Interactions of obesity associated behaviours, BMI, age, sex, and *FTO* genotype

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To my parents, husband and children…

Author's declaration

I hereby declare that:

1. I have not been enrolled for another award of the University, or other academic or professional organisation, whilst undertaking my research degree.

2. None of the material contained in the thesis has been used in any other submission for an academic award.

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4. The work undertaken towards the thesis has been conducted in accordance with the SHU Principles of Integrity in Research and the SHU Research Ethics Policy.

5. The word count of the thesis is 40,846.

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Abstract

Obesity is a complicated condition which occurs due to interactions between many contributing physiological, psychological and genetic factors. Age, sex and body mass index (BMI) are also important in the interaction with obesity-related factors leading to a rise in this epidemic. Knowledge about the interactions that happen between these factors provides a basis for the development of body mass-reducing interventions for people with obesity.

Eating behaviours affect caloric intake and are implicated in the development of obesity. Three types of eating behaviours namely; 1) cognitive restraint, 2) emotional eating and 3) uncontrolled eating have been studied for associations with obesity in various populations. Food cravings refer to an irresistible urge to eat a specific type of food which has been implied to contribute to a loss of control over eating. The experience of food cravings is related to higher BMI and obesity.

Motivation to exercise is also an important factor that influences people´s eating habits as shown in previous studies. A taxonomy where motivation is organised in the form of a continuum that covers the different degrees of self-determination of behaviour, from the non-self-determined, to the self-determined, established three types of motivation (amotivation, extrinsic motivation and intrinsic motivation) and a series of behavioural regulation stages (amotivation, external regulation, introjected regulation, identified regulation and intrinsic regulation).

Problems with emotional regulation may contribute to the development and maintenance of abnormal eating behaviour. Alexithymia is defined as an inability to describe and/or recognise one's own emotions and is considered a common feature in eating disorders. Alexithymia is likely to be associated with problems in modulating affect and with difficulties in the interpersonal and social realm.

The programme of research as part of this PhD was conducted on 424 volunteers from Sheffield Hallam University students and staff, and there were 183 participants of weight-loss interventions. Eating behaviours were measured using the revised Three-

Factor Eating Questionnaire (TFEQ-R18); food cravings were measured by the food cravings inventory (FCI), motivation for exercise using the Behavioural Regulation in Exercise Questionnaire-2 (BREQ-2) and alexithymia was measured by The Toronto Alexithymia Scale (TAS 20).

DNA samples were genotyped using the TaqMan method for the rs9939609 polymorphism in the obesity-associated gene *FTO*. Questionnaire data were analysed for associations between the TFEQ-R18 and FCI, BREQ2 and TAS20 subscales for the whole study group, and the group divided by sex, genotype, age (≤ 25 years vs > 25 years) and BMI (<30kg/m² and ≥30kg/m²). Regression and mediation analyses were used to explore the relationships between BMI, eating behaviours, food cravings, motivation to exercise and alexithymia.

The key findings from each of the experimental chapters in this thesis is 1) Increased cognitive restraint was associated with decreased food craving scores in the ≤ 25 years group; in this group the association between BMI and reduced food cravings was mediated by cognitive restraint indicating that in this age group individuals use cognitive restraint to control their food cravings. 2) Motivation to exercise interacts with eating behaviours and high motivation to exercise is associated with low BMI, people with obesity were less motivated than non-obese, emotional eating is the mediator between external regulations and high BMI. 3) There is a positive relationship between BMI and alexithymia in females, but in contrast there is an inverse relationship in men. The relationship between BMI and alexithymia was stronger in the AA+ AT genotype group than TT genotype. Uncontrolled eating and emotional eating mediate the effect of alexithymia on BMI and this is different between males and females and between genotype groups; particularly in females with the risk genotype, alexithymia were associated with high uncontrolled eating and emotional eating and so higher BMI. Males and/or people with the TT genotype are less at risk of this influence of alexithymia on BMI. These findings will help in the treatment of obesity by informing personal intervention programmes for each person according to his or her situation.

Abbreviations

5-HT - 5-Hydroxytryptamine (serotonin)

5-HT_{2A}R - Serotonin 2A receptor

5-HT_{2C}R - Serotonin 2C receptor

α-MSH - alpha- melanocyte stimulating hormone

ACQ - Attitudes to Chocolate Questionnaire

AgRP - Agouti-related protein

ANKK1-anakyrin receptor

ARC - Arcuate nucleus of hypothalamus

BDNF - Brain-derived neurotrophic factor

(BFP)- Body fat percentage

BMI - Body mass index

BED - Binge eating disorder

CAD - Cardiovascular diseases

CART - Cocaine and amphetamine regulated transcript

CCK -Cholecystokinin

COBLL1- Cordon-Bleu Protein-Like 1

COMT Val108/158Met - Catecholamine-o-methyltransferase

CR - Cognitive restraint

DRD2- Dopamine receptor 2

EE - Emotional eating

FCB - Food craving behaviour

FCQs - Food Cravings Questionnaires

FCI - Food Craving Inventory

FTO - Fat mass obesity related

GABA - Gama amino-butyric acid

GWAS - Genome wide association studies

IRS1 - Insulin receptor substrate 1

LEPR - Leptin receptor

LHA - Lateral hypothalamic area

PVN - Paraventricular nucleus

MAFs - minor allele frequencies

MC4R - Melanocortin-4 Receptor

NCDs - Non-communicable diseases

NPY - Neuropeptide Y

OCQ - Orientation towards Chocolate Questionnaire

PFKP - Platelet type phosphofructokinase

PLA2G6 - phospholipase A2, group VI (cytosolic, calcium-independent)

POMC - Proopiomelanocortin

PYY - Peptide tyrosine tyrosine

RS - Restraint scale

SNP - Single nucleotide polymorphism

T2DM -Type 2 Diabetes Mellitus

TFEQ -Three Factor Eating Questionnaire

TOMM40 - Translocase Of Outer Mitochondrial Membrane 40

UE - uncontrolled eating

VMH - Ventromedial hypothalamus

VTA – Ventral tegmental area

WHO - World Health Organization

WC - Waist circumference

WHR - Waist-to-hip ratio

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1-Satiety- from Origins to Applications, Institute of Child Health London **(2015)**.

