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THE ROLE OF MECHANISMS OF INHIBITION AND ATTENTION IN OBESITY

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List of publications that the dissertation is based upon

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- Tsegaye, A., Guo, L., Stoet, C., Cserjési, G., Kökönyei, G., & Logemann, A. (2022). The relationship between reward context and inhibitory control, does it depend on BMI, maladaptive eating, and negative affect? BMC psychology, 10(1),4. <u>https://doi.org/10.1186/s40359-021-00712-5</u>

Preface

Obesity/ overweight is one of the most demanding and challenging global public health issues of the 21st century (Amro, Euro, & Wpro, 2017; Kelly, Yang, Chen, Reynolds, & He, 2008; Ogden, Yanovski, Carroll, & Flegal, 2007). Obesity is a risk factor for a long list of both immediate and long-term physical, social as well as psychological health consequences, such as type II diabetes, cardiovascular diseases, many types of cancer, sleep apnea, stigmatization, poor self-esteem, and Alzheimer's disease (Craft, 2005; Koch, Matthias, & Pollatos, 2014; Secretan et al., 2016). Moreover, obesity is associated with psychopathologies such as depression and anxiety (Simon, Korff, Saunders, & Diana, 2007).

There is ensuing debate regarding whether obesity can be regarded as a disease/psychopathology (Geisler, 2017; N. D. Volkow, Wang, Tomasi, & Baler, 2013). In that vein, it should be noted that studies show considerable overlap between obesity and addiction with respect to the brain mechanism that drives the problematic behaviour (Robinson, Fischer, Ahuja, Lesser, & Maniates, 2016b; N. D. Volkow, Wang, Fowler, Tomasi, & Baler, 2011; N. D. Volkow et al., 2013).

Obesity relates to executive function (EF), which refers to self-regulatory cognitive processes that contain three components such as inhibitory control, updating and monitoring working memory and mental set shifting (Miyake et al., 2000). Indeed, particularly visuospatial attention and inhibitory control, have been suggested to drive a significant part of the behavioral component in relation to abnormal weight gain (Chantal Nederkoorn, Coelho, Guerrieri, Houben, & Jansen, 2012; D. G. Smith & Robbins, 2013; Zhang, Chen, Chen, Gu, & Xu, 2017). On the other hand, previous research suggests that overexposure to palatable food disrupts the brain mechanism important for reward/inhibitory processing, and may partly drive the observed deficits of inhibitory control and anomalous visuospatial attention, most notably in a reward context (Batterink, Yokum, & Stice, 2010; Robinson, Fischer, Ahuja, Lesser, & Maniates, 2016; Stice, Yokum, Bohon, Marti, & Smolen, 2010). However, previous studies have painted a contradictory picture with respect to the exact role of these processes in obesity. Importantly, a recent study that investigated inhibitory control in relation to BMI has suggested that higher BMI is associated with deficient inhibitory

control, specifically in contexts of palatable food relative to a neutral context (Houben, Nederkoorn, & Jansen, 2014a). This result seems in line with studies that have specifically investigated striatal processing in individuals with obesity during presentation of food cues and food ingestion (Stice, Spoor, Bohon, Veldhuizen, & Small, 2008). But it remains the questions whether the inhibitory deficit really represents a specific deficit in a palatable food context or perhaps a general deficit of executive control in any context of reward. And whether the aforementioned inhibitory deficit could be explained (at least in part) by attentional mechanisms. In addition, less is known about the role of moderating factors stress, rumination, mindfulness, and eating behaviors regarding the relation between BMI and the aforementioned executive factors (i.e. visuospatial attention and inhibitory control) has not yet been investigated. Lastly, as mentioned, there is sizeable overlap between the brain mechanism implicated in obesity and pharmacological addiction. Now, one remaining question was whether the obesity associated behavioural response patterns, especially in contexts of reward, would be mirrored in pharmacological addiction such as nicotine addiction. These main questions were addressed in the current dissertation.

Following the general introduction, in this dissertation includes three empirical studies and one book review chapter. In chapter two, we reviewed the main psychological factors that play a role in the onset and persistence of obesity. In this chapter more discuss the role of emotional and cognitive factors, mood and emotional regulation, sigma and discrimination and personality traits in relation to obesity. Different studies show that individuals with obesity have a stronger attentional bias for and motivational drive (wanting) towards foods rich in fat and sugar food coupled with deficient impulse control in contexts of anticipated palatable food. Currently, obesity is not classified as a mental disorder mainly because of the heterogeneity and uncertainty with respect to its etiology. This may be surprising as this is the case with several other included disorders, and the debate continues. At least part of the issue of current suboptimal treatment approaches is a lack of understanding of the key mechanism implicated in obesity. Hence, increased insight into the main psychological mechanisms could assist in future treatment directions.

Our first empirical study on chapter three, investigated the role of attentional bias/disengagement across conditions that differ in terms of anticipated reward. The results showed that bias was reduced in the food condition relative to the neutral condition, however

this effect was not affected by BMI. Similarly, bias was significantly reduced in the money condition as compared to the neutral condition, but this effect was not affected by BMI. Disengagement was significantly enhanced in the food condition as opposed to the neutral condition, but BMI was not affected. Disengagement increased in the money condition compared to the neutral condition and BMI increased this effect. As regards to moderator factors both self-reported mindfulness and stress did not affect any of the BMI x conditions.

Our second empirical study on chapter four, investigated the role of inhibitory control across three conditions. The results of this study showed that BMI, maladaptive eating and stress were associated with reduced inhibitory control in the food context relative to the neutral context, but not in a money context relative to the neutral context. To conclude our results of this study, the effects of BMI, maladaptive eating behavior, and stress on inhibitory control were specific to the food context and did not generalize to a non-intrinsic reward condition, operationalized with money pictures.

In chapter five, on the third empirical study, we investigated the role of inhibitory control in relation to nicotine addiction in contexts that differ in terms of reward. The results showed that smokers relative to nonsmokers showed less inhibitory control in the specific reward condition relative to the neutral condition. Similarly, smokers relative to nonsmokers also showed reduced inhibitory control in the general reward (i.e., money) condition relative to the neutral condition. Importantly, response time analyses showed that smokers relative to nonsmokers relative to nonsmokers also showed reduced slower in the neutral context relative to reward contexts. We concluded based on our main results smokers as compared to nonsmokers have reduced inhibitory performance in a smoking context which extends to a general reward context. The reduced inhibitory performance may be due to the speeded responses in these conditions, indicating increased reward related response bias.

Chapter six include the discussion of this dissertation started with a brief introduction of main aim of the dissertation and a summary of the main findings of our four published studies. Then discuses briefly our main topics BMI and visuospatial attention in conditions that differ in anticipated reward, BMI and inhibitory control across three reward conditions, different moderator factors that affect the relation of BMI and executive function (visuospatial attention and inhibitory control), and inhibitory control and smoking across different rewarding condition. Finally, the discussion included brief summary of the limitation of our three empirical studies and suggestion for future studies then end with a brief conclusion.

CHAPTER ONE

GENERAL INTRODUCTION

Overview of obesity

The following main sub-topics are discussed in detail in this chapter: the definition, primary cause, and prevalence of obesity; how to measure executive function; the relationship between obesity and executive function; and the overlap of obesity and addiction in terms of anomalous executive control in reward contexts.

Obesity/ overweight is one of the most demanding and challenging global public health issues of the 21st century (Amro et al., 2017; Kelly et al., 2008; Ogden et al., 2007). Obesity is a risk factor for a long list of both immediate and long-term physical, social as well as psychological health consequences, such as type II diabetes, cardiovascular diseases, many types of cancer, sleep apnea, stigmatization, poor self-esteem, and Alzheimer's disease (Craft, 2005; Koch et al., 2014; Secretan et al., 2016). Moreover, obesity is associated with psychopathologies such as depression and anxiety (Simon et al., 2007). Individuals that suffer from negative mood (i.e. depression and anxiety) may experience it challenging to control the intake of food, making healthy food choices and control subsequent weight control (Collins, 2009). In addition, individuals with obesity may overeat as a means to cope with emotional distress (Hunger, Angeles, & Mann, 2016). There is ensuing debate regarding whether obesity can be regarded as a disease/psychopathology (Geisler, 2017; N. D. Volkow et al., 2013). In that vein, it should be noted that studies show considerable overlap between obesity and addiction with respect to the brain mechanism that drives the problematic behaviour (Robinson et al., 2016b; N. D. Volkow et al., 2011, 2013).

Obesity is also associated with a high rate of unemployment, social disadvantages, and reduced quality of life (Blüher, 2019). Perhaps not surprisingly, obesity has become a cause of growing health care costs, recently around two trillion dollars estimated the health care expenses for obesity worldwide this is similar to the annual economic impact of tobacco smokers (i.e. 2.1 trillion US dollar) (McKinsey & Company, 2014). Further, more than five percent of deaths worldwide each year can be attributed to obesity-related diseases and also cause for 120 million individuals' disability (Effects, 2017; McKinsey& company, 2014). Specifically, two-thirds of deaths related to obesity were due to cardiovascular disease (Effects, 2017). This indicates that obesity is the second leading cause of preventable death behind tobacco smoking requiring intervention. However, this is challenging, as obesity is a complex condition with poorly understood genetic, psychological and environmental

interacting factors that drive weight gain (Doolan, Breslin, Hanna, & Gallagher, 2015). One key issue that complicates interventions, is that the exact mechanism that explains the persistence of obesity is still poorly understood. In other words, it is crucial that the mechanism implicated in obesity will be elucidated to fuel future treatment possibilities. Obesity relates to executive function (EF), which refers to self-regulatory cognitive processes that contain three components such as inhibitory control, updating and monitoring working memory and mental set shifting (Miyake et al., 2000). Indeed, results from studies suggest that deficient executive functions (at least in part) drive over consumption of palatable food and associated unhealthy weight gain and persistence. Importantly, a recent study that investigated inhibitory control in relation to BMI has suggested that higher BMI is associated with deficient inhibitory control, specifically in contexts of palatable food relative to a neutral context (Houben et al., 2014a). This result seems in line with studies that have specifically investigated striatal processing in individuals with obesity during presentation of food cues and food ingestion (Stice et al., 2008). But it remains the questions whether the inhibitory deficit really represents a specific deficit in a palatable food context or perhaps a general deficit of executive control in any context of reward. And whether the aforementioned inhibitory deficit could be explained (at least in part) by attentional mechanisms. In addition, less is known about the role of moderating factors stress, rumination, mindfulness, and eating behaviors regarding the relation between BMI and the aforementioned executive factors (i.e., visuospatial attention and inhibitory control) has not yet been investigated. Lastly, as mentioned, there is sizeable overlap between the brain mechanism implicated in obesity and pharmacological addiction. Now, one remaining question was whether the obesity associated behavioural response patterns, especially in contexts of reward, would be mirrored in pharmacological addiction such as nicotine addiction. The work described in the current dissertation entailed the following four main objectives:

- 1. To investigate the relationship between BMI and visuospatial attention in contexts that differ in terms of anticipated reward.
- 2. To investigate the relationship between BMI and inhibitory control in contexts that differ in terms of anticipated reward.

- 3. To assess the potential moderating role of stress, mindfulness, eating behavior, and rumination on the relationship of BMI and executive function across the different contexts.
- 4. To investigate the whether the relationship between BMI and inhibitory control is mirrored in pharmacological addictions.
- 5. To explains the main psychological factors that contributes unhealthy weight gain.

Definition of obesity

Obesity develops when individuals consume excessive amounts of calories compared to what they use over longer periods, and the body stores it as fat deposits (e.g., Hall et al., 2012). However, this not the only cause of obesity and this simplistic biomedical model of obesity does not account for the sizeable individual variability in obesity (partly) due to psychological factors. In that vein it is perhaps not surprising that weight loss interventions based on the mere biomedical model are not very effective, especially not on the long run (Ogden et al., 2007). Obesity is commonly assessed by using weight and height values to calculate a measure of body mass index (BMI). According to the WHO (2016), obesity is defined as body mass index (BMI) that is equal to or exceeding 30 Kg/m². Overweight is defined as a BMI between 25 and 29.9 Kg/m², normal weight is defined as a BMI 18.5 and 24.9 Kg/m², and BMI is less than 18.5 is underweight. Calculating BMI is the most widely used estimate of body fat, although obesity assessing using skinfold or waist circumference measurements, determining waist to hip circumference ratios (Seidell & Flegal, 1997; Visscher & Seidell, 2001).

Prevalence of obesity

The prevalence of obesity has reached the status of an epidemic in 2014, a total of more than 603 million adults are obese and more than 1.9 billion adults are considered overweight (Who, 2016). These concerning facts are not limited to adults as 107.7 million children were considered obese in 2015 (Effects, 2017). The total number of childhood obesity and overweight is expected to reach 60 million in 2020 worldwide (Onis, Blo, & Borghi, 2010). These trends continue, globally by 2030 an estimated in total 2.16 billion overweight and 1.12 billion obese individuals (38 and 20 percent of individuals, respectively) (Kelly et al.,

2008). These data underscore the need to investigate the predisposing and exacerbating factors of the development and persistence of BMI.

Causes of obesity

Executive functions, particularly inhibitory control and visuospatial attention (attentional bias and disengagement) have been suggested to drive a significant part of the behavioral component concerning abnormal weight gain (Chantal Nederkoorn et al., 2012; D. G. Smith & Robbins, 2013; Zhang et al., 2017). On the other hand, previous research also suggests that overexposure to palatable foods may disrupt brain mechanisms important for reward/inhibition processing, and partially drive the observed deficits in inhibitory control and anomalous visuospatial attention, especially in a reward context (Batterink et al., 2010; Robinson et al., 2016a; Stice et al., 2010).

Several risk factors also related to the global increase in incidence of obesity. One of the common assumptions regarding abnormal weight gain is an imbalance between too many calories consumed relative to few energy expenditures (Blüher, 2019; Houben & Jansen, 2015). Environmental and relatedly, socioeconomic factors may promote this imbalance and are important to consider in relation to the increasing incidence. To elaborate, socio-economic factors such as income level, and the effect of industrialization such as community safety (i.e. sedentary life style), easy availability of affordable, palatable and energy and fat dense food and high marking advertisement of food industry are main factors influencing our everyday eating behaviors (Kanter & Caballero, 2012; Swinburn et al., 2011). Indeed, it is clear that high calories dense foods are readily available and individuals reductions of everyday physical activity because of mechanized transportation and sedentariness may cause for developing obesity (Hruby & Hu, 2015). Unfortunately, these circumstances are common in developed countries. The prevalence of insufficient physical activity in developed countries was more than double the prevalence in developing countries in 2016 (Guthold, Stevens, Riley, & Bull, 2018).

It must be emphasized that while a steadily increasing obesogenic environment is plausibly a major contributor to weight gain (Mackenbach et al., 2014). This alone does not explain the sizeable individual variability in the development of obesity. In other words, even in an obesogenic environment, not everyone goes on and develops obesity. The complex interplay between individual factors (i.e., behavior, thoughts, biology), and environment factors such as family and social influences is complex but is key to understanding the obesity epidemic. Importantly, several psychological factors are also thought to contribute to weight gain and persistence of abnormal. For instance, it is shown that individuals with obesity have a stronger sensitivity (attentional bias) for and motivational drive (wanting) towards foods high in fat and sugar (Nora D Volkow, Wang, & Baler, 2011). A growing body of studies have suggested poorer executive functions are cause to obesity (i.e., poor response inhibition associated with increased food intake and overeating) (Gibson, 2012; Houben, Nederkoorn, & Jansen, 2014b; Robinson et al., 2016a).

While it is obvious that humans are generally attracted to food, especially those with high BMI are attracted to palatable foods that are high in fat, salt and sugar content. In a similar vein, especially those with weight problems, these types of foods were often used as a maladaptive coping mechanism when psychologically distressed and/or anxious (Collins, 2009). Predominantly, individuals with higher body mass index and poor inhibitory control may be more vulnerable to cue triggered unhealthy eating behaviours (Bartholdy, Dalton, O'Daly, Campbell, & Schmidt, 2016a). Besides anomalous attentional processes, deficits of inhibitory control have also been implicated in relation to obesity. To elaborate poor inhibitory control are at the core of impulsivity disorder such as attentiondeficit/hyperactivity disorder (ADHD) and poor inhibitory control a negative impact on working memory, self-regulation of affect, motivation and arousal (Barkley, 1997). Studies show that individuals with obesity increased impulsivity might make it more difficult to resist the temptation of foods in high in fat and sugar (Batterink et al., 2010). This was associated with poor performance on cognitive tests which may reflect on frontal lobe function and associated with poor impulse control (Cohen, Yates, Duong, & Convit, 2011). As is evident, obesity is a complex condition with poorly understood genetic, environmental, and psychological interacting factors that drive weight gain (Doolan, Breslin, Hanna, & Gallagher, 2018), and these psychological, social and environmental cause of obesity are can be related from parent to offspring independent of genetic sequence variation. Indeed, several key genes contribute to obesity by interfering with the hypothalamic pathways that regulate satiety and food intake (Houfflyn, Matthys, & Soubry, 2017). Obesity is defined by an abnormal accumulation of fat in adipose tissue, as well as the development of systemic

oxidative stress; thus, excessive calorie intake, mitochondrial overloading, and the generation of oxidative stress in adipose tissues result in adipose tissue dysfunction and obesity (Manna & Jain, 2015; Zhou et al., 2021). Hence, obesity has been linked to disrupted biological functions in energy expenditure, lipid and glucose metabolism, adipose tissue development, and inflammation (Houfflyn et al., 2017). Oxidative stress has also been linked to the pathogenesis of several chronic disorders such as adiposity, insulin resistance, and the metabolic syndrome (Bondia-pons, Ryan, & Martinez, 2012; Manna & Jain, 2015; Verdile et al., 2015), and the pathology of these chronic diseases may begin with oxidative stress. Oxidative stress is caused by an increase in reactive oxygen species or a decrease in antioxidant defenses (Rupérez, Gil, & Aguilera, 2014). To be more specific, oxidative stress occurs when the production of reactive oxygen species (ROS) exceeds the antioxidant defense (Sena, Leandro, Azul, Seiça, & Perry, 2018; Zhou, Li, & Xia, 2021). According to different study's findings suggest that there is a direct link between obesity and oxidative stress (Manna & Jain, 2015; Mazon, Mello, Ferreira, & Rezin, 2017).

