COGNITIVE CONTROL IN YOUTH OBESITY

By

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

BMI	Body Mass Index
IGT	Iowa Gambling Task
RCT	Risky Choice Task
RGT	Risky-Gains Task
CGT	Cambridge Gambling Task
RLT	Randomised Lottery Task
EEfRT	Effort Expenditure for Rewards Task
GET	Grip Effort Task
CST	Concurrent Schedules Task
FCT	Food Choice Task
NAcc	Nucleus accumbens
vmPFC	Ventromedial prefrontal cortex
mOFC	Medial orbitofrontal cortex
OFC	Orbitofrontal cortex
dlPFC	Dorsolateral prefrontal cortex

ABSTRACT

Overweight and obesity, the excess accumulation of adipose tissue, have become increasingly prevalent in youth over the past three decades. This rise represents a substantial public health-burden because excess weight in youth confers an increased lifetime risk for a number of diseases including hypertension, diabetes, polycystic ovarian syndrome and various types of cancer. Neuroscience models postulate that the modern lifestyle with its drastic changes in what and how we eat has moved eating behaviour outside exclusively homeostatic motives, bringing to attention the importance of decision-making abilities in making healthy food choices. In the modern food environment, where the appeal and size of food products is maximized, individual differences in decision-making abilities are likely to predict food preferences and outcomes in weight loss treatment.

This thesis aimed to better understand the neurobehavioural systems that underlie decision-making (i.e., interoception, goal-monitoring and reward-impulsive systems) in overweight and obesity (Aim 1), the impact of weight loss on these systems (Aim 2), and the contribution of decision-making skills to treatment outcome in youth (Aim 3). To achieve Aim 1, I have conducted two Studies: in Study 1, cognitive tasks and functional Magnetic Resonance Imaging (fMRI) were used to cross-sectionally examine to what extent cognitive measures of decision-making under ambiguity and risk are associated with BMI. In Study 2, fMRI was used to cross-sectionally examine whether youth obesity is associated with alterations of insula function (the key brain region for interoception) as indexed by differential correlations between insula activation and perception of interoceptive feedback versus external food cues. To achieve Aim 2, I have conducted Study 3, in which fMRI was used to longitudinally examine if treatment-related weight loss is associated with significant changes in brain activation during risk-based decision-making. To achieve Aim 3, I have

conducted Study 4, in which cognitive tasks were used to longitudinally examine whether effort-based decision-making predicts attrition in a weight loss intervention.

Study 1 examined a sample of 73 young adults (age range: 18-24; BMI range: 18-37) including participants with healthy weight (n=26), overweight (n=26) and obesity (n=21). Participants performed two complementary versions of the Iowa Gambling Task (IGT) and the Risky Choice Task (RCT). The IGT measures decision-making under ambiguity and the RCT measures decision-making under risk. Multiple regression models were applied to examine the association between decision-making and BMI. Study 2 examined a sample of 54 adolescents (age range: 12–18; BMI range: 14-36) with excess weight (n=22) and healthy weight (n=32). Participants performed the Risky-Gains Task (RGT) inside an fMRI scanner, and completed the Heartbeat Perception Task and the Dutch Eating Behaviour Questionnaire outside the scanner. Study 3 examined a sample of 16 adolescents with excess weight (age range: 12-18; BMI range: 22-36). Participants performed the Risky-Gains Task during fMRI both before and after a 12-week weight loss intervention. Study 4 examined a sample of 42 young adults with excess weight (age range: 18-24; BMI range: 25-37). Participants performed the Effort Expenditure for Rewards Task (EEfRT) before undertaking a 12-week weight loss intervention. Logistic regression models were applied to examine to what extent effort-based decision-making predicts attrition in the weight loss intervention.

The findings of this thesis provide evidence that youth obesity is associated with less ability to encode the risk associated with disadvantageous decision-making options. This abnormal risk processing is associated with disrupted tuning of the insula system towards bodily feedback. In obesity, the insula system is tuned towards external eating and not towards interoceptive input during risk-based decision-making. This can be due to pre-existing characteristics or to obesity related neurocognitive adaptations. The findings of this thesis also revealed that this insula deficit recovers following successful weight and adiposity

loss. Furthermore, this thesis links attrition in weight loss intervention to effort-based decision-making. Less willingness to work for uncertain rewards may account for the difficulty experienced by dieters in adhering to treatment.

GENERAL DECLARATION

In accordance with Monash University Doctorate Regulation 17.2 Doctor of Philosophy and Research Master's regulations the following declarations are made:

I hereby declare that this thesis contains no material which has been accepted for the award of any other degree or diploma at any university or equivalent institution and that, to the best of my knowledge and belief, this thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis.

This thesis includes two original papers published and two original paper submitted for publication in peer reviewed journals. The core theme of the thesis is cognitive control in youth obesity. The ideas, development and writing up of all the papers in the thesis were the principal responsibility of myself, Fernanda Gomes da Mata, working within the School of Psychological Sciences under the supervision of Associate Professor Antonio Verdejo-Garcia, Professor Murat Yucel, Professor Helen Truby and Professor Julie Stout.

The inclusion of co-authors reflects the fact that the work came from active collaboration between researchers and acknowledges input into team-based research.

In the case of Chapters 4, 5, 6 and 7 my contribution to the work involved the following:

Thesis Chapter	Publication Title	Status	Nature and % of student contribution	Co-author name(s) Nature and % of Co-author's contribution*	Co-author(s), Monash student Y/N*
4	Body Mass Index is associated with decision-making under ambiguity and risk in young adults	Under Review (*Journal of Youth and Adolescence/ISSN :1573-6601)*	80% (Study conceptualisation, study design, data collection and analysis, interpretation of results and manuscript preparation)	H. Truby, J. Stout, M. Yucel and A. Verdejo-Garcia, manuscript preparation	No
5	Insula tuning towards external eating versus interoceptive input in	Published (*Appetite/ISSN:0195-6663*)	60% (Data analysis, interpretation of results and manuscript preparation)	J. Verdejo-Roman, data collection and analysis C. Soriano-Mas and A. Verdejo-Garcia,	No

	adolescents with overweight and obesity			manuscript preparation	
6	Changes in choice evoked brain activations after a weight loss intervention in adolescents	Published (*Appetite/ISSN:0195-6663*)	60% (Data analysis, interpretation of results and manuscript preparation)	J. Verdejo-Roman, data collection and analysis C. Soriano-Mas, M. Yucel and A. Verdejo-Garcia, manuscript preparation	No
7	Reduced willingness to expend effort for reward in obesity: Link to weight loss outcomes	Under Review *(International Journal of Obesity/ISSN: 0307-0565)*	80% (Study conceptualisation, study design, data collection and analysis, interpretation of results and manuscript preparation)	A. Kwok, data collection M. Treadway, H. Truby, J. Stout, M. Yucel and A. Verdejo-Garcia, manuscript preparation	Yes (Alastair Kwok)

I have renumbered sections of submitted or published papers in order to generate a consistent presentation within the thesis.

Student signature: Fernanda Mata **Date:** 05/09/2016

The undersigned hereby certify that the above declaration correctly reflects the nature and extent of the student's and co-authors' contributions to this work. In instances where I am not the responsible author I have consulted with the responsible author to agree on the respective contributions of the authors.

Main Supervisor signature: **Date:** 05/09/2016

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PREFACE

The content of this thesis by publication discusses and reports findings from four research studies on decision-making in youth obesity, conducted using a multimodal approach consisting of neurobehavioural and psychophysiological measures, and functional magnetic resonance imaging (fMRI) implemented in both cross-sectional and longitudinal studies. The findings of this thesis indicate that a better understanding of the neurobehavioural systems underlying decision-making in overweight and obesity, the impact of weight loss on these systems, and the contribution of decision-making skills to treatment outcome may contribute to the description of cognitive and neural profiles which might benefit from treatment, and thus guide the design of novel and effective interventions.

The present thesis comprises eight chapters. Chapter One includes a narrative *literature review* on evidence from cognitive tests and neuroimaging tools that have been applied to the study of decision-making in the context of obesity. This review includes the current literature relating neurobehavioural measures of decision-making with body mass index (BMI) or eating behaviours in adolescent and adult populations with excess weight and healthy weight. Chapter Two presents the aims and hypotheses of this thesis. Chapter Three provides a description of the *general methodology* employed in the four research studies described in Chapters Four, Five, Six and Seven. This includes a more comprehensive explanation of the methodology utilised in the empirical studies than is possible in these publications, including a description of the cognitive tasks, and a comprehensive description of the weight loss interventions conducted in the research studies described in Chapters Six and Seven. Chapter Four consists of Study 1, entitled: Body mass index is associated with decision-making under ambiguity and risk in young adults. This study aimed to determine to what extent cognitive measures of decision-making under ambiguity and risk are associated with body mass index (BMI) in young adults. Chapter Five consists of Study 2, entitled: Insula tuning towards external eating versus interoceptive output in adolescents with overweight and obesity. This study aimed to examine if obesity is associated with alterations of insula function as indexed by differential correlations between insula activation and perception of interoceptive feedback versus external food cues in adolescents. Chapter Six consists of Study 3, entitled: Changes in choice evoked brain activations after a weight loss intervention in adolescents. This study aimed to examine if treatment-related success in weight loss (i.e., reductions of BMI and fat percentage) is associated with significant changes in choice evoked brain activity in adolescents with excess weight. Chapter Seven consists of Study 4, entitled: Less willingness to work for reward differentiates obesity and overweight and predicts treatment attrition in a weight loss intervention. This study aimed to compare willingness to work for rewards between young adults with healthy weight, overweight and obesity, and examine how individual differences in the willingness to work for rewards predicts adherence to weight loss treatment. Chapter Eight includes a *general discussion and conclusion* of the findings from the four empirical studies reported in the thesis, including the limitations and clinical implications of the research studies.

CHAPTER 1: LITERATURE REVIEW

1. Introduction

1.1. Relevance of decision-making mechanisms in the vulnerability to and pathophysiology of obesity.

Worldwide, the number of individuals who are overweight or obese has increased more than twofold from 857 million in 1998 to 2.1 billion in 2013 (Ogden et al., 2016). This is a major public health concern as obesity confers an increased risk for a wide range of chronic diseases, including metabolic syndrome, cardiovascular disease, diabetes type 2, asthma, obstructive sleep apnoea and several types of cancer (Cheng, Medlow, & Steinbeck, 2016; Kelsey, Zaepfel, Bjornstad, & Nadeau, 2014). Societal changes in food production, marketing and availability over the past half-century have been associated with a dramatic shift in what, when and how we eat, and have played a major role in this rising prevalence of obesity (Berthoud, 2012). Equally important to the development of obesity is how individuals respond to such environmental changes and their food-related decision-making (Rangel, 2013).

Indeed, there are a number of factors in the modern environment that may promote poor food choices. Most notably, the fact that palatable energy dense yet unhealthy foods are highly accessible and affordable is likely to make these foods more appealing than healthy foods, and thus contribute to poor food choices (Drewnowski & Darmon, 2005). Further, there are many external cues that ensure these highly palatable foods and beverages are kept in mind (Berthoud, 2007). This includes food advertisements promoting food choices that are primarily driven by the hedonic pleasure of eating rather than eating for regulatory purposes (Burger & Stice, 2014). Finally, lifestyle changes may contribute to making unhealthy food choices as eating away from home an increasingly common pastime in the lives of many individuals (Poti, Duffey, & Popkin, 2014). It has been proposed that this combination of factors has contributed to the creation of an "obesogenic" environment that overwhelms cognitive control functions relevant to self-regulation, resulting in poor food choices (Davidson & Martin, 2014). To make healthy food decisions, individuals must assign priority to healthiness, which provides long-term benefits, rather than tastiness, which can be linked to health-related risks. That is, healthy food choices require effortful control and goal-directed self-regulation of behaviour that involves cognitive control (Lim et al., 2016; Bruce et al., 2016).

The emerging field of food decision neuroscience uses cognitive neuroscience tools, such as functional resonance imaging (fMRI) and cognitive tasks, to investigate how individuals make decisions regarding food intake. A number of neuroimaging and cognitive studies have reported on the links between obesity and deficits in the decision-making system (Vainik, Dagher, Dube, & Fellows, 2013). In addition, well-controlled animal studies have demonstrated that consuming an energy-rich western diet that is high in sugar and saturated fat can promote not only obesity but also impairments in the brain systems underlying decision-making processes, such as the reward brain system (Vollbrecht, Mabrouk, Nelson, Kennedy, & Ferrario, 2016). In this vein, the modern food environment has been identified as a major contributing factor to excess fat accumulation, bringing to attention the importance of decision-making skills in prioritizing what to eat (i.e., healthy versus unhealthy food). Considering that disadvantageous food choices are associated with obesity and poor weight loss treatment outcomes, early intervention programs targeting decision-making skills may be important to guide food choices towards healthier options and lower energy intake, and to improve outcomes of weight loss and weight maintenance programs (Barlow, Reeves, McKee, Galea, & Stuckler, 2016). Unlike children, adolescents and young adults are more autonomous in their decision-making about food, and are particularly vulnerable to making disadvantageous food choices in the current environment (Lytle, Seifert, Greenstein, & McGovern, 2000).

1.2. Cognitive and neuroimaging tools as a key approach to understand decision-making alterations in obesity.

Decision-making in obesity has been examined from both a cognitive and neuroimaging perspective. Neuroscientific research has identified three key decision-making mechanisms that may be relevant to food choices in obesity: (i) *decision-making under risk,* (ii) *decision-making under ambiguity* and (iii) *effort-based decision-making*.

Neuroimaging research has suggested that at least three interrelated brain systems – (i) *reward-impulsive*, (ii) *interoceptive* and (iii) *goal-monitoring*- are involved in processing food value and regulating food consumption (Volkow & Baler, 2015). The *reward-impulsive* system encompasses the ventral striatum and the amygdala, which are involved in coding the incentive motivational values of available reinforcers (e.g. palatable food) and mediating habitual behaviours that are elicited automatically and spontaneously (Everitt & Robbins, 2005). The *interoceptive* system encompasses the insular cortex, which plays a key role in linking interoceptive signals (e.g. perception of bodily signals of hunger) with external information and reward predictions, as well as somatomotor and cingulate cortices (Craig, 2009). Further, the *goal-monitoring* system encompasses the ventromedial prefrontal cortex (vmPFC). A subregion of the vmPFC, the orbitofrontal cortex (OFC), computes a common internal currency (a common valuation scale) for different food rewards, taking into consideration their basic attributes (e.g. palatability) and the long-term goals associated with the stimuli (e.g. healthiness), and guides behaviour accordingly (Levy & Glimcher, 2012). The dorsolateral prefrontal cortex (dlPFC) is also part of the goal-monitoring system, and is required for higher-order factors, such as healthiness, to be incorporated into the vmPFC/OFC value signal (Hare, Malmaud, & Rangel, 2011).

1.3. Aims of the review

In this chapter, I will review evidence from cognitive and neuroimaging studies concerning the three above-described decision-making systems in the context of obesity. This review includes the current literature relating neurobehavioural measures of decision-making with body mass index (BMI) or eating behaviours in adolescent and adult populations with excess weight and healthy weight. Overweight and obesity are defined by a BMI between 25 and 30 kg/m^2 and BMI $\geq$ 30 kg/m^2, respectively, which results from an excess of body fat accumulation although a regular meal time structure is preserved (Raman, Smith, & Hay, 2013). Conversely, eating disorders are characterised by disturbed patterns of eating behaviour, and comprises Anorexia Nervosa, Bulimia Nervosa and Binge Eating Disorder (Smink, van Hoeken, & Hoek, 2012). For clarity, we will leave aside evidence concerning: (a) eating disorders, and (b) obesity-related comorbidities such as diabetes and hypertension. For each of the decision-making mechanisms, we will review evidence from both cognitive and neuroimaging studies in the context of obesity. We will only review evidence from studies involving fMRI food choice tasks, leaving aside studies that have examined the association between the brain systems underlying food valuation and self-reported everyday food consumption as they are outside of the scope of this review. Finally, as a natural extension to the literature reviewed on cognitive and neural mechanisms of decision-making systems, we will review evidence regarding decision-making and treatment outcomes in obesity.

2. Decision-making mechanisms relevant to obesity

This section reviews empirical studies that have examined the association between different aspects of decision-making with body mass index (BMI) or eating behaviours in adolescent and adult populations with excess weight and healthy weight. A summary of the different aspects of decision-making assessed in the below described studies can be found in Figure 1. A graphical depiction of the cognitive tasks employed can be found in Figure 2.

2.1. Decision-making under ambiguity

In *decision-making under ambiguity,* individuals choose between different options without explicit knowledge about the outcomes or the probabilities for reward and punishment of a specific choice (Brand, Labudda, & Markowitsch, 2006). For example, if an individual on a diet needs to make a decision about whether or not to attend a dinner party, s/he would need to take into account the possibility of being tempted by snacks, sweets and other energy-dense, unhealthy food options. To successfully gauge these situations, one theory posits that the brain relies on probabilistic representations of the world and performs Bayesian inference (i.e., updates the probability of a hypothesis as more evidence of information becomes available) and uses these representations to estimate the outcomes of each choice (Knill & Pouget, 2004).

One of the most frequently used cognitive tasks to assess decision-making under ambiguity is the Iowa Gambling Task (IGT) (Bechara, Damasio, Damasio, & Anderson, 1994) (Figure 1). The IGT requires individuals to choose between four different decks of cards, which are either advantageous or disadvantageous, but the outcome of each choice is uncertain for the participant (Figure 2). Successful completion of the task requires participants to decipher the rules implicitly by taking into account the feedback received after each choice.

2.2. Decision-making under risk

In *decision-making under risk*, the future consequences of specific decisions as well as the probabilities for punishment and reward are explicit (Brand et al., 2006). Positive consequences of selecting a specific food over another include the reward and the hedonic responses associated with tasting a palatable meal, whereas the negative consequences relate to the risk of overconsumption of certain foods for health or dieting goals (Rangel, 2013). Although the health-related consequences associated with the consumption of energy-dense foods are nowadays well-known and accessible via nutrition facts, individuals increasingly make unhealthy food choices leading to obesity (i.e., risky decisions) (Drewnowski, 2004). Although the aggregate risk of having an unhealthy diet is substantial, it has been proposed that most individuals only estimate the risk of unhealthy foods on a meal-by-meal basis, and thus the negative consequences of a single food rarely appear to be exceedingly large (Zald, 2009). As a result, the reward attributes and hedonic pleasure of choosing a palatable food frequently outweigh the negative health-related consequences (Zald, 2009).

The quality of decision-making under risk can be measured with well-validated cognitive tasks. Three examples of commonly used cognitive tasks are the Risky Choice Task (RCT) (Clark et al., 2012), the Cambridge Gambling Task (CGT) (Rogers, Everitt, et al., 1999), and the Randomised Lottery Task (RLT) (Anderson & Mellor, 2008). In the RCT, a neutral gamble associated with even chances of a gain or a loss is pitted against a more risky gamble that varies from highly unfavourable to highly favourable outcomes. In the CGT, participants are presented with an array of ten boxes in varying ratios of ‘Red’ and ‘Blue’, and are required to decide whether a yellow token is hidden under a blue or a red box, staking a proportion of points on this choice being correct. In the RLT, participants are presented with a series of binary lotteries, and each choice consists of a lottery characterised by a randomised winning probability of 50 points (risky option), and a guaranteed payoff that is randomly distributed between zero and 50 points (safe option) (See Figure 2). Furthermore, the Risky-Gains Task (RGT) has been utilised as a measure of decision-making under risk in neuroimaging studies (Paulus, Rogalsky, Simmons, Feinstein, & Stein, 2003). In the RGT, participants are presented with the numbers 20, 40 and 80 in a fixed order in each trial, and they are instructed to acquire as many points as possible by choosing between safe (20 points) and risky (40, 80 points) options.

2.3. Decision-making involving effort

Effort-based decision-making addresses the process of choosing between different actions according to the trade-off between the expected reward (benefit) and the anticipated effort (cost) (Wardle, Treadway, Mayo, Zald, & de Wit, 2011). In this way, the consumption of food is linked to hedonic responses, but it also requires effort (e.g. the time and effort needed to obtain or prepare the food). In real life contexts, individuals are constantly faced with decisions in which they must choose whether or not to make effort for obtaining food. There is evidence that animals, including humans, experience effort as a burden and, when given a choice, tend to avoid effortful actions when reward magnitude is kept constant (Kool, McGuire, Rosen, & Botvinick, 2010). That is, behaviour is driven by the net-value (benefits minus costs) of expected rewards (Bijleveld, Custers, & Aarts, 2012). Nevertheless, effort is not always treated as an inconvenience, and some individuals are indifferent to the high costs of their actions when faced with challenging tasks to obtain a desired reward (Duckworth, Peterson, Matthews, & Kelly, 2007).

The most frequently used effort-based decision-making tasks include: the Grip Effort Task (GET), which assesses willingness to make hard hand grips (90% of personal maximum) versus easy hand grips (50% of personal maximum across three levels of reward) (Mathar, Horstmann, Pleger, Villringer, & Neumman, 2015); the Effort Expenditure for Rewards Task (EEfRT), which assesses willingness to perform hard (larger number of button presses in a relative short time) versus easy (small number of button presses in a relatively long time) tasks across three levels of reward and two levels of probability (Treadway, Buckholtz, & Schwartzman, 2009); and the Concurrent Schedules Task (CST) (Giesen, Havermans, Douven, Tekelenburg, & Jansen, 2010), which assesses willingness to work for high-energy dense food and vegetables on a concurrent schedule of reinforcement (See Figure 2).