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Manuscripts in preparation

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1 CHAPTER 1: Background and literature review

1.1 Introduction

The prevalence of obesity has tripled between 1975 and 2016, reaching epidemic proportions globally (World Health Organisation 2016).According to the World Health Organisation (WHO), 39% of adults were classified as being overweight and 13% obese (World Health Organization 2016). Existing estimates are that 41 million children globally are overweight (Booth *et al.* 2018).

At current rates of increase, it is projected that globally, 2.16 billion (38%) adults will be overweight and 1.12 billion (20%) obese by the year 2030 (Kelly *et al.* 2008). Though obesity was traditionally believed to be a problem primarily faced by populations in developed, high income countries, large scale analyses have revealed it to be a global problem affecting many low income countries (Finucane *et al.* 2011). In the UK, prevalence is gradually increasing with authorised records for England and Wales showing that 20% of children are obese and if trends remain, it has been predicted to increase to 50% by the year 2030 (Wang *et al.* 2011).

The WHO states that the major causes of obesity are twofold: 1) an increasing prevalence of inactive lifestyles in combination with 2) a rise in a diet that contains too much sugar, fat and salt (World Health Organization 2016). The present western environment is particularly obesogenic with the easy accessibility of high calorie, palatable food, and the absence of physical activity (Berthoud and Morrison 2008). It is thought that there are several related causes involved in the development of overweight and obesity including genetic, metabolic, environmental, and socio-cultural aspects but also the individual eating behaviors (Renner *et al.* 2012).

Obesogenic environments have been defined as 'the sum of influences that the surroundings, opportunities, or conditions of life have on promoting obesity in individuals or populations' (Swinburn and Egger 2002).

The built environment is a key contributing factor to the rising prevalence of obesity, through influencing physical activity and dietary behaviours at the individual and community level (Townshend and Lake 2017). The 2014 McKinsey report (Institute MG 2014) highlighted that overcoming obesity requires multiple interventions, involving many sectors from policy and practice through to industry and consumers. The report describes how there is a need to 'reset the default' in order to normalise and make healthy behaviours easier, relying less on the individual (institute MG 2014). Swinburn and colleagues described how 'dramatic actions' are needed, globally, to address food environments and thereby impact the on the rise in obesity and diabetes (Swinburn *et al.* 2015).

The worldwide rise in obesity has been 'driven' by significant changes in the global food system (Swinburn *et al.* 2015). This food system produces readily available, processed food which is marketed to populations (Swinburn *et al.* 2015). Looking at trends in high, middle and low income countries, research has concluded that increases in the food energy supply, alongside increasing sedentary behaviour, explains the increases in population body weight, particularly in high income countries (Vandevijvere *et al.* 2015). The food environment is a contributing factor in the development of obesity, and therefore has a role to play in preventing obesity (Lake 2018).

From nudging and choice architecture (Bucher *et al.* 2016), to conceptualizing how the local food environment influences eating behaviour (Caspi *et al.* 2012) the food environment can be defined as any opportunity to obtain food; it includes physical,

socio-cultural, economic and policy influences at both micro and macro-levels (Townshend *et al.* 2009). The broader food environment includes the home food environment, food policies and school food policies in addition to the neighbourhood food environment (Townshend *et al*. 2017). Story *et al* have developed an ecological framework to illustrate the influences on dietary behaviours (Story *et al.* 2008).

The neighbourhood food environment is defined as a mixture of retail outlets (for example, small convenience stores to supermarkets,) as well as restaurants and take-away ('fast food') outlets and is not limited to the residential neighbourhood (Townshend *et al.* 2017). The neighbourhood food environment influences individual food choice and food intake through the concept of food access. The relatively simple concept of access, in terms of the food environment actually includes five dimensions which are: availability, accessibility, affordability, acceptability, and accommodation (Penchansky *et al.* 1981).

Research has focused on the availability and accessibility of neighbourhood food outlets. Two recent systematic reviews, one exploring the local food environment in relation to obesity (Cobb *et al.* 2015) and one exploring the food environment in relation to diet (Caspi *et al.* 2012) have been inconclusive in their findings. This is, in part, due to the complexity of the measures and the quality of the studies. However some important patterns emerged; for example, in adults, Cobb *et al. (*2015) found evidence that supermarket availability was negatively associated with obesity and fast food availability was positively associated. Janssen *et al*'s review suggested that the strongest determinants of out-of-home food availability are the density of food outlets and deprivation within the built environment (Janssen *et al.* 2017).

The surrounding environment impacts on food choice, ultimately eating behaviour and consequently energy balance, weight gain and obesity (Rosenheck *et al.* 2008). Neighbourhood food environments are important and much attention has been paid to fast food and takeaway outlets. Actually, the food served within these outlets tends to be nutrient poor and energy dense (Jaworowska *et al.* 2013). Public Health England estimate that in 2014 there were over 50,000 fast food and takeaway outlets, fast food delivery services, and fish and chip shops in England and a greater proportion of these are in deprived areas (Public Health England (2017).Data from the UK National Diet and Nutrition Survey indicates that between a fifth and a quarter of people in the UK eat meals out once per week or more (Adams et al. 2015),with one fifth eating take-away meals at home once per week or more (Lake 2018).Being overweight or obese are risk factors for several non-communicable diseases (NCDs) such as coronary heart disease (CHD), cardiovascular disease (CVD), hypertension, stroke, certain types of cancer, diabetes mellitus, gallbladder disease, dyslipidemia, gout, and sleep apnoea (Löffler *et al.* 2015a). Given the increasing concerns about the effect of obesity on public health, it is becoming increasingly important to understand the psychological processes that cause the tendency to overeat unhealthy (high sugar, high fat) foods, especially in obesogenic environments (Booth *et al.* 2018).

1.1.1 Definition of overweight and obesity

WHO defines overweight and obesity as abnormal or excessive body fat accumulation which may impair health. In addition to being a major cause of health-related morbidity and mortality worldwide, obesity represents a growing public health challenge and economic burden to governments and countries (Wang *et al*. 2011).

Obesity is a complicated condition that arises because of an irregularity between energy consumption and use, resulting in abundant fat storage as excess adipose tissue (Razquin *et al.* 2011). The epidemic of obesity combined with poor efficacy of practical weight reduction interventions has encouraged the call for further research to develop effective treatment alternatives (Byrne *et al.* 2006). A deep understanding of the aetiology of weight increase is a clinical necessity (Llewellyn *et al.* 2014).