According to recent research, the environment can alter epigenetic profiles in the exposed people who are exposed to it (Xia & Grant, 2013). The term "Epigenetic mechanisms" refers to heritable gene function modulation that occurs during mitosis and meiosis without affecting DNA sequence (Lawlor, Relton, Sattar, & Nelson, 2012; Ouni & Schürmann, 2020). Hence, environmental factors that do not change the DNA sequence but increased risk for chronic diseases, including obesity (Houfflyn et al., 2017). Epigenome is vulnerable to changes during pregnancy, neonatal development, puberty, and aging. When epigenetic patterning is established at specific genomic loci prior to gastrulation, it results in systematic interindividual variation within one cell type this is referred to as a metastable epiallele (Ouni & Schürmann, 2020). Hence changes in DNA methylation are dynamic and prone to be affected by environmental factors during early development. In fact, human epidemiology studies have shown that prenatal and early postnatal environmental factors influence the adult risk of developing various chronic diseases including, cardiovascular disease, diabetes, and obesity (Centres, 2005; Jirtle, Skinner, & Carolina, 2018). For instance, during the development of male germ cells, epigenetic mechanisms play a critical role. It is widely acknowledged that abnormal DNA methylation is related to male infertility, and although the mechanisms underlying this remain unclear, environmental factors may well

play a key role (Levels et al., 2010; Sharma, 2017; Skinner, Guerrero-bosagna, & Haque, 2015).

In addition to these, studies show that relationship between increased BMI and infertility. Obese women, for instance, have menstrual cycle disturbances, polycystic ovary syndrome and ovulatory dysfunction; however, the majority of obese was not infertile (Disturbances, 2008; Levels et al., 2010). As regards to male, studies show that increased male BMI is associated with lower plasma and sperm concentrations, as well as a high percentage of sperm DNA fragmentation, which leads to infertility (Danielzik, Spethmann, & Müller, 2002; Levels et al., 2010; Palmer, Bakos, Fullston, & Lane, 2012; Sharma, 2017). Indeed, epidemiological studies have found that obese fathers are more likely to father an obese child (Levels et al., 2010). Genetic and epigenetic changes can be silent or alter the quantity, structure and function of RNA and proteins, which can then influence fat mass and distribution

Obesity/overweight and executive functions

Several studies have attempted to elucidate the relationship between BMI and executive functions, but the results have been inconsistent. According to Berg et. al., 2009 review study results showed that obesity might impact executive functioning across one or more executive function domains (Berg, Kloppenborg, Kessels, Kappelle, & Jan, 2009). Indeed, obese individuals requires more blood flow optimal functioning and the reduced blood flow in some parts of the brain, as well as these metabolic abnormalities in the brain, cause deficits in executive functioning (Prickett, Brennan, & Stolwyk, 2015). Furthermore, glucose dysfunction in certain parts of brain may have an impact on prefrontal regions and dopaminergic systems, thereby affecting executive function (Volkow et al., 2008). Increase in adjocytes seen in obese individuals could also lead to deficit of executive function (Gayle & Lee, 2008). Furthermore, recent cross-sectional research results show that obese women have executive function deficit, specifically in the attention, impulsivity and memory domains compared to healthy control groups (Cook et al., 2017). Obesity in middle age may increase the risk of dementia and impair cognitive performance (Gunstad et al., 2007). However, the precise mechanism underlying the link between obesity and deficit executive function remains unknown.

Inhibitory control

The ability to suppress or countermand a goal irrelevant action, thought or feeling is called inhibitory control (Morasch & Bell, 2012; Williams, Ponesse, Schachar, Logan, & Tannock, 1999). To maintain a healthy behavior the individual's self-control ability is needed to overcome unhealthy options. Generally, effective inhibitory control is required in everyday life. Poor inhibitory control contributes to the development of numerous psychiatric, neurological and lifespan development disorders such as (ADHD) (Crosbie, Arnold, Paterson, & Swanson, 2013), substance abuse disorders (Dalley, Everitt, & Robbins, 2011; Luijten, Littel, & Franken, 2011; Verdejo-garc1, Lawrence, & Clark, 2008), internet addiction (Smith, Mattick, Jamadar, & Iredale, 2014), and inappropriate social responding (Hippel & Gonsalkorale, 2005).

A review showed that deficits of executive functions (i.e. deficits in inhibition) are consistently found in ADHD (Pennington & Ozonoff, 1996). Indeed, studies suggest sizeable comorbidity between ADHD and obesity, and the risk of obesity is more higher in adulthood ADHD rather than ADHD childhood (Kooij et.al., 2016). A recent meta-analysis showed that a significant associated between ADHD and obesity/overweight in both children and adults (Cortese, Ph, Moreira-maia, Ph, & Fleur, 2014). This comorbidity between ADHD and obesity show that obesity may be characterized by reduced inhibitory control.

A growing body of research also suggests that poor inhibitory control is related to a higher desire for palatable and fatty foods (Allom & Mullan, 2014; Ramona Guerrieri, Nederkoorn, Schrooten, Martijn, & Jansen, 2009; Powell et al., 2017). In particular, poor inhibitory control predicts future weight gain specifically in childhood and adolescence (Reinert, Po'e, & Barkin, 2013). Hence, poor inhibitory control negative impact on the success of overweight/ obese individuals in reducing weight. While research in this area show that poor inhibitory control put individuals at risk of being obese and high body mass index (BMI) (Bartholdy, Dalton, O'Daly, Campbell, & Schmidt, 2016; Batterink, Yokum, & Stice, 2010; Lavagnino, Arnone, Cao, Soares, & Selvaraj, 2016). Poor inhibitory control is also associated with increased unhealthy eating behavior (i.e. overeating in response to external food cues and response to negative emotional states), as assessed with both direct and indirect measures (Jasinska et al., 2012). Other empirical studies suggests that higher impulsivity

and poor inhibitory control are related with overeating (Guerrieri, Nederkoorn, & Jansen, 2008). Importantly, poor inhibitory control is one of the risk factors for increasing weight.

However, studies did not show a clear relationship between BMI and inhibitory control (Lavagnino, Arnone, Cao, Soares, & Selvaraj, 2016; Lawyer, Boomhower, & Rasmussen, 2015). Several reasons for this apparent inconsistency have been suggested for instance, it might be due to used different methodological approaches to assess inhibitory control and subject states (i.e., individual eating style, stress and hunger levels) as moderators are also important to take into account (Bartholdy, Dalton, O'Daly, Campbell, & Schmidt, 2016). Specifically, with respect to moderators, several studies are worth mentioning. Firstly, Nederkoorn et.al. (2006) contrasted the performance of individuals with obesity to healthy weight controls in the Stop Signal Task (SST) and found obese individuals showed poorer general inhibitory performance as compared to healthy weight control groups, specifically for the last block of the SST, groups differed in terms of Stop Signal Reaction Time (SSRT). This effect may be related to an effect of stress interacting with the factor group. The SST can be regarded as a relatively taxing and stressful task as the task is constructed to yield an approximate 50% inhibition rate. Hence, stress may be induced by task duration and the group x time interaction pertaining SSRT may reflect a moderating role of stress pertaining to the effect of group on inhibitory control. On other words, induced stress may increase the negative effect of obesity on inhibitory control.

In addition, stress can trigger approach behaviour to rewarding stimuli in addicted individuals (Robinson et al., 2016a), and noting the overlap in terms of the neuroadaptive pattern between addicted and obese individuals (Tomasi & Volkow, 2013). In addition reward context also affects inhibitory control according to Loeber et.al., 2012 obese/overweight as well as healthy weight controls show poor inhibitory control for food-associated stimuli relative to neutral condition on a Go/No-Go task (Loeber et.al., 2012). This result suggests that individuals with healthy weight also show higher attentional bias towards food related condition. Similarly, obese/overweight participants showed poor inhibitory control on food-specific conditions but only in dietary restraint participants (Price, Lee, & Higgs, 2015). In another study, children performed the stop signal task and results indicated that overweight children displayed poor inhibitory control for palatable food cues compared to healthy weight children (Chantal Nederkoorn et al., 2012). As mentioned,

reward context may be a moderator of the relationship between BMI and inhibitory control. As noted by Houben and colleagues' previous studies that have explored inhibitory control in neutral contexts in obesity relative to healthy weight controls have yielded inconsistent results. Results of Houben et al., 2014 showed that inhibitory control was negatively affected in a palatable food related context as opposed to the neutral context, but specifically for higher BMI. This result supported with a recent comprehensive systematic review, individuals with obesity may show poor inhibitory control but only in the food-specific reward context (Bartholdy et al., 2016a). However, it remained the question whether the inhibitory deficit really represents a specific deficit in a palatable food context, or perhaps a general deficit of executive control in any context of reward. Results from a recent study seem to support this notion. Specifically, employed a stop-signal task and investigated inhibitory control in relation to BMI in two contexts, a neutral context and (palatable) food context. Results showed that higher BMI is associated with deficient inhibitory control, specifically in a context of palatable food as opposed to the neutral context (Houben et.al., 2014). However, this study has limitation especially presented condition (i.e., lack of counterbalancing), this might cause practice effect on participants.

Visuospatial attention

Naturally, humans are interested in food, and specifically rewarding foods (i.e., high content of sugar, salt and fat). Attentional bias and disengagement are two main part of visuospatial attention and central to everyday functioning (Corbetta & Shulman, 2002). Attentional bias is the observation that related cues tend to grab the attention of our current goals and disengagement refers to the decoupling of attention allowing processing of initially unattended stimuli (Corbetta & Shulman, 2002). According to the incentive sensitization theory, individuals with obesity may be more sensitive to visual food-related cues relative to normal-weight individuals, and relatedly show heightened attentional bias towards food-related stimuli (Nijs, Muris, Euser, & Franken, 2010; Werthmann et al., 2011; Yokum, Ng, & Stice, 2011). Recent studies shown that food-related attentional biases are mediated through top-down processes related to mind-set (i.e., thinking and working memory) (Gibson, 2015; Higgs, Rutters, Thomas, Naish, & Humphreys, 2012). When holding a food cue in working memory, obese individuals were slower than the healthy control group to detect the target in invalid trials compared to valid trials, this indicating that obese individuals

had difficulty disengaging from food related cues when food was in mind (i.e., top-down attentional bias) (Kaisari et al., 2019).

The obesogenic food environment can be promoted via aggressive food marketing, overexposure to palatable and cheap food (Stice, Yokum, Burger, Epstein, & Small, 2011). The availability of high energy and fat dense food is considered one of main environmental risk factors for higher BMI (Nora D Volkow & Wise, 2005). According to incentive sensitization theory rewarding stimuli have the ability to elicit the expectancy of rewarding stimuli availability, and this might induce attentional bias for rewarding stimuli and subjective craving (Field & Cox, 2008).

Attentional bias toward food related cues may also contribute to subsequent weight gain and maintained excessive eating behaviors (Nora D Volkow, Wise, & Baler, 2017; Yokum, Ng, & Stice, 2011). Similarly, frequent exposure to drug related cues has been shown to reduce drug craving and increase drug use, as a results of cue induced dopamine release in the corticostriatal circuit (Franken, 2003). However, studies on attentional bias towards anticipated reward in relation to overweight and obesity show contradictory results (Nijs & Franken, 2012). One contemporary study used both clarification task (i.e., the task measure of attention vigilance for food cues) and spatial cueing tasks to assessed attentional bias towards food related cue in binge eating disorder (Schmitz, Naumann, Trentowska, & Svaldi, 2014). The results shown that obese individuals show high attentional bias towards to palatable food cues, and early attentional processes are very important in food related processing hence, food cues generally hold attention and disengaging attention is relatively difficult for food cues both obese with being eating disorders and obesity without being eating disorder (Schmitz et al., 2014). According to Havermans and colleagues obese and overweight individuals relative to individuals at normal weight, find it challenging refrain from foods with high energy and fat content, and this is more pronounced in male obese individuals (Havermans, Giesen, Houben, & Jansen, 2011). In addition, obese individuals has been shown greater attentional bias towards food cues compared to healthy control groups (Castellanos et.al., 2009; Werthmann et.al., 2011). Subjective craving and attentional bias are direct relation towards rewarding stimuli (such as foods with high energy and fat content) (Franken, 2003). Similarly to obese individuals higher attentional bias towards food related cues, a higher attentional bias for substance-related cues found in addiction individuals (Field & Cox, 2008).

Measurements of Executive Function

To measure executive function, researchers have used several different experimental tasks, the most frequently used paradigms to measure inhibitory control are the stop-signal task (SST)(Logan, Cowan, & Davis, 1984; Verbruggen, Chambers, & Logan, 2013a). Go/no-go task (GNG) (J. Miller, Schtiffer, & Hackley, 1991), and Stroop task (Davidson et al., 2003). These tasks are thought measure different aspect of inhibitory control. For instance, in GNG task withholding a prepared response that has not yet been initiated and in Stop signal task cancellation of a response that is already underway (Wessel, 2017). The probability of responding on a no-go or stop trials depends on the relative finishing time of the go or the stop process. For both tasks, participants are encouraged to respond as far as faster pressing the instructed key button when a presenting go stimulus and withhold the response when an infrequent (i.e. stop or no-go signal/ stimulus) occurs (Wright et al., 2014).

Stop-Signal Task

In the SST, go stimuli to which a response is required, are followed infrequently by stop signals indicating a response should be withheld. The relevant outcome variable is the Stop Signal Reaction Time, reflecting inhibitory control. (Logan et al., 1984). For the most reliable estimation of this measure, the approximate inhibit rate should be 50%. This is accomplished by an adaptive go-stop time interval, that is adjusted per block, or even after each stop trial depending on the performance of the participant. The stop-signal reaction time is calculated according to the independent race model (i.e. subtracting the stop signal delay the delay between go and stop signal that allows correct inhibition on approximately 50% of the stop trials from the mean reaction time) (Verbruggen, Chambers, & Logan, 2013). If the go-related motor response is completed prior to the stop/inhibitory process induced by the stop-signal, the response inhibition is unsuccessful. and a response is executed. Alternatively, the stop-related motor response is completed prior to the go-related motor response process increased by the stop-signal, the response is correctly withheld. Stop signal reaction time difficult to measured directly however, it can be estimated under certain assumptions (i.e. the proportion of inhibitions and reaction time distribution on go stimuli in go trials).

According to Verbruggen et.al., two common estimated methods of SSRT, in integration method to calculated subtracting the Mean Stop Delay (SSD) from the mean finishing time (i.e., nth RT with the nth number corresponding to the number of RTs in the RT distribution x the overall probability of responding [p(respond/signal)]) and in mean method subtracted the mean of the inhibition function from the mean of the RT distribution (Verbruggen et al., 2013). Longer stop-signal reaction time indicates poor inhibitory control and, shorter stop-signal reaction time indicates better inhibitory control (Tannock, Schachar, Carr, Chajczyk, & Logan, 1989; Verbruggen, Chambers, & Logan, 2013).



Figure 1. Stop Signal Task

Go/no-go task

The Go/no-go task is one of the most common psychological tasks used to assess inhibitory control (Verbruggen & Logan, 2008). In this task the go process is triggered by stimulus presentation because of a prepotent response tendency and the stop process is triggered by the identification of the no-go stimulus. In the go/no-go task, generally participants are instructs to respond as fast and accurately as possible to a specific stimulus (i.e. go stimuli)

and withhold a response upon being presented with another stimulus (i.e. no-go stimuli) appears. The fast paced and rare no-go elicited a neural inhibitory control activity contrast to the slow paces and equiprobable go/no-go task. Hence, go/no-go task indicate that a direct relation between with early inappropriate response tendencies on no-go trials and inhibitory control over prefrontal cortex (Wessel, 2017).

The relevant outcome measure in the GNG task is the proportion of successful inhibitions (number of successful inhibitions in no-go trials, divided by the number of no-go trials). It should be emphasized that the extent to which this measure indexes inhibitory control depends on specific task characteristics, intertrial time interval, and the proportion of no-go trials (Wessel, 2017). The most critical component in designing an inhibitory control task is to ensure that motor activity is elicited on each trial.



Figure 2. Go/No-Go Task

Visuospatial cueing task

Another component of executive function is visuospatial attention (i.e. bias and disengagement) which can be measured using the Posner paradigm also called the visuospatial cueing task (VSC) (Posner, 1980).

In this task, a cue (i.e., arrow) is predictive (unless in case of a neutral cue) of the location of a subsequent target to which a response is required. Validity pertains to whether the target was presented at the location indicated by the cue or at the opposite as indicated location. The task included three trials. In neutral trial, the cue was not informative of the location of the target. In invalid trials, the target was presented on the side of the screen contraindicated by the cue. In valid trials, the target was presented on the side of the screen contraindicated by the cue. The task measured two main components of attention (i.e., attentional bias and disengagement). Attentional bias is reflected in the speeded responses to valid targets (targets presented at the location indicated by the cue) relative to neutral targets (targets that do not follow a predictive cue). Specifically, attentional bias is operationalized as the response time to neutral targets minus the response time to valid targets. Disengagement of attention refers to the cost in terms of response time as a consequence of invalid cueing. Specifically, disengagement is reflected in the response time difference between invalidly cued targets minus neutral targets. According to posner there are two ways attention oriented to a stimulus: an endogenous system which is overtly controlled by the subjects intentions and exogenous system which automatically shifts attention according to environmental stimuli (i.e. outside the subjects control and cannot be ignored) (Posner, 1980).



Figure 3. Graphical depiction of a invalid trial of the visuospatial cueing task.

Obesity and addiction: Overlap in terms of anomalous executive control in reward contexts.

Studies have shown similarities between obesity and addiction with respect to inhibitory control, and reward-processing related activity in contexts of (anticipated) reward (García-García et al., 2014; Kenny & Shaw, 2011; N. D. Volkow et al., 2013). Moreover, both palatable food and drugs have powerful reinforcing effects on stimulating human. For instance, the consumption of high fat and sugar content food can enhance human mood and reduce chronic stress (Dallman et al., 2003), and similarly cigarette smoking reduces stress (Re, Science, & Britain, 1995).

Different research findings show that obese and overweight individuals report craving for high-calorie/sugar and fats food, and loss of control over eating (Nijs & Franken, 2012), and decreased activity in prefrontal cortex PFC (N. D. Volkow et al., 2013). The prefrontal cortex (PFC) plays an important role in executive function specifically inhibitory control and, these processes are modulated by D1R and D2R receptors hence, decreased the metabolic activity in PFC in both obesity and addiction that are linked with reward and compulsive behaviors (N. D. Volkow et al., 2011). Moreover, obesity/overweight was inversely related with orbitofrontal cortex (OFC) activation during performance of a Go/no-

go computers task (Batterink et al., 2010). On another study combined Go/no-go task with imaging analyses used magnetic resonance imaging found that obese individuals had lower OFC volume and poor performance on inhibitory control tasks (Maayan, Hoogendoorn, Sweat, & Convit, 2009). These are parallels to reward processing in substance use and addiction behavior. Drug related stimuli produces an increase in dopamine levels specifically in the corticostriatal circuit such as in amygdala and nucleus accumbens, which in turn serves to draw the subjects attention towards a perceived drug stimulus (Franken, 2003).