2.4. Decision-making involving food choices

Food choice tasks (FCT) typically require participants to rate the taste and healthiness of different types of food, and then make a decision regarding their preference for some of these foods. Studies have used both single food choice tasks requiring a yes or no decision, and multiple food choice tasks requiring participants to choose between two food items (e.g. unhealthy versus healthy foods) (Charbonnier, van der Laan, Viergever, & Smeets, 2015; van der Laan, de Ridder, Viergever, & Smeets, 2014) (See Figure 2).

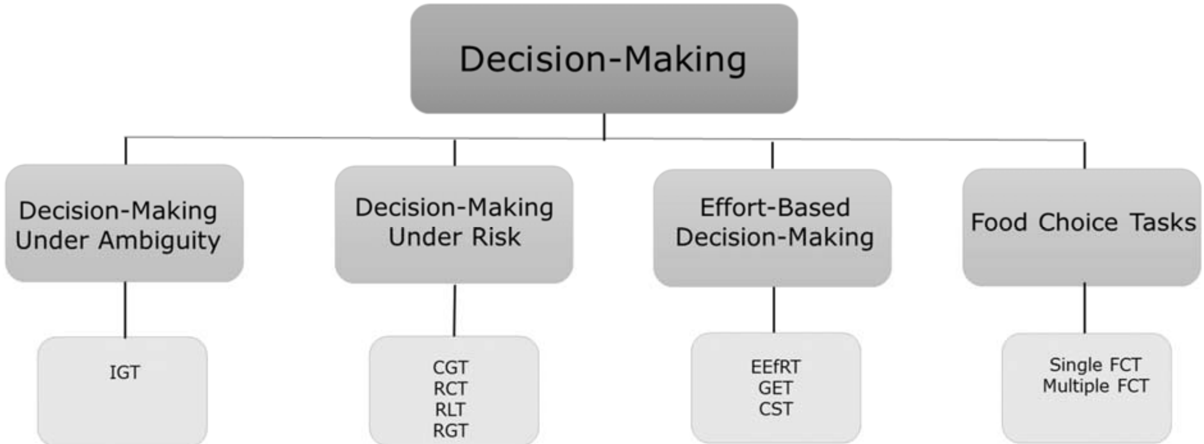

Figure 1: Neurobehavioural tasks used to assess distinct decision-making mechanisms in obesity

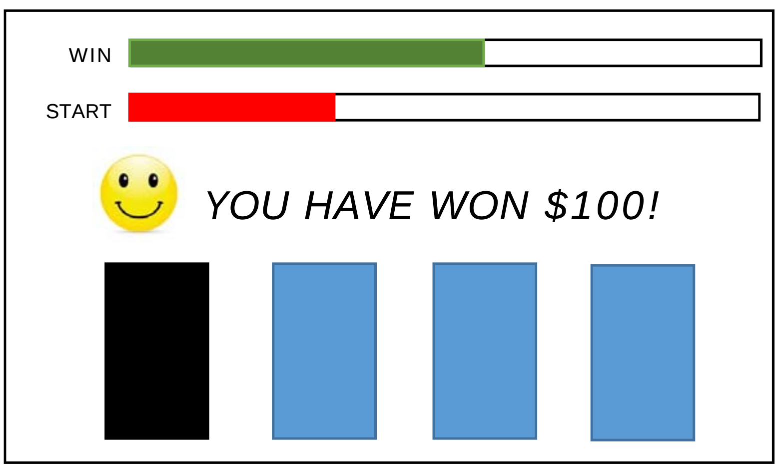

Figure 2. (1) Iowa Gambling Task (IGT) (Bechara et al., 1994).

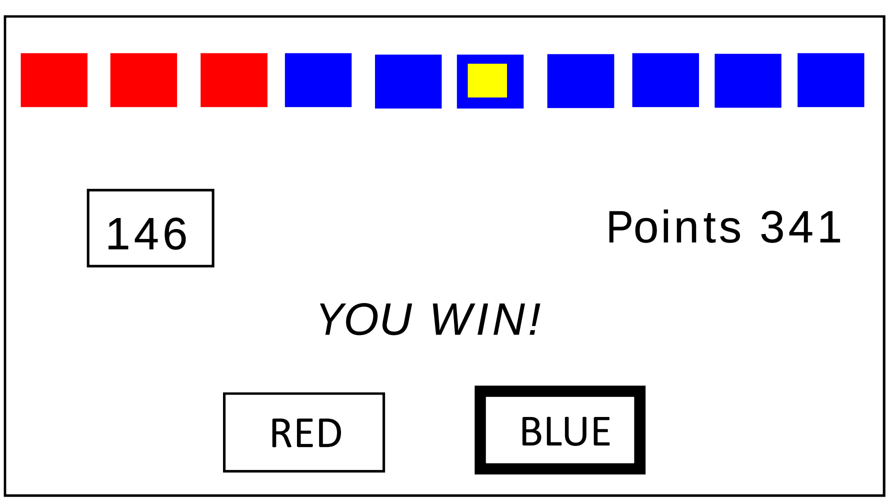

Figure 2. (2) Cambridge Gambling Task (CGT) (Rogers et al., 1999).

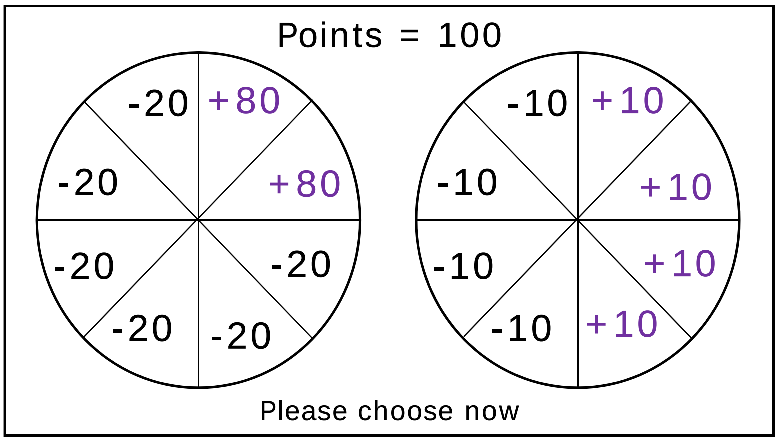

Figure 2. (3) Risky Choice Task (RCT) (Clark et al., 2012).

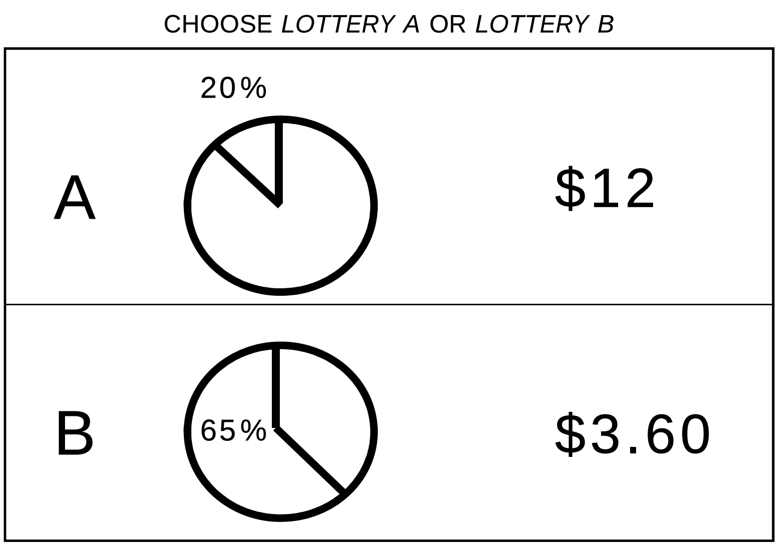

Figure 2. (4) Randomised Lottery Task (RLT) (Anderson & Mellor, 2008).

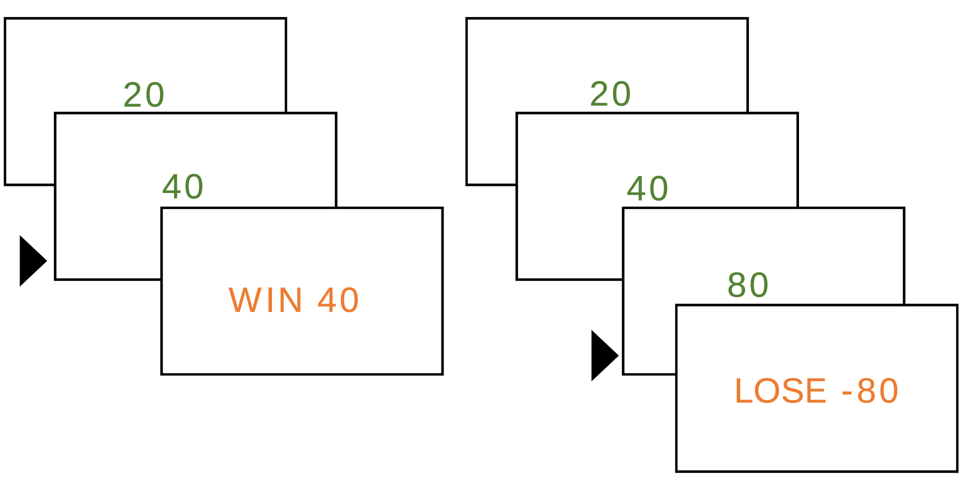

Figure 2. (5) Risky-Gains Task (RGT) (Paulus et al., 2003).

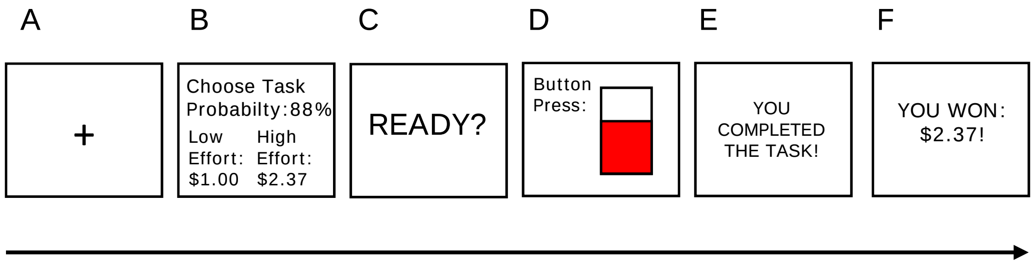

Figure 2. (6) Effort Expenditure for Rewards Task (EEfRT) (Treadway et al., 2009).

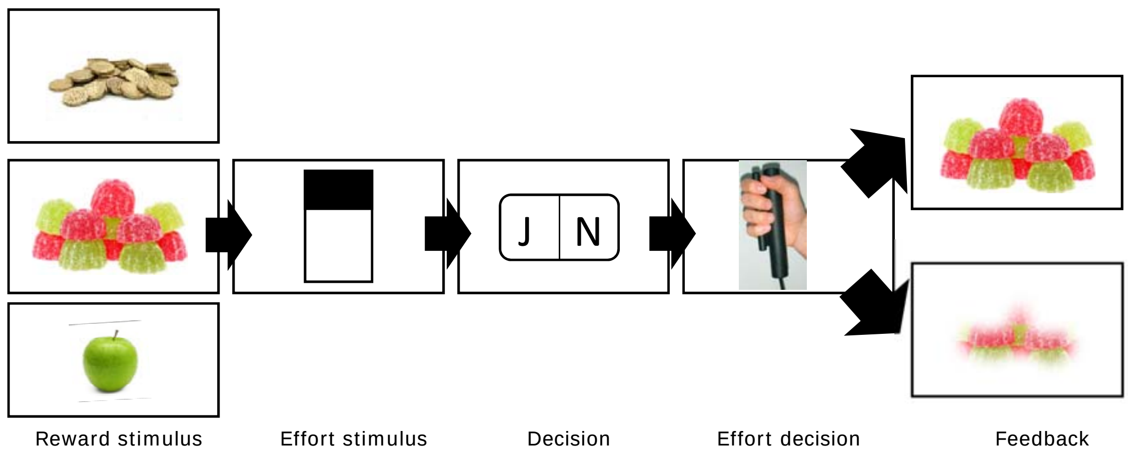

Figure 2. (7) Grip Effort Task (Mathar et al., 2015).

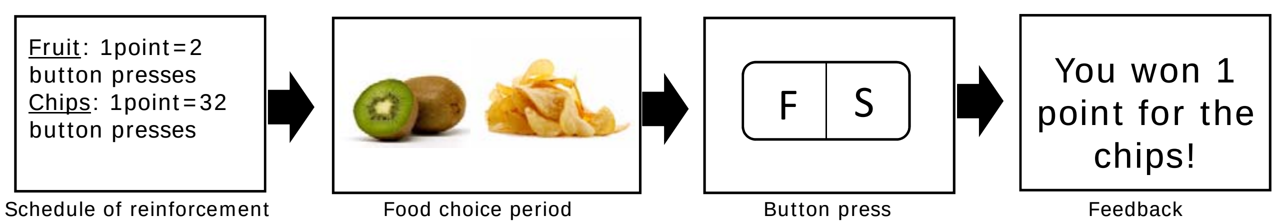

Figure 2. (8) Concurrent Schedules Task (Giesen et al., 2010).

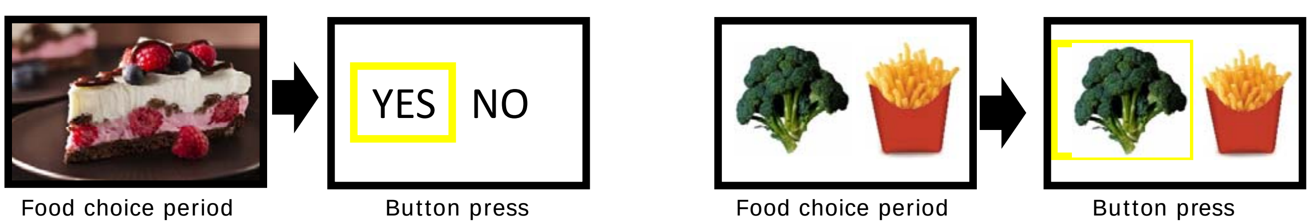

Figure 2. (9) Single Food Choice Task and Multiple Food Choice Task (van der Laan et al., 2014; Charbonnier et al., 2015).

Figure 2: Some common decision-making tasks: (1) Iowa Gambling Task (Bechara et al., 1994); (2) Cambridge Gambling Task (Rogers, Owen, et al., 1999); (3) Risky Choice Task (Clark et al., 2012); (4) Randomised Lottery Task (Anderson & Mellor, 2008); (5) Risky Gains Task (Paulus et al., 2003); (6) Effort Expenditure for Rewards Task (Treadway et al., 2009); (7) Grip Effort Task (Mathar et al., 2015); (8) Concurrent Schedules Task (Giesen et al., 2010); (9) Single Food Choice Task and Multiple Food Choice Task (van der Laan et al., 2014; Charbonnier et al., 2015).

3. Cognitive and Imaging decision-making findings in obese versus healthy weight subjects

3.1. Decision-making under ambiguity

The studies using the Iowa Gambling Task (IGT), as an index of decision-making under ambiguity, have yielded conflicting findings. Most studies have shown that obese adolescents and morbidly obese adults make less advantageous choices compared to their healthy weight counterparts (e.g. Brogan, Hevey, & Pignatti, 2010; Pignatti et al., 2006; Verdejo-Garcia et al., 2010). Conversely, other studies controlling for potential confounders (e.g. comorbid disordes) have shown that excess weight adults perform similarly on the IGT to healthy weight individuals (Navas et al., 2016). These inconsistent findings may be due in part to the age range of the samples employed (i.e., adolescent and older adults tend to perform more poorly than young adults), the inclusion of comorbid disorders such as binge eating disorder in some samples, and the severity of obesity among samples (i.e. morbidly obese appear to display more deficits than excess weight individuals). In sum, the current reearch appears to suggest that deficits in the IGT may be more profound in adolesents and older adults and those with more severe obesity, however, further research is warranted to establish relationships between decision-making under ambiguity using the IGT and obesity.

The brain systems underlying decision-making under ambiguity have only been examined in one study in the context of obesity. This study applied fMRI to investigate the relationship between brain activity during ambiguous decision-making and real-life food choices (He et al., 2014). Increased activity of the striatum was associated with higher consumption of energy-dense snacks. Further, increased activity of the right insula was associated with relatively more snacks and less vegetable consumption. Finally, increased activity of the prefrontal cortex was associated higher consumption of vegetables. This study suggests that unhealthy food choices are associated with increased activation of the striatum and the right insula, whereas healthy food choices are associated with increased activation of the prefrontal cortex.

3.2. Decision-making under risk.

Studies using the Risky Choice Task (RCT) and the Randomised Lottery Task (RLT), as indexes of decision-making under risk, have shown that adults with obesity display riskier decision-making, particularly in conditions that lead to high gains and small losses, compared to individuals with healthy weight and overweight (Anderson & Mellor, 2008; Navas et al., 2016). That is, individuals with excess weight tend to make risky decisions when the outcomes are slightly disadvantageous in the long term. Further, young adults with obesity have shown reduced risk adjustment in decision-making under risk indicated with the Cambridge Gambling Task (CGT) (Chamberlain, Derbyshire, Leppink, & Grant, 2015). These findings indicate that young adults with obesity tend to make riskier decisions when the chance of receiving a reward is low. Therefore, while the evidence is preliminary and further studies are required, there is some indication that poor decision-making under risk is associated with obesity in adulthood.

One study applied fMRI to investigate the brain underpinnings of decision-making under risk, as measured by the Risky Gains Task (RGT), in adolescents with excess weight (Delgado-Rico, Soriano-Mas, Verdejo-Roman, Rio-Valle, & Verdejo-Garcia, 2013). Adolescents with excess weight showed reduced brain activity in the anterior insula and increased brain activity in the striatum and midbrain during anticipation of decisions involving risk and reward compared to their counterparts with healthy weight (Delgado-Rico et al., 2013). The differential patterns of brain activity during decision-making involving risk and reward in adolescents with excess weight are indicative of reduced signalling of risk and increased reactivity to potential reward outcomes (Delgado-Rico et al., 2013).

3.3. Decision-making involving effort

To date**,** few studies have investigated effort-based decision-making in human obesity. One recent study using the Grip Effort Task (GET), as an index of effort-based decision-making, found that individuals with obesity were less willing to engage in physical effort for high-caloric food than their healthy weight counterparts. However, individuals with healthy weight and obesity performed similarly with respect to other reward types (e.g. fruits and money) (Mathar et al., 2015). Saelens and Epstein (1996) used the Concurrent Schedules Task (CST) to measure the differences in reinforcing value of energy-dense foods relative to sedentary activities (e.g. reading the news) between individuals with obesity and healthy weight. It was found that individuals with obesity worked more for food points than for a sedentary activity compared to those with healthy weight (Saelens & Epstein, 1996). Another study using a CST among adults with excess weight and healthy weight examined how hard they would work for energy-dense food compared to low-calorie food (e.g. fruits, vegetables), when both foods are equally liked. It was found that individuals with excess weight worked harder for energy-dense food compared to their counterparts with healthy weight (Giesen et al., 2010). Therefore, from the few studies on effort-based decision-making it appears that compared to healthy weight individuals, individuals with excess weight expend more effort for energy-dense food compared low-caloric food or sedentary activities.

In the only neuroimaging study using effort-based decision-making task, structural MRI was used to investigate whether volume of the nucleus accumbens (NAcc) was associated with willingness to work for rewards in the Grip Effort Task (GET) in adults with excess weight (Mathar et al., 2015). The NAcc was chosen as the main region of interest because a large body of evidence have shown that this region is importantly implicated in coding the incentive motivational values of available rewards during effort-based decision-making (Salamone & Correa, 2012). However, no significant association between NAcc volume and individuals' willingness to work for rewards was found. This may due in part to the small sample size employed in the study (Mathar et al., 2015).

3.4. Decision-making involving food choices.

In relation to tasks involving real food choices (FCTs), one study has examined the differences in the relative speed with which tastiness and healthiness attributes are processed when choosing between tasty and health foods in a sample of young adults (Sullivan, Hutcherson, Harris, & Rangel, 2015). In this study, a food choice task was used in combination with a mouse tracking, which allowed researchers to pinpoint when different attributes (tastiness versus healthiness) were temporally integrated into the decision-making process. Findings showed that tastiness attributes were processed approximately 195ms earlier than healthfulness attributes when making food choices. In addition, dietary self-control in the food choice task decreased with increasing delay between the onset of processing of tastiness and healthfulness attributes.

Neuroimaging studies have applied fMRI to examine brain systems during food choice tasks involving: decisions between different foods and a reference item (Hare, Camerer, & Rangel, 2009; Hare et al., 2011), decisions between high and low calorie food (Charbonnier et al., 2015; van der Laan, Barendse, Viergever, & Smeets, 2016; van der Laan et al., 2014) as well as the impact of food-appearance (e.g. labelling and packaging) on food choices (Grabenhorst, Schulte, Maderwald, & Brand, 2013; Van der Laan, De Ridder, Viergever, & Smeets, 2012). Given that these studies have unique aims and methodologies, it is difficult to draw general conclusions. However, there is evidence to support that: the dlPFC seems to be required for higher-order factors, such as healthiness, to be incorporated into the value-related activity in the vmPFC; high-calorie food choices are associated with increased activity in the *reward-impulsive* system; activity in the *reward-impulsive* system during high versus low calorie food choice is positively associated with steeper delay discounting and non-planning impulsivity; brain regions linked to motor output are activated during food choice, and individuals who demonstrate more successful self-control show increased activity in these brain regions during high-calorie food choice; and healthy food choices could be promoted by presenting healthy foods in more attractive packages with labels that describe their health properties.