1.1.2 Assessment of obesity

Obesity is generally characterised by calculating body mass index (BMI ≥30 kg/m² in adults, and over the 95th percentile in children) and is determined as weight in kg divided by the height in meters, squared (Calle *et al*. 1999, Willett *et al.* 1999). BMI is the most widely utilised measure of weight status in research and data reporting, but is not a direct measure of body fat content (Koni 2013). A person's body mass includes not only fat mass but also muscle and bone mass and these measures may vary significantly between individuals, sex and races. However, BMI remains a cheap and convenient alternative proxy measure of adiposity which is measurable even in large scale studies. Most importantly, BMI is an established indicator of CVD), cardiovascular mortality, type 2 diabetes mellitus (T2DM), hypertension and other co-morbidities (Calle *et al.* 1999, Willett *et al.* 1999).

Waist circumference (WC) and waist-to-hip ratio (WHR) are two other important obesity-related anthropometric measures and reflect abdominal (central) fat deposition. The distribution of body fat is perhaps more important than the total body fat content in predicting adverse health outcomes (Lee *et al.* 2013). The larger proportion of the fat content in the human body is distributed subcutaneously primarily in the abdominal, gluteal and femoral regions. Abdominal obesity is known to

have more detrimental effects on metabolic health compared peripheral fat deposition (Lee *et al.* 2013).

Table 1-1 International definitions of generalised and central obesity [a]

	International criteria
Generalised obesity	(BMI cut-off values in kgm^{-2})
Normal weight	18.00 – 24.99
Overweight	25.00 – 29.99
Obese	≥ 30.00
Obese grade 1	30.00 – 34.99
Obese grade 2	35.00 – 39.99
Obese grade 3	≥ 40.00
Central obesity	(WC cut-off values in cm)
Male central obesity	≥102 cm
Female central obesity	≥ 88 cm

[a] World Health Organisation guideline (WHO Expert Consultation, 2004).

1.1.3 Obesity causes and risk factors

Obesity results from complex interactions between genetic, environmental and lifestyle factors leading to a state of chronic positive energy balance (Tchernof and Després 2013, Marti *et al.* 2004, Das 2010). On a background of relatively stable genetic influences, the more recent increase in obesity could be largely attributable to changes in lifestyle and environmental factors. Rapid urbanisation, commercialisation and associated lifestyle shifts towards sedentary living and consumption of energy dense foods are all factors attributable to the global epidemic of obesity (Arambepola *et al*. 2008). Modernisation occurring in high, middle and low-income countries has

resulted in obesogenic environments that facilitate unhealthy lifestyles (Befort *et al.* 2012)

Contrary to what was traditionally accepted, the protective effects of rural living on obesity are becoming less prominent. Rural living is associated with greater rates of obesity compared to urban areas in developed economies such as the USA (Liu *et al.* 2012), Sweden (Neovius and Rasmussen 2008) and Canada (Bruner *et al.* 2008) and is largely attributed to unhealthy diets, low education levels and ethnic differences. In middle and low-income countries though, urban living is still a strong predictor of obesity. The prevalence of rural obesity is increasing on a par with urban areas in many developing countries (Popkin *et al.* 2012).

1.1.4 Energy homeostasis

The complex physiology underlying energy homeostasis in the human body involves the integrative functions of the brain, gut and adipose tissue (Tchernof and Després 2013, Marti *et al.* 2004, Das 2010). Excessive adiposity develops because of total caloric intake exceeding total energy expenditure and the excess being stored as body fat. The intake of food and expenditure of energy in the form of basal metabolism and physical activity are regulated by the brain. Specifically, the hypothalamus serves as the key site of integration of central and peripheral satiety signals and, therefore, is the central regulator of energy homeostasis (Parker and Bloom 2012, Volkow *et al.* 2008). In states of hunger, the stomach secretes the hormone ghrelin which has the function of stimulating appetite through ghrelin receptors in the hypothalamus (Cummings 2006). Following the ingestion of food, the gastrointestinal tract secretes cholecystokinin (CCK) and peptide tyrosine tyrosine (PYY) hormones which in turn signal the brain to reduce food intake, initiated through feelings of satiety (Little *et al.*

2005, Batterham and Bloom 2003). Adipose tissue secretes leptin which indicates to the brain the level of energy stores available as fat in the body. Leptin is secreted in proportion to adipose tissue mass and inhibits feeding when in high concentrations through actions on the hypothalamus (Halaas *et al.* 1995). In addition, insulin secreted from the pancreas also indicates the levels of energy stores to the brain. Adiponectin, another adipose tissue derived hormone which enhances insulin sensitivity, increases free fatty acid oxidation and reduces glucose and triglyceride concentrations (Kadowaki *et al*., 2008). Serum adiponectin levels reduce with obesity and adiponectin plays a role in energy regulation through functions on the hypothalamus (Kubota *et al.* 2007, Qi *et al.* 2004). The physiology of energy homeostasis is a far more complex process than described and only the key components of the system have been highlighted.

The hypothalamus functions as the key regulator of energy balance in the body. It is a pea sized organ located inferior to the third ventricle of the brain and superior to the pituitary gland. Peripheral nutrient and adiposity signals are received and integrated within the hypothalamus which in turn regulates hunger, satiety and energy expenditure to achieve energy balance (Volkow *et al*. 2008). The hypothalamus consists of several anatomically distinct clusters of neurones or 'nuclei'. Of these, the arcuate nucleus (ARC) of the hypothalamus is of central relevance to appetite control. The ARC contains two distinct neuronal populations which receive and relay on signals relating to peripheral nutrient status and hunger. One cluster contains neurons which produce proopiomelanocortin (POMC) and cocaine and amphetamine regulated transcript (CART) whilst the other cluster produces neuropeptide Y (NPY) and the

agouti-related protein (AgRP) (Mercer *et al*. 2013). These neuronal populations have opposing effects on appetite as displayed in Figure 1.1.