Different studies employed functional magnetic resonance imaging (fMRI) and the results shows that obese/overweight individuals exhibited greater activation in the dorsal striatum and OFC in response to palatable foods (Cohen, Yates, Duong, & Convit, 2011; Rothemund et.al., 2007; Stice, Yokum, Bohon, Marti, & Smolen, 2010). The OFC is involved in regulating impulse behavior, and goal directed behaviors (Schoenbaum, Roesch, & Stalnaker, 2008). The reductions of dopamine receptors related with decreased metabolism (i.e., glucose utilization) in PFC regions in obese/ overweight individuals (Nora D Volkow et al., 2008). Indeed, there is inverse relationship between BMI and dopamine receptors, specifically dopamine receptor decreased in obese proportion to their BMI (Wang et al., 2001). Furthermore, reduction of dopamine receptors reported in different types of drugs addiction individuals (Nora D Volkow et al., 1993; Wang et al., 2001; Wiers et al., 2017). As with drug seeking behaviors, food seeking behaviors are lost when dopamine is depleted from the brain and restored when the ability to synthesize dopamine is restored to the dorsal striatum (Wise & Robble, 2020). In addition, individuals with obesity show abnormal reward processing characterized by a dopaminergic system that is sensitized to food associated cues that have reward value (Nora D Volkow et al., 2017).

Similarly, in addiction the consequence of repeated drug consumption elicits a dopaminergic system that is sensitized to drug and cues significantly increase (Robinson et al., 2016a), and individuals with obesity show abnormal striatal activation in response to anticipation of palatable food related to reward anticipation (Rothemund et al., 2007; Stoeckel et al., 2008). Overall, similar to other types of drug-addiction obese individuals have lower amounts of dopamine D2 receptors in the striatum (Wang et al., 2001). Indeed, dopamine regulates food consumption involving the mesolimbic pathway and the hypothalamus (Nora D Volkow et al., 2011). Similarly, dopamine levels in addiction change

in these two brain regions and plausible that a similar mechanism of reinforcing effects on food and drug (Salamone, Cousins, & Snyder, 1997; Singh, 2014; Wang & Volkow, 2004). Indeed, the dopamine D2 receptor mediates reinforcing responses (i.e., obesity might mirror a reward deficiency syndrome) (Blum K., Eric R., Jay M., Joel F, Vincent J., David, Judith O., Thomas J.H. & David E., 2000). Dopamine is not the sole cause of addiction however a motivational properties and play important role in addictions behaviors (Wise & Robble, 2020). Recent review study showed that reduction of dopamine receptors can also contribute to addiction behavior with modulates motivation and reward circuits (Nora D Volkow et al., 2017; Wang et al., 2001). Moreover, dopamine is implicated in the reward system (D. G. Smith & Robbins, 2013; N. D. Volkow et al., 2011). And facilitates the development of cellular modifications of glutamate and these determine the effectiveness of reward predictors to control subsequent search behaviors (Wise & Robble, 2020).

In drug-addicted individuals, the reduction of striatal D2R availability is related to decreased activity of OPF, anterior cingulate gyrus, and dorsolateral prefrontal cortex that drives reward processing (N. D. Volkow et al., 1997, 2013; Wang et al., 2001). It must be noted that reward processing is also subserved by striatal regions and D2 availability, and reward processing is also has been reported to be negatively affected in obese individuals (Robinson et al., 2016a), and obese individuals show abnormal striatal activity in response to palatable food cues (Rothemund et al., 2007) Indeed, higher neural activation in obese/ overweight related to the healthy control group in response to palatable food reward, and this is similar to reward processing in substance addiction (Horstmann, Jurado, Garolera, Chaudhry, & Margulies, 2014). A recent review study shows that there is an overlapping between obesity/ overweight and addiction to the brain mechanism in the context of rewarding (Nora D Volkow, Wise, & Baler, 2017).

Aims of the thesis

As mentioned, previous studies strongly suggest that high BMI is associated with increased attentional bias, and reduced inhibitory control, most predominantly in a context of anticipated food reward. The unresolved questions were whether this enhanced attentional bias and poor inhibitory control extends to other conditions of reward. In addition, the role of plausible subject-related moderators (affective factors, rumination, and mindfulness) regarding the relation between BMI and the aforementioned executive functions (i.e., visuospatial attention and inhibitory control) has not yet been investigated. Lastly, the overlap between obesity and pharmacological addiction with respect to the aforementioned potential relationships is yet unclear. The aims of the described projects were to address these important questions. Specifically, in chapter 2, we repot on the main psychological factors that affect obesity. In chapter 3 we report on the role of attentional bias/disengagement across conditions that differ in terms of anticipated reward (i.e., neutral, specific, general). Most previous studies employed either one (neutral) or two conditions (i.e., neutral and specific). However, in this study we added a general reward condition (operationalized by money related stimuli). We hypothesized that participants would display increased attentional bias and decreased disengagement in the specific condition relative to the neutral condition, and that this effect would be more pronounced in individuals with higher BMI. Similarly, that participants would display increased attention to the general condition relative to the neutral condition, and that this effect would be more pronounced in individuals with higher BMI.

Chapter 4 reports on the role of inhibitory control across conditions that differ in terms of anticipated reward (i.e., neutral, specific, general). Similar to our study one in chapter 3 we employed similar stimuli for each condition. In this study we postulated the following hypotheses. Firstly, we hypothesized that high vs low BMI would be associated with reduced inhibitory control in the food-related condition relative to a neutral condition. Similarly, participants that high vs low BMI would be associated with reduced inhibitory (i.e., General) related condition relative to a neutral condition.

Chapter 5 reports on the relation between nicotine addiction and inhibitory control in contexts that differed in terms of reward, and we explored to role of rumination and stress as potential moderators. In this study we postulated the following hypotheses. First, smokers relative to nonsmokers would present with reduced inhibitory control in the specific reward condition relative to the neutral condition. Second, this would also apply for the general reward condition relative to the neutral condition. Thirdly, the relative reductions in inhibitory performance would be mirrored by speeded responses to go trials.

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CHAPTER TWO

The psychological basis of obesity¹

¹This chapter based upon Tsegaye, A., Kökönyei, G., Baldacchino, A., Urbán, R., Demetrovics, Z., & Logemann, H. N. A. (2020). Chapter 4 - The psychological basis of obesity. In T. A. Mahmood, S. Arulkumaran, & F. A. B. T. Chervenak (Eds.), *Obesity and obstetrics* (2nd ed., pp. 37–44). Elsevier https://doi.org/https://doi.org/10.1016/B978-0-12-817921-5.00004-7

General Introduction

Overweight and obesity is characterized by a BMI equal to and exceeding 25 Kg/m² and 30 Kg/m², respectively (Who, 2016). Body Mass Index is calculated by dividing mass (in kilograms) by squared height (in meters). Although some differences have been reported, both overweight and obesity are linked to an increased risk of serious health conditions, such as cardiovascular disease, ischemic strokes, and diabetes (Chu et al., 2018). A systematic review reported an elevated risk of mortality in obesity relative to normal weight, however quite surprisingly overweight was associated with a lower risk of mortality relative to normal weight (Flegal, Kit, Orpana, & Graubard, 2013). However, several factors may have affected the results and could have negatively affected the validity of the interpretation of results, and it should be noted that such "biases" were not completely controlled for. In an extensive recent systematic review by the Global BMI Mortality Collaboration, biases were controlled for, and it was shown that overweight was also associated with elevated risk for mortality (The Global BMI Mortality Collaboration, 2016). It is thought that one of the main drivers of obesity is energy intake that exceeds energy output (Romieu et al., 2017). This traditional biomedical view, however, does not sufficiently explain individual variability in weight gain and persistence of abnormal weight. In a related vein, treatment approaches solely directed at the imbalance between energy intake and expenditure have failed to render effects on the long run (Garner & Wooley, 1991).

As will be elaborated, psychological factors that drive the onset and persistence of obesity have been consistently reported. In fact, several lines of research indicate substantial overlap with addiction, noting the phenomenological characteristics(Robinson et al., 2016b) as well as the brain mechanism(Tomasi & Volkow, 2013). Indeed, Volkow et al.("Issues for DSM-V : Should Obesity Be Included as a Brain Disorder ?," 2007) have suggested obesity to be included in the DSM-V, but perhaps surprisingly, the Eating Disorders Work Group of the Diagnostic and Statistical Manual of Mental Disorders concluded that "Obesity is a heterogeneous condition with a complex and incompletely understood etiology, and thus cannot be considered a mental disorder" (p. 434)(Marcus & Wildes, 2012) but the debate continues.

As with many other DSM-included disorders (i.e. Schizophrenia (Tandon et al., 2013), Attention Deficit / Hyperactivity Disorder (del Campo, Müller, & Sahakian, 2012). Obesity is relatively heterogeneous disorder meaning that there is individual variability within that group. However, several key psychological factors implicated in obesity have consistently been reported. For example, it is shown that individuals with obesity have a stronger sensitivity (attentional bias) for, and motivational drive ("wanting") towards, foods high in fat and sugar (palatable food)(N. D.

Volkow et al., 2011) in combination with deficient impulse control in contexts of anticipated palatable food (Bartholdy et al., 2016b). Several factors are important in relation to obesity and connected eating behaviours such as depression (Atlantis & Baker, 2008; Heo, Pietrobelli, Fontaine, Sirey, & Faith, 2006; Luppino et al., 2010) (John, College, & Blaine, 2008); personality (Petry, Barry, Pietrzak, & Wagner, 2008); anxiety (Strine et al., 2008); stigma and discrimination (Puder & Munsch, 2010; Puhl M. & Brownell D., 2003; R. Puhl, Brownell, & Bias, 2001); shame (Sjo, 2005). Individuals that suffer from negative-mood (i.e. anxiety, depression) may experience it challenging to control the intake of food, making healthy food choices and control subsequent weight control (Collins, 2009). To elaborate, individuals with obesity may overeat (excessive intake of palatable food) as a means to cope with (alleviate) emotional distress (Hunger et al., 2016). The resulting alleviation from distress (negative reinforcement) enhances the likelihood that this behaviour occurs more frequently through the known process of operant conditioning. As mentioned, obesity thus shares some phenomenological characteristics with pharmacological addiction. In fact, the (brain) mechanism has also been reported to show considerable overlap with addiction (Robinson et al., 2016b; Tomasi & Volkow, 2013; N. D. Volkow et al., 2011), and there is a striking comorbidity of eating disorders with substance use disorder (SUD) (Gregorowski, Seedat, & Jordaan, 2013). For example, Bulimia Nervosa and Binge Eating Disorder are both characterized in part by excessive food intake within a short time-span (binging) and are both associated with alcohol abuse (Gregorowski et al., 2013). Perhaps a transdiagnostic approach that considers such overlap would be beneficial, and transdiagnostic approaches to eating disorders are recently being applied (Garke, Sörman, Jayaram-Lindström, Hellner, & Birgegård, 2019; Rancourt, Ahlich, Levine, Lee, & Schlauch, 2019).

In the discussion of the contribution of psychological factors that are involved in the onset and persistence of obesity, moderating factors such as gender / biological sex and age should also be considered. Specifically, gender has been shown to moderate the relation between BMI and mental health related variables. In short, girls that are obese are more disadvantaged to dating partners compared to boys that are obese (Chen & Brown, 2005; R. M. Puhl & Heuer, 2009). Cognitive deficits seem more consistently reported in obese women, and plausibly related, obese women relative to men report stronger temptations pertaining to eating, and report to be generally more concerned about body weight and shape (i.e. body image) compared to lean women (Hay, Mond, Darby, Owen, & Rodgers, 2006). Overall, it is very important to take into consideration the demographic aspects (such as age and gender), both in understanding the mechanism, but also from a clinical treatment perspective. Clinical treatment of obesity and overweight should not only focus on diet and exercise but should also include psychological factors (Sjo, 2005).

Eating behavior

Generally, individuals eat because it provides an intrinsic incentive, and/or external incentive. Pertaining to the first, and simplified, eating is associated with a pleasurable feeling, and especially palatable food is associated with stimulation of opioid systems in the brain responsible for the feeling of pleasure (Bodnar, 2019). Secondly, individuals consume because of social pressures. Indeed, eating habits are formed in part by early socialization processes (Fiese et al., 2002). Human eating behavior is determined by a complex set of interacting genetical, physiological, psychological, and environmental factors, and in its simplest conceptualization eating behaviour is driven by both internal and external factors (Bilman, van Kleef, & van Trijp, 2017; Emilien & Hollis, 2017). To elaborate, eating behaviour can be triggered by internal cues, such as ghrelin hormone levels which has been shown to affect meal initiation (Klok, Jakobsdottir, & Drent, 2007; Mihalache et al., 2016), and by the sight of external cues. External cues could be actual pictures of nice food or anything (e.g. smell) that is associated with nice foods (Cornell, Rodin, & Weingarten, 1989) and are also known to affect internal signals that drive the percept of hunger plausibly mediated by ghrelin (Bilman et al., 2017) , and motivational drive (feeling of "wanting") mediated by enhanced dopaminergic neurotransmission. (N. D. Volkow et al., 2011).

With respect to unhealthy eating behaviours, it is not surprising that the risk for unhealthy eating patterns such as overeating and/or consumption of palatable foods is determined by a variety of interacting social, environmental, and psychological factors (Brug, Kremers, Lenthe, Ball, & Crawford, 2008). For instance, especially early (childhood) eating behaviours are significantly influenced by social factors and parenting practices and thus family and in a broader context, the social environment may promote obesity (Birch & Fisher, 1998; Reilly et al., 2005). In the current obesogenic world palatable foods are also aggressively presented by media (i.e., on TV advertisement) and these stimuli are often strongly associated with emotional information (e.g., social desirability and happiness) making it more likely that individuals will adopt unhealthy consummatory behaviours. In connection with this, in the media, specific food is paradoxically presented as reflecting temptations that need to be resisted or classified as unhealthy but are advertised frequently. These effects enhance the preference towards specific foods (Maio, Haddock, & Jarman, 2007).

As mentioned, eating styles vary markedly across individuals, and differences between individuals with obesity and individuals with normal weight have been reported. Specifically, it has been shown that obesity is related to an elevated sensitivity to external cues over internal cues. In other words, irrespective of internal signals (hunger), obese individuals are more susceptible to social and environmental stimuli that are related to (especially palatable) foods (Bilman et al., 2017). In addition, individuals with obesity are more likely to engage in comfort eating in response to negative mood (Hunger et al., 2016). This comfort eating is associated with a shift towards preference of palatable food, foods high in fats and sugars (Oliver, Wardle, & Gibson, 2000).

One important question is why obese individuals are so driven to engage and persist in overexposure of palatable unhealthy foods. It should be emphasized that especially palatable food rich in fats and sugars strongly engage the "pleasure center" of the brain via its effect on the opioid system (Bodnar, 2019) and dopaminergic system (Nora D Volkow et al., 2017). Importantly, over time through an associative learning process the dopaminergic system becomes selectively sensitized to cues that are associated with intrinsic reward from palatable food. The mere anticipation of palatable food in turn results in selective enhancement of dopaminergic neurotransmission and associated experience of "wanting", or motivational drive that is not necessarily connected to the "liking" experience (N. D. Volkow et al., 2011; Nora D Volkow et al., 2017). This can ultimately result in rigid impulsive and compulsive responding towards palatable food or stimuli associated with palatable food (Nora D Volkow et al., 2017).

Cognition

Individuals with obesity have an inflated chance for developing dementia of the Alzheimer's type, characterized by serious progressive cognitive deficits (Fratiglioni et al., 2005; Gustafson, Lissner, Bengtsson, & Björkelund, 2004; Parikshak et al., 2009). In addition to the increased risk for Alzheimer's disease, other cognitive deficits (pertaining to i.e. learning, flexibility, attention and inhibitory control) have been associated with obesity (Fergenbaum et al., 2009; Li, Dai, Jackson, & Zhang, 2008; Sellbom & Gunstad, 2012; E. Smith, Hay, Campbell, & Trollor, 2011). Not surprisingly, the cognitive deficits are associated with abnormal brain functioning (Garolera et al., 2015; Liang, Matheson, Kaye, & Boutelle, 2014; Sellbom & Gunstad, 2012). For some of the aforementioned cognitive deficits it may be difficult to disentangle whether these deficits precipitate the onset of obesity, or whether they are a result of obesity. In that vein it should be noted that intake of foods high in fats is linked to inflammation of brain structures (A. A. Miller & Spencer, 2014), which may impair cognitive performance over time.

In addition, it has been suggested that overexposure to palatable food can induce abnormal reward-related processing within the striatum (Johnson & Kenny, 2010). Hence, these studies suggest that (at least partly) obesity may induce these cognitive deficits and related structural and functional changes of the brain. Perhaps one of the most predominant psychological factors connected to obesity is diminished impulse control, or specifically inhibitory control. It has been

suggested that the external cues in the current obesogenic environment put pressure on our internal system (driven by bodily signals) (Bilman et al., 2017). In that vein, impulse control is essential, and hence deficient impulse control could be implicated in obesity. Indeed, results from some studies suggest such link. To elaborate, there is comorbidity of obesity with Attention Deficit / Hyperactivity Disorder, and there is overlap in terms of the implicated brain mechanism (Hanć & Cortese, 2018). Similar to ADHD (Nora D. Volkow et al., 2009), reduced striatal D2 receptor availability has been reported in obesity (Nora D Volkow et al., 2008). This system is important in reward processing, but also in inhibitory control (Logemann et al., 2017). However, there is no straightforward relation between impulse control and obesity. Studies have not consistently shown detrimental inhibitory control in obesity (Bartholdy et al., 2016b), but deficits do become apparent when motivational drive for consumption is enhanced such in case of specific subject-states as in dietary restraint (Jansen et al., 2009), or during the experience of hunger (C. Nederkoorn, Guerrieri, Havermans, Roefs, & Jansen, 2009). Indeed, as mentioned, anticipatory responses can be induced by external cues (Bilman et al., 2017), and indeed, several studies have shown that obesity is associated with deficient inhibitory control, specifically in food related contexts (Bartholdy et al., 2016b).