Interim Conclusion

Excess weight in adolescent and adult populations is associated with an increased propensity to make risky choices during decision-making under conditions of explicit risk. Studies investigating decision-making under ambiguity and decision-making involving effort have yielded conflicting findings. Excess weight in adolescent and adult populations has been associated with poor decision-making under ambiguity, however, no differences have been found between healthy weight and excess weight young adults. In relation to decision-making involving effort, two studies indicate that obese adults may be more willing to invest higher effort to obtain energy-dense food than healthy weight individuals, whereas one study showed that obese adults are less willing to expend effort for energy-dense food. The tasks used as a measure of effort-based decision-making (GET versus CST) and/or the rewards types (food versus money) used in these tasks vary across studies, which may further contribute to the inconsistent results. In relation to decision-making with real food choices, one study showed that tastiness attributes were processed earlier than healthfulness attributes, and individual differences in dietary self-control abilities were explained by differences in the speed with which these attributes were processed. During decision-making under conditions of explicit risk, adolescents with excess weight showed decreased brain activity in brain regions importantly involved in the interoceptive system, such as the insula, and increased activity in brain regions involved in the reward-impulsive system, such as the striatum. During decision-making under ambiguity, increased activity in the brain regions involved in the reward-impulsive system, such as the striatum, appears to be associated with unhealthy food choices. Moreover, increased activity in brain regions involved in the goal-monitoring system, such as the prefrontal cortex, is associated with healthy food-choices in young adults. In line with this, in relation to decision-making with real food choices, an increased activity of the striatum is associated with high-calorie food choices and impulsivity, and the activation of the dorsolateral prefrontal cortex (dlPFC) is required for healthiness attributes to be incorporated into the decision-making process (See Box 1).

4. Cognitive and Imaging decision-making findings in relation to weight loss outcomes

Treatment of obesity is complex and costly, and can involve various weight management approaches including behavioural, pharmacological, and surgical interventions in the more extreme cases of morbid obesity (Dietz et al., 2015; Hollinghurst, Hunt, Banks, Sharp, & Shield, 2014). Critically, successful weight loss is often compromised by poor attendance and treatment attrition, which impacts, on average, 32% of the individuals who start a weight loss intervention, depending on the type and setting of the treatment program (Finley et al., 2006). Therefore, a better understanding of factors that may be predictive of successful weight loss could facilitate more effective tailoring of treatment to patient characteristics, and may improve completion rates and produce enduring weight changes.

In light of the cognitive and neural mechanisms of decision-making systems discussed in this review, it is possible such systems have clinically meaningful relevance to weight loss outcomes. This section will summarise evidence from cognitive and neuroimaging studies regarding the relevance of decision-making mechanisms to weight management outcome (e.g. magnitude of weight loss and attrition). For clarity, we will only review evidence directly related to behavioural interventions, leaving aside pharmacological and surgical interventions as they are outside of the scope of this review.

4.1. Decision-making under ambiguity

To date two studies have examined the relationship between decision-making under ambiguity as measured by the Iowa Gambling Task (IGT) and weight loss in adults. Specifically, Witbracht and colleagues (2012) investigated whether decision-making under ambiguity predicts magnitude of weight loss following an intervention focused on reduction of calorie intake. Findings showed that better performance on the IGT longitudinally predicted a greater amount of body weight and fat mass reduction (Witbracht, Laugero, Van Loan, Adams, & Keim, 2012). Furthermore, Koritzky and colleagues (2015) examined whether recency effects during decision-making under ambiguity (i.e., the reliance on recent information at the expense of time-distant information) predicted magnitude of weight loss following a lifestyle intervention (Koritzky, Rice, Dieterle, & Bechara, 2015). Successful dieters (those who lost at least 5% of their initial body weight) had lower recency scores than non-successful dieters. These findings show that successful dieters tend to consider long-term information during the decision-making process whereas non-successful dieters tend to rely on recent outcomes as a source of information.

Only one study has examined whether sensitivity to reward (i.e., subjective emphasis that individuals assign to gain versus losses) during decision-making under ambiguity as measured by the IGT predicts treatment attrition in the context of a lifestyle intervention (Koritzky, Dieterle, Rice, Jordan, & Bechara, 2014). Findings showed that sensitivity to reward during decision-making predicted attrition, and the individuals who dropped out the intervention had higher sensitivity to reward than completers. Excess weight individuals who have lower sensitivity to reward may find it easier to adhere to a weight management program.

4.2. Decision-making under risk

No studies have examined the relationship between decision-making under risk and magnitude of weight loss after treatment or the utility of decision-making under risk to predict attrition rates in weight loss interventions. To date only one study has examined whether treatment-related success in weight loss (i.e., reductions of BMI and fat percentage) is associated with changes in brain activation during decision-making under risky in adolescents with excess weight (Mata et al., 2016). Greater success in weight loss was selectively associated with the greatest increases in activation in the insula-related interoceptive system. These findings are reported in detail in Chapter Six of this thesis, entitled: Changes in choice evoked brain activations after a weight loss intervention in adolescents.

4.3. Decision-making involving effort and decision-making involving food choices

No studies have examined the association between decision-making involving effort and decision-making involving food choices with magnitude of weight loss or attrition in weight loss interventions, or the utility of these decision-making mechanisms to predict attrition rates in weight loss interventions.

Interim Conclusion

Decision-making under ambiguity measured by the Iowa Gambling Task (IGT) has consistently shown to predict weight treatment outcome. Specifically, indices of recency and reward sensitivity during decision-making predicted magnitude of weight loss and attrition in treatment, respectively. There is neuroimaging evidence showing that greater success in weight loss is associated with greater normalisation of the interoceptive system (See Box 1). No studies have examined the association between decision-making involving effort and decision-making involving food choices with magnitude of weight loss or attrition in weight loss interventions.

5. Discussion and Conclusions

Research on the decision-making systems in excess weight adolescents and adults has been increasing during the last decade, and it is expected to continue to grow over the coming years. The above-described studies have shown that obesity in adolescent and adult populations is associated with significant decision-making deficits, generally characterised by increased propensity to make risky choices under condition of explicit risk. Studies investigating decision-making under ambiguity and decision-making involving effort in adolescent and adults with excess weight, compared to their healthy weight counterparts, have yielded conflicting findings. However, there is evidence showing that decision-making under ambiguity consistently predicts weight loss and attrition in treatment. In regards to the brain underpinnings of decision-making, there is consistency in the link between (i) increased activity in the *reward-impulsive* system and unhealthy food choices, (ii) increased activity in the *goal-monitoring* system and healthy food choices, and (iii) an altered interoception system and obesity (See Box 1). Critically, more research is need on decision-making under ambiguity and decision-making involving effort in obesity, and longitudinal studies are warranted to investigate the impact of weight loss on the decision-making system.

Box 1: What we know and what is still unknown and will be novel in this thesis

What we know

- Adolescent and adult populations with excess weight show poor decision-making under conditions of explicit risk.
- Increased activity in the brain's reward-impulsive system during decision-making is associated with unhealthy food choices.
- Increased activity in the brain's goal-monitoring system during decision-making is associated with healthy food choices.
- Altered decision-making under ambiguity predicts worse treatment outcome.

What is still unknown and will be novel in this thesis

- To what extent decision-making under ambiguity and risk are associated with body mass index (BMI).
- The association between insula activation in decision-making and interoceptive feedback versus external food cues.
- The relationship between weight loss and changes in activity of the brain systems underlying decision-making.
- The link between decision-making involving effort and treatment outcome.

CHAPTER 2: AIMS AND HYPOTHESES

This chapter summarises the aims and hypotheses arising from the literature reviewed in Chapter One. There are three aims of this thesis, which are addressed in four separate yet related research studies.

Aim 1: To characterise the neurobehavioural systems that underlie decision-making (i.e., reward-impulsive, goal-monitoring and interoceptive) in adolescents and young adults with excess weight versus a comparison group with healthy weight.

To achieve this aim, I conducted two cross-sectional studies using cognitive tasks, as well as functional Magnetic Resonance Imaging (fMRI) (Studies 1 and 2).

Hypothesis: Adolescents and young adults with excess weight would show poorer decision-making under risk and ambiguity, linked to greater activation of the reward-impulsive system to reward cues, decreased activation of the interoceptive system to interoceptive input, and decreased activation of the goal-monitoring system during cognitive control.

Aim 2: To examine if treatment-related success in weight loss (i.e., reductions of BMI and fat percentage) is linked to significant changes in choice evoked brain activity in adolescents with excess weight.

To achieve this aim, I conducted one longitudinal study using fMRI (Study 3).

Hypothesis: More successful weight loss would be associated with normalisation of the insula-related interoceptive system during decision-making.

Aim 3: To examine how individual differences in willingness to expend effort for rewards predict adherence to weight loss treatment.

To achieve this aim, I conducted one cross-sectional study cognitive tasks (Study 4).

Hypothesis: Willingness to expend effort for the most uncertain rewards would distinguish between weight loss intervention completers and drop-outs.

CHAPTER 3: GENERAL METHODS

Introduction to General Methods

This chapter is an overview of the general methodology employed in the four studies that make up Chapter Four (Study 1), Chapter Five (Study 2), Chapter Six (Study 3) and Chapter Seven (Study 4). The chapter provides a more comprehensive explanation of the methodology than is possible in the associated articles. This includes a table outlining each study's methods, a description of the cognitive tasks, and a detailed description of the weight loss interventions conducted in Study 3 and Study 4.

In this thesis, I used a multimodal approach consisting of neurobehavioural and psychophysiological measures, and functional magnetic resonance imaging (fMRI) implemented in both cross-sectional and longitudinal studies. These varied designs and tools provide different but complementary insights into the neurobehavioural systems underlying decision-making processes in overweight and obese individuals. Neurobehavioural measures provide accurate estimations of the current function of specific cognitive processes (e.g. decision-making), and allow inferences about the brain systems relevant to these processes (Vainik et al., 2013). Functional magnetic resonance imaging (fMRI) permits direct observation of the brain underpinnings of cognitive measures, as well as insights about the dynamic interplay between different brain systems (He et al., 2014).

The table below outlines each study's methods, including a detailed account of the study's design, participants, cognitive tasks and analytical technique implemented in each study. All procedures from Studies 1 and 4 were approved from the Monash University Human Research Ethics Committee – project approval number: CF14/1599 - 2014000769. Procedures from Studies 2 and 3 were approved from the University of Granada (Spain) Human Research Ethics Committee – project approval number: PSI2010-17290.

Table 1. Description of each study's methods: design, participants, cognitive tasks and analytical technique

Study	Design	Inclusion/Exclusion criteria	Participants	Cognitive Tasks	Analytical Technique
1	Case-control cross-sectional behavioural study	Inclusion criteria: (i) age range between 18 and 24 years old; (ii) BMI between 18kg/m^2 and 40kg/m^2; (iii) absence of history or current evidence of neurological, psychiatric and eating disorders, assessed on survey responses using DSM-V criteria; (iv) absence of current comorbid medical conditions associated with excess weight (e.g. type II diabetes, hypertension) Exclusion criteria: (i) has undergone weight loss surgery; and (ii) has taken weight loss drugs	Seventy-three young adults (age range: 18-24; BMI range: 18-37) with healthy weight (n=26), overweight (n=26) and obesity (n=21)	Risky Choice Task and Iowa Gambling Task	Multiple regression models were applied to examine the association between decision-making and body mass index (BMI)
2	Case-control cross-sectional magnetic resonance imaging (MRI) study	Inclusion criteria: (i) age range between 12 and 18 years old; (ii) BMI values falling within the intervals categorized as excess weight according to the IOTF (BMI percentile > 85th); (iii) absence of history or current evidence of neurological or psychiatric disorders, assessed by participants and parents interviews; (iv) absence of history of brain injury involving loss of consciousness for longer than 5 min and; (v) absence of significant abnormalities on MRI or any contraindications to MRI scanning	Fifty-four adolescents (age range: 12-18; BMI range: 14-36) with healthy weight (n=32) and excess weight (n=22)	Risky-Gains Task	Correlation analyses between insula activation and (1) the percentage of errors in the heartbeat perception task, and (2) eating behaviour scores were conducted to examine whether obesity is associated with differential correlations between insula activation and perception of interoceptive feedback versus external food cues

3	Longitudinal magnetic resonance imaging (MRI) study	Inclusion criteria: (i) age range between 12 and 18 years old; (ii) BMI values falling within the intervals categorized as excess weight according to the IOTF (BMI percentile > 85th); (iii) absence of history or current evidence of neurological or psychiatric disorders, assessed by participants and parents interviews; (iv) absence of history of brain injury involving loss of consciousness for longer than 5 min and; (v) absence of significant abnormalities on MRI or any contraindications to MRI scanning	Sixteen adolescents with excess weight (age range: 12-18; BMI range: 22-36)	Risky-Gains Task	Correlation analyses were conducted to examine whether success in a weight loss program (i.e., reductions in BMI and fat percentage) was associated with changes in choice evoked brain activation
4	Longitudinal behavioural study	Inclusion criteria: (i) age range between 18 and 24 years old; (ii) BMI between 18kg/m^2 and 40kg/m^2; (iii) absence of history or current evidence of neurological, psychiatric and eating disorders, assessed on survey responses using DSM-V criteria; (iv) absence of current comorbid medical conditions associated with excess weight (e.g. type II diabetes, hypertension) Exclusion criteria: (i) has undergone weight loss surgery; and (ii) has taken weight loss drugs	Forty-two young adults (age range: 18-24; BMI range: 25-37) with overweight (n=23) and obesity (n=19)	Effort Expenditure for Rewards Task	Logistic regression models were applied to examine to what extent effort-based decision-making predicted attrition in a weight loss intervention

Cognitive Tasks

Iowa Gambling Task – Version ABCD (IGT-ABCD) (Bechara et al., 1994): The IGT is a computerised task used to assess decision-making under ambiguity. The original version of the IGT consists of four decks of cards, decks A', B', C' and D'. Each time a participant selects a card, a specified amount of played money is awarded. However, interspersed amongst these rewards are probabilistic punishments (monetary losses with different amounts). Two of the decks of cards, decks A' and B', are associated with high immediate rewards, but with higher unpredictable losses resulting in negative long-term outcomes. The other two decks, decks C' and D', are considered advantageous, as they are associated with small, immediate rewards, but with even lower unpredictable losses and thus result in positive long-term outcomes. The primary dependent measure for this task was the difference in the number of cards selected from the advantageous versus the disadvantageous decks: $[(C + D) - (A + B)]$ throughout the task.

Iowa Gambling Task – Version EFGH (IGT-EFGH) (Bechara et al., 1994): The variant version of the IGT consists of four decks of cards, decks E', F', G' and H'. Again, there are two advantageous decks (E' and F') and two disadvantageous decks (F' and H'). In this version of the task, each card choice results in an immediate punishment (monetary losses), with delayed reward. Instructions for the participants are similar to the instructions for task ABCD, however, this time they are told that they will lose money every time they pick a card and win money occasionally. The primary dependent measure for this task was the difference in the number of cards selected from the advantageous versus the disadvantageous decks: $[(E + F) - (G + H)]$ throughout the task.

Risky Choice Task (RCT) (Clark et al., 2012): This is a computerised task used to assess decision-making under risk. Participants are instructed that the goal of the task is to win as many points as possible. In each trial, participants are presented with two wheels of fortune on the computer screen, and they have to choose between a control and an experimental wheel. Each wheel consists of eight segments that have differing amounts they can win or lose displayed in different colours. The control wheels have a 50-50% chance of either winning or losing 10 points (thus an expected value of 0; see below). The experimental wheel varies systematically in terms of the probability of winning or losing points (75% or 25%), the magnitude of a gain (20 or 80 points), and the magnitude of a loss (20 or 80 points) to yield eight possible trial types. These types vary in their relative expected value (ΔEV), which is the difference between the two wheels with which the participants are presented. For example, in most trials the control wheel has an EV of 0 (.5 × 10 + .5 × –10), whereas an experimental wheel with 25% probability of losing 80 points and 75% probability of winning 20 points has an EV of –5 (.25 × –80 + .75 × 20). In this example, the ΔEV of choosing the experimental gamble is –5. There were several dependent measures of risky decision making which related to the eight different trial types.

Table 2. The ten trial types presented in the Risky Choice Task

	Risky gamble		Control gamble		
Trial type	p(win)/win	p(loss)/loss	p(win)/win	p(loss)/loss	ΔEV
-80(20)	.25/+20	.75/-80	.50/+10	.50/-10	-55
-80(80)	.25/+80	.75/-80	.50/+10	.50/-10	-40
-20(20)	.25/+20	.75/-20	.50/+10	.50/-10	-10
20(-80)	.75/+20	.25/-80	.50/+10	.50/-10	-5
-20(80)	.25/+80	.75/-20	.50/+10	.50/-10	5
20(-20)	.75/+20	.25/-20	.50/+10	.50/-10	10
80(-80)	.75/+80	.25/-80	.50/+10	.50/-10	40
80(-20)	.75/+80	.25/-20	.50/+10	.50/-10	55

Notes: The trial type notation refers to the risky gamble, with the initial value denoting the high probability outcome and the value in parentheses denoting the low probability outcome. ΔEV = Difference between the expected values of the risky and control gambles, with the trials ranked in increasing order of ΔEV.

Risky-Gains Task (RGT) (Paulus et al., 2003)*:* This task was utilised as the neuroimaging task of decision-making under risk. Participants are presented with the numbers 20, 40 and 80 in a fixed order in each trial, and they are instructed to acquire as many points as possible by choosing between safe (20 points) and risky (40, 80 points) options. Each number (20, 40 or 80) is presented on the screen for 1 s, and the participant is instructed to press a button while the selected number is on the screen in order to win the corresponding amount of points. If participants fail to press the button within the allocated time, a 'too late' message is displayed on the screen and they miss the points for that trial. The first number in the sequence is always a safe choice, and participants are told that if they choose to press the button while the 20 is on the screen they would always receive 20 points. Moreover, participants are told that they have the option to wait and select one of the two subsequent choices (40 and 80); in that case they could win either 40 or 80 points, but that would be a chance (i.e., the probability is uncertain) that these options lead to losses of 40 or 80 points, respectively. Hence, although the subject may gain more points per trial by waiting until the 40 or 80 choices appear on the screen, there is also a risk of losing 40 or 80 points. Points accumulate from trial to trial and the stake is shown at the top of the screen, and these information is continuously updated. Participants receive feedback immediately after making a response, so they can adapt their behaviour to the feedback received. The task consists of 96 trials, each trial lasting 5 s (total of 8:05 min). Fifty-four trials (56.25%) are non-punished trials, where participants can get as much as 80 points. Twenty-four trials (25%) are punished -40 and 18 trials (18.75%) are punished -80 trials. The expected value of the three options (20, 40 and 80) is the same (i.e., the penalties are set in a way that there is no advantage in selecting the 40 and 80 options). Thus, there is no advantage in selecting the risky response (40 or 80) over the safe response.

Effort Expenditure for Rewards Task (EEfRT) (Treadway et al., 2009): This is a computerised task used to assess effort-based decision-making. In each trial, participants are given the opportunity to choose between two different task difficulty levels, an "easy task" and a "hard task", which require different amounts of speeded manual button pressing. Successful completion of the easy task requires 30 repeated button presses in seven seconds on a keyboard using the dominant index finger, while successful completion of the hard task requires 100 presses with the non-dominant finger in 21 seconds. Participants are told that successful trial completion does not guarantee winning money (a "win trial") but rather it is possible that successful completion could result in not winning money (a "no win" trial). Before making a choice between an "easy task" and a "hard task", participants are provided with information about (1) the reward probability of a 'win' or 'no win' trial upon successful trial completion, and the (2) reward magnitude for successfully completed 'win' trials. Trials have three levels of probability: "high," 88% probability of being a win trial, "medium" 50%, and "low," 12% (reward probability). Probability levels apply to both the hard task and easy task. For easy-task choices, participants are eligible to win the same amount, $1.00, on each trial if they successfully complete the task. For hard-task choices, participants are eligible to win higher amounts that vary per trial within a range of $1.24 – $4.30 (reward magnitude). The dependent measures for this task were the proportion of hard-task choices for the three probability levels (12, 50 and 88%).

Weight loss intervention conducted in Study 3

The multicomponent weight loss intervention was conducted in small groups (10-12 participants each), and was implemented for 12 consecutive weeks (one session/week) between baseline and second assessments. The intervention included three modules: (a) a nutritional module, (b) a physical activity module, and (c) a psychosocial module. The nutritional module involved a caloric restriction regimen as a function of participant's age, gender and BMI z-score, and consisted of tailored dietary advice and monitoring of dietary compliance (Moreno et al., 2006). Dietary counseling was implemented during sessions 2, 5 and 8, and a minimum energy intake of 1500 kilocalories per day was applied to all participants. Monitoring of dietary compliance was conducted every week during appointments of the participants and their parents with the psychologist and the nutritionist. During these sessions, compliance was monitored through interview and review of meal registries, and supported by counseling on strategies to facilitate adequate observance (Martinez-Gomez et al., 2009). The physical activity module involved encouraging participants to undertake at least 60 minutes of moderate-to-vigorous intensity aerobic exercise for three to five days a week, depending on the physical activity level. The psychosocial module was implemented in weekly meetings dedicated to the training of cognitive (inhibitory control, planning, and conflict resolution) and affective (emotional expression and regulation) skills.