The NPY/AgRP neurones, when stimulated by peripheral signals have the overall effect of increasing appetite and therefore are orexigenic in nature. Conversely, POMC/CART neurones inhibit appetite and are therefore anorexigenic in nature. In addition, POMC/CART neurones are under inhibition of NPY/AgRP via gamma amino-butyric acid (GABA). Both neuronal populations contain multiple receptors for hormonal signals arising from the periphery. The stomach, large and small intestine, pancreas and adipose tissue provide primary peripheral signals of nutrient and energy status to the ARC. In states of hunger, ghrelin activates the NPY/AGRP via ghrelin receptors (Cummings 2006). Conversely, the CCK and PYY released following meals have inhibitory effects on NPY/AgRP (Little *et al.* 2005). Leptin acts via leptin receptors (LEPR) present in both NPY/AgRP and POMC/CART neurones (Cheung *et al*. 1997, Wardlaw 2011). The agonist action of leptin on POMC/CART activates the anorexigenic pathways whilst inhibiting orexigenic signals by hyperpolarisation of LEPR on NPY/AgRP neurones. Leptin concentration does not acutely fluctuate with meals and therefore provides a more long-term signal on the level of adiposity. Insulin released from the pancreas following meals binds to the insulin receptors on POMC neurones thus contributing to satiety induction (Wardlaw 2011).

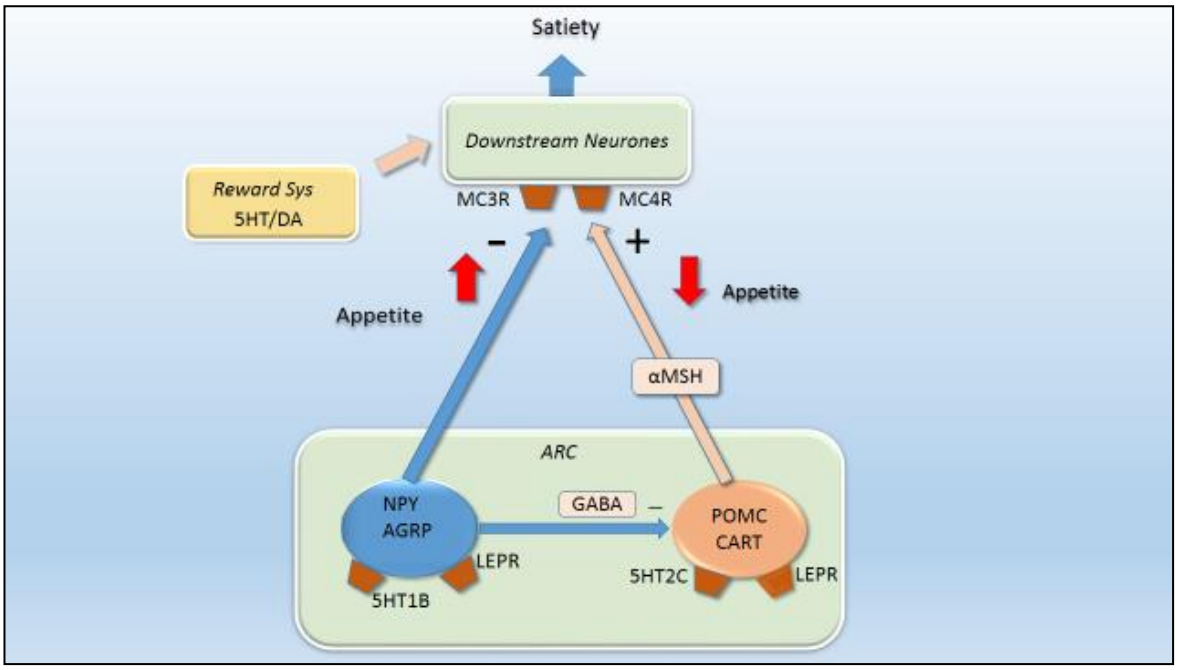


Figure 1-1 Simplified depictions of hypothalamic appetite control pathways.

Two distinct populations of neurones within the ARC nucleus, POMC/CART and NPY/AGRP receive peripheral hunger and adiposity signals. Upon stimulation, POMC undergoes post-translational modification to produce α– melanocyte stimulating hormone which is an agonist at the MC4R receptor which initiates downstream signalling to induce satiety. In contrast AgRP is a competitive antagonist at the MC3R and MC4R receptors and stimulation results in increased energy intake. The POMC neurones are therefore stimulated in states of energy excess whereas AgRP is activated in states of negative energy balance. NPY/AgRP inhibits activity of POMC/CART neurones through GABA mediation. In addition, signals from the serotonin and dopamine neurotransmitters related to brain rewards systems are integrated to this system to affect appetite and eating behaviour. POMC-Proopiomelanocortin, CART-Cocaine and amphetamine regulated transcript, AgRP- Agouti related protein, NPY-Neuropeptide Y, GABA-Gamma amino-butyric acid, LEPR- Leptin receptor, 5HT1B – 5-Hydroxytryptamine 1B receptor, 5HT2C – 5- Hydroxytryptamine 2C receptor, ARC-Arcuate nucleus, α-MSH- Alpha melanocyte stimulating hormone, MC3R-Melanocortin 3 receptor, MC4R – Melanocortin 4 Receptor, 5HT- Serotonin, DA- Dopamine.

Signals from the ARC are relayed to second order neurones in other nuclei of the hypothalamus. These include the lateral hypothalamic area (LHA), paraventricular nucleus (PVN) and ventromedial hypothalamus (VMH) (Yeo and Heisler 2012). The PVN is believed to be the primary anorexigenic centre in the brain due to its actions on the central melanocortin system (Wardlaw 2011). The melanocortin-4 receptor (MC4R) which is expressed in neurones of the PVN acts as a site of convergence for anorexigenic and orexigenic pathways (Yeo and Heisler 2012). Agonism of the MC4R inhibits food intake and increases metabolic rate (Adan *et al.* 2006). Upon stimulation by leptin primarily, POMC neurones produce POMC which undergoes post-

translational modification to produce alpha- melanocyte stimulating hormone (α-MSH) (Wardlaw 2011).

The α-MSH functions as an agonist at the MC4R. In contrast, AgRP acts as an antagonist at MC4R thus counteracting the effects of α-MSH (Ollmann *et al.* 1997). The LHA also contains MC4R expressing neurones but in addition also express orexin which stimulates food seeking (Yeo and Heisler 2012). NPY acts through its Y receptors located in most of the hypothalamic nuclei. The VMH contains neurones which secrete the brain-derived neurotrophic factor (BDNF) which is essentially an anorexigenic factor. Whilst the VMH receives innervations from the POMC and AgRP neurones, the expression of BDNF is acutely regulated by MC4R. Here reduced MC4R signalling has been shown to reduce the expression of BDNF (Abilés *et al.* 2010, Xu *et al.* 2003).

