangio quanto vorrei, perché sono consapevole del mio disagio verso il cibo.	
Spesso mangio poco quando sono con altre persone, perché mangiare di fronte ad altri mi imbarazza.	
Mi vergogno così tanto di mangiare troppo, che per farlo scelgo i momenti in cui nessuno mi vede. In effetti, mangio di nascosto.	

13.

Faccio tre pasti al giorno e occasionalmente uno spuntino.	
Faccio tre pasti al giorno e normalmente anche gli spuntini.	
Quando faccio molti spuntini, salto i pasti regolari.	
Ci sono periodi in cui mi sembra di mangiare continuamente, senza pasti regolari.	

14.

Non penso molto a controllare gli impulsi a mangiare non desiderati.	
Almeno qualche volta, la mia mente è occupata dal pensiero di come controllare i miei impulsi a mangiare.	
Sento che spesso passo molto tempo a pensare a quanto ho mangiato o a come fare per non mangiare più.	
Mi sembra che la maggior parte del mio tempo la mia mente sia occupata da pensieri sul mangiare. Mi sembra di essere continuamente in lotta per non mangiare.	

15.

Non penso molto al cibo.	
Mi capita di avere un forte desiderio di cibo, ma solo per brevi periodi di tempo.	
Ci sono giorni in cui non penso ad altro che al cibo.	
La maggior parte delle mie giornate è occupata da pensieri sul cibo. Mi sembra di vivere per mangiare.	

16.

Di solito se sono affamato/a oppure no, prendo la giusta porzione per saziarmi.	
Occasionalmente, sono incerto/a se ho fisicamente fame oppure no. In questi momenti, mi è difficile capire quanto cibo ci vorrebbe per saziarmi.	
Anche se sapessi quante calorie dovrei mangiare, non ho idea precisa di quanto sarebbe una "normale" quantità.	

Power Of Food Scale (PFS)

.

	Per niente d'accordo	**Un po' d'accordo**	**Piuttosto d'accordo**	**D'accordo**	**Fortemente d'accordo**
1. Mi ritrovo a pensare al cibo anche quando non sono fisicamente affamato.					
2. Quando mi trovo in una situazione nella quale sono presenti cibi deliziosi, ma devo aspettare per mangiarli, è difficile per me aspettare.					
3. Ricavo molto più piacere nel mangiare che per ogni altra cosa.					
4.Sento che il cibo è per me come un liquore per un alcolista.					
5. Se vedo o sento l'odore di un cibo che mi piace, ho un urgente bisogno di assaggiarlo.					
6. Quando è presente un cibo grasso(calorico) che mi piace molto, è difficile per me trattenermi dall'assaggiarlo.					
7. Penso spesso a quali cibi potrei mangiare nel corso nella giornata.					
8. E' spaventoso pensare al potere che il cibo ha su di me.					
9. Quando assaggio un cibo che mi piace provo intenso piacere .					
10. Quando so che un cibo che mi piace è disponibile, non riesco a trattenermi dall'idea di averne un po'.					
11. Mi piace così tanto il sapore di certi cibi, che non riesco ad evitare di mangiarli anche se non mi fanno bene.					
12. Vedere cibi appetitosi negli annunci o spot pubblicitari mi mette voglia di mangiare.					

	Per niente d'accordo	**Un po' d'accordo**	**Piuttosto d'accordo**	**D'accordo**	**Fortemente d'accordo**
13. Ho la sensazione che sia il cibo a controllarmi, piuttosto che il contrario.					
14. Poco prima di assaggiare un cibo che mi piace, lo pregusto in modo intenso.					
15. Quando mangio un cibo appetitoso, mi focalizzo molto sul buon sapore che ha.					
16. A volte, mentre sto svolgendo attività quotidiane, sento di punto in bianco il bisogno di mangiare senza una ragione .					
17. Credo che mi piaccia mangiare molto di più delle altre persone.					
18.Sentire qualcuno che descrive un buon pasto, mi fa venire voglia di mangiare qualcosa.					
19.Penso molto spesso al cibo.					
20. Per me è molto importante che i cibi che mangio siano particolarmente gustosi .					
21. Prima di mangiare un cibo che mi piace la mia bocca inizia a riempirsi di saliva.					