Table 3. Detailed description of the multicomponent behavioural intervention: distribution of sessions, duration, goals and attendants for each session

Session	Duration (minutes)	Goals	Individual or family session
1	60	Introduction	Family session
2	150	Tailored dietary advice and physical activity programs	Family session
3	70	Monitoring and planning of physical activity Psychosocial Module I: Attention - Healthy Lifestyles	Individual
4	70	Monitoring of physical activity Psychosocial Module II: Attentional slips - Self-stem	Individual
5	130	Monitoring of physical activity Diet adjustments Psychosocial Module III: Stimulus control and reinforcement management	Family session
6	70	Monitoring of physical activity Psychosocial Module IV: Inhibitory control of behaviour and emotions	Individual
7	120	Physical activity: ongoing assessment and adjustment Psychosocial Module V: Working memory - Expression and processing of positive and negative emotions	Family session
8	120	Diet adjustments Psychosocial Module VI: Goal planning - Coping with critiques	Individual
9	70	Monitoring of physical activity Psychosocial Module VII: Goal achievement - Planning, decision-making and monitoring. Social skills: 'Learning to say no'	Individual
10	60	Psychosocial Module VIII: Relapse prevention: identification/management of 'at risk' situations. Asking for help	Individual
11	70	Monitoring of physical activity Psychosocial Module IX: Relapse prevention - Problem solution	Individual
12	60	Rehearsal of key points	Family session

Weight loss intervention conducted in Study 4

The multicomponent weight loss intervention was implemented for 12 consecutive weeks between baseline and second assessments, and consisted of individual counseling. The intervention included two modules: (a) a nutrition module and (b) a physical activity module. The nutrition module included a modified intermittent fasting regimen that consisted of tailored dietary advice based on the Australian Dietary Guidelines on five days of the week with a focus on optimizing intake from the five core groups and an overall reduction in energy intake. Supplementary milk-based protein shakes were provided for the other two 'fasting days' of the week. Participants were also instructed to consume a pre-prepared meal, vegetables and fruit on the two 'fasting days'. The total energy intake for each 'fasting day' was approximately 800-1000 calories per day. The nutritional module was supported by six face-to-face sessions with an Accredited Practicing Dietitian, which were scheduled at baseline, week 1, week 2, week 4, week 8 and week 12. Monitoring of weight and dietary compliance was conducted during these sessions. Nutrition information and education on different aspects of healthy eating were also provided at each face-to-face session. The physical activity module consisted of encouraging participants to undertake at least five days/week of light to moderate physical activity with duration of 30 to 60 minutes per day. Each participant was provided with a pedometer and a pedometer log to increase their motivation for physical activity and instructed to aim for 10,000 steps or more each day.

CHAPTER 4: BODY MASS INDEX IS ASSOCIATED WITH DECISION-MAKING UNDER AMBIGUITY AND RISK IN YOUNG ADULTS

Declaration for Thesis Chapter 4

Monash University

In the case of Chapter Four, the nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
Study conceptualisation, study design, data collection and analyses, interpretation of results and manuscript preparation	80%

The following co-authors contributed to the work. If co-authors are students at Monash University, the extent of their contribution in percentage terms must be stated:

Name	Nature of contribution	Extent of contribution (%) for student co-authors only
Antonio Verdejo-Garcia	Study conceptualisation, study design, interpretation of results and manuscript preparation	n/a
Julie Stout, Murat Yucel and Helen Truby	Interpretation of results and manuscript preparation	n/a

The undersigned hereby certify that the above declaration correctly reflects the nature and extent of the candidate's and co-authors' contributions to this work.

Candidate's signature: Fernanda Mata Date: 05/09/2016

Main supervisor's signature: Date: 05/09/2016

Body mass index is associated with decision-making under ambiguity and risk in young adults

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Abstract

Objective: This study aimed to determine to what extent cognitive measures of decision-making under ambiguity and risk are associated with body mass index (BMI) in young adults.

Method: Seventy-three young adults (age range: 18-24) with healthy weight (n=26), overweight (n=26), and obesity (n=21) participated in the study. We used two complementary versions of the Iowa Gambling Task (IGT) to assess decision-making under ambiguity, and the Risky Choice Task (RCT) to assess decision-making under risk. Multiple regression models were applied to examine the association between decision-making measures and BMI.

Results: Decision-making under ambiguity and risk were significantly associated with BMI. More advantageous choices on the version of the IGT involving high punishment and high reward, and more risky choices that are sightly disadvantageous in the long-term on the RCT were associated with higher BMI. Conversely, risky choices that are advantageous in the long-term on the RCT were negatively associated with BMI. Risky choices that are sightly disadvantageous in the long-term made the most significant contribution to BMI.

Conclusions: Decision-making under ambiguity and risk is associated with BMI in young adulthood. Risky choices that are slightly disadvantageous in the long-term are the most significant correlate of high BMIs.

Keywords: Decision-making, Ambiguity, Risk, BMI, Young adults.

Introduction

Over 30% of young adults in developed countries are overweight or obese (Ng et al., 2014). Young adults are a particularly vulnerable group to develop obesity, as they gain weight at a higher rate than at any other age group (Lewis et al., 2000). The importance of this link cannot be underestimated given that obesity in young adulthood is associated with a higher risk of mortality later in life (Hirko et al., 2015). Therefore, research is needed to understand the individual differences among young adults that are associated with the susceptibility to develop obesity. Notwithstanding the relevance of metabolic factors, higher order cognitive processes such as decision-making skills relevant to food choices have a significant influence on the variation of body weight (van der Laan et al., 2015). Young adults are newly autonomous decision-makers and consumers, and thus diet choices based on energy-dense and high-fat food have been associated with excess weight in this age group (Te Morenga et al., 2013). Therefore, determining the contribution of decision-making skills to body weight in young adulthood is highly relevant to explain obesity in this age period.

Obesogenic environments promote the availability of highly palatable and calorie-dense food, which is not necessarily healthy (Berthoud, 2012). In this context, we need to constantly weigh up the positive and negative properties of food choices (Hare et al., 2011). Positive properties of food include the reward and hedonic responses associated with tasting a palatable meal, whereas negative properties are concerned with the risks of overconsumption of certain foods on health or dieting goals. Therefore, in an obesogenic environment selecting foods involves making decisions, and it is assumed that individuals aim to maximize some subjective measure of expected value (the sum of all possible outcomes of a particular choice multiplied by their probabilities) (Rangel, 2013). That is, decision-makers tend to choose actions with the highest aggregate return over a sequence of such choices.

There are different classes of decision-making with respect to potential outcomes: decision-making under ambiguity and decision-making under risk (Brand et al., 2006). In decision-making under ambiguity, individuals choose between different options without explicit knowledge about the outcomes or the probabilities for reward and punishment. To assess decisions under ambiguity, the Iowa Gambling Task (IGT) is one of the most frequently used tasks to measure this type of decision-making (Bechara et al., 1994). The IGT requires individuals to choose between four different decks, which are either advantageous or disadvantageous, but each choice is uncertain regarding the outcome. In decision-making under risk, the future consequences of specific decisions as well as the probabilities for reward and punishment are explicit (Brand et al., 2006). Two examples of commonly used tasks that utilize decisions involving risk are the Risky Choice Task (RCT) (Clark et al., 2012) and the Cambridge Gambling Task (CGT) (Rogers et al., 1999). In the RCT, a neutral gamble associated with even chances of a gain or a loss is pitted against a more risky gamble that varies from highly unfavourable to highly favourable outcomes. In the CGT, participants are presented with an array of blue and red boxes, and are required to decide whether a yellow token is hidden under a blue or a red box. Previous studies indicated that adolescents and adults with obesity display decision-making deficits under ambiguity in the IGT (Davis et al., 2004; Verdejo-Garcia et al., 2010). IGT performance has also been associated with treatment response to weight loss interventions (Witbracht et al., 2012). In addition, young adults with obesity show reduced risk adjustment (modulation of the amount risked as a function of probability of receiving the reward) in decision-making under risk indicated with the CGT (Chamberlain et al., 2015). Therefore, overweight and obesity have been generally associated with decision-making deficits, but the outstanding questions are whether decision-making under ambiguity and decision-making under risk are differentially associated with individual differences in body mass index (BMI), and to what extent they account for these individual differences. These questions are particularly pertinent in young adults, as weight gain seems to be largely driven by dietary choices in this group (Larson et al., 2011).

In this study, we aimed to determine to what extent cognitive measures of decision-making under ambiguity and risk are associated with BMI in young adults. We used two different versions of the Iowa Gambling Task (IGT) to assess decision-making under ambiguity and the Risky Choice Task (RCT) to assess decision-making under risk. We hypothesised that poorer performance on the IGT and more risky choices on trial types of the RCT with negative expected values would be associated with higher BMIs in young adults.

Method

Participants

Seventy-three young adults (age range: 18-24 years) with healthy weight (n=26), overweight (n=26), and with obesity (n=21) participated in the study. Participants' socio-demographic characteristics (age, gender and IQ), BMIs and fat percentage are displayed in Table 1.

Participants were recruited via community advertisements posted in the Monash University campus and clinics and via social media. The inclusion criteria for participants were defined as follows: (i) age range between 18 and 24 years old; (ii) BMI between 18kg/m^2 and 24.9kg/m^2 (Healthy weight group), 25kg/m^2 and 29.9kg/m^2 (Excess weight group) and 30kg/m^2 and 39.9kg/m^2 (Obesity group); (iii) absence of history or current evidence of neurological, psychiatric and eating disorders, assessed on survey responses; and (iv) absence of current comorbid medical conditions associated with excess weight (e.g. type

II diabetes, hypertension). This study was approved by the Monash University Human Research Ethics Committee. Written informed consent was obtained from participants.

Measures

Cognitive Tasks

We utilised two computerised tests to evaluate decision-making skills: Iowa Gambling Task (IGT), which included two complementary versions: original (ABCD) and variant (EFGH), and the Risky-Choice Task (RCT).

Iowa Gambling Task (IGT): This task measures decision-making under ambiguity (Bechara et al., 1994).

Version ABCD: The original version of the IGT involves four decks or cards, decks A', B', C', and D'. Each time a participant selects a card, a specified amount of play money is awarded. However, interspersed among these rewards, there are probabilistic punishments (monetary losses with different amounts). Two of the decks of cards (A' and B') produce high immediate gains, however, in the long run, these two decks will lead to greater losses relative to gains, and are therefore considered to be the disadvantageous decks. The remaining two decks (C' and D') are considered advantageous, as they result in small, immediate gains, but will yield greater gains relative to losses long run. Each game consists of 100 card choices. Net scores were calculated according to the formula [(C+D) – (A+B)] for the total 100 trials. Optimal performance on the IGT requires that participants begin to learn the contingencies in each deck as the task progresses, and to shift their strategy accordingly (choosing from advantageous decks mostly).

Version EFGH: This version involves decks E', F', G', and H'. Again, there are two advantageous decks (E' and G') and two disadvantageous decks (F' and H'). In this version of the task, each card choice results in an immediate punishment (loss of money) with delayed reward. The advantageous decks (E' and G') are those with high immediate punishment, but higher future reward. The disadvantageous decks (F' and H') are those with low immediate punishment, but lower future reward. Instructions for the participants are similar to the instructions for task ABCD, however, this time they are told that they will lose money every time they pick a card and win money once in a while. Net scores were calculated according to the formula [(E + G) − (F + H)] for the total 100 trials.

Risky-Choice Task: This task measures decision-making under risk (Clark et al., 2012). Participants are instructed that the goal of the task is to win as many points as possible. Participants are told that they will see two wheels of fortune on the computer screen, one on the left and one on the right, and they have to choose the wheel that will give them the best chance of winning as many points as possible. Each wheel consists of eight segments that have differing amounts they can win or lose each time. The participants have to choose between control and experimental wheels. The control wheels have a 50-50% chance of either winning or losing 10 points (thus an expected value of 0). The experimental wheel varies systematically in terms of the probability of winning or losing points (75% or 25%), the magnitude of a gain (20 or 80 points), and the magnitude of a loss (20 or 80 points) to yield eight possible trial types. These trial types vary in their relative expected value from -55 to 55 ([ΔEV], which is the difference between the two wheels with which the participants are presented). The experimental gamble of the eight trial types are: -80(20), -80(80), -20(20), 20(-80), -20(80), 20(-20), 80(-80) and 80(-20), and the ΔEV for each trial type is -55, -40, -10, -5, 5, 10, 40 and 55, respectively. In the trial type notation of the experimental gamble, the initial value refers to the high probability outcome and the value in parentheses refers to the low probability outcome (for details, see Clark et al., 2012).

The Wechsler Abbreviated Scale of Intelligence – Second Edition (WASI-II) Full Scale IQ – 2 subtest (FSIQ-2): It was administered to measure general cognitive ability (Wechsler, 2011). It consists of the Vocabulary task (31 items requiring definition of words) and Matrix Reasoning task (30 items requiring selection of a response option to correctly complete a set of matrices).

Body Mass Index (BMI)

Height and weight were measured using a stadiometer and a Seca scale (SECA Group, Hamburg, Germany), respectively. BMI was calculated for each participant as weight in kilograms divided by the square of height in meters.

Body composition

Body composition was measured with Dual Energy X-ray Absorptiometry (iDXA; Lunar Prodigy, GE Medical Systems, Madison, WI). A whole-body scan with the participant lying supine on the DXA bed was then obtained, according to the manufacturer's guidelines. DXA is able to calculate percentage fat. DXA percentage body fat was determined as total fat mass divided by total body mass.

Statistical Analysis

Statistical analyses were implemented in SPSS v.21 (SPSS, Chicago, IL). We first explored the dependent variables to identify missing data points and outliers, and check the normality of distributions via Kolgomorov-Smirnov tests. IGT-EFGH data from one participant with excess weight and RCT data from 4 participants (3 participants with excess weight and 1 participant with healthy weight) were missed due to technical problems. One outlier was detected in the RCT distribution (defined by the Explore command of SPSS v.21) and this subject was removed from further analysis. The majority of the dependent measures from the RCT and the IGT-ABCD were not normally distributed. However, suitable transformations neither improved this situation nor altered the overall conclusions concerning statistical significance. Therefore, we used: the (1) the number of advantageous minus disadvantageous choices of the IGT-ABCD (net score IGT-ABCD) and IGT-EFGH (net-score IGT-EFGH), and (2) the proportion of risky choices for each trial type of the RCT without transformation for the analysis.

Due to the relatively small sample size with regard to the high number of predictors, we first used a series of setwise regression analyses. The purpose of these analyses was to obtain the best fitting subset of predictor variables for BMI. The best fitting model was defined as the one with the highest R^2-adjusted value, lesser number of predictors and smallest Mallow's Cp. By performing these analyses, we significantly reduced the number of predictor variables, which optimized the stability of the subsequent regression model (Hair et al., 2000). To check the study's hypothesis, a multiple regression analysis was carried out including the best fitting model as the set of predictors and BMI as the dependent variable.

Results

Associations between decision-making indices linked to ambiguity and risk and BMI

To examine the predictive capacity of the decision-making under ambiguity and risk indices on BMI, we first carried out a series of setwise regression analyses. These analyses were aimed at obtaining the best subset of predictor variables for BMI. As predictor variables, we included the number of advantageous minus disadvantageous choices of the IGT-ABCD (net score IGT-ABCD), the IGT-EFGH (net-score IGT-EFGH), and the proportion of risky choices for each trial type of the RCT [-80(20), -80(80), -20(20), 20(-80), -20(80), 20(-20), 80(-80) and 80(-20)]. BMI was included as the dependent variable. We found that the net score of the IGT-EFGH IGT (where punishment is immediate and reward is delayed), and the proportion of risky choices in the trial types 20(-80) and 80(-20) of the RCT were the best predictors of BMI (R^2-adjusted =13.4). Sets of four or more predictors were associated with slightly higher R^2-adjusted values, but largest Mallow's Cp.

Regression of decision-making predictors on BMI

Next we carried out a multiple regression analysis using as predictor variables the best subset of predictors obtained in the setwise analyses for BMI: the net score of the IGT-EFGH IGT and the proportion of risky choices in the trial types 20(-80) and 80(-20). The results showed the regression model was statistically significant $F(3, 64)=4.44$, $p = 0.007$, $R^2=17.2$, R^2-adjusted=13.4, and Cohen's $f^2 = 0.20$. The proportion of risky choices for the trial type 20(-80) of the RCT was the only individual significant predictor of BMI, $p < 0.003$. The relationship between the selected decision-making indexes and BMI is displayed in table 2.

Table 1: Participants' socio-demographic characteristics, BMIs, fat percentage and descriptive scores on the IGT and RCT.

Variable	Healthy weight Mean (S.D[a])	Excess weight Mean (S.D[a])	Obesity Mean (S.D[a])
Age, years	21.69(2.11)	21.72(1.7)	21.37(1.53)
Gender (%Men/Women)	38/62	36/64	14/86
IQ	107.23(12.43)	104.25(11.92)	108.05(10.48)
BMI	21.52(1.96)	27.41(1.41)	33.12(2.16)
Fat (%)	25.12(6.36)	38.42(6.9)	43.97(6.36)
IGT-ABCD	11.31(26.93)	11.84(29.85)	13.9(23.48)
IGT-EFGH	19.54(33.08)	26.58(29.94)	32.60(38.26)
RCT -80(20)	0.03(0.10)	0.02(0.07)	0.07(0.14)
RCT -80(80)	0.08(0.17)	0.05(0.12)	0.2(0.27)
RCT -20(20)	0.07(0.15)	0.09(0.14)	0.06(0.13)
RCT 20(-80)	0.7(0.31)	0.87(0.20)	0.88(0.15)
RCT -20(80)	0.24(0.23)	0.23(0.22)	0.25(0.26)
RCT 20(-20)	0.97(0.08)	0.95(0.09)	0.92(0.11)
RCT 80(-80)	0.9(0.19)	0.9(0.20)	0.92(0.14)
RCT 80(-20)	0.99(0.05)	0.97(0.10)	0.96(0.12)

[a]Standard Deviation

Table 2: Relationship between the selected decision-making indexes (best fitting models) and BMI.

Dependent variable	Predictors	B (95% CI)	*β*	*t*	p
	IGT-EFGH	0.019(-0.016-0.054)	0.127	1.091	0.279
BMI	RCT 20(-80)	7.389(2.554-12.225)	0.358	3.053	0.003
	RCT 80(-20)	-11.266(-23.898-1.365)	-0.207	-1.782	0.080

Note. B=unstandardized coefficient

CI=confidence interval

β =standardized regression parameter

t=t-score

p=alfa error

Discussion

Performance on cognitive measures of decision-making under ambiguity and risk is associated with BMI in young adults. Specifically, more advantageous choices on the version of the IGT involving high punishment and high reward, and more risky choices that are sightly disadvantageous in the long-term on the RCT (i.e., associated with small, negative expected values) were associated with higher BMI. Conversely, risky choices that are advantageous in the long-term on the RCT (i.e., associated with high positive expected values) were negatively associated with BMI. Risky choices that are sightly disadvantageous in the long-term made the most significant contribution to BMI.

Better performance on the variant version of the IGT (where punishment is immediate and reward is delayed) was associated with higher BMIs. In this version, net winning requires choosing largely from decks with higher initial punishment coupled with higher delayed reward. That is, participants are required to accept the "pain" of more up-front punishment in order to obtain greater long-term reward (Bauer et al., 2013). Therefore, our findings suggest that higher BMIs are associated with greater tolerance to punishment and greater motivation for reward in uncertain decision-making scenarios. We did not find performance on the original IGT to be associated with BMI. Previous studies had found a negative association between these variables, but in this study we controlled for several potential confounders that may have contributed to this association in previous studies, such as age (i.e., adolescent and older adults tend to perform more poorly in the task), binge eating and relevant medical comorbidities (Davis et al., 2010).

Risky choices associated with small, negative expected value and yielding a high loss (-80) were associated with higher BMIs. Conversely, risky choices associated with positive expected values and yielding a moderate loss (-20) were associated with lower BMIs. These findings indicate that risk-taking choices involving small, negative expected values are linked to overweight and obesity in youth, and imply that greater BMI relates to less ability to encode the risk of disadvantageous choices. This notion is consistent with the results of a recent study in which young adults with obesity failed to adjust risk-taking to the probability of winning in the CGT (Chamberlain et al., 2015). Reduced risk adjustment has been previously identified in individuals with damage in the insular cortex (Clark et al., 2008), a brain region involved in modulating risk-seeking choices to minimize losses (Werner et al., 2009). We have previously shown that adolescents with overweight and obesity display poorer insula activation preceding risk-taking decisions (Delgado-Rico et al., 2013). Therefore, consistent evidence indicates that risk-based decision-making is poorer in young adults with higher BMIs (Delgado-Rico et al., 2013; Chamberlain et al., 2015).

Taken together, uncertain choices involving high punishment and high reward and risky choices sightly disadvantageous in the long-term are associated with higher BMI in young adults. Risky choices that are slightly disadvantageous in the long-term were the main correlate of high BMIs. In more general terms, risky decision-making in young adulthood could be translated into food choices driven by the rewarding properties of palatable food despite awareness of its health-related risks and impact on diet goals. Strengths of this study include the measures selection of young adults with healthy and excess weight; this selection allowed us to elegantly test the neuropsychological assumptions without any medical or psychological confounder. However, our findings should be interpreted taking into consideration that decision-making skills accounted for only 13.4% of the variance for BMI in young adulthood. The modest amount of variance explained by the model suggests that factors other than decision-making skills, such as environmental influences and individual differences in trait measures, contribute to variation of body weight in young adulthood.

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CHAPTER 5: INSULA TUNNING TOWARDS EXTERNAL EATING VERSUS INTEROCEPTIVE INPUT IN ADOLESCENTS WITH OVERWEIGHT AND OBESITY

Declaration for Thesis Chapter 5

Monash University

In the case of Chapter Five, the nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
Data analysis, interpretation of results and manuscript preparation	60%

The following co-authors contributed to the work. If co-authors are students at Monash University, the extent of their contribution in percentage terms must be stated:

Name	Nature of contribution	Extent of contribution (%) for student co-authors only
Antonio Verdejo-Garcia	Study conceptualisation, study design, interpretation of results and manuscript preparation	n/a
Carles Soriano-Mas	Manuscript preparation	n/a
Juan Verdejo-Roman	Data collection and analysis	n/a

The undersigned hereby certify that the above declaration correctly reflects the nature and extent of the candidate's and co-authors' contributions to this work.