The central importance of the neurotransmitter serotonin (5-Hydroxytriptamine, 5-HT) on appetite regulation is well established and evidenced by the number of anti-obesity pharmacological agents developed over the years (Garfield and Heisler 2009). Serotonin transmission is inversely related to appetite and the serotonergic system in closely integrated into the hypothalamic feeding circuitry (Lam *et al.* 2010).

The anorexigenic actions of 5-HT are mediated through the serotonin 1B (5-HT_{1B}), 2A (5-HT_{2A}) and 2C (5-HT_{2C}) receptors located in the various hypothalamic and brain regions related to reward pathways. The 5-HT_{2C} receptors are expressed in the POMC neurones in the ARC and their stimulation activates POMC and thus the anorexigenic pathway (Xu *et al.* 2008). In contrast, serotonin causes hyperpolarisation of 5-HT_{1B} receptors on NPY/AgRP neurones thus reducing GABA mediated inhibition of POMC (Heisler *et al.* 2006). The 5-HT_{2A} receptors mainly located in the PVN inhibit feeding through inhibition of NPY mediated eating (Currie *et al.* 2002). The 5-HT_{2C} receptors

are also found in the ventral tegmental area (VTA) in the midbrain where serotonin and dopamine mediate functions of the reward system (Baik 2013, Yeo and Heisler 2012). Furthermore, serotonin and dopamine modulate feeding through the VMN (Meguid *et al.* 2000). Food reward elevates dopamine levels in the brain and therefore the hypothalamic appetite control circuitry is therefore closely integrated with the dopamine system.

1.2 Eating behaviour

Understanding the underlying mechanisms of becoming overweight and obese is of utmost importance. Understanding why food is consumed and the motivational factors driving food choices is significant to addressing the epidemics of obesity, diabetes and CVD as food consumption is an important factor impacting the development and management of these disorders (Grimm and Steinle 2011).

Obesity is a dysfunction of hunger and satiety, which are controlled by several combined physiological mechanisms. Other influences affect energy intake like the impact of socio-cultural, environmental and psychological effects that reduce appetite control, and control of the motivation to eat (Broberger 2005). In addition to the role of genetic and physiological factors, evidence for the influence of eating behaviour dimensions on energy intake and, therefore, susceptibility to weight gain is growing (French *et al.* 2012). The psychology of eating behavior e.g. the cognitive, behavioral and emotional features of eating habits, call for more consideration, given the growing prevalence of obesity and other eating related problems. Disordered eating in different forms and of various degrees of severity are common, especially among adolescent girls and young women (Hautala *et al.* 2008).

The idea that various measurable 'psychological constructs' underlie overeating behaviours and thus affect body weight has interested psychologists and researchers for decades (Oda-Montecinos *et al.* 2013, van Strien *et al*., 2012, Wardle *et al.* 2001). Various dimensions of eating behaviour such as food responsiveness, satiety responsiveness, eating in the absence of hunger, disinhibition of eating, etc., have been studied and reported in the literature (French *et al*. 2012).

Whilst the quantification of caloric and nutrient intake has traditionally provided useful information in obesity studies, the study of the 'psychological structure' of an individual's eating behaviour offers another approach to addressing the problem of adiposity. Focusing on 'why' a person overeats as opposed to `what' is eaten allows for a unique perspective on how increased caloric intake and adiposity occurs. Overeating types founded on various psychological theories thus have their own aetiologies and treatment methods. Characterisation of individuals into eating behaviour phenotypes, therefore, can allow for more targeted interventions in an evolving field of personalized medicine (Kass *et al.* 2013).

1.2.1 Definition of eating behaviour

Eating behaviours could be described as behaviours related to food intake which influence the frequency, meal size, meal content and attitude to meals in general. Therefore, eating behaviours can influence the amount of energy consumed by an individual and thus predispose towards obesity (Blundell and Cooling 2000).

Eating behaviour is a complex interaction of social, physiologic, psychological and genetic factors that affect meal timing, quantity of food intake and food preference (Magni *et al.* 2009). Active investigation involving the genetics of taste, food

preference, pathological eating behaviours, meal size, and meal selection is rapidly increasing our understanding of how and why we eat (Grimm and Steinle 2011).

Three eating behaviour constructs are typically measured i.e.: 1) cognitive restraint (CR), considered by numerous dietary prohibitions and limitations frequently linked with desire to lose weight (Apfeldorfer and Zermati 2001, Lowe and Timko 2004), 2) uncontrolled eating (UE), defined as the loss of self-control when the individual is exposed to various non-healthy foods (Gilhooly *et al.* 2007), and 3) emotional eating (EE), which is directly associated with mood and stress levels; increase in stress leads to increase in food intake (Rutters *et al.* 2009).

1.2.2 Assessment of eating behaviours

1.2.2.1 Three Factor Eating Questionnaire (TFEQ)

The Three Factor Eating Questionnaire, (TFEQ), is one of the most commonly used tools in the field of eating behavior studies developed by (Stunkard and Messick 1985a). Initially, this self-assessment questionnaire was planned to measure cognitive and behavioral mechanisms of eating in people with obesity. It comprises 51 items, combined into three scales: "Cognitive Restraint", "Disinhibition" and "Hunger" (Anglé *et al.* 2009). Nevertheless, some studies have raised concern about the factor structure and the factor stability of the 51-item TFEQ (Karlsson *et al.* 2000a, Hyland *et al*. 1989).

According to the psychometric analyses, a revised version of the questionnaire was constructed, including three factors: "Cognitive Restraint", "Emotional Eating" and "Uncontrolled Eating". Using the most effective items to rise the convergent and discriminant strength of the new scales lastly led to a revised, shorter, 18-item version of the tool, the Three Factor Eating Questionnaire (TFEQ – R18) (Anglé *et al.* 2009).

In sum, the questionnaire measures three different aspects of eating behaviour: (a) restrained eating (defined as conscious restriction of food intake aimed to control body weight and/or to promote weight loss); comprised of six items (e.g., "I consciously hold back at meals in order not to gain weight), (b) uncontrolled eating (the tendency to eat more than usual due to a loss of control over intake with a subjective feeling of hunger); comprised of nine items (e.g., "When I see a real delicacy, I often get so hungry that I have to eat right away"), and (c) emotional eating (inability to resist emotional cues, eating as a response to different negative emotions). Comprised of three items (e.g. "When I feel blue, I often overeat"). The questionnaire comprises 18 items that are measured on a 4-point Likert response scale (definitely true: 4, mostly true: 3, mostly false: 2, definitely false: 1) and item scores are summated into subscale scores: CR, UE and EE. Previous studies have reported that TFEQ-R18 has adequate internal consistency reliability coefficients for the three subscales, as well as for the whole questionnaire (ranging between 0.75 and 0.87) (Karlsson *et al.* 2000).