Eating Attitudes Test-26 (EAT-26)

	Sempre	**Normalmente**	**Spesso**	**A volte**	**Raramente**	**Mai**
1. Sono terrorizzato di essere in sovrappeso.	O	O	O	O	O	O
2. Quando ho fame evito di mangiare.	O	O	O	O	O	O
3. Penso al cibo con preoccupazione.	O	O	O	O	O	O
4. Mi è capitato di mangiare con enorme voracità sentendomi incapace di smettere.	O	O	O	O	O	O
5. Ho l'abitudine di sminuzzare il cibo.	O	O	O	O	O	O
6. Faccio molta attenzione al potere calorico degli alimenti che mangio.	O	O	O	O	O	O
7. Evito in particolare gli alimenti con un alto contenuto di carboidrati (ad esempio, pane, riso, patate, ecc).	O	O	O	O	O	O
8. Sento gli altri che vorrebbero che mangiassi di più.	O	O	O	O	O	O

	Sempre	**Normalmente**	**Spesso**	**A volte**	**Raramente**	**Mai**
9. Vomito dopo aver mangiato.	O	O	O	O	O	O
10. Mi sento molto in colpa dopo aver mangiato.	O	O	O	O	O	O
11. Mi tormenta il desiderio di essere più sottile.	O	O	O	O	O	O
12. Mi sottopongo a esercizi fisici intensi per bruciare calorie.	O	O	O	O	O	O
13. Altri pensano che io sia troppo magra.	O	O	O	O	O	O
14 Mi preoccupa l'idea di avere del grasso sul mio corpo.	O	O	O	O	O	O
15. Impiego più tempo degli altri per mangiare.	O	O	O	O	O	O
16. Evitare cibi dolci.	O	O	O	O	O	O
17. Mangiare cibi dietetici.	O	O	O	O	O	O
18. Sento che il cibo controlli la mia vita.	O	O	O	O	O	O
19. Mi piace mostrare un grande autocontrollo verso il cibo e dominare la fame.	O	O	O	O	O	O

	Sempre	**Normalmente**	**Spesso**	**A volte**	**Raramente**	**Mai**
20. Sento che gli altri fanno pressione su di me perché io mangi.	O	O	O	O	O	O
21. Dedico al cibo troppo tempo e troppi pensieri.	O	O	O	O	O	O
22. Mi dispero se mangio dei dolci.	O	O	O	O	O	O
23. Mi impegno in programmi di dieta.	O	O	O	O	O	O
24. Mi piace che il mio stomaco sia vuoto.	O	O	O	O	O	O
25. Ho l'impulso di vomitare dopo mangiato.	O	O	O	O	O	O
26. Mi piace provare nuovi cibi elaborati.	O	O	O	O	O	O

Dutch Eating Behavior Questionnaire (DEBQ)

1= "mai" 2= "raramente" 3= "a volte" 4= "spesso" 5= "molto spesso"