Candidate's signature: Date: 05/09/2016

Main supervisor's signature: Date: 05/09/2016

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Research report

Insula tuning towards external eating versus interoceptive input in adolescents with overweight and obesity ☆

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ABSTRACT

This study was aimed to examine if adolescent obesity is associated with alterations of insula function as indexed by differential correlations between insula activation and perception of interoceptive feedback versus external food cues. We hypothesized that, in healthy weight adolescents, insula activation will positively correlate with interoceptive sensitivity, whereas in excess weight adolescents, insula activation will positively correlate with sensitivity towards external cues. Fifty-four adolescents (age range 12–18), classified in two groups as a function of BMI, excess weight (n = 22) and healthy weight (n = 32), performed the Risky-Gains task (sensitive to insula function) inside an fMRI scanner, and completed the heartbeat perception task (measuring interoceptive sensitivity) and the Dutch Eating Behaviour Questionnaire (measuring external eating as well as emotional eating and restraint) outside the scanner. We found that insula activation during the Risky-Gains task positively correlated with interoceptive sensitivity and negatively correlated with external eating in healthy weight adolescents. Conversely, in excess weight adolescents, insula activation positively correlated with external eating and negatively correlated with interoceptive sensitivity, arguably reflecting obesity related neurocognitive adaptations. In excess weight adolescents, external eating was also positively associated with caudate nucleus activation, and restrained eating was negatively associated with insula activation. Our findings suggest that adolescent obesity is associated with disrupted tuning of the insula system towards interoceptive input.

Introduction

The current food environment is full of cues that keep thoughts of palatable, energy-dense food almost constantly in mind (Swinburn et al., 2011). Therefore, individual differences in the relative value given to external food cues versus current homeostatic needs (e.g. hunger, satiety) may contribute to understanding the increasing prevalence of obesity (Carnell, Benson, Pryor, & Driggin, 2013). In this context, obesity is viewed as a condition characterized by difficulties in resisting the urge to respond to external food cues, which may override homeostatic control of food intake (Blundell & Finlayson, 2004). The insula is the brain hub that integrates homeostatic feedback with external information and expected outcomes (Craig, 2009), and therefore it is key to understanding the neural balance between interoceptive and external information. Recent research suggests that during adolescence insula function is sensitized towards external reward cues and comparatively less sensitive to risk (Smith, Steinberg, & Chein, 2014). It is however yet unclear whether this pattern translates into greater insula weighing of external versus interoceptive information in adolescents with overweight and obesity. This question is relevant as in that case insula related adaptations may contribute to the establishment and maintenance of a highly palatable yet unhealthy (hence risky) diet.

Risky decision-making involves cognitive evaluation of potential rewards and outcomes, but it is also critically modulated by homeostatic signals that project to the insula cortex (Paulus, 2007). The insula receives the major sources of interoceptive input (i.e., gut, hormonal) and gives rise to awareness of homeostatic states, which guide behaviour in the direction of satisfying body needs (Craig, 2009). The insula is centrally involved in basic functions related to perception of physiological needs such as thirst and hunger as evidenced by animal (Hollis, McKinley, D'Souza, Kampe, & Oldfield,

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2008; Saker et al., 2014) and human studies (Craig, 2009; Frank, Kullmann, & Veit, 2013). In relation to food intake, the insula cortex receives gut motility and hormonal signals of appetite and satiety, processes sensory and gustatory aspects of food and guides food related decisions (Frank et al., 2013; Volkow, Wang, & Baler, 2011). Moreover, the insula is typically engaged when subjects make risky decisions involving gains and potential losses (Preuschoff, Quartz, & Bossaerts, 2008) and specifically involved in signalling the probability of aversive outcomes (Bossaerts, 2010; Venkatraman, Payne, Bettman, Luce, & Huettel, 2009). Therefore, it is reasonable to assume that the insula plays a relevant role on food decisions involving reward, but potentially associated with health related costs.

Adolescents with excess weight have decreased activation of the insula during anticipation of higher rewards in the Risky-Gains task, which opposes a less rewarding safe choice with more rewarding risky choices (Delgado-Rico, Soriano-Mas, Verdejo-Roman, Rio-Valle, & Verdejo-Garcia, 2013). The insula also plays a crucial role in interoceptive sensitivity, which is decreased in individuals with excess weight (Herbert & Pollatos, 2014). Importantly, individual differences in interoceptive sensitivity modulate decision-making processes regarding food intake. Higher interoceptive sensitivity has been shown to predict adaptive eating behaviours (guided by awareness of internal cues of hunger or satiety), which indeed is negatively associated with BMI levels (Herbert, Blechert, Hautzinger, Matthias, & Herbert, 2013). Conversely, poor interoceptive sensitivity in the face of the current obesogenic environment may predispose obese individuals to rely on external cues rather than on internal feedback on physiological states (e.g., hunger and satiety) (Schachter, 1968).

In this study, we used functional magnetic resonance imaging to examine whether insula activation during risk-based decision-making is associated with sensitivity towards external food cues versus perception of interoceptive feedback in adolescents with excess weight. Decision-making was challenged using the Risky-Gains task (Paulus, Rogalsky, Simmons, Feinstein, & Stein, 2003), which reliably induces recruitment of insula activation (Delgado-Rico et al., 2013). The perception of interoceptive feedback was measured by a heartbeat perception task (Schandry, 1981). It has been demonstrated that cardiac interoception is strongly correlated with gastric interoception, which indicates that this is a general index of interoceptive sensitivity (Herbert, Muth, Pollatos, & Herbert, 2012). Sensitivity towards external food cues was measured by the external eating subscale of the Dutch Eating Behaviour Questionnaire (Van Strien, Frijters, Bergers, & Defares, 1986). We hypothesized that in excess weight adolescents insula activation would positively correlate with external eating, at difference with positive correlations with interoceptive sensitivity in healthy weight controls.

Methods

Participants

Fifty-four adolescents (age range 12–18) participated in this study. They were classified in two groups (excess weight [n = 22] or healthy weight [n = 32]) according to their age- and sex-adjusted BMI percentile, following the criteria of the International Obesity Task Force (IOTF) defined by Cole and Lobstein (2012). The demographic data, BMI, percentage of fat and the biochemical parameters are summarized in Table 1. The two groups did not differ significantly in age, sex or any biochemical parameter. Participants were recruited from the pediatrics and endocrinology services of the Hospital "Virgen de las Nieves" in Granada, Spain, and from schools located in the same geographical area. The inclusion criteria were as follows: (i) aged between 12 and 18 years old, (ii) BMI values falling within the intervals categorized as excess weight or healthy weight according to the IOTF, (iii) absence of history or current evidence of neurological or psychiatric disorders, assessed by participants and parents interviews and the Eating Disorder Inventory (Garner, 1994, (iv) absence of significant abnormalities on MRI (Magnetic Resonance Imaging) or any contraindications to MRI scanning (including claustrophobia and implanted ferromagnetic objects) and (v) absence of history of brain injury involving loss of consciousness (LOC) for longer than 5 minutes. All of them had normal or corrected-to-normal vision. The study was approved by the Ethics Committee of the University of Granada. All participants and their parents were briefed about study aims and detailed procedures, and both signed an informed consent form certifying their voluntary participation.

fMRI task

We used the Risky-Gains task described by Paulus et al. (2003). In each trial, participants are presented with the numbers 20, 40 and 80 in a fixed order. The task requires the participant to acquire as many points as possible by choosing between safe (20 points) and risky (40, 80 points) options. Each number (20, 40 or 80) is presented on the screen for 1 s, and the participant is instructed to press a button while the selected number is on the screen in order to win the corresponding amount of points. If participants fail to press the button within the required time, a 'too late' message is displayed on the screen and they miss the points for that trial.

The first number in the sequence (20) is always a safe choice. Participants are told that if they choose to press the bottom while the 20 is on the screen they would always receive 20 points. Moreover, participants are told that they have the option to wait and select one of the two subsequent choices (40 and 80); in that case they

Table 1
Socio-demographic characteristics, BMI, percentage of fat and biochemical parameters for each group.

	Excess weight (n = 22) Mean (SD[b])	Healthy weight (n = 32) Mean (SD)	p-value
Demographic variables			
Age	15.14 (2.03)	15.53 (1.70)	0.443
Sex (male/female)	11/21	10/12	0.412
BMI[a]	29.40 (3.00)	21.17 (2.24)	<0.001
Fat (%)	33.14 (8.85)	19.01 (6.73)	<0.001
Biochemical parameters			
Insulin	45.58 (59.90)	39.13 (38.69)	0.635
Basal glucose	92.34 (3.91)	92.17 (7.19)	0.91
Triglycerides	71.70 (31.80)	65.15 (29.05)	0.437
HDL[c]	55.15 (13.13)	56.88 (10.81)	0.6
Total cholesterol	154.64 (27.77)	146.00 (18.34)	0.174

[a] Body Mass Index.
[b] Standard deviation.
[c] High-density lipoprotein.

could win either 40 or 80 points, but that there would be a chance (i.e., the probability is uncertain) that these options lead to losses of 40 or 80 points, respectively. Thus, although the subject may gain more points per trial by waiting until the 40 or 80 choices appear on the screen, there is also a risk of losing 40 or 80 points. Points accumulate from trial to trial and the stake is shown at the top of the screen, being continuously updated. Participants received feedback immediately after making a response, so they could adapt their behaviour to the feedback received.

The task consisted of 96 trials of 5 seconds. Fifty-four trials were non-punished trial type, where participants could get as much as 80 points, while 24 trials were –40 punished and 18 were –80 punished trial types. The expected value of the three options (20, 40 and 80) is the same (i.e., the penalties are set in a way that there is no advantage in selecting the 40 and 80 options). Therefore, there is no advantage in selecting the risky response (40 or 80) over the safe response (20).

Imaging data acquisition and processing

A 3.0 T clinical MRI scanner (Intera Achieva, Philips Medical Systems, Eindhoven, The Netherlands), equipped with an eight-channel phased-array head coil, was used during task performance to obtain a T2*-weighted echo-planar imaging (EPI) sequence with the following parameters: repetition time (TR) = 2000 ms, echo time (TE) = 35 ms, field of view (FOV) = 230 × 230 mm, 96 × 96 matrix, flip angle = 90°, 21 4 mm axial slices, 1 mm gap, 243 scans. A sagittal three-dimensional T1-weighted turbo-gradient-echo sequence (3D-TFE) (160 slices, TR = 8.3 ms, TE = 3.8 ms, flip angle = 8°, FOV = 240 × 240, 1 mm^3 voxels) was also obtained in the same experimental session for anatomical reference. Stimuli were presented through magnetic resonance-compatible liquid crystal display goggles (Resonance Technology Inc., Northridge, CA, USA), and responses were recorded through Evoke Response Pad System (Resonance Technology Inc.).

The brain images were analyzed using Statistical Parametric Mapping (SPM8) software (Wellcome Department of Cognitive Neurology, Institute of Neurology, Queen Square, London, United Kingdom), running under Matlab R2009 (MathWorks, Natick, MA, USA). Preprocessing steps were slice timing correction, reslicing to the first image of the time series, normalization (using affine and smoothly nonlinear transformations) to an EPI template in the Montreal Neurological Institute (MNI) space, and spatial smoothing by convolution with a 3D Gaussian kernel (full width at half maximum = 8 mm).

Inside scanner behavioural measures

The main performance measures were safe and risky choice rates (proportion of safe/risky election by total trials) and safe and risky choice rates after punishments (proportion of safe/risky election after a punishment trial).

Outside scanner behavioural measures

Heartbeat perception task

We used the heartbeat perception task (Schandry, 1981), as described by Ehlers and Breuer (1992). In each trial participants were required to count how many heartbeats they felt over a period of time while the real number of heartbeats were measured by electrocardiogram (ECG). In order to determine whether subjects could calculate their number of heartbeats by simply estimating the time interval of the trial, a time estimation test was included. Participants completed three heartbeat trials (35, 25 and 45 s), three time trials (23, 56 and 40 s) and then three further heartbeat trials (23, 56 and 40 s). Prior to testing, participants were asked to remove their watch and instructed not to take their pulse with their fingers or to hold their breath. Time and heartbeat perception inaccuracy was calculated by taking the modulus of the actual value minus the estimated value, dividing this by the actual value and multiplied by 100 to express the inaccuracy as a percentage: $(|AV-EV|)/(AV) \times 100$, where AV is the actual value and EV is the estimated value.

Electrocardiogram (ECG) was recorded at rest and during performance of the heartbeat perception task at a sampling rate of 2000 Hz through a Biopac MP150 (Biopac Systems Inc., USA). Electrodes (Ag/AgCl) were placed according to Einthoven's II derivation attaching them to the participants' right and left ankles and wrist of the non-dominant hand. The ECG raw signal was processed using the software AcqKnoledge 3.8.1.

Dutch eating behaviour questionnaire

The Dutch Eating Behaviour Questionnaire (DEBQ) (Van Strien et al., 1986) was used to measure trait-eating behaviours. It is a 33-item questionnaire consisting of three subscales measuring the constructs of emotional eating (13 items), external eating (10 items) and restrained eating (10 items). Responses are made via a 5-point Likert scale ranging from "Never" (1) to "Very often" (5). It has good reliability and internal and discriminant validity (Van Strien et al., 1986).

Data analysis

Behavioural analysis

Behavioural data were analyzed with the Statistical Package for the Social Sciences version 19 (SPSS 19; Chicago, IL, USA). We conducted independent-sample t-tests (two-tailed) to compare the two groups on relevant sociodemographic variables, and inside and outside scanner behavioural measures.

Neuroimaging analysis

The time series were convolved with the SPM8 canonical hemodynamic response function and a high-pass filter was used to remove low-frequency noise (1/128 Hz). We defined 2 conditions of interest: (i) safe response (20 points trials), (ii) risky response (40, –40, 80 and –80 points trials). Conditions were modelled as the time elapsed from the beginning of the trial to the participants' response or punishment feedback appears. Our contrast of interest was defined to study risky related brain activations: risky versus vs. safe choices.

One-sample t-test was conducted to assess intra-group activations (healthy weight and excess weight) in the contrasts of interest. Between-group comparisons were conducted using a two-sample t-test, masking results by the activation maps derived from the one-sample t-tests. The statistical threshold used for creating this mask was $p < 0.005$, with a minimum cluster size extent (KE) of 10 contiguous voxels. Regarding brain–behaviour associations, voxel-wise correlation analyses with our variables of interest (i.e., percentage of error in heartbeat perception and eating behaviour scores) were masked by two anatomical masks of the insular cortex and caudate nucleus, corresponding to the regions activated by risky choices in our study groups (see below). Such masks were created using the automated anatomical labelling (Tzourio-Mazoyer et al., 2002) from the WFU Pick Atlas Tool, version 3.0, integrated into SPM8 (Maldjian, Laurienti, Kraft, & Burdette, 2003). The main analysis were conducted within these masks within group correlations as well as between-group comparisons of correlation values (i.e., interactions).

All these analyses were corrected for multiple comparisons with a combination of voxel intensity and cluster extent thresholds. The spatial extent threshold was determined by 1000 Monte Carlo simulations using AlphaSim as implemented in the SPM REST toolbox (Song et al., 2011) (Ward, 2013). The input parameters included an insula and a caudate mask of 5383 and 1239 voxels, respectively,

Table 2
Behavioural measures.

	Healthy weight (n = 32) Mean (SD[a])	Excess weight (n = 22) Mean (SD)	p-value
Body perception task			
Error in heartbeat perception (%)	33.74 (16.17)	36.35 (18.02)	0.581
Error in time perception (%)	17.94 (15.96)	18.32 (13.57)	0.928
Dutch Eating Behaviour Questionnaire			
Emotional Eating	23.13 (7.52)	22.86 (8.91)	0.908
Restrained Eating	20.50 (8.61)	24.68 (8.28)	0.081
External Eating	30.06 (7.40)	28.68 (7.01)	0.494
Risky Gains Task			
Safe choices (%)	50.39 (17.04)	53.66 (13.96)	0.46
Risky choices (%)	49.61 (17.04)	46.34 (13.96)	0.46
Safe choices after punishment (%)	61.69 (26.97)	65.41 (24.44)	0.607
Risky choices after punishment (%)	38.31 (26.97)	34.59 (24.44)	0.607

[a] Standard deviation.

an individual voxel threshold probability of 0.005 and a cluster connection radius of 5 mm, considering the actual smoothness of data after estimation. A minimum cluster extent (KE) of 34 voxels was estimated to satisfy a Family-wise error (FWE) corrected P value of $P_{FWE} < 0.05$.

Finally, in order to calculate the correlation coefficients (r) and depict correlation plots, the beta eigenvalues from each cluster of significant brain differences between groups were extracted for each participant, and then correlated with behavioural measures in SPSS. We performed fisher r-to-z transformation to calculate between-group interactions in these correlations.

Results

Behavioural results

There were no between-group differences in any of the behavioural measures (Table 2).

Neuroimaging results

Risky–safe contrast

One-sample t-tests showed that both groups commonly activated the caudate nucleus and a cluster comprising inferior frontal gyrus and anterior insula bilaterally. Excess weight group additionally activated the midbrain. We did not observe significant differences between the groups at the selected threshold (Table 3).

Main analysis – correlations between brain activation patterns and behavioural measures

A negative correlation between percentage of errors in the heartbeat perception task and bilateral posterior insula activation was found in healthy weight participants (x, y, z = 40, −4, 8, z score = 3.61; x, y, z = −36, −10, 12, z score = 3.52). Conversely, the percentage of errors in the heartbeat perception task (x, y, z = −36, 6, −12, z score = 3.54; x, y, z = 32, 6, −12, z score = 2.81) and external eating scores (x, y, z = −46, 2, −10, z score = 3.61) were positively correlated with posterior insula activations in excess weight participants (see Fig. 1).

Results showed significant between-group (normal weight vs. excess weight) interactions in the correlations between the percentage of heartbeat perception errors and external eating scores and posterior insula activation (z score = 3.84, p = 0.0001, and z score = 2.77, p = 0.0056, respectively) (see Fig. 1).

Moreover, bilateral insula activation correlated positively with Restrained Eating scores in normal weight participants (x, y, z = −40, −20, −2, z score = 3.27; x, y, z = 34, −22, 14, z score = 3.27) whereas this correlation was negative in excess weight participants (x, y, z = 36, 4, 12, z score = 3.08). The direct comparison between these correlations revealed a significant difference (z score = 4.13, p < 0.0001) (see Fig. 2).

Finally, although there were no significant correlations between caudate activation and any of the behavioural measures in the healthy weight group, a significant and positive correlation with external eating (x, y, z = −6, 8, 10, z score = 3.10) was observed in the excess weight group (see Fig. 3).

Discussion

In agreement with the initial hypothesis, we found that insula activation during risk-based decision-making is positively associated with external eating and negatively associated with interoceptive sensitivity in adolescents with excess weight. The opposite pattern was observed in adolescents with healthy weight.

Table 3
Brain activations observed in risky versus safe choices in within-group (one-sample) whole-brain analyses.

	BA[a]	Side	MNI coordinates			Ke[b]	T-value
			X	Y	Z		
Healthy weight							
Inferior frontal gyrus/Insula	47/13	L	−30	26	−10	384	6.77
Caudate		R/L	−8	12	−6	1261	6.7
Inferior frontal gyrus/Insula	47/13	R	30	28	−8	21	3.36
Excess weight							
Inferior frontal gyrus/Insula	47/13	L	−34	26	−2	234	4.47
Midbrain		R/L	−2	−18	−28	241	4.39
Caudate		R/L	8	10	−4	473	4.31
Inferior frontal gyrus/Insula	47/13	R	32	24	−8	60	3.99

[a] Brodmann area.
[b] Cluster extent in voxels.

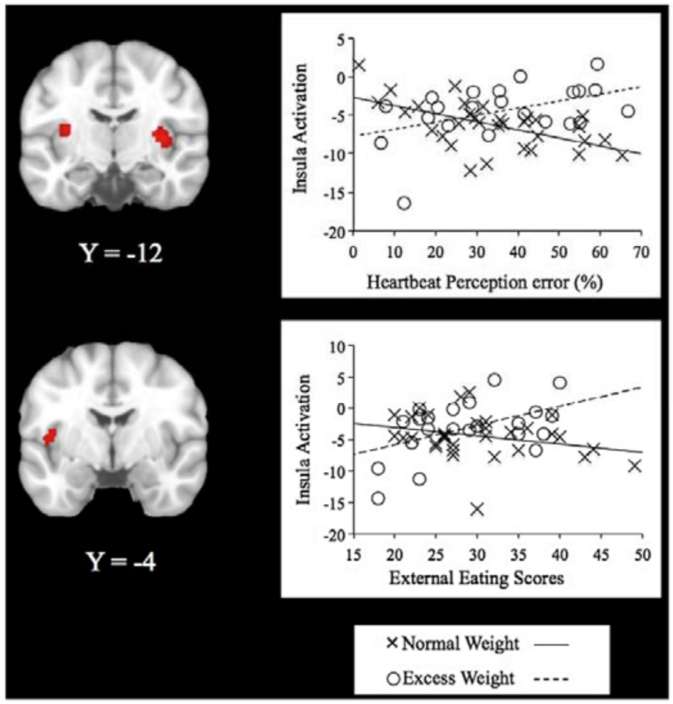

Fig. 1. Significant interaction between heartbeat perception error and external eating scores and posterior insula activation during Risky > Safe contrast. Y denotes coordinate in standard MNI space. Right hemisphere is displayed on the right.