The TFEQ-R18 progressed the psychometrics of eating behavior. it has been revealed to be suitable in different populations, although it was created using information from obese adults (Elfhag and Linné 2005), the TFEQ-R18 was also found to be easy and clear to the participants. It has been shown to distinguish between different eating habits in a general population, for example in a study where it was used in French adolescents and adults (Elfhag and Linné 2005).

To understand the relationships between eating and health and to provide nutritional prevention plans in light of the worldwide obesity epidemic, better knowledge of the various eating behaviors and their frequency in the general population would be

helpful in assessment of obesity correlates and risk factors. Due to the prominence of measuring eating behaviour a detailed discussion of each behaviour is warranted.

1.2.3 Types of eating behaviours

1.2.3.1 Cognitive restraint

Cognitive restraint, which appears to be common in current societies, is indeed suggested to play a fundamental role in the development of eating disorders and obesity (Blundell and Gillett 2001).

The term dietary restraint, cognitive restraint, restraint, or restrained eating has been one of the most essential and argued concepts in the study of human eating behaviour since the restraint theory of obesity (Herman and Mack 1975). Restraint refers to a tendency to continually and consciously restrict one's food intake instead of using physiological cues of hunger and satiety as controllers of food intake. Dieting and restrained eating are not one and the same. Restrained eaters eat less food that they would like to eat but not necessarily less than they need to keep energy balance (Beiseigel and Nickols-Richardson 2004, Lowe and Timko 2004).

The concept of dietary restraint has played an important role in the study of human eating behaviour. Restraint theory suggests that attempts to regulate food intake in order to control body weight and body shape cause episodic overeating and, moreover, the model posits a causal role of frequent restraint in the development of eating disorders and obesity. Research along this course is far-reaching and has yielded conflicting results (Karlsson *et al.* 2000).

Much consideration has been given to the methodological and applied challenges involved with the investigation of restraint and varied perspectives have been

generally argued. However, debate still exists concerning the most suitable method to measure cognitive restraint, and further cautious assessment of the validity and acceptability of the varied strategies is required to increase theoretical clarity and enhance estimation precision (Karlsson *et al.* 2000).

De Lauzon, *et al.* stated that in present-day societies characterised by bounteous and easily available food, cognitive restraint may be a versatile behaviour to avoid an increase in body weight (de Lauzon *et al.* 2004). However researchers propose that any benefit from this eating behaviour might be short-term and may lead to long term excessive weight gain (de Lauzon-Guillain *et al.* 2006).

Before the use of the TFEQ, the Restraint Scale (RS) was commonly used to assess patients with obesity since there was a high association observed between restraint scores and severity of obesity. However criticisms regarding this measure were made due to the RS's lack of distinction between items on the scale pertaining to anxiety about body weight variation, and those probing anxiety related to dieting, and the lack of distinction between restraint and disinhibition.

The Three Factor eating Questionnaire overcomes these limitations by separating cognitive restraint, uncontrolled eating and emotional eating (Boschi *et al.* 2001). The original version of the TFEQ (Boschi *et al.* 2001) consolidated the RS into three subscales: strategic dieting behaviour, attitude to self-regulation, and avoidance of fattening foods. Westenhoefer *et al*., (1999) offered a different break down of cognitive restraint, dividing it into two subscales depending on its relationships with both BMI and disinhibition or UE (Westenhoefer *et al.* 1999). The subscales were flexible control, a more relaxed version of restraint associated with both low UE and

low BMI, and rigid control, a more severe restrictive state associated with both high UE and high BMI (Westenhoefer *et al.* 1999).

1.2.3.2 Uncontrolled Eating (UE)

Uncontrolled eating refers to a tendency to overeat, with the feeling of being out of control (Anglé *et al.* 2009). Uncontrolled eating is recognised as an eating habit style that is characterised by the overeating of unhealthy food in response to exterior food stimulus, occasionally called external eating and has been related to obesity and high calorie food consumption in adult populations (Booth *et al.* 2018). Uncontrolled eating is similar to the idea of loss of control during drinking, which has been considered as an underlying description for overconsumption of alcohol (Lyvers 2000). Certainly, studies propose that treatment-seeking people with overeating behaviors who are subsequently diagnosed with binge eating disorder (BED) report uncontrolled eating episodes as particularly debilitating (Spitzer *et al.* 1992). Likewise, uncontrolled eating is strongly connected with obese status (Verzijl *et al.* 2018, Rohrer *et al. 2009).*

According to Anglé *et al.,* uncontrolled eating refers to a tendency to overeat with the feeling of being out of control (Anglé *et al.* 2009). de Lauzon *et al.* (2004) adds to this definition, stating UE as the tendency to eat more than usual due to loss of control over intake accompanied by subjective feelings of hunger (de Lauzon *et al.* 2004). High disinhibition has been linked to women with higher BMI (Boschi *et al.* 2001). Questions pertaining to UE in the questionnaire describe habitual and situational susceptibility to disinhibition (Bond *et al*. 2001). Two psychological processes have been defined in the literature, which may account for individual differences in uncontrolled eating. The first is (reduced) cognitive control, such as impulsive personality style, which has been found to be a key predictor of obesity in children (Thamotharan *et al.* 2013).The

second is automatic action tendencies to approach appetitive food cues in the environment, which is thought to be modulated by reward networks in the brain and be inflated in certain individuals, such as those at risk of obesity (Booth *et al.* 2018, Mogg *et al.* 2012).

1.2.3.3 Emotional Eating

Emotional eating means the tendency to eat in response to negative emotions as a result of stressful situations (Anglé *et al.* 2009). Cappelleri *et al*. (2009) described emotional eating (EE) as overeating during dysphoric mood states. De Lauzon *et al*. (2004) reported that the inability to resist emotional cues and has been associated with the consumption of snack foods, especially fatty and salty foods (de Lauzon *et al.* 2004). Karlsson *et al*., defines emotional eating as the tendency to eat in response to negative emotions (Karlsson *et al.* 2000). Lluch *et al.* associates higher scores of emotional eating with a higher BMI (Lluch *et al.* 2000). Originally derived from theories of obesity, emotional eating occurs in an effort to reduce emotional distress (Bruch 1973, Kaplan and Kaplan 1957) and is similar to theories and supporting evidence that individuals use alcohol to cope with negative affect. Emotional eating research indicates that individuals diagnosed with BED report an association between anxiety-related emotional eating and more frequent binge-eating episodes (Verzijl *et al.* 2018).