Another system that is key in our everyday behaviour, and which is known to operate differently in obesity, is attention. The processing of stimuli that are in the focus of attention is facilitated (attentional bias), and processing of stimuli that are not within the focus of our attention is suppressed (Corbetta, Patel, & Shulman, 2008; Corbetta & Shulman, 2002a). As such, attention fulfills an important task in resource-management and prioritizing, and is essential to adaptive behaviour. Attention can be consciously driven by our goals and task-set, or can be engaged by environmental cues (Corbetta et al., 2008; Corbetta & Shulman, 2002a). It may not be too surprising that several studies have reported that obesity is associated with enhanced attentional bias for (palatable) food related stimuli relative to neutral stimuli (Castellanos et al., 2009; Werthmann et al., 2011). To elaborate, individuals with obesity show abnormal reward processing characterized by a dopaminergic system that is sensitized to food associated cues that have reward value (Nora D Volkow et al., n.d.), and individuals with obesity show abnormal striatal activation in response to anticipation of palatable food (Rothemund et al., 2007; Stoeckel et al., 2008). This is thought to drive the heightened motivation for palatable food (Nora D Volkow et al., n.d.), and is plausibly associated with the facilitated processing of associated cues.

Stigma and discrimination

According to Tomiyama, weight stigma can be defined as the devaluation and abuse of a person by a group of individuals/ society based on body size (Tomiyama, 2014). Weight stigmatization is

manifested by discriminations, prejudice, and rejection in society based on the body status of the individuals (Harriger & Thompson, 2012).

Studies show that obese/overweight individuals are more likely to face societal stigmatization compared to healthy weight individuals (R. Puhl et al., 2001; R. M. Puhl & Heuer, 2009; Stunkard, 2018). Weight stigma and discrimination affect obese individuals in different domains of their life, educational such as workplace, healthcare center. settings, and interpersonal relationships. Individuals with obesity often encounter stereotypical attitudes in the workplace from co-workers and are often disadvantaged because of their weight class (R. M. Puhl & Heuer, 2009). Such attitudes are varied and can be perceptions of obese individuals as being lazy, careless, less conscientious, unmotivated, and bad work habits (Puhl M. & Brownell D., 2003). Sadly, stigmatization is even encountered in healthcare centers, as it is reported that health care professionals routinely express negative stereotypes regarding their obese patients (Moskovich, Hunger, & Mann, 2012). These are important findings, especially since weight-related stigma and discrimination is a risk factor for substance use disorder and has detrimental effects on social and psychological well-being (Moskovich et al., 2012).

Stress and mood disorders

Commonly known, psychological stress encountered in childhood and adolescence is a non-specific factor for mental health problems. Stress can also contribute to the development of emotional eating, which could be one precipitating factor in the onset of obesity. More specifically, it has been shown that physical or psychological abuse during childhood was associated with an elevated chance on developing obesity. Importantly, this relation was partially mediated by maladaptive coping with stress via palatable food intake (Greenfield & Marks, 2009). It is consistently shown that stress results in alteration of the hypothalamic-pituitary-adrenal (HPA) axis (Bose, Oliván, & Laferrère, 2009) and it should be emphasized that stress tends to shift food preferences towards palatable foods (Oliver et al., 2000). Specifically, chronic stress results in elevated cortisol and insulin levels, and this may in part promote preference towards more palatable food and result in visceral fat (Adam & Epel, 2007). Indeed, increased cortisol levels are associated with obesity, although individual variability exists (van der Valk, Savas, & van Rossum, 2018).

Depression is associated with a substantial number of unhealthy conditions and behaviours, including obesity, smoking, binge drinking and heavy/high consumption of palatable food (Strine et al., 2008). Several studies showed that obesity is associated with depression (Atlantis & Baker, 2008; Heo et al., 2006; Luppino et al., 2010), and poor body image (Schwartz & Brownell, 2004; Xanthopoulos et al., 2011). The relation between obesity and depression is bidirectional (Goldfield

et al., 2010; Luppino et al., 2010). A number of cross-sectional and longitudinal studies have assessed the association between obesity and depression. One study has shown that depression could be predicted by BMI class (Roberts, Deleger, Strawbridge, & Kaplan, 2003), however, it should be noted that the association of BMI with depression seems specifically apparent when not controlling for visceral fat (Rivenes, Harvey, & Mykletun, 2009). Similar to stress, hypothalamic-pituitary-adrenal (HPA) axis dysregulation might partly explain the relation between obesity and depression(Luppino et al., 2010). It should be noted that several factors (sociocultural, stigma and discrimination) increase the risk of depression in obese individuals (Atlantis & Baker, 2008). The relation between BMI and depression is complex and the effect varies as a function of several moderators. For example, a recent extensive systematic review that included 76 studies in the dataset showed that overall obesity is associated with depression (Jung et al., 2017). However, gender affected the relation between overweight status and depression where overweight was associated with a higher chance for depression in females, whereas the inverse relation was found for males (Jung et al., 2017), further stressing the moderating role of gender. Several factors may explain the development of depression due to weight gain.

As mentioned, consequences of weight gain such as negative body percept stigma and discrimination may negatively affect mood, but direct effects have also been suggested. Pertaining to the latter, it has been suggested that a diet characterized by high fat and sugars, especially during adolescence, may have a detrimental effect on neuroendocrine systems important in adaptive responses to stressors and on neuroanatomical correlates of emotional regulation processes (Baker, Loughman, Spencer, & Reichelt, 2017). As mentioned, depression (and anxiety) has also been reported to precipitate the development of obesity in different age groups (Gaysina et al., 2011). Weight gain following depression or anxiety is thought to be mediated via side-effects inherent to pharmacological treatment and/or due to maladaptive coping strategies such as comfort eating (Wurtman & Wurtman, 2018).

Personality traits

Personality traits in the context of the Five Factor Model (Neuroticism, Extraversion, Openness to Experience, Agreeableness, and Conscientiousness) have been linked to different outcomes of psychological and physical health behaviors (Goodwin & Friedman, 2006; Sutin, Ferrucci, Zonderman, & Terracciano, 2012). Although considered rather non-specific factors, personality traits are thought to play an important role in relation to obesity and are though important in the context of the development of treatment options (Gerlach, Herpertz, & Loeber, 2015). Among the five traits, conscientiousness is the most consistently associated with adiposity(Jokela et al., 2013;

Sutin et al., 2012). To elaborate, high conscientiousness indicates high self-control, orderliness and devotion to social norms, and is associated with lower obesity risk (Jokela et al., 2013). Neuroticism is a construct composed of anxiety, anger-hostility, depression, impulsivity, and vulnerability and high neuroticism is associated with obesity, particularly with abdominal obesity (Sutin et al., 2012). These factors are additive, and high neuroticism and low conscientiousness both increase the likelihood to engage in unhealthy eating behaviour (Provencher, Polivy, & Herman, 2009) and in gaining weight (Sutin, Ferrucci, Zonderman, & Terracciano, 2011). Sociocultural factors of a population might affect the association between neuroticism and obesity, however, the relation between neuroticism and obesity remains stable (Gerlach et al., 2015).

Emotion regulation

Experimental and theoretical approaches concerning emotional eating clearly draw attention to the relevance of emotional processing and emotional regulation in the background of the formation and subsistence of obesity/overweight. Suppression of emotions, for example, significantly enhances greater intake of energy dense foods such as sweet and high fat snacks (Evers, Stok, & Ridder, 2016). Moreover, emotional eating is associated with elevated calorie intake in self-threatening situations (in situations when the value of one's self is questioned) (Wallis & Hetherington, 2004). Emotional eating can be regarded a maladaptive emotional regulation strategy that involves indulging in immediate impulses to eat (Evers et al., 2016; Tice, Bratslavsky, & Baumeister, 2001). According to Polivy and Herman in case of restrained eaters, who wilfully restrict their food intake to control their body weight, distress induced emotional eating is explained by the fact that eating can distract them from the true source of distress (Polivy & Herman, 1998). The difference between emotional eaters and restrained eaters is the following: emotional eaters in distressful situations eat in order to reduce negative emotions, while restrained eaters eat more in emotional distress situations, because emotions undermine their cognitive control of restricted eating patterns (Boon, Stroebe, Schut, & Ijntema, 2002) (Macht, 2008). A two-component emotional regulation model of binge eating has been proposed (Leehr et al., 2015). Specifically, both negative emotions and distress are considered to play a role in overeating, and consequently overeating is suggested to provide relief from negative emotions/distress.

In a systematic review that included several experimental studies that tested the triggering effect of negative emotions on eating, it was concluded that overeating or binge eating during the experience of negative emotions in individuals with obesity could be predicted as a function of the presence or absence of binge eating disorder (Leehr et al., 2015). However, a recent meta-analysis emphasizes that there is substantial individual variability pertaining to this triggering effect of negative emotions in relation to overeating in obesity (Evers, Dingemans, Junghans, & Boevé,

2018). This is not surprising, noting that obesity is characterized by substantial heterogeneity. Regarding the short- or long-term relief component of overeating/binge eating in obesity, more experimental and naturalistic studies are needed.

The possible emotion regulation function of overeating and binge eating raises the question whether people with overweight or obesity have poorer emotion regulation skills and/or use more maladaptive emotion regulation strategies. In general, studies using self-report questionnaire support this notion (Görlach, Kohlmann, Shedden-Mora, Rief, & Westermann, 2016; Tan, Xin, Wang, & Yao, 2017), but also point out that certain characteristics (e.g. the presence of binge eating disorder (Fernandes, Ferreira-Santos, Miller, & Torres, 2018)) may moderate the association between emotion regulation and obesity. In addition, based on questionnaire studies, impairments in the identification stage of emotion regulation (Sheppes, Suri, & Gross, 2015), particularly difficulties in identifying feelings (which is a key facet of alexithymia) is pronounced in obesity (Fernandes et al., 2018). Alexithymia and habitual use of maladaptive strategies may be relevant in the (personalized) treatment of obesity.

Summary

Obesity is a condition characterized by a body mass index that is equal to or exceeds 30 kg/m^2 (Who, 2016), and is associated with many serious health consequences (The Global BMI Mortality Collaboration, 2016). It is highly concerning that the prevalence is increasing, and treatment regimens based on the traditional biomedical approach have failed to render successful effect (Garner & Wooley, 1991). Studies show that individuals with obesity have a stronger sensitivity for and motivational drive ("wanting") towards foods high in fat and sugar (palatable food) in combination with deficient impulse control (Robinson et al., 2016b; N. D. Volkow et al., 2011). This is evident on multiple levels, from subjective-self report, objective performance measures and brain activity patterns (Tomasi & Volkow, 2013; N. D. Volkow et al., 2011; Nora D Volkow et al., 2017). Studies suggest that this condition may be (in part) acquired via repeated exposure to palatable food and a consequential associative learning process (N. D. Volkow et al., 2011; Nora D Volkow et al., 2017). Depression can precipitate obesity, but can also be a result of obesity(Goldfield et al., 2010; Luppino et al., 2010), and in general, negative mood can induce motivation towards intake of palatable food (Oliver et al., 2000), resulting in further weight gain. Overall, several lines of research show substantial overlap with substance use disorder, both in terms of phenomenology (craving, lack of control) and brain activity measures (i.e. striatal deficits) in contexts of anticipated rewards (N. D. Volkow et al., 2011; Nora D Volkow et al., 2017). However, currently obesity is not characterized as a mental disorder mainly because of heterogeneity and an unclear etiology (Marcus

& Wildes, 2012). That can be a valid consideration, yet surprising as heterogeneity and ambiguity with respect to the etiology is the case with several other disorders that are included in the DSM. The decision is an important one, especially in clinical context.

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CHAPTER THREE

Attentional bias and disengagement as a function of Body Mass Index in conditions that differ in anticipated reward²

²This chapter based upon Tsegaye, A., Bjørne, J., Winther, A., Kokonyei, G., Cserjesi, R., & Logemann, H. N. A. (2020). Attentional bias and disengagement as a function of Body Mass Index in conditions that differ in anticipated reward. *Journal of Behavioral Addictions*, *9*(3), 818–825. https://doi.org/10.1556/2006.2020.00073

Introduction

Attentional bias and disengagement are central to the functioning of everyday life (Corbetta & Shulman, 2002). Attention is generally directed to relevant elements in our environment (attentional bias), leading to facilitated processing of these elements. Stimuli may be relevant because they are salient, or because they are relevant in relation to our current goals/tasks (Corbetta & Shulman, 2002). Previous studies suggest that an abnormally heightened attentional bias to food cues can be triggered by overexposure to palatable foods (Eric Stice, Yokum, Burger,Epstein, & Smaii, 2011). In turn, attentional bias to food cues predicts subsequent weight gain and maintains excessive eating behaviors (Yokum et al., 2011). However, there are some conflicting results on attentional bias in obesity (Nijs, & Franken, 2012), which may be due, at least in part, to the use of different measures of executive processes.

With respect to moderators, studies suggest that stress can increase food palatability (Groesz et al., 2012; Tomiyama, Dallman, & Epel, 2011). This may not be too detrimental effect of high BMI on behavioural control. Firstly, previous studies have shown that increased perceived stress or actual stress exposure induces stronger eating drive and ingestion of palatable food (Groesz et al., 2012; Tomiyama, Dallman, & Epel, 2011). This may not be too surprising, as the ingestion of palatable foods has been associated with short-term pleasure and relief from stress (Dallman, Pecoraro, & La Fleur, 2005). Most noteworthy is the study of (Nederkoorn et al., 2006). In that study, the relationship between BMI and inhibitory control was investigated using a stop signal task, which can be regarded as a relatively taxing (and plausibly relatively stressful) task. There was an inverse relationship between BMI and inhibitory control, but only at the end of the task. Hence, as stress may be induced as time on task increases, this may indicate that the relationship between BMI

and inhibitory control varies as a function of (induced) stress. With mindfulness, individuals with normal BMI relative to abnormally high BMI, showed better inhibitory performance. Noting the task characteristics, this could plausibly be interpreted as indicating a moderating role of stress on the relationship between BMI and inhibitory control. Mindful, individuals focus on internal and external events in a perceptive, attentive and open manner (Carlson, 2009). Mindfulness-based interventions are currently being used to reduce abnormal weight(gain), and findings suggest that this approach may be beneficial weight loss (Olson & Emery, 2015; Tapper et al., 2009). Indeed, obesity is associated with relatively low (compared to high) dispositional mindfulness (Carlyle et al., 2015). In terms of mechanism, mindfulness has been shown to negatively correlate with levels of depression and anxiety (Brown & Ryan, 2003). Low mindfulness may a cause to increased intake of palatable food, and it should be emphasized that in individuals with relatively high mindfulness, the correlation between stressors and stressful eating is lower, which is due to a potentially high mechanism/ability to cope with stress (Cotter & Kelly, 2018). On the other hand, there is also evidence of a direct relationship between a mindful state and executive control. Specifically, mindfulness-based interventions have been shown to reduce ADHD symptomatology in adults and children (Cairncross & Miller, 2016; Janssen et al., 2018). In addition, specific effects on executive processes have been reported following mindfulness-based training. Improved mindfulness was associated with improved attentional control (Sibalis et al., 2017), and improved inhibitory control (Gallant, 2016).

In this study, the following hypotheses were postulated. Firstly, it was hypothesized that BMI would be positively associated with increased attentional bias, predominantly in both reward contexts as opposed to the neutral context. Secondly, a negative relationship was expected between BMI and disengagement in the reward contexts as opposed to the neutral context. Finally, it was hypothesized that higher perceived stress would enhance the aforementioned effects, and the opposite was expected for trait mindfulness.

METHODS

Participants

Participants were included if they were between 18-50 years old, were not pregnant and had no known current mental disorder (by own admission), if they were not currently using drugs affecting cognitive functioning and had normal or corrected-to-normal vision. The final sample for the analyses consisted of in total eighty-seven individuals (24 males and 63 females; age: M=30.1, SD=8.3; body mass index (BMI): M=24.2, SD=4.67).

Measures

Visuospatial Cuing (VSC) Task

The VSC task was modelled after (Clark, Geffen, & Geffen, 1989; Logemann et al., 2017), and developed using Canvas for HTML5. The task was implemented on a Raspberry Pi3 with Linux operating system and Apache2 as webserver for online use. In a typical trial, a fixation dot was presented for 600 ms, after which a cue was presented centrally for 400ms. The cue (width:60 pixels; height:60 pixels) indicated the likely location (unless in case of a non-informative cue) of a subsequent target to which a response was required. After presentation of the cue, the fixation dot was presented again for 600 ms after which the target was presented for 200 ms. The target was always a portrait-oriented bar-shaped stimulus, and presented at the vertical midline of the display, at the left or right side of the display. The required response depended on whether the bar (width: 200 pixels) was either long (height: 400 pixels) or short (height: 320 pixels). The current implementation included non-cued, invalid, and valid trials. In a non-cued trial, the cue was not informative of the location of the target. In invalid trials, the target was presented opposite to the location indicated by the cue. In valid trials, the target was presented on the side of the screen indicated by the cue (figure 1). The task consisted of three conditions, a neutral condition, a money and food condition. The conditions differed only with respect to the target-pictures, the dimensions of the two (short and long) types of pictures did not differ between conditions. In the neutral condition, targets were solid grey filled bars. For the food condition, the short or long bar was always one out of four potential pictures representing palatable food (chips, chocolate, chocolate chip cookies, cashew nuts) similar to Houben et al. (Houben et al., 2014a). For the money condition, the short or long bar was always one out of four potential pictures representing money. Presentation of each picture, and type of target (short/long) was equiprobable. Condition order as well as responsetarget (short/long) assignment was counterbalanced over participants. Each condition consisted of 48 valid trials, 16 invalid trials and 16 trials that consisted of non-informative cues. Trial order was randomized for each participant and trials could not be predicted from previous trials. Early (<150ms) and late responses (>1400 ms) were discarded from the analyses. The relevant outcomes of the VSC task were attentional bias, and disengagement. Bias was operationalized as the mean response time to non-cued targets minus the mean response time to validly cued targets. Disengagement was operationalized as the mean response time to invalidly cued targets minus the mean response time to non-cued targets. For both measures, the measurement level is milliseconds(ms).



Fig 1 Graphical depiction of a valid trial in the food condition of the visuospatial cueing task.

Self-report measures implemented in Qualtrics (Qualtrics, Provo, UT, 2019):

Depression, Anxiety and Stress Scale (DASS-21) (Lovibond & Lovibond, 1995).

The DASS-21 consists of three self-report scales that is thought to measure the subjective degree of depression, anxiety and stress. The subscales of DASS-21 have been reported to have a high reliability (Cronbach's $\alpha > .85$) (Sinclair et al., 2012). In our sample (N=87), the stress subscale also showed a good reliability (Cronbach's alpha: 0.891).

Mindful attention awareness scale (MAAS) (Brown & Ryan, 2003)

The MAAS is a 15-item scale that measures trait mindfulness. The questionnaire shows high internal consistency (Cronbach's $\alpha > .80$) (Brown, West, Loverich, & Biegel, 2011), and in our sample (N=87) Cronbach's alpha was 0.853.