1. Se sei aumentato di peso, mangi meno di quello che sei solito fare?	**1**	**2**	**3**	**4**	**5**
2. Provi a mangiare meno all'ora dei pasti rispetto a quanto ti piacerebbe mangiare?	**1**	**2**	**3**	**4**	**5**
3. Quanto spesso rifiuti cibi o bevande offerte perché sei preoccupato del tuo peso?	**1**	**2**	**3**	**4**	**5**
4. Guardi esattamente cosa mangi?	**1**	**2**	**3**	**4**	**5**
5. Volutamente mangi cibi dimagranti?	**1**	**2**	**3**	**4**	**5**
6. Quando hai mangiato troppo, mangi meno del solito nei giorni seguenti?	**1**	**2**	**3**	**4**	**5**
7. Mangi volutamente meno per non diventare più grasso?	**1**	**2**	**3**	**4**	**5**
8. Quanto spesso provi a non mangiare perché stai attento al tuo peso?	**1**	**2**	**3**	**4**	**5**
9. Quanto spesso alla sera provi a non mangiare perché stai attento al tuo peso?	**1**	**2**	**3**	**4**	**5**
10. Prendi in considerazione il tuo peso con quello che mangi?	**1**	**2**	**3**	**4**	**5**
11. Hai il desiderio di mangiare quando sei irritato?	**1**	**2**	**3**	**4**	**5**
12. Hai il desiderio di mangiare quando non hai niente da fare?	**1**	**2**	**3**	**4**	**5**
13. Hai il desiderio di mangiare quando sei depresso o scoraggiato?	**1**	**2**	**3**	**4**	**5**
14. Hai il desiderio di mangiare quando ti senti solo?	**1**	**2**	**3**	**4**	**5**
15. Hai il desiderio di mangiare quando qualcuno ti delude?	**1**	**2**	**3**	**4**	**5**
16. Hai il desiderio di mangiare quando sei arrabbiato?	**1**	**2**	**3**	**4**	**5**
17. Hai il desiderio di mangiare quando stai vivendo qualcosa di spiacevole?	**1**	**2**	**3**	**4**	**5**

18. Hai il desiderio di mangiare quando sei ansioso, preoccupato o teso?	**1**	**2**	**3**	**4**	**5**
19. Hai il desiderio di mangiare quando le cose vanno contro di te o quando vanno male?	**1**	**2**	**3**	**4**	**5**
20. Hai il desiderio di mangiare quando sei spaventato?	**1**	**2**	**3**	**4**	**5**
21. Hai il desiderio di mangiare quando sei deluso o insoddisfatto?	**1**	**2**	**3**	**4**	**5**
22. Hai il desiderio di mangiare quando sei annoiato o inquieto?	**1**	**2**	**3**	**4**	**5**
23. Hai il desiderio di mangiare quando sei emotivamente turbato?	**1**	**2**	**3**	**4**	**5**
24. Se ti piace il sapore di un cibo, mangi più del solito?	**1**	**2**	**3**	**4**	**5**
25. Se un cibo per te ha un buon odore e un bell'aspetto, mangi più del solito?	**1**	**2**	**3**	**4**	**5**
26. Se vedi o senti l'odore di un cibo gustoso, hai il desiderio di mangiarlo?	**1**	**2**	**3**	**4**	**5**
27. Se hai qualcosa di gustoso da mangiare, lo mangi subito?	**1**	**2**	**3**	**4**	**5**
28. Se passi vicino ad un forno, hai il desiderio di comprare qualcosa di delizioso?	**1**	**2**	**3**	**4**	**5**
29. Se passi affianco ad un bar o una caffetteria, hai il desiderio di comprare qualcosa di delizioso?	**1**	**2**	**3**	**4**	**5**
30. Se vedi altri che mangiano, hai il desiderio di mangiare?	**1**	**2**	**3**	**4**	**5**
31. Riesci a resistere alla tentazione di mangiare cibi deliziosi?	**1**	**2**	**3**	**4**	**5**
32. Mangi più del solito quando vedi altri che mangiano?	**1**	**2**	**3**	**4**	**5**
33. Mentre prepari un pasto, tendi a mangiare qualcosa?	**1**	**2**	**3**	**4**	**5**

APPENDIX B

Likert Scales Hunger/Satiety/Desire to eat

Come definiresti il tuo stato attuale rispetto alle seguenti espressioni riguardanti l'assunzione di cibo?

In questo momento mi sento

Estremamente affamato										Per nulla affamato
-5	-4	-3	-2	-1	0	1	2	3	4	5

Per nulla sazio										Estremamente sazio
-5	-4	-3	-2	-1	0	1	2	3	4	5

Desideroso di mangiare										Non desideroso di mangiare
-5	-4	-3	-2	-1	0	1	2	3	4	5