1.2.4 Eating behaviours and weight loss

Emotional eating or eating in response to feelings could be an important factor related to weight loss results in adults with obesity. Fifty-seven percent of overweight adults report frequent incidents of emotional eating (Péneau *et al.* 2013). Emotional eating is

accompanied with a higher frequency of snacking (O'connor *et al.* 2008), greater consumption of energy-dense, high-fat foods, as measured in the laboratory (Oliver *et al.* 2000) and via self-report (Camilleri *et al.* 2014),and eating in response to everyday stressors (O'connor *et al.* 2008). Additionally, emotional eating seems to be a significant factor associated with body weight over time (Keller and Siegrist 2015).

While the relationships between the emotional eating and weight loss success and maintenance have only been examined in a few studies, the results show that emotional eating may be inversely related to successful outcomes. Two earlier studies have investigated the association between emotional eating, as opposed to general disinhibition (i.e., eating in response to internal and external cues), and weight loss in treatment-seeking samples of overweight adults. Results showed that a higher level of self-reported emotional eating before treatment was significantly related to less weight reduction in behavioural (Niemeier *et al.* 2007) and surgical interventions (Canetti *et al*. 2009). Blair *et al.* (1990) examined a non-treatment-seeking sample of adults who experienced a decrease in emotional eating over the course of a year and observed a significantly higher weight loss compared to adults who reported a constant level of emotional eating. Therefore, it is probable that adults who decrease emotional eating during behavioural weight loss treatment may be more likely to achieve successful weight loss compared to adults who are unable to modify this tendency. If emotional eating is a reliable predictor of weight loss, it may be clinically useful to assess in behavioural weight loss treatments, which generally target weight loss through reduced-energy diet and increased physical activity (Knowler *et al*. 2002).

1.3 Food cravings

Nowadays, the obesogenic environment encourages sweet and high fat foods to be consumed at amounts higher than daily requirements (Cleobury and Tapper 2014, McKiernan *et al.* 2008), indicating the significance of non-homeostatic elements of food intake (Lowe and Butryn 2007). One of these elements is the involvement of food cravings, typically described as 'an intense desire to eat specific foods' (White *et al.* 2002) which can happen in the absence of hunger (Pelchat and Schaefer 2000).

Food cravings are different from hunger (which is defined as the susceptibility to internal or external hunger signs (Löffler *et al.* 2015)) and can be elicited without food deprivation. Consuming a monotonous diet triggers food craving without any nutritional deficit (Pelchat and Schaefer 2000). Food cravings are specific in that they can only be satisfied by consuming the desired food or similar (Bruinsma and Taren 1999). Food cravings are prevalent in societies characterised by rich food environment (Pelchat 1997, Weingarten and Elston 1991) and craved foods are generally high in sugar and fat, with chocolate reported to be the most commonly craved food in Western societies (Rozin *et al.* 1991).

1.3.1 Definition of food craving

Cravings refer to an intense desire or longing for a particular food (Weingarten and Elston 1991). In relation to food, this irresistible urge to eat a specific type of food has been suggested to contribute to a loss of control over eating. For instance, the experience of food cravings is related to higher BMI or binge eating behaviours (Abilés *et al.* 2010). Food craving is extremely common; it is experienced by more than ninety percent of the population (Hill 2007). Types of food craving are commonly defined and studied (Hallam *et al.* 2016) and are categorised by both appetitive and aversive components (Rodriguez *et al.* 2005). Therefore, it has been proposed that food

cravings can be prompted by certain emotional conditions, such as psychological and physical stress, anxiety, depression, anger, or psychological reactions to food (Karlsson *et al.* 2000).

1.3.2 Food craving behaviour

Food craving behaviour (FCB) is demonstrated as a positive emotion. This can lead to repetitive food intake leading to obesity and counterproductive emotional states (Karlsson *et al*. 2000). The prevalence of FCB stated from earlier studies varies globally with incidence ranges from 28% to 97% (Pelchat 1997). This phenomenon is observed more commonly in females because of a biological approach related to psycho-endocrinology. For example, changes in eating behaviours during the menstrual cycle and states of mood variations are more frequently described in female subjects, however, there are inadequate studies evaluating FCB in females and the underlying causes are not completely clear (Lafay *et al*. 2001).

1.3.3 The importance of food craving

Food cravings are multi-dimensional experiences with behavioural, motivational, and cognitive facets (Cepeda-Benito *et al.* 2000). As indicated by the explained interruption hypothesis of desire, craving is a consequence of a psychological elaboration of disturbing thoughts about a desired object (Kavanagh *et al.*, 2005), highlighting the role of food-related thoughts as a prerequisite for the emergence of food cravings. Thus, food cravings are not necessarily caused by the presence of food stimuli but can also occur spontaneously through mental images of the craved foods (Hallam *et al.* 2016). These feelings can lead to consumption of the craved food, particularly when cravings are strong (Appelhans *et al*. 2016). There are also obvious, and constant inter

individual variances in the occurrence and strength of food craving experiences, proposing that some individuals think more often, crave more strongly and therefore consume more snack foods than others (Boswell and Kober 2016).

1.3.4 Types of craving

State food craving is completely experienced as a temporary state in a particular moment (Richard *et al.* 2017). It is defined as a feeling of craving in a particular moment, regardless of whether a cue is present; thus, it can be described as either tonic or cue-induced craving assessed in a present moment (Hallam *et al.* 2016).

Trait food craving refers to the experience of food cravings in general (Richard *et al.* 2017), however, it can also refer to craving in the presence of cues in general. For example, the Food Craving Questionnaire- Trait contains questions about the tendency to experience both tonic craving (e.g., "If I am craving something, thoughts of eating it consume me") and cue-induced craving (e.g., "Whenever I go to a buffet I end up eating more than what I needed" (Cepeda-Benito *et al.* 2000). Conversely, the Food Craving Questionnaire-State includes questions asking about the present moment only, which could include cue-induced or tonic craving (e.g., "I have an urge for a specific food") (Cepeda-Benito *et al*. 2003).