Procedure

The study was advertised on digital (social) media such as Facebook. The advertisement provided some brief information regarding the study, contact details of the investigator and included a link to the online Qualtrics survey platform that included the information letter/informed consent form. After providing their informed consent, participants started with the questionnaires also implemented in Qualtrics. First, participants were requested to provide their age, gender, and hunger

level. Hunger level was assessed with one question "Please state on a scale from 1(not hungry at all) - 5(very hungry) how hungry you currently are". Subsequently, participants filled out the DASS-21 and MAAS. Upon completion, participants were directed to the online VSC task. For this task, participants were instructed to respond to the targets as fast and as accurately as possible. After performing the VSC task, the experiment was completed. The total duration of the experiment was approximately 30 minutes.

Statistical Analysis

Data preprocessing (to calculate the relevant outcome variables) was done using R (R Development Core Team, 2017) and statistical analyses were performed using SPSS (IBM Corp., 2019). Similar to Houben et al. (Houben et al., 2014a), we employed repeated measures ANCOVAs. Specifically, for evaluating the effects regarding attentional bias, we tested the BMI x condition (neutral/food) x validity (non-cued/valid) interaction with respect to response time (in ms level of measurement). In addition, we tested the BMI x condition (neutral/money) x validity (non-cued/valid) interaction with respect to response time. For disengagement, we performed the same tests, except the validity levels were non-cued/invalid. Lastly, we tested whether mindfulness and stress moderated the aforementioned interactions. Alpha was set at .05, and we controlled for age, gender and hunger level. These variables were included in all analyses as covariates of no interest. All variables, except the within-subjects factor "condition" were continuous.

Ethics

The study was approved by the Research Ethics Committee at ELTE Eötvös Loránd University, Faculty of Education and Psychology (reference number:2017/218, date: 2017/10/25), and has been performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

RESULTS

Descriptive data for age, BMI, mindfulness, stress and hunger level are shown in table 1. Data regarding the inferential statistics are reported in table 2. Importantly, the well-known validity effect was replicated in the current study. Specifically, irrespective of condition, the validity effect was significant with shorter response times (RTs) to validly cued targets and longer RTs to invalidly cued targets relative to non-cued targets, F(1,86) = 109.61, P < 0.001 (partial $\eta^2 = 0.560$), and F(1,86) = 6.37, P = 0.013 (partial $\eta^2 = 0.069$) respectively.

	Max	Min	Μ	S.D
	(maximum)	(minimum)	(Mean)	(std. deviation)
Age	50.00	18.00	30.10	8.30
BMI	44.08	17.50	24.20	4.67
Mindfulness	6.00	1.93	4.06	0.74
Stress	40.00	0.00	13.10	9.05
Hunger level	5.00	2.00	4.18	0.84

Table 1. Descriptive statistics of age, BMI, mindfulness, stress and hunger level (N = 87).

Table 2. Primary analyses: attentional bias (top four rows) and disengagement (bottom four rows).

Factor	F(1,82)	Р	partial η2		
condition (neutral/food) x validity (non-	9.77	0.002	0.106		
cued/valid)					
BMI x condition (neutral/food) x validity (non-	2.37	0.128	0.028		
cued/valid)					
condition (neutral/money) x validity (non-cued	6.53	0.012	0.074		
l/valid)					
BMI x condition (neutral/money) x validity	2.53	0.116	0.030		
(non-cued /valid)					
condition (neutral/food) x validity (non-cued	8.23	0.005	0.091		
/invalid)					

BMI x condition (neutral/food) x validity (non-	3.27	0.074	0.038	
cued /invalid)				
condition (neutral/money) x validity (non-cued	5.94	0.017	0.068	
/invalid)				Note:
BMI x condition (neutral/money) x validity	5.95	0.017	0.068	
(non-cued /invalid)				

Dependent variable is response time in ms.

Performance data with respect to bias and disengagement are graphically depicted in figure 2 and figure 3, respectively. Inferential statistics are shown in table 2. As indicated by the condition (neutral/food) x validity (non-cued/valid) interaction, bias was reduced in the food condition relative to the neutral condition, but this effect was not affected by BMI. Similarly, as indicated by the condition (neutral/money) x validity (non-cued/valid) interaction, bias was significantly reduced in the money condition as compared to the neutral condition, and this effect was not affected by BMI. As indicated by the condition (neutral/food) x validity (non-cued/invalid) interaction, disengagement was significantly enhanced in the food condition as opposed to the neutral condition and BMI did not affect this effect. Disengagement increased in the money condition compared to the neutral condition, as indicated by the condition (neutral/money) x validity (non-cued/invalid) interaction and BMI did not affect this effect. Posthoc testing indicated that higher BMI was associated with increased disengagement in the money condition F(1,82) = 7.29, P = 0.008), but not in the neutral condition, F(1,82) = 0.95, P = 0.334.

With respect to the secondary explorative analyses, both self-reported mindfulness and stress did not affect any of the BMI x condition interactions that were described in table 2 (all partial $\eta^2 < 0.023$).

Fig 2 Graphical depiction of the relationship between BMI and bias (response time to non-cued targets minus validly cued targets, higher values indicate stronger bias) in the three conditions.



Fig 3 Graphical depiction of the relationship between BMI and disengagement (response time to invalidly cued targets minus non-cued targets, lower values indicate stronger disengagement) in the three conditions.



DISCUSSION

Previous studies have suggested that attentional bias may vary as a function of BMI. In addition, inhibitory control, and its associated process of attentional disengagement has also been implicated in relation to high BMI. However, the exact role of these aspects of visuospatial attention and the complex interaction between BMI with environment contexts of reward and subject variables (stress and trait mindfulness) had not yet been thoroughly investigated. Addressing this main gap in the literature, was the main aim of the current study.

The lack of a significant relationship between BMI and attentional bias to reward related stimuli relative to neutral stimuli was unexpected. Previous studies have suggested that high BMI (i.e. Yokum et al., 2011) and specifically obesity (Nijs et al., 2010; Werthmann et al., 2011) is associated with increased attentional bias to food cues. However, it has also been noted that studies have yielded contradictory effects that may be accountable to differences in the exact methodology employed (Nijs & Franken, 2012). It is plausible that attentional bias for a specific location (as opposed to i.e. stimulus characteristics) is not affected by BMI.

With respect to disengagement, results are opposite to what was expected. Interestingly, higher BMI was associated with speeded responses to unexpected stimuli in the money condition (but not in the food condition) relative to the neutral condition. Results may imply that inhibitory control operates differently in the visuospatial cueing task as opposed to the stop signal task employed by Houben et al. (2014). Specifically, in the stop signal task the prepotent response to a stimulus that has reward value must be inhibited subsequent to a stop-stimulus. In this case, the requirement for inhibition contradicts with the primary task requirement (responding as fast and accurate as possible to the go stimuli). In the visuospatial cueing task however, disengagement of attention is congruent with the requirement to respond as fast and accurate as possible to the unattended target. In that vein, inhibition/disengagement may be speeded with increased perceived reward value of targets in the visuospatial cueing task, but negatively affected in the stop signal task (or go/no-go task).

It should be noted that there were some extreme values (defined as three times the interquartile range) with respect to bias (n=2) and disengagement (n=4). In view of the stringent exclusion criteria (erroneous responses were excluded, see materials) there is no reason to assume these represent erroneous data. Nevertheless, excluding the extreme cases did not change the significance of the BMI x condition (neutral/money) interaction with respect to disengagement.

With respect to the moderators, we did not find evidence for a moderating effect of stress on the aforementioned effects. This might seem to contrast previous studies on obesity that have suggested a moderating role of stress (Chantal Nederkoorn, Smulders, Havermans, Roefs, & Jansen, 2006). However, we did not specifically focus on obesity, and we did not induce acute stress but assessed self-reported stress experience via the DASS-21 questionnaire which might not interact with BMI

with respect to attentional/inhibitory control. Indeed, previous studies have shown a complex relation between stress and food intake. Although acute stress may affect food intake (Rutters, Nieuwenhuizen, Lemmens, Born, & Westerterp-Plantenga, 2009), a very recent study has suggested that the relationship between chronic stress and food intake may depend on the degree of impulsive-risk taking tendencies (Mason, Schleicher, Coccia, Epel, & Aschbacher, 2018).

Our results do not support a clear effect of trait mindfulness on the relationship between BMI and inhibitory control across the conditions. Previous studies have shown that mindfulness training improves executive control (Gallant, 2016; Sahdra et al., 2011), which in turn may promote weight loss. Indeed, with respect to obesity and weight-loss some systematic reviews have indicated that mindfulness-based training may promote weight loss (Carrière, Khoury, Günak, & Knäuper, 2018), but others have reported inconsistent findings (Rogers, Ferrari, Mosely, Lang, & Brennan, 2017; Ruffault et al., 2017). The main issue is that there are numerous mindfulness-based methods, which may differ in terms of rendered effects. In fact, a recent review suggests that specifically mindful eating, not mindfulness, is associated with subsequent weight loss (Dunn et al., 2018). To the best of our knowledge, the relation between mindfulness and executive mechanisms has not previously been thoroughly investigated in relation to BMI in contexts of reward.

The relationship between BMI and disengagement in the money condition was not evident in the food condition. One important difference between these conditions is the type of reinforcer. Food can be regarded as a primary reward/reinforcer whereas money becomes a secondary reinforcer via a conditioning process over time. Indeed, some differences exist with respect to the exact brainregions that are activated subsequent to processing pictures of food and money, but both types of stimuli have been shown to activate the primary brain circuitry responsible for reward processing, and neural processing of these stimuli has been suggested to be modulated by metabolic state (Yousuf, Heldmann, Göttlich, Münte, & Doñamayor, 2018). The reason why the differential modulation of disengagement by BMI was limited for the contrast of the money versus neutral condition, might be due to the operationalization of the condition. Specifically, responses were more varied in the latter condition, negatively affecting statistical power. One limitation of the current study is that stimuli were not matched on salience. Thus, it might be that the enhanced variability in the food condition may be due to stimulus differences across conditions (i.e. salience). Other limitations should also be noted. Firstly, height and weight were assessed by self-report, which can be affected by self-representation bias. However, as noted by Houben et al. (2014), it is not plausible that self-representation bias affects the overall rank-order of BMI values in the sample. Secondly, this was an online study. We should emphasize that studies suggest that the reliability of online cognitive experiments is comparable to those conducted in the lab (Hilbig, 2016). Most importantly,

the overall validity effect was replicated in our study, confirming the validity of the employed paradigm. In a related vein, it has been suggested that the effects of cueing on performance is more substantial when perceptual demands and potential target locations are increased (Meinke, Thiel, & Fink, 2006). Indeed, in the current employed paradigm, participants plausibly quickly learned that there are only two possible target locations which might reduce the effect of cueing on response times. However, we should also emphasize again that the effect of cuing on response time was significant in the current paradigm and employment of a more taxing VSC task may result in a higher level of attrition. Lastly, although we controlled for gender, it should be noted that only four male participants had a BMI below the median. Excluding male participants, and performing the analyses on the female sample did not yield a different outcome (data available upon request). However, appropriate nuance should be applied in generalizing results to the male population.

In conclusion, our results suggest that higher BMI is associated with facilitated processing of unexpected stimuli that have general reward value. This might imply that individuals with overweight or obesity are sensitive to unexpected reward related stimuli and suggests that reward context should be considered in clinical context.

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CHAPTER FOUR

The relationship between reward context and inhibitory control, does it depend on BMI, maladaptive eating, and negative affect?³

³This chapter based upon Tsegaye, A., Guo, L., Stoet, C., Cserjési, G., Kökönyei, G., & Logemann, H. N. A. (2022). The relationship between reward context and inhibitory control, does it depend on BMI, maladaptive eating, negative affect? BMC psychology, 10(1),4. https://doi.org/10.1186/s40359-021-00712-5

Introduction

Previous studies have not shown a consistent relationship between BMI and inhibitory control in neutral contexts (Bartholdy et al., 2016). The results of a relatively recent study suggest that high BMI is associated with a specific reduction in inhibitory control in a palatable food context (Houben, Nederkoorn, & Jansen, 2014). However, it is not clear whether this reduced inhibitory control extends to other reward contexts. This question was explored in the current study. Additionally, we examined the role of eating behaviors, rumination, and stress as a moderator.

Several plausible moderators should also be noted. First, eating behaviors may directly affect inhibitory control, but may also moderate the relationship between BMI and inhibitory control. For instance, emotional eating has been reported to be associated with reduced inhibitory control, specifically in a food related context (Svaldi, Naumann, Trentowska, & Schmitz, 2014). Rumination and associated stress may also play a role. For instance, there is evidence for a negative association between the trait rumination and inhibitory control (Yang, Cao, Shields, Teng, & Liu, 2017), but in the context of overweight/obesity, we do not know how they are related when responses to rewards need to be inhibited. Of note, stress has been associated with shifts in preference for palatable foods (Oliver, Wardle, & Gibson, 2000). Moreover, in a context of negative mood tasty food can be a powerful negative reinforcer in the case of stress and rumination (Moskovich, Hunger, & Mann, 2012). Although eating behaviors, stress and rumination may influence inhibitory control, and the relationship between BMI and inhibitory control, particularly in the context of a food, it is not clear whether this is not true for a condition reflecting general reward.

To answer our research questions, we used an adapted Go/No-Go task with three conditions, a neutral, a food and a general reward condition (the latter operationalized with stimuli representing money). In this study, the following hypotheses were formulated. First, it was hypothesized that higher BMI would be associated with decreased inhibitory control in the food-related condition compared to a neutral condition. Second, we expected that higher BMI would be associated with reduced inhibitory control in the money-related condition compared to a neutral condition. Finally,

we examined the potential moderating role of eating behaviors (uncontrolled eating, restrained eating, and emotional eating), stress, and trait rumination on the relationship between BMI and response inhibition across contexts.

Methods

Participants

Participants were recruited predominantly via advertisements on social media (e.g. Facebook, LinkedIn). Participants were excluded if they had any known current mental disorder, if they currently used drugs affecting cognitive functioning, if they had color blindness and if they were pregnant. Participants had to be between 18 - 50 years old. Participants who did not complete the experiment were excluded. The final sample for final analyses consisted of in total forty-six participants (39 % males and 61 % females), ranging in age from 19 to 50 years old (M = 30.80, SD = 9.32) and Body mass index BMI (kg/m²), (M = 23.49, SD = 3.85). In total 34 participants had normal BMI (range 19 to 25, M=21.75, SD=1.80) with a gender distribution of 40% males and 60% females respectively, and 12 participants (BMI range 25 to 39, M=28.42, SD=3.92; equal gender distribution) presented with overweight (n=8) or obesity (n=4). The study was approved by the Research Ethics Committee and conducted following the declaration of Helsinki.

Materials

Go/no-go task

The go/no-go task (Wessel, 2018) was employed to assess inhibition. A single trial consisted of the presentation of a target stimulus, a central go stimulus (400x400 pixels) requiring a space-bar response or no-go stimulus (400x400 pixel go stimulus but surrounded a 50-pixel white border) to which no response should be made. The duration of the target stimulus was 150ms and subsequently a fixation dot was presented until the next target stimulus was presented. The trial-to-trial duration was 1500ms. Probability of a go stimulus was 80% and of a no-go stimulus 20%. The task consisted of one practice block and three experiment blocks (neutral, food and money condition). The practice block consisted of 8 trials and feedback was provided in case of an error of commission or error of omission. The three experimental blocks/conditions consisted of 40 trials. The main difference between the blocks were the pictures. In the practice block, the target stimulus was respectively one of four possible solid color filled squares (olive, green, blue, orange), pictures of food or pictures of money. The measure of inhibitory control was the proportion of successful inhibitions to no-go trials (number of successful inhibitions to no-go trials divided by the total number of no go-trials).



Figure 1. Schematic representation of two trials in the food specific condition of the Go/no-go task

Self-report measures implemented in Qualtrics

Three-Factor Eating Questionnaire-R18V2 (Cappelleri et al., 2009).

The participants eating behavior was assessed by the short version of the three-factor eating questionnaire (TFEQ-R18). Previous research has shown that the TFEQ-R18 yields a good measure of uncontrolled and emotional eating and has a good factor structure and reliability with Cronbach's alpha ranging between 0.78 and 0.94 (Cappelleri et al., 2009). The TFEQ-R18 has three subscales: cognitive restraint of eating (conscious restriction of food intake in order to control body weight, three items), uncontrolled eating (tendency to eat more than usual due to a loss of control, nine items) and emotional eating (inability to resist emotional cues/ responding to negative emotions by eating, six items), in total 18 items. Participants rate each item to the extent that the item-content applies to his or her thoughts, feelings and behaviors on a scale of 1 to 4, scoring 1 equal to "definitely false" and scoring 4 equal to 'definitely true.' The range of possible scores for each subscale is 9 to 36, 6 to 24, and 3 to 12 points for the uncontrolled eating, emotional eating scale, and cognitive restraint respectively. Higher scaled scores for each subscale suggest greater UE, CR or EE characteristics the internal consistency of subscale showed good reliability (Cronbach's alpha: 0.89, 0.78 and 0.94, respectively) (Cappelleri et al., 2009). Cronbach's alpha in our study 0.776, 0.733 and 0.959.

Ruminative Response Scale (RRS) (Treynor et al., 2003).

The RRS is one of the most popular instruments to assess ruminative responses (Treynor et al., 2003), and has excellent reliability with a Cronbach's alpha across studies of about 0.9. The RRS is

a 22-item scale capturing trait-like ruminative thoughts ("What am I doing to deserve this?") when experiencing low mood. Items are answered on a 4-point Likert – type scale, ranging from 1 "almost never" to 4 "almost always"; higher scores reflect higher rumination. In our study Cronbach's alpha was 0.943.

Depression, Anxiety and Stress Scale (DASS-21) (Lovibond & Lovibond, 1995).

The DASS-21 is a widely used instrument to assess levels of depression, anxiety and stress by self-report, also in relation to clinical symptomatology. The instrument has a good overall reliability with a Cronbach's alpha of 0.91, 0.84 and 0.80 for the Depression, Stress and Anxiety subscale, respectively (Sinclair et al., 2012). Each of the three subscales contains 7 items. Items are answered on a 4-point Likert-type scale, ranging from 0 "Never" to 3 "Almost always". Scores for stress, anxiety and depression scales are determined by summing the scores for the relevant 7 items and multiplying by 2. For the current study, we only focused on the stress scale and Cronbach's alpha for this scale was 0.867.