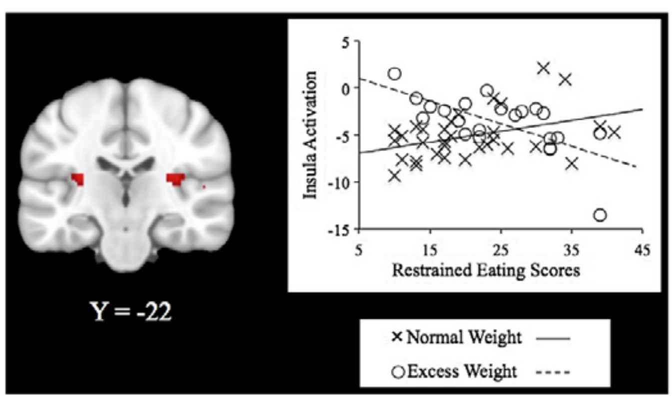

Fig. 2. Significant interaction between restrained eating scores and posterior insula activation during Risky > Safe contrast. Y denotes coordinate in standard MNI space. Right hemisphere is displayed on the right.

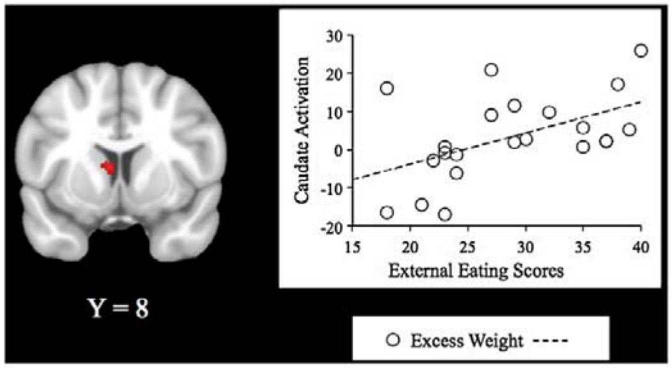

Fig. 3. Correlation between external eating scores (X axis) and caudate activation during Risky > Safe contrast (Y axis). Y denotes coordinate in standard MNI space. Right hemisphere is displayed on the right.

Therefore, the distinctive insula tuning towards external compared to internal information likely reflects neurocognitive adaptations associated with obesity. In excess weight adolescents, external eating was also positively associated with caudate nucleus activation, and restrained eating – which refers to an effort to restrict food intake for the purposes of maintenance or weight loss – was negatively associated with insula activation. These correlations emerged in the absence of significant between-group differences on brain activations or behavioural measures.

Our findings indicate that adolescents with excess weight have an altered association between insula function and processing of interoceptive information. This neuroimaging finding resonates with previous behavioural results showing that obesity is associated with poorer perception of interoceptive signals in adults (Herbert & Pollatos, 2014). The insula is the key brain system for interoceptive processing, but growing evidence suggests that adiposity may interfere with the normal perception of interoceptive input. For instance, adult obese patients display reduced posterior insula activation in response to mechanically-induced gastric distention (Tomasi et al., 2009). Therefore, adolescents with excess weight may have decreased insula sensitivity towards interoceptive stimuli (i.e., signals of hunger and satiety, bodily representations of the risk of aversive outcomes) and comparatively increased sensitivity towards external rewards (Smith et al., 2014). In agreement with this notion, our findings suggest that adolescent obesity is associated with disrupted tuning of the insula system towards interoceptive input. At the same time, insula activity correlates with external eating patterns, which speculatively suggest that adolescents with excess weight might have a distinctive insula tuning towards external eating cues. This is consistent with previous neuroimaging studies showing that adolescents with excess weight and adolescents at risk of obesity (by virtue of family history) have increased insula activation in response to food images (Batterink, Yokum, & Stice, 2010) and monetary rewards (Stice, Yokum, Burger, Epstein, & Small, 2011), during reallocation of attention to appetizing food images (Yokum, Ng, & Stice, 2011), and during anticipation and actual consumption of milkshakes (Stice, Spoor, Bohon, Veldhuizen, & Small, 2008). Obese men have been shown to activate the posterior and middle insula upon exposure to a meal whereas lean individuals deactivate the middle insula and show no response in the posterior insula (DelParigi et al., 2004). The insula sensitivity towards external cues has important public health implications as insula activation in response to food cues has been shown to predict ensuing consumption of high energy foods (Mehta et al., 2012) and weight gain (Demos, Heatherton, & Kelley, 2012). Furthermore, postprandial insula activation is associated with subsequent selection of high energy foods in an "ad libitum" buffet (Mehta et al., 2012).

In addition, in adolescents with excess weight, caudate nucleus activation (related to the reward – impulsive system) was positively correlated with external eating and insula activation was negatively correlated with restrained eating (related to the goal-monitoring systems). Collectively, our findings suggest that obesity may be associated with a disruption of the interoception system involved in ongoing mapping of homeostatic signals and subsequent moderation of reward-impulsive versus goal-monitoring systems (Noel, Brevers, & Bechara, 2013). Specifically, engaging the insula system during risk-based decision-making in obesity might increase the vulnerability to eat in response to external food cues (regardless of physiological needs) by exacerbating activity within the reward-impulsive system and weakening activity of the goal-monitoring systems. Sensitization of the dopaminergic reward-impulsive system might serve to increase the salience of food cues in the environment and make them more attractive (Robinson & Berridge, 1993). This is consistent with the finding that obese versus healthy weight individuals show increased brain activation in the caudate nucleus while viewing appetizing versus bland food (Nummenmaa et al., 2012). The caudate nucleus also shows increased connectivity with the posterior insula in obese individuals while they are seeing appetitive versus bland food (Nummenmaa et al., 2012). Moreover, a recent systematic review of the literature suggests that the striatum and the amygdala (reward-impulsive system) and the insula are hyper-reactive to visual food cues in obese individuals, parallelled by decreased response in the lateral and medial prefrontal areas (goal-monitoring system) (Garcia-Garcia et al., 2013).

The main conclusion of this study is that insula activation during risky versus safe choices is positively associated with external eating and negatively associated with interoceptive sensitivity in adolescents with excess weight, which is opposite to the "normal" pattern predicted by theory and observed in healthy weight controls. Moreover, in excess weight adolescents, the activation of the caudate nucleus also positively correlates with external eating, and the activation of the insula also negatively correlates with restraint. Collectively these findings suggest that, in excess weight adolescents, both interoceptive and reward related regions are tuned towards external cues, which may hamper efforts to restrain excessive eating behaviour. These findings give therefore support to cognitive interventions focused on enhancing appraisal of internal body signals as well as hunger and satiety awareness (Bloom, Sharpe, Mullan, & Zucker, 2013). These findings should be however interpreted in the context of relevant limitations. First, the data are correlational and therefore cannot speak of the causality of these alterations. Second, the correlations between brain activations and behaviour emerged in absence of significant group differences in brain or behaviour, likely because at difference with previous studies (Delgado-Rico et al., 2013), the present study was not adequately powered to detect such between-group differences. Future studies using longitudinal designs, larger samples sizes and ecologically valid food choice tasks are warranted to validate our findings and to examine their public health implications. In essence we speculatively propose that altered insula tuning towards external rather than interoceptive cues may underlie unhealthy ("risky") food choices in adolescents with overweight and obesity.

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CHAPTER 6: CHANGES IN CHOICE EVOKED BRAIN ACTIVATIONS AFTER A WEIGHT LOSS INTERVENTION IN ADOLESCENTS

Declaration for Thesis Chapter 6

Monash University

In the case of Chapter Six, the nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
Data Analysis, interpretation of results and manuscript preparation	60%

The following co-authors contributed to the work. If co-authors are students at Monash University, the extent of their contribution in percentage terms must be stated:

Name	Nature of contribution	Extent of contribution (%) for student co-authors only
Antonio Verdejo-Garcia	Study conceptualisation, study design, interpretation of results and manuscript preparation	n/a
Carles Soriano-Mas and MuratYucel	Manuscript preparation	n/a
Juan Verdejo-Roman	Data collection and analysis	n/a

The undersigned hereby certify that the above declaration correctly reflects the nature and extent of the candidate's and co-authors' contributions to this work.

Candidate's signature: Fernanda Mata Date: 05/09/2016

Main supervisor's signature: Date: 05/09/2016

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Changes in choice evoked brain activations after a weight loss intervention in adolescents

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ABSTRACT

This study was aimed to investigate if treatment-related success in weight loss (i.e., reductions of BMI and fat percentage) is linked to significant changes in choice evoked brain activity in adolescents with excess weight. Sixteen adolescents with excess weight (age range: 12–18; BMI range: 22–36) performed the Risky-Gains Task during functional Magnetic Resonance Imaging (fMRI) both before and after a 12-week weight loss intervention. Success in weight loss was selectively associated with increased activation in the anterior insula. We concluded that adolescents with the greatest increases in activation of the insula-related interoceptive neural circuitry also show greater reductions in BMI and fat mass.

1. Introduction

A quarter of the adolescent population in the United States and other developed countries are classified as 'obese', which places them at increased risk for premature mortality and physical morbidity in adulthood (Ogden, Carroll, Kit, & Flegal, 2014; Reilly & Kelly, 2011). Therefore, tackling obesity at an early stage of life, when obesity-related diseases are still preventable, remains a public health priority and, consequently, a major aim of Healthy People 2020 (Department of Health and Human Services, 2014). One key factor promoting obesity is the enormous pressure on maintaining energy balance provided by the modern food environment, wherein highly palatable yet unhealthy foods are abundant and proliferate (Zheng & Berthoud, 2007). In this context, a high burden is placed on the individual's ability to make healthy food choices (Rangel, 2013), particularly at a time when cognitive-emotional systems are still maturing and therefore, vulnerable to non-adaptive choices (Verdejo-Garcia et al., 2010). In line with this, longitudinal evidence has demonstrated an association between poor food choices and excess weight in adolescents (Te Morenga, Mallard, & Mann, 2013). Consequently, there is a need for more research into decision-making process underlying food choices in adolescence.

Risky decision-making, characterised by a tendency to select immediate, rewarding options despite the potential negative consequences, has been observed in adolescents with excess weight (Verdejo-Garcia et al., 2010). Further, studies investigating the neural mechanisms of such associations have utilised functional brain imaging and found that overweight and obese adolescents are characterised by alterations in their brain function including: (i) greater activation of the orbitofrontal cortex in response to food commercials (Rapuano, Huckins, Sargent, Heatherton, & Kelley, 2015), and during anticipation of risky decision-making (Delgado-Rico, Soriano-Mas, Verdejo-Roman, Rio-Valle, & Verdejo-Garcia, 2013); (ii) reduced activation of the lateral areas of the prefrontal cortex when attempting to inhibit prepotent responses to images of appetizing foods (Batterink, Yokum, & Stice, 2010); and (iii) reduced activation of the left anterior insula during anticipation of risky

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decision-making (Delgado-Rico et al., 2013). Further, growing evidence indicates that decision-making skills are associated with treatment success in weight loss interventions. For instance, overweight adults showing poorer decision-making skills are less able to lose weight and fat mass during a standard 12-week calorie-reduced intervention (Witbracht, Laugero, VanLoan, Adams, & Keim, 2012).

Longitudinal studies of brain activation during passive observation of food cues suggest that weight loss is associated with recovery of these brain alterations (Bruce et al., 2012). For instance, decreases in body mass index (BMI) after bariatric surgery are associated with diminished brain activation in the mesolimbic system, including the ventral striatum, putamen, and its cortical outputs such as the dorsomedial prefrontal cortex in response to high calorie food cues (Ochner et al., 2011). Moreover, increased brain activation in the anterior insula in response to high-calories food pictures pre-intervention predicts poor weight loss during treatment (Murdaugh, Cox, Cook, & Weller, 2012). There is recent evidence suggesting that brain alterations in obesity are sensitive to weight loss interventions that target enhancements in cognitive control (i.e., decision making) during rewarding stimuli in adolescents (Delgado-Rico et al., 2012; Kulendran et al., 2014). However, it remains unknown if the brain systems underlying risky decision-making recover after successful weight loss. This question is relevant as normalisation of brain activity during risky decision-making may be relevant to healthy food choices and weight loss.

In this study, we used functional magnetic resonance imaging to investigate if treatment-related success in weight loss (i.e., reductions of BMI and fat percentage) is associated with changes in brain activation during risky decision-making in adolescents with excess weight. Risky decision-making was challenged with the Risky-Gains Task (Paulus, Rogalsky, Simmons, Feinstein, & Stein, 2003), which has been shown to robustly activate the brain systems involved in reward-related risky choices (Delgado-Rico et al., 2013). We hypothesised that greater increases in anterior insula activation during anticipation of higher rewards (risky vs. safe choices) from pre-to post-treatment would be associated with more successful weight loss.

2. Methods and procedures

Participants

The sample was comprised of sixteen adolescents (age range: 12–18; mean age: 13.94; standard deviation: 1.65; twelve females; all right handed) with excess weight according to the criteria of the International Obesity Task Force (IOTF) (Cole & Lobstein, 2012). This is a subsample of participants from a previously published intervention study in which fMRI was conducted prior to and following the weight loss intervention (Delgado-Rico et al., 2012). The sample size of the present study was calculated to detect weight loss changes associated with the intervention. The present study introduces for the first time the longitudinal imaging component of this larger study.

Participants' socio-demographic characteristics, BMI, fat percentage and baseline blood-count based biochemical parameters are displayed in Table 1. A Whole Body Composition Monitor (TANITA SC-330) was used to obtain participant's BMI and fat percentage. Participants were recruited from the paediatrics and endocrinology services of the Hospital "Virgen de las Nieves" in Granada, Spain, and from schools located in the same geographical area. The inclusion criteria were as follows: (i) aged between 12 and 18 years old; (ii) BMI values falling within the intervals categorized as excess weight according to the IOTF (BMI percentile > 85th); (iii) absence of history or current evidence of neurological or psychiatric disorders, assessed by participants and parents interviews; (iv) absence of significant abnormalities on MRI (Magnetic Resonance Imaging) or any contraindications to MRI scanning (including claustrophobia and implanted ferromagnetic objects), and; (v) absence of history of brain injury involving loss of consciousness for longer than 5 min. All participants had normal or corrected-to-normal vision. The study was approved by the local Ethics Committee of the University of Granada. All participants and their parents were debriefed about study aims and detailed procedures. Participants signed an assent form certifying their voluntary participation and their parents signed a parental permission form authorizing the participation of their children in the study.

All participants partook in a 12-week multicomponent behavioural intervention, consisting of cognitive behavioural therapy, structured physical activity and dietary counselling (Delgado-Rico et al., 2012). Two fMRI sessions were conducted. Each fMRI scan took place at 6 pm and prior to this the participants had fasted for approximately 3 h. The first session was conducted within 11.88 days (SD = 10.22) prior to the start of the intervention and the other within 18.19 days (SD = 7.93) following completion of the treatment.

fMRI task

The Risky-Gains task described by Paulus et al. (2003) was utilised as the neuroimaging task of choice. In each trial, participants are presented with the numbers 20, 40 and 80 in a fixed order. The task requires the participant to acquire as many points as possible by choosing between safe (20 points) and risky (40, 80 points) options. Each number (20, 40 or 80) is presented on the screen for 1 s, and the participant is instructed to press a button while the selected number is on the screen in order to win the corresponding amount of points. If participants fail to press the button within the required time, a 'too late' message is displayed on the screen and they miss the points for that trial.

The first number in the sequence is always a safe choice. Participants are told that if they choose to press the button while the 20 is on the screen they would always receive 20 points. Moreover, participants are told that they have the option to wait and select one of the two subsequent choices (40 and 80); in that case they could win either 40 or 80 points, but that there would be a chance (i.e., the probability is uncertain) that these options lead to losses of 40 or 80 points, respectively. Thus, although the subject may gain more points per trial by waiting until the 40 or 80 choices appear on the screen, there is also a risk of losing 40 or 80 points. Points accumulate from trial to trial and the stake is shown at the top of the screen, being continuously updated. Participants received feedback immediately after making a response, so they could adapt their behaviour to the feedback received.

The task consisted of 96 trials, each trial lasting 5 s (total of 8:05 min). Fifty-four trials (56.25%) were non-punished trials, where participants could get as much as 80 points, while 24 trials (25%) were punished −40 and 18 trials (18.75%) were punished −80 trials. The expected value of the three options (20, 40 and 80) is the same (i.e., the penalties are set in a way that there is no advantage in selecting the 40 and 80 options). Therefore, there is no advantage in selecting the risky response (40 or 80) over the safe response (20).

Inside scanner behavioural measures

The primary behavioural performance measures were safe and risky rates (proportion of safe/risky election by total trials).

Imaging data acquisition and pre-processing

The subject's head was immobilised inside the MRI coil with

Table 1
BMI, fat percentage and biochemical parameters.

	Before treatment mean (SD)[b]	Range	After treatment mean (SD)	Range
Demographic variables				
BMI[a]	27.95 (4.29)	22.06–36.36	26.46 (4.37)	21.93–36.14
Fat (%)	35.5 (6.20)	22.30–45.60	32.14 (6.30)	20.40–40.40
Biochemical parameters				
Insulin (mcU/ml[c])	11.78 (4.34)	4.90–20.40		
Basal glucose (mg/dl[d])	86.00 (9.70)	71.00–106.00		
Triglycerides (mg/dl[d])	96.69 (29.64)	56.00–167.00		
HDL[e] (mg/dl[d])	53.44 (12.53)	34.00–74.00		
Total cholesterol (mg/dl[d])	166.69 (31.44)	113.00–222.00		

[a] Body Mass Index.
[b] Standard-deviation.
[c] Micro-units per milliliter.
[d] Milligrams per deciliter.
[e] High-density lipoprotein.

foam cushions to reduce head motion. We used the same data acquisition and pre-processing protocol for both time-points. A 3.0 T MRI scanner, equipped with an eight-channel phased-array head coil, was used in both sessions (Intera Achieva, Philips Medical Systems, Eindhoven, The Netherlands). During each task performance, a T2*-weighted echo-planar imaging (EPI) was collected, (repetition time (TR) = 2000 m, echo time (TE) = 35 ms, field of view (FOV) = 230 × 230 mm, 96 × 96 matrix, flip angle = 90°, 21 × 4 mm axial slices, 1 mm gap, 243 scans). A sagittal three-dimensional T1-weighted turbo-gradient-echo sequence (3D-TFE) (160 slices, TR = 8.3 ms, TE = 3.8 ms, flip angle = 8°, FOV = 240 × 240, 1 mm^3 voxels) was obtained for anatomical reference. Stimuli were presented through magnetic resonance-compatible liquid crystal display goggles (Resonance Technology Inc., Northridge, California, USA), and responses were recorded through Evoke Response Pad System (Resonance Technology Inc., Northridge, California, USA).

The brain images were pre-processed using Statistical Parametric Mapping (SPM8) software (Wellcome Department of Cognitive Neurology, Institute of Neurology, Queen Square, London, United Kingdom), running under Matlab R2009 (MathWorks, Natick, Massachusetts, USA). First the images were re-sliced to the first image of the time series, followed by slice timing correction, normalisation (using affine and smoothly nonlinear transformations) to an EPI template in the Montreal Neurological Institute (MNI) space, and spatial smoothing by convolution with a 3D Gaussian kernel (full width at half maximum = 8 mm). Head motion was corrected during the pre-processing procedure. None of the scans exceeded cut-off for excessive motion (3 mm or 3° in any direction).

Statistical analyses

Behavioural analyses

Behavioural data were analysed with the Statistical Package for the Social Sciences version 19 (SPSS 19; Chicago, IL, USA). Paired-sample t-tests (two-tailed) were conducted to compare participants' clinical measurements and performance between the two-time points.

Neuroimaging analyses

The time series were convolved with the SPM8 canonical hemodynamic response function and a high-pass filter was used to remove low-frequency noise (1/128 Hz). We defined 2 conditions of interest: (i) safe response (20 points trials), and; (ii) risky response (40 and 80 points trials). Conditions were modelled as the time elapsed from the beginning of the trial to the participants' response or punishment feedback appears. The risky vs. safe choices contrast was defined to study risky related brain activations.

Voxel-wise correlation analyses were conducted in SPM8 to map the association between post-treatment versus pre-treatment changes in brain activity and differences in clinical measures. We created individual maps subtracting the contrasts images to obtain brain change images. Then we correlated activity in these maps with BMI and fat percentage reduction. Consistent with our main analyses, the statistical threshold was set $p < 0.005$, with a minimum cluster size extent (KE) of 10 contiguous voxels.

A one-sample *t*-test was conducted to assess significant brain activations in each time-point. Further, a paired *t*-test analysis was conducted to assess longitudinal differences before and after treatment. In both analyses, the statistical threshold was set at $p < 0.005$, with a minimum cluster size extent (KE) of 10 contiguous voxels, which provides a good balance between Type I and II errors (Lieberman & Cunningham, 2009). The results are reported in the Supplementary Material.

3. Results

Changes in body composition

There was a significant reduction in BMI ($t = 4.62$, $p < 0.001$, Cohen's $d = 0.34$) and Fat percentage ($t = 4.17$, $p = 0.001$, Cohen's $d = 0.54$) after treatment.

Behavioural performance in the risky gains task

There was no significant difference in task performance after the intervention (see Table 2). Safe choices increased from 56.32% to 56.89% ($p = 0.827$) whereas risky choices decreased from 43.68% to 43.11% ($p = 0.827$).

Correlations between changes in body composition and changes in brain activation

Changes in insula activation between baseline and post-intervention positively correlated with reduction in BMI (x, y, z = 38, 2, 16, z score = 3.79, $r = 0.81$, $p < 0.001$) and with fat percentage reduction (x, y, z = 32, 16, 12, z score = 3.56, $r = 0.61$, $p = 0.013$) (Fig. 1).

4. Discussion

Adolescents showing greater treatment-related success in weight loss (i.e., reductions of BMI and fat percentage) had a concurrent and selective increase in the anterior insula activation. These correlations emerged in the absence of significant differences

Table 2
Percentage of safe and risky responses before and after the intervention.

	Before treatment mean (SD)[a]	After treatment mean (SD)	p-value
Risky gains task			
Safe choices (%)	56.32 (17.92)	56.89 (13.16)	0.827
Risky choices (%)	43.68 (17.92)	43.11 (13.16)	0.827

[a] Standard-deviation.

on behavioural choice, such that they genuinely reflect different neural approaches to the risky decision-making task. Overall, these findings indicate that adolescents showing greater reductions in weight and fat mass have greater normalisation of the insula-related interoceptive system.