Procedure

The assessments were completed online, via Psytoolkit (Stoet, 2010, 2017). All participants were provided with basic information regarding the study and procedures and read and signed the online version of a digital consent form. After providing informed consent, the experiment started with self-report general questions that included question regarding age, gender, weight, height, smoking status, handedness, hunger level and amount of sleep last night. Subsequently, participants filled out psychometric scales. Finally, participants performed the go/no-go task. During this task, pictures were presented sequentially, and participants were required to respond via pressing the spacebar unless the picture was surrounded by a white border. In the latter case, a response was required to be withheld. Upon completion of the go/no-go task, the study was concluded. The total duration of the study (questionnaires and experiment) was approximately 25 minutes.

Statistical approach

Repeated measures ANCOVAs were performed for the primary analyses, with alpha level set at 0.05. Analyses were based on the ones performed in Houben et al. (2014), and one of the aims was to test whether their results were replicable. Hence, we first tested the BMI x condition (neutral/food) interaction regarding the proportion of inhibitions to no-go trials. In addition, we tested the BMI x condition (neutral/money) interaction. As the relationship between BMI and inhibitory control does not necessarily follow a linear relationship, as described in Houben (2014), we also included BMI

as categorical variable in the model (repeated measures ANOVA) as a secondary approach. Specifically, to maintain equal sample sizes we transformed BMI to a categorical variable via median-split, creating two levels (below median/above median). Lastly, we tested the interactions between maladaptive eating (uncontrolled and emotional eating), rumination and stress on the one hand and condition (neutral/food and neutral/money) on the other.

Results

Descriptive data for age, BMI, eating behavior, rumination, stress and subjective hunger level is shown in table 1.

Table 1. Descriptive data Eating behavior, Rumination, Stress, Age, BMI, and Subjective hunger level (N = 46).

	Scale-range	Max	Min	Μ	S.D
	(max-min)	(obtained)	(obtained)	(Mean)	(std. deviation)
Age	50-18	50	19	30.8	9.3
BMI	N/A	39	19	23.5	3.9
Stress	42-0	28	0	9	7
Rumination	88-22	73	23	42	12
Hunger level	5-1	4	1	2	1
Uncontrolled eating	36-9	33	11	19	5
Cognitive restraint	12-3	12	3	6	3
Emotional eating	24-6	21	6	11	4

Primary analyses: BMI and inhibitory control across different conditions.

The relationship between BMI and inhibitory control did not significantly vary as a function of condition (neutral/food/money), F (2,88) = 0.48, p = 0.622, partial η^2 = 0.011. The secondary

analysis, including BMI as categorical variable based on split by median (=22.43) yielded a BMI (above median/below median) x condition (neutral/food/money) interaction that trended to significance, F (2,88) = 2.73, p = 0.071, partial $\eta^2 = 0.058$. Post-hoc analyses indicate that above median BMI relative to below median BMI was associated with reduced inhibitory control in the food condition relative to the neutral condition, F (1,44) = 4.12, p = 0.049, partial $\eta^2 = 0.086$ (see figure 2). This relation was not evident for the neutral/money contrast, F (1,44) = 0.20, p = 0.660, partial $\eta^2 = 0.004$. Lastly, there was no main effect of condition regarding inhibitory control, F (2,88) = 1.01, p = 0.369, partial $\eta^2 = 0.022$



Figure 2. Mean proportion of inhibitions for both BMI groups across the three conditions, neutral, food, and money. Error bars indicate +/-2 standard errors from the mean.

Secondary analyses: Maladaptive eating behavior, rumination, stress and inhibitory control across the different conditions.

As shown in table 2, there were no significant main effects or interactions with condition with respect to eating behaviors, rumination and stress regarding inhibitory control. Explorative correlational analyses indicated that maladaptive eating, rumination and stress were associated with reduced inhibitory control, specifically in the food context. Only rumination was negatively associated with inhibitory control in the money context.

Table 2 Inferential statistics regarding eating behavior, rumination and stress with respect to inhibitory control.

Factor	F(1,42)	Р	partial
			η2
Uncontrolled eating x condition (neutral/food)	4.20	0.047*	0.091
Emotional eating x condition (neutral/food)	6.73	0.013*	0.138
Rumination x condition (neutral/food)	4.65	0.037*	0.100
Stress x condition (neutral/food)	2.52	0.141	0.051
Stress x BMI x condition (neutral/food)	1.71	0.198	0.039
Uncontrolled eating x condition (neutral/money)	0.57	0.455	0.013
Emotional eating x condition (neutral/ money)	2.67	0.110	0.060
Rumination x condition (neutral/ money)	0.09	0.769	0.002
Stress x condition (neutral/ money)	0.01	0.938	< 0.001
Stress x BMI x condition (neutral/money)	< 0.01	0.964	< 0.001

Note: * significant at the 0.05 level

Table 3. Post-hoc explorative correlational analyses, regarding the relationship between self-report measures and inhibitory control in the neutral, food, and money condition (n=46).

	Neutral	Food	Money
Uncontrolled eating	0.065	-0.2481	-0.026
Emotional eating	0.013	-0.319*	-0.167
Rumination	-0.147	-0.390**	-0.299*
Stress	-0.038	-0.323*	-0.053

N.B.: *. Correlation is significant at 0.05 level (2-tailed); **. Correlation is significant at 0.01 level (2-tailed); ¹Trending to significance, p < 0.1

Discussion

Our results indicate that higher BMI is associated with reduced inhibitory control in a food context relative to a neutral one. In addition, explorative correlational analyses seem to indicate that maladaptive eating and negative effect were associated with reduced inhibitory control in the food context. In contrast to our hypotheses, effects with the exception of rumination, did not generalize to the money context.

In a previous study, it was already reported that higher BMI was associated with reduced inhibitory control in a food context relative to a neutral context. However, one important limitation challenged the interpretation of effects. More specifically, in Houben et al. (2014) counterbalancing of conditions was omitted, meaning that all participants were provided with the same order of tasks, neutral condition first followed by the food condition. This means that the interaction between BMI and condition regarding inhibitory performance, could also be explained by an interaction between BMI and time. Importantly, a previous study from Nederkoorn et al. (2006), in which only a neutral stop task was employed, reduced inhibitory control in the group with obesity relative to the normal weight group, was only evident at the last part of the task. This means, that the effect reported in Houben et al. (2014), could potentially be due to time (and potentially induced stress) instead of reward context. This limitation was addressed in the current study in which counterbalancing of condition order was employed. As mentioned, results are congruent with previous findings (Batterink et al., 2010; Houben et al., 2014).

In line with previous reports (Svaldi et al., 2014), the explorative correlational analyses suggest that maladaptive eating patterns that promote overconsumption of palatable food (uncontrolled eating and emotional eating) were associated with challenged inhibitory control in the food context relative to the neutral context. This is an important finding as, to the best of our knowledge, previous studies have not thoroughly assessed food specific inhibitory effects, as most studies omitted a control condition that included non-reward stimuli. As hypothesized, rumination was also associated with reduced inhibitory control in the food- relative to neutral context. This finding supports the notion that trait rumination may affect reward-related information processing. Interestingly, in a previous report, using the monetary incentive delay (MID) task in a never-depressed sample a significant positive association was found between trait rumination and neural response in areas of the Salience Network to monetary reward anticipation (reward cues) compared to loss anticipation (loss cues) (Kocsel et al., 2017). However, the MID task differs from the go/no-go task used in our study in many ways, both studies show that reward processing might be altered in relation to rumination. Further studies need to investigate whether the relationship between

rumination and reward processing may vary as a function of the type of the reward or the process (e.g., inhibition, switching, anticipation etc.) implemented in task performance.

Considering previous studies, it was surprising that stress did not affect inhibitory control and did not moderate the relation between BMI and inhibitory control, especially in the food context. This could be (at least partly) due to the method of measuring stress. Specifically, we assessed the level of stress with the DASS-21 self-report questionnaire, where individuals report on experienced stress over the past week. This was one limitation of the current study in that we only assessed relatively prolonged stress and it has been reported that the association between chronic stress and unrestrained food ingestion varies as a function of the level of impulsive risk-taking (Mason et al., 2018).

As mentioned, it was expected that the negative association between BMI, maladaptive eating, and stress on the one hand and inhibitory control on the other in the food context relative to the neutral context, would be mirrored in the contrast between the money context relative to neutral context. However, our results did not support that notion. One might argue that this implies that the challenged inhibitory control is restricted to food contexts and may not generalize to other reward contexts. However, one limitation of the current study may be the operationalization of the nonfood, reward condition operationalized by stimuli representing money. We employed the money condition because stimuli of money are obviously different than food, but are also known to trigger primary reward related activity (Yousuf et al., 2018). However, it should be noted that money not only represents a different reward object, but also a different class of reward. To elaborate, whereas food can be regarded as an intrinsic reward, money related stimuli become rewarding/reinforcing only after an operant learning process over time. Now as mentioned, the mechanism implicated in obesity shows significant overlap with that implicated in substance use disorder (Matikainen-Ankney & Kravitz, 2018), and cross sensitization for different substances and associated stimuli may (at least partly) explain comorbidity between maladaptive eating and substance use disorder. However, following our results, one might argue that cross sensitization is more restricted to reward related stimuli that are intrinsically rewarding as opposed to non-intrinsic reward related stimuli. The latter would be one question that could be addressed in future studies.

On the other hand, results from Godefroy et al. (2016), may suggest an alternative explanation. They employed a structural equation modeling approach and showed that effortful control was associated with enhanced self-regulation in eating, which in turn, was associated with reduced appetite reactivity. This may suggest that, even though cross-sensitization may enhance motivational and response tendencies towards other reward-associated stimuli (in line with e.g.

Tsegaye et al. (2020)), maladaptive eating and associated adiposity due to reduced temperamental inhibitory control, may be specifically evident in a palatable food context.

It should be noted that the relation between BMI and inhibitory control in the food context relative to the neutral context was only statistically significant in our exploratory analysis when including BMI as a categorical (median split) variable. Following Houben et al. (2014), we decided to perform such approach as the relationship between BMI and inhibitory control is not necessarily linear. One may note that one disadvantage of a median split strategy is that it can make results relatively sample dependent, as groups are not formed based on an apriori criterion regarding group assignment. For instance, the latter would entail assigning participations to an overweight/obesity group and control group based on BMI value. However, in the current study the aim was not to specifically focus on overweight and/or obesity, but to assess the general relationship between BMI and inhibitory control. Importantly, testing the difference between the overweight/obese group and normal healthy weight controls would result in unequal sample sizes and especially small sample size of the overweight/obese group. One other limitation, at least perceptually, is that the study was conducted online. However, it should be emphasized that recent studies consistently show that online cognitive psychological experiments can generate reliable and valid data, comparable to those conducted in a controlled lab environment (Hilbig, 2016; Kim et al., 2019). Of course, it is still possible that participants did not take the experiment seriously or did not understand the task. However, we controlled for this potential issue and excluded those participants that did not respond consistently to go trials, indicated by the proportion of omissions to those trials.

Furthermore, the use of the go/no-go task as opposed to the stop signal task, to measure inhibitory control, could be viewed as a limitation. Firstly, there is substantial heterogeneity of go/no-go task implementations in terms of task specifics. Until recently, it was not entirely clear what task characteristics were essential to induce inhibitory control. However, as shown in Wessel et al. (2018), a fast-pace go/no-go task (with 1500ms intertrial interval), with infrequent (20%) no-go trials triggers inhibitory control, comparable to that commonly reported in stop signal paradigms. In that vein, as our go/no-go task used these same task characteristics, the relevant outcome variable (proportion of inhibitions) is thought to reflect inhibitory performance.

Our results indicate that higher BMI, maladaptive eating patterns (uncontrolled eating and emotional eating) are associated with challenged inhibitory control when perceiving palatable food related stimuli relative to neutral stimuli. We could not confirm that the effect generalizes to a different, and non-intrinsic reward context operationalized by money. The results have clinical implications in that

interventions aimed at improving inhibitory control may benefit from a focus on inhibitory control in a context of palatable food.

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CHAPTER FIVE

Inhibitory performance in smokers relative to nonsmokers when exposed to neutral, smoking and money-related pictures ⁴

⁴This chapter beasd up on Tsegaye, A., Guo, C., Cserjési, R., Kenemans, L., Stoet, G., Kökönyei, G., & Logemann, A. (2021). Inhibitory Performance in Smokers Relative to Nonsmokers When Exposed to Neutral, Smoking- and Money-Related Pictures. *Behavioral Sciences*, *11*(10), 128. https://doi.org/10.3390/bs11100128

Introduction

It is commonly known that smoking represents a serious public health problem and approximately eight million people die of smoking-related diseases each year (World Health Organization, 2019). Even in light of this common knowledge, the global prevalence of tobacco smoking in adults is around 20% (World Health Organization, 2019). This underscores the need for a more thorough understanding of the mechanism that accounts for the persistence of smoking behavior. Perhaps not surprising, previous studies suggest that inhibitory control may be impaired in smokers (Anokhin & Golosheykin, 2016; Luijten, Littel, & Franken, 2011), though some studies do not suggest such a clear relation (H. N A Logemann, Böcker, Deschamps, Kemner, & Kenemans, 2014). As suggested by Luijten et al. (Luijten et al., 2011), the relationship may depend on reward context. However, the exact role of reward context on the relation between inhibitory control and nicotine addiction has not yet been thoroughly explored.

Inhibitory control can be defined as the general ability of an individual to suppress a planned or prepotent response and has been commonly assessed using the Stop Signal Task and Go/No-go task (de Jong, Coles, Logan, & Gratton, 1990; Wessel, 2017). Inhibitory control is important in everyday functioning, and deficits of inhibitory control have been reported in various addictions, such as cocaine addiction (Fillmore & Rush, 2002), nicotine dependence (Charles-walsh, Furlong, Munro, & Hester, 2014; Luijten et al., 2011), alcohol dependence (Kreusch, Vilenne, & Quertemont, 2013; Lawrence, Luty, Bogdan, Sahakian, & Clark, 2009; Li, Luo, Yan, Bergquist, & Sinha, 2009), and methamphetamine abuse (Monterosso, Aron, Cordova, Xu, & London, 2005). It has recently been shown that deficits of inhibitory control are also implicated in behavioral addiction such as internet addiction (Smith, Smith, Mattick, Jamadar, & Iredale, 2014); and obesity characterized by high Body Mass Index (BMI) (Bartholdy, Dalton, O'Daly, Campbell, & Schmidt, 2016; Batterink, Yokum, & Stice, 2010; Lavagnino, Arnone, Cao, Soares, & Selvaraj, 2016). Indeed, there seems to be sizeable overlap in terms of the brain mechanism and behavioural manifestation implicated in both pharmacological and non-pharmacological addictions (Robinson, Fischer, Ahuja, Lesser, & Maniates, 2016; Volkow, Wise, & Baler, 2017).

With respect to the mechanism, addiction has been associated with a disruption of the dopamine motive system as postulated by Volkow et al. (Volkow et al., 2017). To elaborate, on the biological level, motivation and associated approach behaviour is driven (at least in part) by striatal dopaminergic (DA) neurotransmission. Generally, percept of stimuli that are associated with any type of reward (e.g. palatable food) increases striatal DA neurotransmission, and increases the chance of approach behaviour towards the reward (Tsegaye, Kökönyei, et al., 2020). As mentioned, this dopamine motive system may be dysregulated in addicted individuals due to repeated exposure to potent rewards. Specifically, in addiction the repeated exposure to reward may result in an overactivation of the DA system and sensitization to reward related stimuli, as well as a net downregulation of striatal dopamine D2 receptors (Koob & Volkow, 2016; Volkow et al., 2017). This is congruent with the incentive sensitization (IS) theory as postulated by Robinson (Robinson et al., 2016). Similarly, IS theory entails that repeated exposure to rewarding substance(s) results in heightened sensitivity to these drugs and associated stimuli, which in turn is related to heightened motivation or approach bias to reward related stimuli. This is relevant in relation to inhibition, as increased approach tendencies may challenge inhibitory performance. In addition, it should be noted that the striatum is not only important for reward processing but striatal D2 drives (at least in part) inhibitory control (H. N Alexander Logemann et al., 2017).

Taken together, it follows that the mentioned inhibitory deficits may be more pronounced in a context of reward (at least partly) due to higher response tendencies in such conditions. It is also important to note that IS theory predicts cross-sensitization, in that heightened sensitization to one drug or reward related stimulus may extend to other rewards (Robinson et al., 2016) This notion is further supported by the known comorbidity between nicotine addiction and addiction to other substances (Kalman, Morissette, & George, 2005). Hence, it may be suggested that the inhibitory deficits may extend to other conditions of reward.

The relation between nicotine addiction and inhibitory control in a smoking context relative to a neutral context has been addressed, at least partly, with a go/no-go task (Luijten et al., 2011; Mashhoon, Betts, Farmer, & Lukas, 2018). In short, in a standard go/no-go task, go stimuli and no-go stimuli are sequentially presented in random order. Go stimuli require a simple response (i.e., space-bar) and no-go stimuli require a response to be withheld (Wessel, 2017). The relevant outcome variable is the proportion of inhibitions (number of successful inhibitions in no-go trials, divided by the number of no-go trials). Although this measure is plausibly affected by response tendencies, it is thought to reflect (at least partly) inhibitory control (Wessel, 2017).

In the go/no-go task implementation of Luijten et al. (Luijten et al., 2011), smoking related go and no-go stimuli were included in addition to neutral go/no-go stimuli. Results showed that

smokers relative to nonsmokers presented with an overall reduced proportion of inhibitions in nogo trials. However, stimulus type (neutral/smoking related) did not moderate the relationship. In other words, results did not confirm that individuals that smoke relative to those that do not smoke presented with a more pronounced deficit of inhibitory control in the smoking context relative to a nonsmoking context.

Though the aforementioned result may indicate that reward context does not moderate the relationship between smoker status and inhibitory control, there are alternative explanations. For instance, noting that a valid go/no-go task is a relatively fast-paced task, it may have been problematic that in one experimental block both reward-related pictures and neutral pictures were randomly interleaved. This way, no relatively consistent and predictable reward context was created, which may have negatively impacted the ecological validity of the paradigm and effect size. Specifically, in the paradigm as implemented by Luijten et al. (Luijten et al., 2011), participants could not know whether a given trial would be reward related or not and response bias to reward related stimuli may be reduced. Houben et al., 2014 carried out a relatively similar task (Stop Signal Task - SST) with a more stable reward context; stimulus type (neutral/reward related) was separated across two conditions (a reward related condition and neutral condition). This latter study supports the notion that inhibitory control (in this case in individuals with obesity) varied as a function of reward context. One may expect the same applies to nicotine addiction, because inhibitory deficits seem most pronounced in a context of reward.