Of note, we found that adolescents showing greater weight loss also showed increases in the anterior insula activation during anticipation of risky choices. The present finding complements our previous studies linking insula de-activation with distorted representations of bodily feedback (i.e., heartbeat sensations) and deficits in social-emotional decision-making (Mata, Verdejo-Roman, Soriano-Mas, & Verdejo-Garcia, 2015; Verdejo-Garcia et al., 2015). Here we show that this insula deficit can recover following successful weight reduction. Furthermore, it has been shown that the anterior insula is typically engaged when subjects make risky decisions involving gains and potential losses and specifically involved in signalling the probability of aversive outcomes (Bossaerts, 2010; Preuschoff, Quartz, & Bossaerts, 2008). Our findings indicate that weight and fat loss in adolescents with excess weight are associated with alteration of insula function during risky decision-making (i.e., increased activation during risky choices). In agreement with our findings, it has been observed that adults taking part in a behavioural weight loss intervention show increased connectivity pre-to post-meal between the insula and the precuneus, which is involved in processing self-referential information (Lepping et al., 2015). Further, in studies reporting pre-to post-bariatric surgery outcomes, changes in activity in the insula in

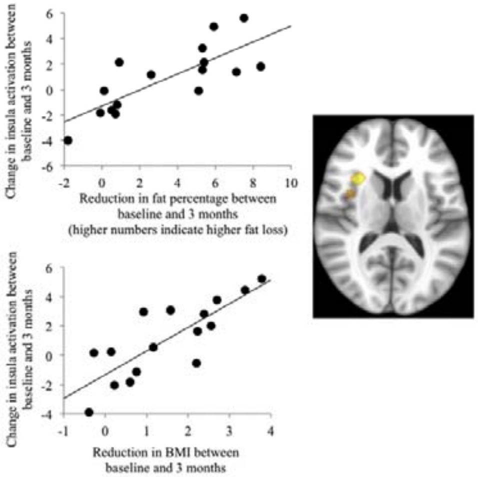

Fig. 1. Brain areas showing a significant correlation between brain activation during risky vs. safe choices and reductions in fat percentage (top panel) and BMI (bottom panel).

response to visual food cues have also been reported following decreases in BMI (Bruce et al., 2012).

The main conclusion of this study is that adolescents showing greater increases in activation of the interoceptive system (insula) also show greater loss of weight and fat mass. Future studies are needed to determine whether greater choice-related insula activation promotes increased awareness of body signals monitoring feelings of hunger and satiety, and therefore serve as mechanism for weight and fat loss. In addition, future studies are warranted to investigate whether greater insula activation during risky decision-making improves awareness of the long term-risks of energy-dense, but unhealthy food choices, and therefore, contribute to weight loss. Knowledge concerning the mechanisms by which normalisation of the interoceptive brain system promote successful weight loss in adolescents with excess weight has important clinical and policy implications.

Our findings should be interpreted in the context of relevant limitations. Given that our study did not include a non-intervention group and because there were no changes in performance on the decision-making task, the changes in brain activation from pre to post-treatment (Supplementary Material) cannot be attributed to treatment or change in risky decision-making. Future studies using a wait list design with a non-intervention group are needed to clarify if the reported changes reflect intervention-related normalisation of brain function. Furthermore, future studies with bigger samples are warranted to clarify if the changes in brain activation from pre to post-treatment emerged in the absence of significant differences in behaviour because: (1) successful weight loss is associated with meaningful brain activation but not behavioural changes, or (2) successful weight loss is associated with meaningful behavioural changes, however, the present study was not adequately powered to detect such changes. Finally, future studies using more ecological food-choice paradigms are warranted to determine if experimental findings are relevant to real-life food choices.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.appet.2016.04.002.

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Supplementary Material

Neuroimaging results

Task Effects

One sample t-tests showed that before treatment, participants displayed significant activations in the right anterior insula extending to inferior frontal gyrus, the caudate and the midbrain during risky vs. safe choices. After treatment, participants only showed significant activations in the anterior insula/inferior frontal gyrus region (see Table 3).

Changes in brain activation during risky versus safe choices between baseline and follow-up

Participants showed a significant reduction of brain activation in the midbrain, the striatum (dorsal caudate and ventral putamen), the hippocampus, the superior temporal gyrus and the lateral OFC (see Table 3 and Fig. 2). No brain regions showed significant increases in activation at the selected threshold.

Table 3: Brain activations observed in risky vs. safe choices in within-group (one sample) before and after treatment and paired t-test.

	MNI Coordinates			Ke[a]	T-value
	X	Y	Z		
One-Sample					
Before Treatment					
Anterior Insula / Inferior Frontal Gyrus	34	20	-14	635	7.69
Midbrain	6	-22	-12	353	4.52
Caudate	8	12	4	18	3.18
After Treatment					
Anterior Insula / Inferior Frontal Gyrus	44	22	0	331	4.6
Paired t-test					
Midbrain	14	-16	-6	183	5.81
Lateral Orbitofrontal Cortex	46	54	-2	647	5.12
Putamen	-20	14	-6	44	3.26
Hippocampus	-28	-16	-8	141	4
Caudate	-16	12	16	11	3.65
Superior Temporal Gyrus	42	10	-32	83	4.34

[a]Cluster extent in voxels

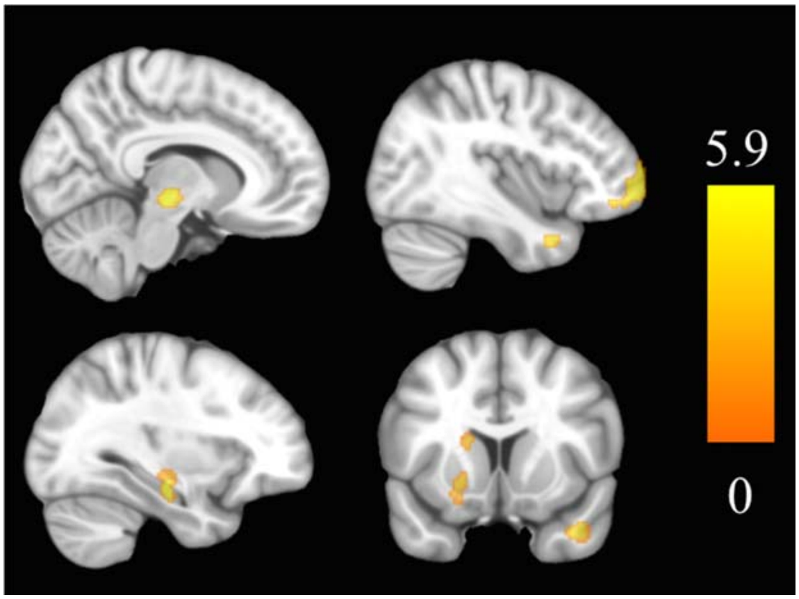

Figure 2: Brain regions showing significant reduction activation during risky vs. safe contrast after the treatment.

CHAPTER 7: REDUCED WILLINGNESS TO EXPEND EFFORT FOR REWARD IN OBESITY: LINK TO WEIGHT LOSS OUTCOMES

Declaration for Thesis Chapter 7

Monash University

In the case of Chapter Seven, the nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
Study conceptualisation, study design, data collection and analysis, interpretation of results and manuscript preparation	80%

The following co-authors contributed to the work. If co-authors are students at Monash University, the extent of their contribution in percentage terms must be stated:

Name	Nature of contribution	Extent of contribution (%) for student co-authors only
Antonio Verdejo-Garcia	Study conceptualisation, study design, interpretation of results and manuscript preparation	n/a
Michael Treadway, Julie Stout, Murat Yucel and Helen Truby	Interpretation of results and manuscript preparation	n/a
Alastair Kwok	Data collection	20%

The undersigned hereby certify that the above declaration correctly reflects the nature and extent of the candidate's and co-authors' contributions to this work.

Candidate's signature: Fernanda Mata Date: 05/09/2016

Main supervisor's signature: Date: 05/09/2016

TITLE

Reduced willingness to expend effort for reward in obesity: Link to weight loss outcomes.

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KEYWORDS: Effort-based decision-making, Obesity, Young adults, Weight loss intervention

ABSTRACT

Objective: (1) To compare willingness to expend effort for rewards between healthy weight, overweight and obese young adults; and (2) To examine how individual differences in willingness to expend effort for rewards predict adherence to weight loss treatment.

Methods: 73 participants (26 healthy weight, 26 overweight and 21 obese) completed the Effort Expenditure for Rewards Task (EEfRT). Of those 73 participants, 42 excess weight young adults (26 overweight and 20 obese) took part in a 3-month weight loss intervention after completing the EEfRT. Generalized Estimating Equations (GEE) models were used to compare the healthy weight, overweight and obese groups in the EEfRT, and the interactions between group, reward magnitude and probability on willingness to expend effort for rewards. Logistic regression models, including the proportion of hard-task choices for each reward probability condition as predictors (12, 50 and 88%), were conducted to longitudinally predict attrition in the weight loss intervention.

Results: Obese young adults were significantly less willing to expend effort for high magnitude rewards compared to overweight participants ($p=0.05$), although neither of the obese or overweight groups differed from controls with healthy weight ($p>0.05$). Willingness to expend effort for uncertain rewards (50% probability) distinguished between completers and dropouts in the weight loss intervention ($\chi2 = 5.04$, $p< 0.02$).

Conclusion: Obese young adults, compared to their overweight counterparts, have diminished motivation to expend effort for obtaining high magnitude rewards. Less willingness to expend effort for the most uncertain rewards predicts poor adherence to weight loss treatment.

Introduction

Over 30% of young adults (18-24 years old) in developed countries are overweight or obese (Ng et al., 2014). Young adults are a particularly vulnerable group to develop obesity, as they gain weight at a higher rate than any other age group (Lewis et al., 2000). Weight gain has been shown to have a dynamic course, in which initially enhanced motivation to approach rewards shifts to diminished interest in these rewards as body mass index (BMI) increases (Davis, Strachan, & Berkson, 2004). Thus, obesity is often associated with motivational deficits, as indicated by less subjective engagement in and enjoyment of rewarding behaviours (Pagoto, Spring, Cook, McChargue, & Schneider, 2006). In this context, it is important to examine effort-based decisions, in which potential rewards are weighed against the effort required to achieve them (Gendolla & Krusken, 2002). In the modern food environment, palatable energy-dense foods do not require much effort to be obtained given these foods are readily available at a minimal cost for a large segment of the population (Berthoud, 2012). Conversely, willingness to expend effort to lose weight is essential for adherence to weight loss interventions (Lantz, Peltonen, Agren, & Torgerson, 2003).

Effort-based decision-making varies as a function of reward probability (Bonnelle et al., 2015), and the relationship between individual sensitivity to this reward property and BMI ranges follow an inverted U-shaped curve (Davis et al., 2004). Therefore, it is relevant to examine effort-based decision-making across the three BMI categories (healthy weight, overweight and obesity). However, few studies to date have examined effort-based decisions in individuals with excess weight, and these studies have not differentiated between overweight and obesity. Among the available studies, two studies have used concurrent schedules of reinforcement tasks, adapted from the animal literature, in which button presses were used as a measure of relative effort. Participants were required to choose between earning points for high-calorie snacks or sedentary activities, and between standard foods and high-caloric snacks, and findings showed that adults with excess weight were willing to expend greater effort to obtain high-caloric food than healthy weight individuals (Epstein et al., 2007; Giesen et al., 2010). In another study, physical effort was measured by hand-grip force and participants had to make a decision about whether they wanted to put effort to receive both food and non-food rewards. Contrary to the above-described findings, obese individuals were less willing to put effort for high-caloric food than their healthy weight counterparts (Mathar et al., 2015). It is thus important to further evaluate effort-based decision-making, using better-validated tasks and different BMI ranges, to clarify its link to obesity. Among the available measures of this construct, the Effort Expenditure for Rewards Task has shown to reliably assess the weight of both reward magnitude and probability, and to correlate with the relevant traits of reward sensitivity and reward-related motivation (Geaney, Treadway, & Smillie, 2015).

Effort-based decision-making may also be relevant to predict the clinical outcome of weight loss programs. Recent studies have examined whether variation in reward sensitivity and motivation, and their related influences on decision-making under ambiguity are associated with both the adherence to, and the outcome of, weight loss interventions (Koritzky et al., 2014; Witbracht et al., 2012). These studies suggest that individuals who are more sensitive to reward during decision-making, and assign higher weights to gains (rewards) versus losses in the evaluation of alternatives, are more likely to drop out of a weight loss intervention (Koritzky et al., 2014). It has been proposed that heightened sensitivity to reward is associated with more difficulty to withdraw from very drive-gratifying behaviour, such as consumption of palatable energy-dense yet unhealthy food (Koritzky et al., 2014). As such, intact sensitivity to reward and motivation may be necessary prerequisites to advantageous decision-making in the long-term and successful treatment completion. To our knowledge, no study has focused on the prognostic utility of more cost/benefit aspects of decision-making, such as those related to the willingness to expend effort for rewards. This lack of research is striking given the link between anhedonia, characterised by an inability to feel pleasure in rewarding activities, obesity and poor treatment outcome (Komulainen et al., 2011). Hypothetically, dieters may be willing to expend more effort for the most uncertain rewards to successfully complete a weight loss intervention given the likelihood that the reward of losing weight will be accomplished even if the diet is completed is uncertain. Indeed, there is evidence indicating that only a minority of participants in behavioural weight loss interventions lose a significant amount of weight (5% or more of the original weight) (Heshka et al., 2003). However, despite the intuitive appeal of such a relationship, it is yet unclear whether willingness to expend effort for uncertain rewards predicts attrition in weight loss interventions.

The aims of this study were: (1) To compare willingness to expend effort for rewards between healthy weight, overweight and obese young adults; and (2) To examine how individual differences in willingness to expend effort for rewards predicts adherence to weight loss treatment. The Effort Expenditure for Rewards Task (EEfRT) (Treadway et al., 2009) was used as a measure of willingness to expend effort for rewards. We hypothesized that: (i) the obese group would be less willing to expend effort for rewards than the overweight group and the overweight group would in turn be more willing to expend effort for rewards than the healthy weight group, and (ii) willingness to expend effort for the most uncertain rewards (50% probability) would distinguish between weight loss intervention completers and drop-outs.

Methods and Procedures

Participants

Seventy-three young adults (age range: 18-24; 26 healthy weight, 26 overweight and 21 obese) completed the baseline assessment. Participants' baseline characteristics are displayed in Table 1.

Table 1 - Baseline characteristics of healthy weight, overweight and obese young adults.

Variable	Healthy weight Mean (S.D[a])	Overweight Mean (S.D[a])	Obese Mean (S.D[a])	F/Chi square	p
Age	21.69(2.11)	21.72(1.7)	21.37(1.53)	0.23	0.79
Gender (%Male/Female)	38/62	36/64	14/86	3.73	0.15
Full Scale IQ	107.23(12.43)	104.25(11.92)	108.05(10.48)	0.67	0.51
BMI[b]	21.52(1.96)	27.41(1.41)	33.12(2.16)	227.08	0.000

[a]Standard deviation

[b]Body Mass Index

Overweight and obese participants were offered the opportunity to take part in a 12-week weight loss intervention. Of the 47 participants with overweight and obesity, 42 (89.3%) took part in the weight loss intervention.

Participants were recruited via community advertisements posted in the Monash University campus and clinics and via social media. The selection criteria for participants were defined as follows: (i) aged between 18 and 24 years; (ii) BMI between: 18kg/m2 and 24.9kg/m2 (Healthy weight group), 25kg/m2 and 29.9kg/m2 (Overweight group) and 30 kg/m2 and 40kg/m2 (Obesity group); (iii) no history or current evidence of neurological and psychiatric disorders, assessed via survey reports based on DSM-V criteria; (iv) no comorbid medical conditions associated with excess weight (e.g. type II diabetes, hypertension); (v) has not undergone weight loss surgery; (vi) and has not taken/is not taking medications for weight loss.

Measures

Effort Expenditure for Reward (EEfRT) (Treadway et al., 2009): The EEfRT is a measure of willingness to expend effort to obtain a monetary reward under different conditions of reward probability and reward magnitude (Treadway et al., 2009). In each trial, participants were given an opportunity to choose between two tasks with different levels of difficulty, a 'hard task' and an 'easy task', which require different amounts of speeded manual button pressing. Participants were told that successful trial completion did not guarantee winning money. Before making a choice, participants were provided with information that varied from trial to trial regarding the (1) reward probability (12%, 50% and 88%) of winning the money, and (2) reward magnitude of the hard task for successfully completed winning trials. The reward magnitude is $1.00 for easy tasks and higher amounts that varied per trial within a range of $1.24 – $4.30 for hard tasks. Successful completion of hard task trials requires 100 button presses, using the non-dominant little finger within 21 seconds, while successful completion of easy-task trials requires 30 button presses, using the dominant index finger within 7 seconds. Participants all were given 20 minutes to perform the task, thus the number of trials varied across the participants.

Wechsler Abbreviated Scale of Intelligence – Second Edition (WASI-II) Full Scale IQ – 2 subtest (FSIQ-2): The WASI-II is a measure of general cognitive ability (Wechsler, 2008). It consists of the Vocabulary task (31 items requiring definition of words) and the Matrix

Reasoning task (30 items requiring selection of a response option to correctly complete a set of matrices).

Body Mass Index

Height and weight were measured using a Holtain stadiometer and an electronic scale (SECA Group, Hamburg, Germany), respectively, as part of the first phase of the study. BMI was calculated for each participant as the ratio of weight in kilograms and divided by the square of height in meters.

Weight Loss Intervention

The multicomponent weight loss intervention consisted of individual counseling and was implemented for 12 consecutive weeks between the baseline and second assessments. The intervention included two modules: (a) a nutrition module and (b) a physical activity module. The nutrition module involved a modified intermittent fasting regimen that consisted of tailored dietary advice based on the Australian Dietary Guidelines on five days of the week with a focus on optimizing intake from the five core food groups and an overall reduction in energy intake. On the other two days of the week, supplementary milk-based protein shakes were provided for these 'fasting days'. Participants were also advised to consume a pre-prepared meal, vegetables and fruit on the 'fasting days'. The total energy intake for each 'fasting day' was approximately 800-1000 calories per day. The nutritional module was supported by six face-to-face sessions with an Accredited Practicing Dietitian which were scheduled at baseline, week 1, week 2, week 4, week 8 and week 12. Monitoring of weight and dietary compliance, via 24-hour dietary intake recalls, were conducted during these sessions. Nutrition information and education on different aspects of healthy eating were also provided at each session. The physical activity module involved encouraging participants to undertake at least five days/week of light to moderate physical activity with duration of 30 to 60 mins/day. Each participant was provided with a pedometer and a pedometer log to increase their motivation for physical activity and recommended to aim for 10,000 steps or more each day.

Data reduction and statistical analysis

As per instructions, participants performed the EEfRT during 20 minutes, and the number of trials completed during that time varied among them (Mean trials completed =61.76, SD =4.65, Range=52-73 trials). For consistency of analysis, only the first 50 trials were used, consistent with the original study using the EEfRT (Treadway et al., 2009). There were significant group differences in total trials completed, $F(2, 67)=3.25$, $p=0.045$, with the obese group (Mean trials completed=63.86, SD=5.28, Range=55-73 trials) completing more trials than the healthy weight (Mean trials completed=60.81, SD=4.05, Range=52-71 trials) and the overweight groups (Mean trials completed=60.91, SD=4.23, Range=53-69 trials).

GEE models were performed to test the effects of group, and the interactions between group, reward magnitude and probability on the willingness to expend effort for rewards. We used an exchangeable matrix and a binary logistic distribution to model the dichotomous outcome of choosing the hard versus the easy task in the EEfRT. Wald chi-square statistics were tested with a type III sums of squares approach. All GEE models included reward magnitude, reward probability and expected value. Furthermore, each model included trial number as a covariate to control for possible effects of fatigue over the course of the task. Reward magnitude was converted to a categorical variable with three levels: low (<$2.30), medium ($2.31 to $3.29), and high (>$3.30).

We examined attrition in three separate logistic regression models, including the proportion of hard-task choices for each probability condition as predictors (12, 50 and 88%).

Results

Comparison of effort-based decision-making between young adults with healthy weight, overweight and obesity

Three independent GEE models were tested (See Table 2). Model 1 tested for a main effect of Group on preference for hard tasks, but did not find an evidence for a significant main effect, χ^2 (2) = 4.42, $p = 0.10$. The three groups did not differ in willingness to expend effort to obtain a monetary reward. Model 2 tested for the interaction between Group and Reward magnitude, and found a significant interaction, χ^2 (6)=14.85, p=0.02. Post-hoc pairwise comparisons indicated that within trials with a low and medium reward magnitude, the three groups showed similar preferences for hard and easy tasks (all ps > 0.05). Within trials with a high reward magnitude, however, the obesity group showed a lower probability of making hard-task choices compared to the overweight group (p=0.05). Nonetheless, neither the obesity nor the overweight group were significantly different from the healthy weight group (p > 0.05) in choosing the hard task in trials with a high reward magnitude. Model 3 tested for an interaction between Group and Reward probability, but did not find evidence for the interaction, χ^2 (6)= 7.75, $p = 0.25$. Therefore, we did not find a difference between the three groups in their sensitivity to reward probability when choosing hard tasks.

Table 2. GEE Models

				95% CI		
	χ	b	SE	Lower	Upper	*p*
Model 1						
Reward magnitude	18.10					0.00
Medium	6.58	0.41	0.16	0.09	0.73	0.01
High	15.24	0.84	0.21	0.41	1.26	0.00
Reward probability	12.41					0.00
Medium	2.05	0.31	0.21	-0.11	0.73	0.15
High	8.38	0.96	0.33	0.31	1.61	0.00
Expected Value	22.10	0.78	0.16	0.45	1.11	0.00
Trial number	9.15	-0.01	0.00	-0.01	0.00	0.00
Group	4.42					0.10
Overweight	0.14	-0.08	0.22	-0.52	0.35	0.70
Obese	3.97	-0.05	0.25	-1.00	0.00	0.04
Model 2						
Reward magnitude	18.27					0.00
Medium	3.91	0.52	0.26	0.00	1.04	0.04
High	5.11	0.67	0.29	0.09	1.26	0.02
Reward probability						0.00
Medium	2.07	0.31	0.22	-0.11	0.75	0.15
High	8.26	0.97	0.34	0.31	1.64	0.00
Expected value	21.34	0.78	0.16	0.44	1.11	0.00
Trial number	9.25	-0.01	0.00	-0.01	0.00	0.00
Group*Reward magnitude	14.85					0.02
Model 3						
Reward magnitude	18.03					0.00
Medium	6.55	0.41	0.16	0.09	0.73	0.01
High	15.18	0.83	0.21	0.41	1.25	0.00
Reward probability	12.50					0.00
Medium	5.74	0.67	0.28	0.12	1.22	0.01
High	7.87	1.21	0.43	0.36	2.06	0.00
Expected value	22.65	0.79	0.16	0.46	1.11	0.00
Trial number	9.20	-0.1	0.00	-0.01	-0.00	0.00
Group*Reward probability	7.75					0.25

Note. All models included reward magnitude, reward probability and trial number. χ^2 = Wald chi-square; *b* = regression coefficients are linear predictors of the likelihood of choosing the hard-task; CI = confidence interval. Estimations were computed in relation to the low reward magnitude level, low reward probability level and the healthy weight group, the parameters for which are therefore redundant.

Prediction of attrition in the weight loss intervention

There was a significant reduction in BMI ($t=4.43$, $p<0.001$, Cohen's $d=0.33$) after treatment. Of the original 42 participants, 25 (59.5%) completed the intervention, and 17 (40.5%) did not. This attrition rate is similar to those reported in the literature in this age group (Moroshko, Brennan, & O'Brien, 2011; Skelton, Goff, Ip, & Beech, 2011).

We examined attrition in three separate logistic regression models, including the proportion of hard-task choices for each probability condition as predictors (12, 50 and 88%). Only the logistic regression model for the 50% probability condition was statistically significant, $\chi^2 = 5.04$, $p < 0.02$, indicating that this model was able to distinguish between weight loss intervention completers and drop-outs. The predictor (hard-task choices for 50% probability) was significant as well, $p < 0.04$. This model explained between 12.1% (Cox and Snell R Square) and 16.4% (Nagelkerke R Squared) of the variance in drop-out status, and correctly classified 69.6% of completers and 50% of drop-outs.

Table 3: Regression models predicting intervention attrition using the proportion of hard-task choices for each probability as the predictors

	Model 1[a]	Model 2[b]	Model 3[c]
Model Chi-square	1.9(p<0.16)	5.04 (p<0.02)	0.331(p<0.56)
Cox & Snell R Square	0.04	0.12	0.00
Nagelkerke R Square	0.06	0.16	0.01
Predictor (Wald Statistic)	1.68(p<0.19)	4.18 (p<0.04)	0.329(p<0.56)
Completers corrected classified	100%	69.6%	95.70%
Drop-outs corrected classified	0%	50.0%	12.50%

[a] Proportion of hard-task choices for 12% probability

[b] Proportion of hard-task choices for 50% probability

[c] Proportion of hard-task choices for 88% probability

Discussion

Consistent with our hypotheses, obese young adults displayed less willingness to expend effort for rewards than their overweight counterparts. Specifically, compared to overweight young adults, those who were obese were less willing to expend effort for the rewards with the highest magnitude. Willingness to expend effort for the most uncertain rewards (50% probability) reliably distinguished between weight loss intervention completers and drop-outs. Weight loss intervention completers expended significantly more effort for uncertain rewards than drop-outs. Our results suggest that willingness to expend effort for uncertain rewards is relevant to characterize obesity, and to predict adherence to weight loss interventions.

One reason why obese individuals, compared to their overweight counterparts, may have expended less effort for the greatest rewards is that the obese group does not increase their preference for the hard tasks during high rewards as the overweight group does. This notion resonates with the findings of previous cross-sectional self-report studies showing that obese individuals are less sensitive to reward than overweight individuals (Davis et al., 2004). Furthermore, individuals with obesity report less engagement in rewarding activities (Pagoto et al., 2006) and are less willing to engage in physical effort for high-caloric food (Mathar et al., 2015). One potential mechanism to explain less willingness to work for reward in obesity is the rewiring of the brain's reward system associated with long-lasting consumption of high energy-dense food (Volkow et al., 2011; Wang et al., 2001). Prolonged overeating has been associated with alterations in the dopaminergic reward system, and these alterations have been shown to result in hyposensitivity to reward in obesity (Volkow et al., 2011). In our study, however, performance of obesity and overweight groups did not differ significantly from the healthy weight group, although with the $p = .10$, the possibility exists that a larger sample may be needed to reveal such differences.

Our weight loss attrition findings suggest that intervention completers may be willing to overcome the ambiguity and effort-related costs of desired rewards when making effort-based decisions. Despite the lack of guarantee of receiving the reward (successfully losing weight), intervention completers may have more motivation than drop-outs to comply with treatment requirements (effort costs), such as not consuming energy-dense food and coping with the discomfort that arises from reducing caloric intake and physical activity (e.g., food cravings, physical discomfort that can accompany exercising). Therefore, willingness to expend effort for uncertain rewards may reflect an adaptive mechanism that increases the likelihood of goal pursuit in situations where rewards are uncertain and cannot stimulate appetitive responding (Hughes, Yates, Morton, & Smillie, 2015). In contrast, for the participants who did not complete the weight loss intervention, the lower level of willingness to exert effort for the most uncertain rewards may be associated with greater estimated effort costs in relation to the probability of attaining the reward. Based on this high estimated effort, drop-outs may be less motivated to complete a weight loss intervention, where the lack of guarantee of reward (successfully losing weight) would be expected to tax motivation maximally. That is, intervention drop-outs may be more sensitive to effort costs, particularly under circumstances of lack of guarantee of reward, and thus not willing to complete a weight loss intervention.

Our findings may have important clinical implications. First, they underline the usefulness of cognitive measures to identify patients at risk of dropping out of a weight loss intervention. Second, they suggest that effort-based decision-making skills may be a promising target for interventions promoting better treatment outcomes in overweight and obese young adults. Treatments aimed at altering the value of rewards by manipulating the brain's reward system using dopaminergic modulation may promote a greater willingness to exert effort to achieve weight loss. Furthermore, our findings support the importance of the clinical cut-off points overweight versus obese and the examination of the three BMI categories (healthy weight, overweight and obese). Frequently, overweight and obese individuals are examined as a whole (overweight/obese versus healthy weight) or only obese and healthy weight individuals are investigated.

We conclude that obese young adults, compared to their overweight counterparts, demonstrate diminished motivation to expend effort for high magnitude rewards. Furthermore, willingness to work for uncertain rewards may be crucial to adhere to weight loss intervention and complete treatment objectives. Future studies are warranted to longitudinally assess effort-based decision-making using food rewards in young adults with overweight as they progress to obesity.

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CHAPTER 8: GENERAL DISCUSSION

Introduction to General Discussion

This final chapter provides an integrated discussion of the key findings of this thesis, which are reviewed in the context of the original research aims and the existing literature regarding decision-making abilities in youth overweight and obesity. A discussion of the clinical implications, as well as the strengths of the research will follow. Next, limitations of the research and suggestions for future research will be proposed and finally a conclusion of the thesis findings will be presented.

Key Findings of the Thesis

The following section summarises the key findings of this thesis which aimed to examine (i) the neurobehavioural systems that underlie decision-making (i.e., the interoception, goal-monitoring and reward-impulsive systems) in overweight and obesity (Chapters Four and Five), (ii) the impact of weight loss on these systems (Chapter Six), and (iii) the contribution of decision-making skills to treatment outcome in youth (Chapter Seven). The first empirical paper examined to what extent cognitive measures of decision-making under ambiguity and risk were associated with body mass index (BMI) in young adults. This study utilised two complementary versions of the Iowa Gambling Task (IGT) (Bechara et al., 1994) to assess decision-making under ambiguity, and the Risky Choice Task (RCT) (Clark et al., 2012) to assess decision-making under risk. It was found that decision-making under ambiguity and risk was significantly associated with BMI. However, decision-making skills explained a relatively small proportion of the variance (13.4%) for BMI. More advantageous choices on the version of the IGT involving high punishment and high reward, and more risky choices that are slightly disadvantageous (i.e., associated with small, negative expected values) on the RCT were associated with higher BMI. Conversely, risky choices that are advantageous (i.e., associated with high, positive expected values) on the RCT were negatively associated with BMI. Risky choices that are slightly disadvantageous were the most significant correlate of excessive BMI. These findings suggest that young adults with excessive BMI are prone to make risky choices when the anticipated reward is equal or slightly higher than the expected loss. The relevance of these findings for real-life choices is that risky choices in young adulthood could be translated into food choices driven by the rewarding properties of palatable food despite awareness of its health-related risks and impact on diet goals. Although the aggregate risk of having an unhealthy diet is substantial, it has been proposed that the risk of consuming unhealthy foods is typically estimated on a meal-by-meal basis, and thus the negative consequences of a single food rarely appear to be exceedingly large (Zald, 2009). As a result, the reward attributes and the hedonic pleasure linked to choosing a palatable yet unhealthy food frequently outweighs the risk of negative health-related consequences. In support to this notion, neuroimaging studies have shown that adolescents with overweight and obesity display increased activation in regions signaling reward (midbrain) and decreased activation in regions signaling risk (left anterior insula) preceding risk-taking decisions (Delgado-Rico et al., 2013).

Extending on the findings from the first study, the second empirical study aimed to examine if adolescent obesity was associated with alterations of the insula-related interoceptive system during decision-making under risk. Specifically, functional magnetic resonance imaging (fMRI) was used to investigate whether adolescent obesity was associated with alterations of the interoceptive system as indexed by differential correlations between insula activation and perception of interoceptive feedback versus external food cues. This study utilized the Risky-Gains Task (Paulus et al., 2003) as a measure of decision-making under risk, the Heartbeat Perception Task (Schachter, 1968) as a measure of perception of interoceptive feedback, and the external eating subscale of the Dutch Eating Behaviour

Questionnaire (Van Strien, Frijters, Bergers, & Defares, 1986) as a measure of sensitivity towards external food cues. Insula activation positively correlated with external eating and negatively correlated with interoceptive sensitivity in excess weight adolescents. The opposite pattern was observed in healthy weight adolescents. These findings suggest that excess weight may interfere with the normal perception of interoceptive input (i.e., signals of hunger and satiety, bodily representations of the risk of aversive outcomes). Disrupted perception of internal bodily signals (e.g. satiety cues) may result in overeating based on the reduced ability of satiety signals to curb response evocation by external food cues in the modern food environment (Hargrave, Jones, & Davidson, 2016; Wansink, Payne, & Chandon, 2007).

In excess weight adolescents, external eating – which refers to a heightened responsiveness to external food-related cues - was also positively associated with caudate nucleus activation, and restrained eating – which refers to an effort to restrict food intake for the purpose of maintenance and weight loss – was negatively associated with insula activation. When considered together, these findings indicate that both interoceptive and reward related brain regions are tuned towards external cues in excess weight adolescents. In this way, the ability of external food cues to evoke appetite and eating behaviours may become stronger than the ability of internal satiety signals to inhibit those responses (Sample, Jones, Hargrave, Jarrard, & Davidson, 2016), which may hamper efforts to restrain overeating. This relative external control of food intake may be central to the emergence and maintenance of obesity in the modern environment, characterised by a high prevalence of external cues that are associated with highly palatable, energy-dense foods (Sample, Martin, Jones, Hargrave, & Davidson, 2015).

The third empirical study aimed to examine if treatment-related success in weight loss (i.e., reductions of BMI and fat percentage) was linked to significant changes in choice evoked brain activity in excess weight adolescents. Excess weight adolescents performed the Risky-Gains Task during functional Magnetic Resonance Imaging (fMRI) both before and after a 12-week weight loss intervention. The Risky-Gains Task was used as a measure of risky decision-making (Paulus et al., 2003). Findings showed that adolescents showing greater reductions in weight and fat mass also showed increases in activation of the insula-related interoceptive system during anticipation of risky choices from pre- to post-intervention. These findings complement the second study that had linked insula activation during risky decision-making with poorer perception of bodily feedback (i.e., heartbeat sensations) during risky decision-making in excess weight adolescents. The third empirical study revealed that this insula deficit can at least partly recover following successful weight loss. These results demonstrate that successful weight loss is accompanied by greater perception of interoceptive input (i.e., signals of hunger and satiety, bodily representations of the risk of aversive outcomes) preceding risk-taking decisions. Interoceptive sensitivity significantly shape decision-making processes; for example, individuals with good interoceptive sensitivity tend to select less risky choices in a decision-making task (Werner, Jung, Duschek, & Schandry, 2009). The relevance of these findings for real-life choices is that adolescents showing more successful weight loss may be more able to detect internal bodily signals (e.g. satiety cues) and stop eating when they feel full. Indeed, relying on internal bodily signals for meal cessation, rather than on situational or external food cues, has been shown to improve eating patterns (Wansink et al., 2007).

The fourth empirical study aimed to (1) compare willingness to expend effort for rewards between healthy weight, overweight and obese young adults, and (2) examine how individual differences in willingness to expend effort for rewards predict adherence to weight loss treatment. Healthy weight and excess weight young adults completed the Effort Expenditure for Rewards Task (EEfRT) (Treadway et al., 2009) as a measure of willingness to expend effort for rewards. Excess weight young adults took part in a 3-month weight loss intervention after completing the EEfRT. Findings showed that young adults with obesity were significantly less willing to expend effort for high magnitude rewards compared to participants with overweight, although neither of the obese or overweight groups differed from controls with healthy weight. One reason why obese individuals, compared to their overweight counterparts, may have expended less effort for the greatest rewards is that the obese group does not increase their preference for the hard tasks during high magnitude rewards as the overweight group does. This finding may suggest that obesity is associated with lower behavioural adaptation to changes in the motivational value of reward (e.g. reward magnitude). Indeed, obese individuals have been shown to be less sensitive to changes in motivational value of snack food, as induced via a devaluation procedure, compared to their healthy weight counterparts, which results in automatic overeating patterns in obesity (Horstmann et al., 2015). The potential mechanisms for the less willingness to work for the greatest rewards in obesity includes the rewiring of the brain's reward system linked to prolonged consumption of high energy-dense food (Kroemer & Small, 2016). There is increasing evidence that overconsumption of rewarding food can lead to changes in the dopaminergic reward system, which results in hyposensitivity to reward and heightened habit-like responding among populations with obesity (Volkow, Wang, & Baler, 2011).

Willingness to expend effort for the most uncertain rewards distinguished between completers and dropouts in the weight loss intervention. Intervention completers may be more motivated to engage and complete the weight loss intervention than dropouts despite the lack of guarantee of receiving the reward. i.e., successfully losing weight. Our results suggest that attrition in the weight loss intervention may be related to the way the uncertainty of receiving the reward affects the estimation of effort costs, and more particularly manifest as decreased willingness to exert effort when the probability of receiving the rewards is ambiguous. That is, the participants that drop out weight loss interventions may have less tolerance for the effort-related costs of uncertain rewards (e.g., foregoing a favorite dessert and coping with the discomfort that arises from physical activity). Conversely, intervention completers may be willing to overcome the ambiguity and effort-related costs of desired rewards when making effort-based decisions. Overall, these findings suggest that willingness to expend effort for uncertain rewards is relevant to adhere to weight loss intervention. In support to these findings, several studies have linked pre-treatment motivation with treatment outcomes in obesity (Bean et al., 2015; Kearney, Rosal, Ockene, & Churchill, 2002).

Collectively, the findings of this thesis suggest that adolescent and youth obesity is associated with alterations in the function of the insula-related interoceptive system and the reward-impulsive system during decision-making, which may result in poor food choices and overeating. Obese youths display disrupted tuning of the insula-related interoceptive system towards internal signals (i.e., signals of hunger and satiety). Both interoceptive and reward-impulsive related brain regions are tuned towards external cues in obesity. In this way, overeating in the face of rewarding external food cues may be related to reduced responsivity to interoceptive input (i.e., satiety signals, bodily representations of the risk of aversive outcomes) among populations with obesity (Sample et al., 2016). The findings of this thesis suggest that reduced responsivity to interoceptive input in obesity is associated with less ability to encode the risk associated with choices that are slightly disadvantageous in the long term (e.g. health-related risks of poor food choices). Youths showing greater treatment-related weight loss (i.e., reductions of BMI and fat percentage) have greater normalisation of the interoceptive system. This may result in greater perception of interoceptive input (i.e., signals of hunger and satiety, bodily representations of the risk of aversive outcomes) and less risky food choices (Werner et al., 2009). This thesis also provides evidence that attrition in weight loss intervention is linked to effort-based decision-making. Willingness to expend effort for uncertain rewards may be crucial to adhere to weight loss intervention and complete treatment objectives.

Clinical Implications

The findings from the research studies reported in this thesis have important clinical implications for the development of early intervention and therapeutic programs for youth obesity. The ability to provide evidence-based treatment strategies for young people with obesity may serve to avert more severe manifestations of obesity and obesity-related adverse outcomes, including metabolic syndrome, cardiovascular disease, diabetes type 2, and several types of cancer (Cheng et al., 2016).

The findings of this thesis suggests that overweight and obese youths showing greater success in weight loss have greater normalisation of the insula-related interoceptive system. These findings support the potential utility of cognitive interventions focused on enhancing appraisal of internal body signals as well as hunger and satiety awareness (Bloom, Sharpe, Mullan, & Zucker, 2013). These cognitive interventions are based on the premise that excess weight individuals frequently eat in response to situational or external cues, rather than eating when they are hungry and stopping when they are full. In these interventions, excess weight individuals are encouraged to increase eating in response to moderate internal hunger and satiety cues, and reduce eating in response to external-food related cues (Hill, Craighead, & Safer, 2011).

Successful weight loss is often compromised by poor attendance and treatment attrition, which impacts, on average, 32% of the individuals who start a weight loss intervention (Dietz et al., 2015). From the findings of this thesis, willingness to expend effort for uncertain rewards is a relevant mechanism to explain adherence and completion of treatment objectives. These findings suggest that treatment strategies aimed at strengthening effort-based decision-making skills may prove useful to increase treatment adherence. For instance, strategies that reinforce treatment attendance and engagement with immediate, tangible rewards (e.g., cash) may increase treatment completion (Morean et al., 2015). Moreover, treatments aimed at altering the value of rewards by manipulating the brain's reward system using dopaminergic modulation may promote a greater willingness to exert effort to achieve better treatment outcomes (Wardle et al., 2011).

Strengths of the Thesis

While decision-making in obesity has been extensively examined in children and adults, this research provides novel insights about decision-making in adolescents and young adults. It has been shown that youth is a particularly vulnerable group for developing obesity as suggested by epidemiological evidence showing significant and rapid weight gains during this developmental period (Ng et al., 2014). Furthermore, unlike children, youth are more autonomous in their decision-making about food, which means this is a crucial developmental stage for establishing cognitive control and decision-making in relation to eating habits (Stok et al., 2015).

Another important strength of this thesis include the measured selection of adolescents and young adults with excess weight, who were matched to their healthy weight counterparts in biochemical and psychological indices; this selection allowed me to elegantly test the neurobehavioural assumptions without relevant medical or psychological confounders. In addition, specific well-validated tasks of three key decision-making mechanisms that may be relevant to food choices in obesity were used in this thesis: (i) decision-making under risk, (ii) decision-making under ambiguity and (iii) effort-based decision-making; the utilisation of these indices allowed me to examine how different decision-making mechanisms are associated with obesity and weight loss treatment outcomes.

Limitations of the Thesis and Future Research Directions

The findings of this thesis must be appraised in the context of some relevant limitations. An important limitation relates to the samples employed in the first and fourth studies of this thesis (Chapters Four and Seven). Given that participants were predominantly recruited from university campuses they are likely to have higher than average levels of intelligence and a middle class socio-economic background (CSHE, 2008). Furthermore, in the fourth study (Chapter Seven), performance of obesity and overweight groups did not differ significantly from the healthy weight group, although with the $p = .10$, the possibility exists that a larger sample may be warranted to reveal such differences. Given these limitations, replication with more diverse and larger samples is needed to enhance the generalisability of the findings.

A second limitation of this thesis relates to the decision-making tasks utilised in the research studies given that these tasks included only non-food stimulus (e.g., monetary rewards). Behavioural and functional magnetic resonance imaging (fMRI) studies employing more ecological food-choice paradigms are needed as they could determine whether the findings of this thesis are relevant to real-life food choices.

Conclusion

Youth obesity is linked to less ability to encode the risk associated with choices that are slightly disadvantageous in the short-term and can be significantly disadvantageous in the long term. This abnormal risk processing is characterised by disrupted tuning of the insula towards bodily feedback (e.g. heartbeat sensations) during decision-making. Both interoceptive and reward-impulsive related brain regions are tuned towards external cues in obesity. This insula-related interoceptive deficit recovers following successful weight loss (i.e., reductions in weight and fat mass). Youths showing greater success in weight loss have greater normalisation of the insula-related interoceptive system. Attrition in weight loss intervention is linked to effort-based decision-making. Willingness to expend effort for uncertain rewards may be crucial to adhere to weight loss intervention and complete treatment objectives.

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