The main aim of the current study was to assess the relation between nicotine addiction and inhibitory control in contexts that differed in terms of reward. We employed a go/no-go task modeled after version 4 as described in Wessel et al. (Wessel, 2017). The task consisted of a neutral, smoking (smoking related pictures) and money (pictures of money) condition. The following hypotheses were postulated. Firstly, we hypothesized that individuals that smoke relative to people that do not smoke would present with reduced proportion of inhibitions in the smoking condition relative to the neutral condition. Secondly, we hypothesized that this would also apply for the money condition relative to the neutral would be mirrored by speeded responses to go trials.

Materials and Methods

Participants

We used convenience sampling, and participants were recruited via advertisements via various social media (most predominantly facebook). The advertisements included a link to the website that included the information letter and link to provide informed consent and the subsequent link to the experiment. The final sample consisted of seventy-eight participants (55% male, 45% female). The

mean age of the group that consists of individuals that smoke (n=43) was 28 years old (range 18-44, median = 27, SD=6), and for the individuals that do not smoke (n=35) the mean age was 23 years old (range 18-33, median = 23, SD=3). Participants could not participate if they were using drugs (except nicotine) within seven days prior to participating. Participants had to be between 18-50 years old and healthy (by self-report). Participants could only be included in the smoker group in case of smoking approximately ten or more cigarettes per day in the past year. This inclusion criterion was based on several studies that have used the same or similar criterion (Ashare & Jr, 2012; Luijten et al., 2011; Powell, Tait, & Lessiter, 2002). The level of craving as assessed with the tobacco craving questionnaire, was overall relatively high (median = 72, SD = 14.9). Participants could be included in the non-smokers group if they never smoked on a daily basis and if they did not smoke at all in the three months prior to participation (Potter, Bucci, & Newhouse, 2012). Participants participated voluntarily and did not receive a monetary compensation. The study was approved by the Research Ethics Committee of the Eötvös Loránd University (ELTE) and conducted following the declaration of Helsinki.

Materials and Procedure

Tobacco Craving Questionnaire (TCQ)

The short version of TCQ instrument (*Heishman, Singleton, & Pickworth, 2008*) assesses tobacco craving across four subscales (emotionality, expectancy, compulsivity, and purposefulness). Each of the four scales is measured with three items. Items are scored on a likert scale ranging from 1 (strongly disagree) to 7 (strongly agree). The final craving score is computed as the sum of all item scores. The final craving score can range from 12 to 84. Higher scores reflects stronger craving. The subscales are known to show good reliability (Cronbach's alpha: 0.90, 0.89, 0.78 and 0.69, respectively) (Heishman et al., 2008).

Go/no-go task

The go/no-go task was employed to assess inhibitory control and was modeled after the go/no-go task (version 4) as described in Wessel et al. (Wessel, 2017). Each condition started with the instruction followed by a fixation dot which was presented for 2000 ms. A single trial in each condition started with a go or no/go stimulus presented centrally for 150 ms, followed by a fixation dot presented for 1350 ms. Hence, the trial-to-trial interval was 1500 ms. Go stimuli (400x400 pixels) required a space-bar response and no-go stimuli (500x500 pixels) were similar to go stimuli but included a white border and required a response to be withheld. Each participant completed three separate conditions. In each trial in the neutral condition, the target stimulus (go or no-go stimulus) was one of four possible color filled squares. In each trial in the smoking condition, the target

stimulus was one of four possible pictures related to smoking (figure 1), and for the money condition, target stimuli consisted of one of four possible pictures of money. The pictures were in the public domain, and royalty free to use, download, copy modify and adapt. Trials and condition order were randomized. For each condition, the probabilities of go and no-go stimuli were .8 and .2, respectively. The total number of trials per condition was 40. The conditions were preceded by a practice block consisting of 12 trials in which target stimuli were gray squares. Inhibitory performance was indexed by the proportion of inhibitions to no-go trials. In other words, the proportion of inhibition was calculated as the number of successful non-responses to no-go stimuli divided by the total number of no-go trials. Response time was based on go-trials only, and fast/accidental (<150 ms) and delayed responses (>1500 ms) were discarded from the analyses.



Figure 1. Schematic representation of two trials in the smoking-related condition of the go/no-go task

Procedure

The assessments were implemented online, via Psytoolkit (Stoet, 2010, 2017). All participants were fully informed and signed the digital informed consent paper prior to participation. Subsequently, participants provided demographic information and performed the go/no-go task. The average total duration of the experiment was approximately 15 minutes.

Statistical Analyses

The sample size was determined using G*power (Erdfelder, FAul, Buchner, & Lang, 2009; Faul, Erdfelder, Lang, & Buchner, 2007) based on results provided in Luijten et al. (Luijten et al., 2011). Specifically, the main effect (η p2) of group regarding accuracy on no go trials (relevant index of inhibitory control), was estimated via F*(df1)/(F*(df2) + (df1)) (Lakens, 2013). η p2 was estimated to be 0.098 which translates to an f effect size of 0.33 (Erdfelder et al., 2009; Faul et al., 2007). With power set at 0.8, and alpha at 0.05, the optimal sample should be approximately n=76. In total 154 individuals expressed initial interest in participating (reflected by the number of clicks on the experiment link). However, the final sample size (n= 78) was lower due to either not meeting the inclusion criteria or due to not completing the experiment. In addition, we excluded participants (n=4) that had an omission rate that exceeded 3 standard deviations from the mean omission rate. Effectively those participants were excluded with over 40% omissions as this can indicate task non-adherence. For remaining analyses repeated measures ANCOVAs were performed, and we controlled for age differences. Specifically, age was included as a covariate.

Results

Smoking status and inhibitory control across conditions.

As is evident from table 1 and figure 2, the group of individuals that smoke relative to those that do not smoke showed a lower proportion of inhibitions in the smoking condition relative to the neutral condition. Specifically, this group x condition interaction was significant with F(1,75) = 22.08, P <.001, partial $\eta 2 = .23$. Similarly, smokers relative to nonsmokers also showed a reduced proportion of inhibitions in the money condition relative to the neutral condition. This group x condition interaction was significant with F(1,75) = 7.31, P = .008, partial $\eta 2 = .09$. The reductions in inhibitory performance were mirrored by reductions in response time, described in table 2, and visually depicted in figure 3. Specifically, smokers relative to nonsmokers showed reduced response time in both the smoking condition and the money condition relative to the neutral condition. These group x condition interactions were significant, respectively F(1,75) = 25.40, P < .001, partial $\eta 2 = .25$ and F(1,75) = 25.67, P < .001, partial $\eta 2 = .26$. With respect to the proportion of omissions, there was no significant group x condition interaction (for both, partial $\eta 2 < .003$).

Table 1. Proportion of inhibitions to no-go trials for smokers and nonsmokers in the neutral, smoking, and money condition.

Condition	Group	Mean	Std. Deviation
neutral	smokers	0.85	0.19
	nonsmokers	0.69	0.24
smoking	smokers	0.45	0.27
	nonsmokers	0.70	0.18
money	smokers	0.56	0.24

nonsmokers	0.64	0.25

Note: Proportion of inhibitions: the number of successful non-responses to no-go stimuli divided by the total number of no-go trials.

Table 2. Mean response time in milliseconds in go trials for smokers and nonsmokers in the neutral, smoking, and money condition.

Condition	Group	Mean	Std. Deviation
neutral	smokers	570	165
	nonsmokers	390	68
smoking	smokers	355	74
	nonsmokers	422	65
money	smokers	373	71
	nonsmokers	423	74

Table 3. Proportion of omissions in go trials for smokers and nonsmokers in the neutral, smoking, and money condition.



Figure 2. Mean proportion of inhibitions (the number of successful non-responses to no-go stimuli divided by the total number of no-go trials) for the smokers and nonsmokers group across the neutral, smoking, and money condition. Error bars indicate +/- 2 standard errors from the mean.



Figure 3. Mean reaction time (RT) for both smokers and nonsmokers groups across the neutral, smoking, and money condition. Error bars indicate +/- 2 standard errors from the mean.

Inhibitory performance and response speed in the neutral, smoking and money context as a function of craving in smokers: an ad-hoc exploratory analysis

Craving was associated with a larger reduction of the proportion of inhibitions in the smoking relative to the neutral condition, as well as in the money condition relative to the neutral condition (respectively, F(1,40) = 29.51, P < 0.001, $\eta p2 = 0.425$; F(1,40) = 9.21, P = 0.004, $\eta p2 = 0.187$). Effects are visualized in figure 4. Please note that to visualize the direction of effects, craving was transformed to a categorical variable using median split.



Figure 4. Proportion of inhibitions as a function of craving across conditions.

With respect to response time to go-stimuli, the craving x condition interactions were also significant. Specifically, as visualized in figure 5, craving was associated with an reduced response time to smoking related stimuli and money stimuli relative to neutral stimuli, F(1,40) = 43.35, P < 0.001, $\eta_p^2 = 0.520$; and F(1,40) = 36.16, P < 0.001, $\eta_p^2 = 0.475$, respectively.



Figure 5. Mean response time as a function of craving across conditions.

It should be noted that the distribution of craving scores showed a significant negative skew, with skewness = -1.720. Although it is known that analyses of variance are relatively robust against deviations from normality, we rerun the above analyses on normalized data using a common log-transform to the inverse distribution. Specifically, we subtracted all scores from the maximum score in the distribution and subsequently applied the log-transform. The repeated measures ANCOVAs did not result in a different outcome regarding significance of the contrasts (data available in publicly available repository).

Discussion

Our results showed that individuals that smoke relative to those that do not smoke have less inhibitions in a smoking and money context relative to a neutral context. Importantly, response time analyses showed that individuals that smoke relative to those that do not smoke responded slower in the neutral context relative to the reward contexts.

It should be noted that smokers' relatively lower number of inhibitions in both reward contexts as compared to the neutral context may also be (at least in part) due to the slowed responses in the neutral context. Specifically, the response time data indicate that individuals that smoke may adopt a waiting strategy in the neutral context and engage in faster responding in both reward contexts which may at least contribute to reduced inhibitory performance. Smokers' relative speeded responses in reward contexts is congruent with IS theory (Robinson et al., 2016) as well as with Volkow's dopamine motive model, as outlined in the introduction (Volkow et al., n.d.). In short, IS theory predicts a higher approach or response bias in those individuals afflicted by nicotine addiction, to stimuli that have reward value, which in turn may contribute to poorer inhibitory performance in such context, which is exactly what our results suggest.

Importantly, the lower inhibitory performance in the money condition relative to the neutral condition in individuals that smoke may indicate a generalized reduced inhibitory control in any context of reward, or alternatively/additionally, increased response bias. Interestingly, these performance effects seem to extend to other contexts of learned rewards, such as a context of money.

Further explorative analyses regarding inhibitory control as a function of craving also seem in line with what would be expected from IS theory and the dopamine motive model. In particular, to the extent that tobacco craving is associated with heightened motivational tendencies and associated attentional bias as well as reduced inhibition towards cigarette associated stimuli, the same would be predicted for other reward related stimuli. Indeed, our results indicate that craving in smokers is associated with challenged inhibitory control and enhanced attentional bias in relation to both smoking-related cues as well as money-related cues relative to a neutral context.

It may be surprising that results of Luijten et al. (2011) did not support a reward context specific inhibitory deficit in individuals that smoke relative to individuals that do not smoke. There was quite some overlap between our study and the one from Luijten et al., 2011 in terms of the paradigm and in- and exclusion criteria. However, one important difference was the operationalization of a reward context. In contrast with our study and the one from Houben et al., 2014 (which also showed that inhibitory control varied as a function of reward context, albeit in individuals with obesity), reward context was not stable and relatedly, reward related targets were not predictable. Specifically, no separate conditions were implemented, and an experimental run included both reward-related and neutral pictures. One other important difference was that individuals in the study from Luijten et al., 2011, were not allowed to smoke within an hour prior to participation which might have induced some heightened craving which might explain the more general reduction of inhibitory control. A slightly different interpretation is that acute nicotine-induced cognitive enhancement in the present study may have induced proactive slowing; but in the reward conditions this is counteracted by the enhanced approach tendency.

Indeed, the slowed responses in the neutral condition in individuals that smoke is mirrored by a more than two-fold higher standard deviation relative to the other conditions. Though at first glance this might reflect the presence of outliers, we should emphasize that there were no extreme response times characterized as values exceeding three standard deviations from the mean. Hence, the larger response time variability indicates higher individual differences in the smokers group in terms of response speed.

It should be emphasized that the exact brain mechanism that explains the effects on inhibitory control, and speed of responding, is yet to be elucidated. Certainly, the proportion of inhibitions as assessed in the implementation of the go/no-go task in our study reflects (at least partly) inhibitory control and is associated with an electrophysiological (brain-activity) measure of inhibition (Wessel, 2017). Even so, other cognitive brain processes most plausibly contribute to the observed behavioural effects. For instance, congruent with IS theory, addicted individuals may present with enhanced attentional bias for reward-related stimuli. It follows that when

attentional bias and related approach behavior is sizeable for a no-go stimulus that is related to reward, inhibitory control is challenged. Based on performance measures alone, it is difficult, if not impossible, to disentangle the relative contributions of attentional processes from inhibitory processes. Combining the go/no-go paradigm with brain activity measures of attention and inhibitory control may address this unanswered question and provide more information on the neurophysiological and neuroanatomical correlates of involved attentional and inhibitory processes.

Another limitation concerns the stimuli used for the induction of reward-related activity. Smoking-related pictures were based on Luijten et al., 2011, and money stimuli were based on our previous report (Tsegaye, Bjørne, et al., 2020). However, though it is very plausible, based on previous studies, that reward-related activity is induced by the rewardrelated stimuli (with the possible exception of smoking-related stimuli in relation to nonsmokers) (Robinson et al., 2016; Volkow et al., 2017), we do not know the degree of activation as a function of exact stimulus. Hence, for future studies it would be interesting to complement the behavioral measures with brain activity measures of reward-processes to further scrutinize the exact role of reward-processing in the observed behavioral effects. Pertaining to the latter, one suggested interesting approach would be to implement a reward prediction violation task that includes the different reward contexts and combine it with fMRI and/or EEG. During this task reward predicting stimuli are presented which are sometimes followed by an unexpected consequence. Importantly, it has been shown using such task that reward delivery and reward prediction are driven by different neural mechanisms (Martin, Potts, Burton, & Montague, 2009). How these mechanisms operate in nicotine addiction across different conditions of reward and drive behavioral performance remains an open question.

A somewhat related limitation of the current study is that the conditions were not matched on stimulus complexity and the stimuli in the reward contexts may be viewed a more complex, thus one might argue that our observed effects reflect at least partly the interaction between smoker status and stimulus complexity. However, the response time results contrast such notion. To elaborate, significantly higher stimulus complexity would yield increased response times. Yet, no increased response time in the reward contexts relative to the neutral context was observed. In fact, for individuals that smoke, response times decreased significantly in the reward contexts. Taken together, it is not plausible that the observed effects are due to the interaction of smoker status with stimulus complexity. The age restriction could also be seen as a limitation. The main reason for the age limit was based on recent studies that suggest inhibition-mechanisms might be affected by aging, especially around and over the age of 60 (Hsu & Hsieh, 2021; Lin & Cheng, 2020). To avoid any such potential age-related effects, we employed a strict age restriction. Of course, one may argue that as age progresses in individuals that smoke, their exposure to nicotine and associations also increases. That could be the case, but then the observed group x condition effects would most plausibly be even more (not less) pronounced.

Lastly, one might argue that the online implementation of the study is a limitation. It has been questioned whether data can be acquired reliably in online cognitive psychological experiments that require fast split-second logging of event durations and response times. However, recent studies have shown that online experiments, including those that have stringent timing-criteria, can record valid and reliable data comparable to data acquired in labs using dedicated hardware and software (Hilbig, 2016; Kim, Gabriel, & Gygax, 2019). Similarly and specific for the Psytoolkit platform, results of previous studies indicate that experiments with stringent timing criteria for logging data can generate reliable and valid data (Kim et al., 2019; Stoet, 2017). Of course, that does not mean that online experiments do not include any challenges. Individuals performing an online experiment cannot ask for additional information as easy as in a lab environment, and task understanding and adherence may be challenged. In our study, we took this into account and used the proportion of omissions as an index of task To elaborate, omissions to go stimuli are quite rare in a fast-paced go/no-go task adherence. (Mashhoon et al., 2018), and hence we excluded those participants who displayed a relatively high rate of omissions. Lastly, we believe that the online format effectively increased ecological validity while reducing common biases. Pertaining to the latter, desirability and acquiescence bias is deemed minimal due the anonymous nature and due to the implemented objective measures together with lack of information about how the constructs are reflected in actual responses. Order bias may affect condition effects; however, any potential/plausible order effects are controlled for via counterbalancing. Certainly, sampling bias is a challenge in almost any type of empirical research including online studies. However, we tried to minimize sampling bias by means of advertising across a wide variety of different social media channels, and not focus on one isolated social media group.

Our results suggest that individuals that smoke as compared to nonsmokers have reduced inhibitory performance in a smoking context which may extend to another learned reward contexts. The reduced inhibitory performance may be due to the speeded responses in these conditions, indicating increased reward-related response bias. Taken together, the results seem consistent with IS theory and cross-sensitization. In terms of clinical implications, our results might imply that challenged inhibitory control in pharmacological addiction and craving may extend to other reward contexts. This may be considered in treatment approaches.

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CHAPTER SIX

GENERAL DISCUSSION

The main overarching goal was to gain more insight into the role and mechanism of attention and inhibitory control in obesity. Previous studies have shown higher BMI is associated with poor inhibitory control, particularly in contexts with palatable food compared to a neutral context (Houben et al., 2014a). This result seems in line with studies showing that food related stimuli elicit activation in ventrolateral prefrontal cortex in obese individuals compared to healthy controls (Batterink et al., 2010). However, the question remained whether the inhibitory deficit is a specific deficit related to palatable food or perhaps a general deficit of executive control in any reward context. And whether the aforementioned inhibitory deficit can be explained (at least in part) by attentional mechanisms. In our projects, these limitations were largely addressed. In Chapter 2, we addressed the basic psychological determinants of obesity; In Chapter 3, we examined the role of visuospatial attention in contexts that differ in terms of anticipated rewards. In Chapter 4, we investigated the role of inhibitory control across conditions that differ in terms of anticipated reward. In addition, we examined the role of maladaptive eating behaviors (uncontrolled and emotional eating), and stress. In Chapter 5, we examined the role of inhibitory control in relation to nicotine addiction in contexts that differ in terms of reward. Finally, we discuss the overlap between obesity and pharmacological addiction in light of the aforementioned potential associations noted above and the clinical implication of our main empirical study findings.

Summary of the main results

In Chapter 2, we addressed the basic psychological determinants of obesity. We integrated previous findings and showed that individuals with obesity have greater sensitivity to and motivation for palatable foods, and that poor impulse control related to expected higher sugar content foods and negative moods has been shown to be associated with obesity and to lead to excessive intake of palatable foods. In addition, obesity has also been associated with stigma, discrimination, bullying and stereotypical portrayals in the media. In Chapter 3, we examined the role of attentional bias/disengagement across conditions that differ in terms of anticipated reward (i.e., neutral, specific, general).

Our results showed that higher BMI was associated with facilitated processing of unexpected stimuli that had general reward value but no specific reward value. Stress had no effect on the aforementioned effects. In Chapter 4, we investigated the role of inhibitory control across conditions that differ in terms of anticipated reward. Our main results showed that BMI, maladaptive eating (uncontrolled and emotional eating), and rumination were associated with reduced inhibitory control in a food context relative to the neutral context, but not in a money context compared to a neutral context. There was no evidence for a moderating role of stress. In Chapter 5, we investigated the relationship between nicotine dependence and inhibitory control in different anticipated rewards. Our main findings showed that smokers exhibited lower inhibitory control compared to non-smokers in both reward contexts compared to a neutral context.

BMI and visuospatial attention under conditions differing in terms of anticipated reward

Psychological factors, particularly attention and inhibitory control, have been suggested to play an important role in the human behavioral component associated with abnormal weight gain and drug use (Dohle, Diel, & Hofmann, 2017; Favieri, Forte, & Casagrande, 2019). A recent study suggests that poor inhibitory control is negatively affected in obesity, particularly in the context of palatable foods (Houben et al., 2014a). However, it remained to be elucidated whether attention contributes to this effect and in what context abnormal functioning of these mechanisms occurs.

In Chapter 3, we examined the relationship between BMI and visuospatial attention in contexts that differ in terms of anticipated reward. In this study, we included three conditions (i.e., food, neutral and money). In the food condition, the targets are palatable foods, similar to Houben et al. (2014). In the neutral condition the targets are gray bars. In the general condition the targets that represent novel money. In this study, our results showed that BMI did not significantly affect attentional bias in the reward conditions (food and money) compared to the neutral condition.

Disengagement was also not affected by BMI for the specific reward condition relative to the neutral condition. However, for general reward condition, BMI significantly enhanced attentional disengagement relative to the neutral condition. As discussed in the literature in chapter one, several studies suggest that higher BMI and obesity are associated with a more pronounced attentional bias towards food-related cues (Nijs et al., 2010; Werthmann et al., 2011; Yokum et al., 2011a). This effect is more pronounced in patients with binge-eating disorder (Schmitz et al., 2014). Indeed, obese individuals have a greater top-down attention bias towards food cues however, there is no difference in bottom-up attentional bias between obese and healthy weight (Kaisari et al., 2019). Similarly, a higher attentional bias for substance-related cues have produced inconsistent results, possibly due to differences in precise methodology (Nijs & Franken, 2012). It is plausible that attentional bias for a particular location (as opposed to stimulus characteristics) is not influenced by BMI. One of the previous studies used a go/no-go task with food-related stimuli found that obese and health weight participants showed bias in approaching food-related stimuli (Loeber et al., 2012).

In our study, higher BMI was associated with a faster response to unexpected stimuli in the money condition (but not in the food condition) compared to the neutral condition. However, in this study we did not compare individuals with obesity to individuals who are lean, and we only looked at a narrow range of BMI scores. Although there was no effect of BMI on attentional bias toward expected reward stimuli, susceptibility to unexpected reward related stimuli was found to be increased with higher BMI. This, in turn is consistent with the findings from the go/no-go task paradigm, in which higher BMI was associated with decreased inhibitory control, which may be explained in part by an increased susceptibility to stop-trials, which carry increased unpredictability. More specifically, in the stop signal task, the prepotent response to a reward stimulus must be inhibited after a stop stimulus. In this case, the inhibition requirement contradicts primary task requirement (to respond as quickly and accurately as possible to the go stimuli). Notably, both inhibition and disengagement of attention processes are triggered by abrupt changes in task demands, and are driven by overlapping neurocircuits (Logemann et al., 2017). Importantly, it could be argued that the deficit in inhibitory control measured by the SSRT in the SST is due in part to an increased attentional bias toward the primary go stimulus when the stimulus is a reward (i.e., food). In the simplest notion, increased attentional bias toward the Go stimulus would make it more difficult to withhold the prepotent response when the Go stimulus is followed by a stop signal. In the visuospatial cueing task, the disengagement of attention is congruent with the requirement to respond as quickly and accurately as possible to the unattended target. In this sense, inhibition and disengagement may be speeded with increased perceived reward value of targets in the visuospatial

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cueing task, but negatively affected in the stop signal task (or go/no-go task). It should be noted that there were some extreme values (defined as three times the interquartile range) with respect to bias (n = 2) and disengagement (n = 4). In view of the stringent exclusion criteria (incorrect responses were excluded), there is no reason to believe that these were erroneous data. Nevertheless, excluding the extreme cases did not change the significance of the BMI x condition (neutral/money) interaction with respect to disengagement. In summary, in this empirical study higher BMI is associated with facilitated processing of unexpected stimuli that have general reward value.

Inhibitory control, BMI and smoking across different rewarding context

In terms of inhibitory control and BMI, our main findings in chapter 4 revealed that a high BMI is associated with lower inhibitory control in a food context compared to a neutral. However, the relationship between BMI and inhibitory control in the money context was not statistically significant when compared to the neutral context. As previously stated, the findings are consistent with previous findings (Batterink et al., 2010; Houben et al., 2014), as well as previous resports that increased BMI is associated with altered sensitivity to food-related stimuli (Hendrikse et al., 2015). Similar to study two, our third study on chapter 5 smokers revealed that they had lower inhibitory control in specific context compared to a neutral. It should be noted that smokers' relatively lower number of inhibitions in both reward contexts as compared to the neutral context may also be (at least in part) due to the slowed responses in the neutral context.

Specifically, the response time data indicate that smokers may adopt a waiting strategy in the neutral context and engage in faster responding in both reward contexts which may at least contribute to reduced inhibitory performance. Previous studies have suggested overlap between obesity and (pharmacological) addiction, both in terms of reward processing related activity in contexts of reward. For instance, a recent review study showed that there is an overlapping between obesity and addiction to the brain mechanism in the context of rewarding (Nora D Volkow, Wise, & Baler, 2017). Our results are consistent with the incentive salience theory (Robinson et al., 2016b). In short, incentive sensitization theory predicts a higher approach or response bias in (nicotine) addicted individuals to stimuli that have reward value, which in turn may contribute to poorer inhibitory performance in such context. This model postulates that repeated pairings of reward from food intake and cues that predict impending food intake result in a hyper-responsivity of dopamin-based reward circuitry to food cues, contributing to overeating. The model suggests that abnormalities in responsivity of the dopamine-based reward circuitry could contribute to an enhanced attentional bias and thus to elevated approach tendencies toward food and food cues (Volkow, Wise, & Baler, 2017).

In addition, studies have reported that high BMI is associated with differential striatal functioning that drives reward processing and this pattern overlaps with the one associated with different drug addiction (Volkow, Wise, & Baler, 2017). Importantly, smokers' lower inhibitory performance in the money condition relative to the neutral condition may indicate a generalized reduced inhibitory control in any context of reward, or alternatively/additionally, increased response bias. Interestingly, as money is a learned reinforcer (in contrast to food), these performance effects seem to extend to contexts of learned rewards. Thought smokers and individuals with relatively high BMI overlap in terms of reduced inhibitory control in a specific reward context (cigarette stimuli and food stimuli respectively), they also differ. Specifically, results in chapter 3 and 4 did not support that the reduced inhibitory control in individuals with relatively high BMI extends to a different reward context operationalized by money.

Moderators of the relationship between BMI and Executive functions

Respect to the moderation effect on relation between BMI and visuospatial (i.e., bias and disengagement), in chapter 3 our results showed that stress did not affect the aforementioned effects. Similarly, stress did not affect in chapter 4 related to inhibitory control. This might seem to contrast previous studies on obesity that have suggested a moderating role of stress (Nederkoorn et al., 2006). However, our study we did not specifically focus on obesity, and we did not induce acute stress but assessed self-reported stress experience via the DASS-21 questionnaire which might not interact with BMI with respect to attentional/inhibitory control. Hence, we assessed relatively prolonged stress and it has been reported that the association between chronic stress and unrestrained food ingestion varies as a function of the level of impulsive risk-taking (Mason, Schleicher, Coccia, Epel, & Aschbacher, 2018). Indeed, previous studies have shown a complex relation between stress and food intake. Although acute stress may affect food intake (Rutters, Nieuwenhuizen, Lemmens, Born, & Westerterp-Plantenga, 2009). In our books review chapter, include this thesis on chapter 2, stress may enhance the association between BMI and behavioral control and palatable food may provide a negative reinforcement in a context of stress. Specifically, chronic stress results in elevated cortisol and insulin levels, and this may in part promote preference towards high content of fat and sugar food (Adam & Epel, 2007). Indeed, a very recent study has suggested that the relation between chronic stress and food intake may depend on the degree of impulsive-risk taking tendencies (Mason et al., 2018).

Trait mindfulness seems to have a moderating role, however cognitive functions is not the only general capacity of mindfulness related function (Anicha, Ode, Moeller, & Robinson, 2011). In chapter 3 our results showed that trait mindfulness did not affect the relation between BMI and

executive function across the condition. Previous studies have shown that mindfulness training improves executive control (Gallant, 2016; Sahdra et al., 2011), which in turn may promote weight loss. Indeed, with respect to obesity and weight-loss some systematic reviews have indicated that mindfulness-based training may promote weight loss (Carrière, Khoury, Günak, & Knäuper, 2018; Dunn et al., 2018), but others have reported inconsistent findings (Rogers, Ferrari, Mosely, Lang, & Brennan, 2017; Ruffault et al., 2017). The main issue is that there are numerous mindfulness-based methods, which may all differ in terms of rendered effects. In fact, a recent review suggests that specifically mindful eating, not mindfulness, is associated with subsequent weight loss (Dunn et al., 2018). There is some support for a direct relation between a mindful state and executive control. Specifically, enhanced mindfulness has been associated with generally improved attention (Sibalis et al., 2019), and improved inhibitory control (Gallant, 2016). To the best of our knowledge, the relation between mindfulness and executive mechanisms has not yet been thoroughly investigated in relation to BMI in contexts of reward. In chapter 4, we investigated eating behaviors may affect inhibitory control and the relation between BMI and inhibitory control, especially in a rewarding context. Our results showed that uncontrolled eating and emotional eating significantly associated with challenged inhibitory control in the food relative condition to the neutral context. But were not significant for the money relative condition. These results line with previous reports (Svaldi et al., 2014), maladaptive eating patterns that promote overconsumption of palatable food (uncontrolled eating and emotional eating) were associated with challenged inhibitory control in the food context relative to the neutral context.

Limitation of studies

This dissertation, just like any other empirical studies has limitations. Most of these limitations listed below.

First, the operationalization of the general reward condition. In our three empirical studies including in this dissertation, we used similar general reward stimuli (i.e., money). On study 1 and study 2, for the specific condition four palatable food pictures and in study three smoking related pictures used for specific condition. One important difference between these two conditions is the type of reinforcer. Food can be regarded as a primary reward/ reinforcer whereas money becomes a secondary reinforcer via a conditioning process over time. However, although some difference exist with respect to the exact brain regions that are activated subsequent to processing pictures of food and money, both types of stimuli have been shown to activates the primary brain circuitry responsible for reward processing and neutral processing of these stimuli has been suggested to be modulated by metabolic state. Second, the stimuli were not matched on salience. Thus, it might be

that the enhanced variability in the specific reward condition may be due to stimulus differences across conditions (i.e., salience).

Other limitation specifically, in study 1 and 2, we focused on the relation between BMI and executive control and in these two empirical studies height and weight were assessed by self-report, might affected by self-representation bias. Although results are relevant in relation to obesity, appropriate nuance should be applied when generalizing our results. Future research should include more participants the BMI equal or greater than 30 this might reduce lack of power, due to the small sample size of experimental group. In our three empirical studies the total sample size relatively small (i.e., n = 87 in first study, n = 46 in the second study and n = 78 in the third study). Our three empirical studies were employed online. This improves feasibility with respect to data acquisition but provides a less controlled environment as opposed to conducting the study in a lab. This also explains the relatively high attrition rate and potentially higher response variability. And it could be argued that performing the tree conditions of the visuospatial cueing task and Go/no-go task is relatively taxing and may induce fatigue which may affect results and cause for small sample size. However, in contrast to Houben et al. (2014), the induction of fatigue as a function of time could not have negatively impacted the validity of our data as we employed counterbalancing across individuals. However, it should be emphasized that recent studies consistently show that online cognitive psychological experiments can generate reliable and valid data, comparable to those conducted in a controlled lab environment (Hilbig, 2016; Kim et al., 2019). Future studies are needed to systematically examine in more control lab environment and successfully assess weight group differences. However, we controlled for this potential issue and excluded those participants that did not respond consistently to go trials, indicated by the proportion of omissions to those trials specifically, on experiment 2 and 3. With respect to our VSC task in study 1 chapter 3, our participants quickly learned that there are only two possible target locations (valid and invalid) which might reduce the effect of cueing on response times. The go/no-go task the frequent trials of go stimuli out put partly interpreting attentional bias but in our chapter 3 we implement the posner paradigm also to asses attentional bias. Overall, behavioral effects do not give a clear view regarding the neuroanatomical correlates that drive the observed effects. Further research is needed to systematically examine combined both behavioral measurements and functional magnetic resonance imaging (fMRI) to more understand and replicated in both environments' lab and online.

Conclusions

To conclude, the present dissertation yielded novel and theoretically relevant results. To the best of our knowledge in our studies the first time we addressed important previous limitations and included

the operationalization of money as reward condition. In sum, the results of the current dissertation showed that individuals with obesity are associated with a specific reduction of inhibitory control when perceiving palatable food. However, do not indicate that individuals with obesity are associated reduction of inhibitory control extends to a different reward related context operationalized by money pictures. In addition, higher BMI is associated with facilitated processing of unexpected stimuli that have general reward value. Smokers as compared to nonsmokers have reduced inhibitory performance in a smoking context which extends to a general reward context. The reduced inhibitory performance may be due the speeded responses in these conditions, indicating increased reward related response bias. Similar to smokers, high BMI individuals to compared to health weight have reduced inhibitory performance in a food context but did not extends to money context reward like smokers. Overall, our findings contribute to a better understanding of the theoretical role of executive function in obesity and drug addiction (i.e., smoking), as well as to the development of interventions that focus on strengthening executive function and integrating it with other psychological factors.

Clinical implications

Our results imply that obesity is characterized by reduced inhibitory control when perceiving palatable food, combined with heightened sensitivity for unexpected reward related stimuli. In contrast to pharmacological addiction, specifically nicotine addiction, obesity does not seem to be characterized by cross sensitization. In other words, though challenged inhibitory control I pharmacological addiction seems to extend to other reward-contexts, obesity associated challenged inhibitory control seems restricted to a palatable food context. This may be important for clinical intervention aimed at weight reduction, to specifically focus on increasing inhibition ability to food related stimuli.

A growing body of research indicates that computer inhibitory training is one of the most promising strategies for changing eating habits and losing weight (Adams, Lawrence, Verbruggen, & Chambers, 2017; Houben & Jansen, 2011; Verbeken, Braet, Naets, Houben, & Boendermaker, 2018; Yang et al., 2019). Specifically, specific training of inhibition to food cues, in particular could help reduce palatable food consumption as well as increased craving for healthy foods (Boswell, Sun, Suzuki, & Kober, 2018). A recent study shows that by administering a food specific inhibition training to address food related impulsivity among patients with being eating seemed to increase inhibitory control (Eichen, Matheson, Appleton-knapp, & Boutelle, 2017) (Elisabeth et al., 2017). Indeed, strengthening inhibitory control can help obese individuals regain control over the consumption of high calories and energy content foods, making obese individuals less vulnerable to the temptations of palatable food and higher restrict food intake (Houben & Jansen, 2011). Further, inhibitory control training particularly beneficial to individuals who have difficulties in implementing healthy eating behaviors. For instance, individuals diagnosed with an eating disorder, binge eating disorder (BED) inhibitory training helps reduce weight, decrease binge eating and improve inhibitory control (Elisabeth et al., 2017; Preuss, Schnicker, & Legenbauer, 2017). Mostly, food specific computerized tasks such as stop-signal and Go/no-go tasks main aim are to increase the ability to delay, stop and change a behavioral response specifically to palatable foods cue by practicing the inhibition of a pre-potent behavior (Jones et al., 2016). Indeed, repeated response inhibition also affects the motivational component of impulsivity by leading to a devaluation of the appetitive cue (Elisabeth et al., 2017; Jones et al., 2016).

In the context of obesity, attention bias modification training works by training attention away from appetitive food cues and towards control alternatives (Kemps, Tiggemann, Orr, & Grear, 2014). Indeed, attention bias modification training is designed to change attentional processing via consistent and systematic practice in diverting attention away from unhealthy food cues, directing attention instead towards healthy food cues (Kemps et al., 2014). Hence, attention bias modification training was effective at changing attention bias to food cues (i.e., decrease obese individuals attention bias towards palatable food cues) (Kemps et al., 2014; Yang, Shields, & Chen, 2019). Further, in clinical samples also reduce reward and attention region response to high calorie food cues, reduced body fat and palatability rating of high calorie dense foods (Preuss et al., 2017; Stice, Yokum, Veling, Kemps, & Lawrence, 2017). Inhibition training and attention bias modification training can produce beneficial changes in eating behavior and lose weight. However, these intervention methods moderated by the food novelty and the training tasks types.

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DECLARATION FORM for disclosure of a doctoral dissertation

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Name of the author: Afework Tsegaye Abebe

MTMT-identifier: 10071854

Title and subtitle of the doctoral dissertation: The role of mechanisms of inhibition and attention in obesity.

DOI-identifier⁸⁷: 10.15476/ELTE.2022.011

Name of the doctoral school: Doctoral School of Psychology

Name of the doctoral programme: Clinical Psychology and Addiction

Name and scientific degree of the supervisor: Dr. Alexander Logemann and Dr. Gyöngyi

Kökönyei

Workplace of the supervisor: Eötvös Loránd University

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