Tonic craving reflects a general feeling that is experienced either over time or in a particular moment, in the absence of environmental stimuli. It is often related to abstinence from a specific food (e.g., consistently craving chocolate when on a diet) (Jansen 1998) and is typically measured with multi-item self-report scales/questionnaires, including the Food Craving Inventory (e.g., "I frequently desire fried chicken"). Such measures of tonic craving are typically higher in restrained eaters

and increase after deprivation. Nevertheless, tonic craving is not the same as hunger, and can be experienced in the absence of caloric need.

Cue-induced craving is an acute period of craving, elicited by environmental/external stimuli (e.g., craving chocolate after seeing a commercial advert (Boswell and Kober 2016).

1.3.5 Causes of food cravings

Although the primary causes of food cravings remain poorly understood, there have been several theories regarding their origin (Gilhooly *et al.* 2007). There is also limited agreement relating to the biological, psychological, and behavioural factors that control food cravings. To date, three primary themes have been discovered about the association between food cravings and eating disorders. These are the physiological or homeostatic theories, learning theories including sensory aspects of food and psychological or affect-correlated theories (White *et al.* 2002).

Another study has focused on the biological underpinnings of food cravings and has raised the possibility that cravings represent a learned appetite for energy that develops, for example, through the reinforcing effects of eating specific foods when hungry (Gibson 2001). Neurological explanations for reinforcement include responses to eating mediated by the release of dopamine in the nucleus accumbens and neostriatum (Martel and Fantino 1996, Berridge 1996) or altered endogenous opioid peptide synthesis and release, which have been proposed to induce food cravings by increasing perceptions of palatability (Mercer and Holder 1997). However, the latter suggestion is also supported by reports that food cues and sensory stimulation cause a rise in food cravings and intake whether in a hungry or satiated state (Lambert *et al.*

1991), representing a role for conditioning independent of any metabolic requirement for food. Further studies have stated that factors such as mood and food images are common antecedents to food cravings (Tiggemann and Kemps 2005).

Some studies have considered the role of cravings for specific food classes (e.g., carbohydrates, sweets, and fats) and have confirmed differences in the types of foods craved according to sex, age, hunger state, time of day, and phase of the menstrual cycle. Carbohydrate craving has been most frequently studied (White *et al.* 2002). Craving has also been suggested as corresponding to addiction, and as such, is reliant on the percentage of dopamine to acetylcholine in the nucleus acumbens (Leibowitz and Hoebel 2004).

1.3.6 Food craving assessment

To measure food craving, several ways have been established (Meule and Hormes 2015). Earlier studies regarding the assessment of food cravings in normal life, however, used paper-and-pencil methods such as the craving record sheet (Hill, Weaver and Blundell 1991). In this type of measure, participants entered craving episodes by hand each time they had felt a need to eat a specific type of food regardless of consumption. It was found that momentary cravings co-occurred with thoughts about craved foods or the presence of these foods (Richard *et al.* 2017).

Nowadays, different procedures have been established such as the Food Cravings Questionnaires (FCQs, including a state and a trait version; (Cepeda-Benito *et al.* 2000), the Attitudes to Chocolate Questionnaire (ACQ; (Benton *et al*., 1998)), the Orientation towards Chocolate Questionnaire (OCQ; (Cartwright and Stritzke 2008)) and the Food Craving Inventory (FCI; (White *et al.* 2002)). Each of these measures represents different approaches to the craving construct (White *et al.* 2002). Both the ACQ and

OCQ are considered to estimate cravings specifically correlated to chocolate and highlight the association between craving and feelings of guilt. The FCI measures cravings connected to different types of food (carbohydrates/starches, fast-food fats, high fats, sweets).

1.3.6.1 The Food Craving Inventory (FCI)

The Food Craving Inventory (FCI) is of particular interest, given that differently from other measurements, it emphases specific foods. This inventory divides its 28 items into four subscales ("Sweets," (brownies, cookies, candy, chocolate, donuts, cake, cinnamon rolls, ice cream), "High fats," (fried chicken, sausage, gravy, fried fish, bacon, cornbread, hot dogs, steak), "Carbohydrates/starches," (rolls, pancakes/ waffles, biscuits, sandwich bread, rice, baked potato, pasta, cereal), and "Fast food fats" hamburger, French fries, chips, pizza) (White *et al.* 2002). The FCI evaluates how frequently each food was desired over the previous month on a 5-point Like scale ranging from 1 (never) to 5 (always/almost every day) (Chao *et al.* 2015).

The FCI has been modified for the UK population by Nicholls and collaborators and it displayed the same factors as the original FCI (Nicholls and Hulbert-Williams 2013). There are Spanish and Japanese versions with differences, these have three- and five-factor solutions, respectively. However, they all show in general a clear discrimination in craving for different food groups, with "Sweets," "High fats," and "Fast food" dependable across the three studies (Tarragon *et al.* 2017).

The FCI has established satisfactory reliability in the field of eating behaviours, with discriminant validity with the restraint scale of the TFEQ, and concurrent validity with the Conceptual Craving Scale. The FCI has been demonstrated to have acceptable

internal consistency, reliability and test-retest reliability in adults (White *et al.* 2002). Further psychometric support for the FCI has been established in varied public and scientific samples (Barnes *et al.* 2010, White and Grilo 2005) and has been demonstrated to be valid in evaluating food craving. After the validation of the original instrument, later studies replicated the results with regard to both structure and category.

1.3.7 Food craving and food intake

Although experiencing food cravings does not always result in subsequent food intake, previous studies reported positive associations between state (Meule and Hormes 2015) and trait food craving (Martin *et al.* 2008) with consumption of the craved food in the lab (Richard *et al.* 2017), Questionnaire-based and laboratory studies revealed that individuals with elevated levels of trait food craving (i.e., high trait food cravers) seem to prefer high-calorie foods and are more susceptible to experiencing food cravings spontaneously or when confronted with external food cues. Studies that applied food diaries, however, have been less consistent. For example, food cravers reported a descriptively, but not significantly, higher energy intake than non-cravers in a small sample (Meule *et al*. 2017).

High trait food cravers also stated higher craving intensity when they were asked to imagine their preferred food (Tiggemann and Kemps 2005) or were shown images of appetising foods (Meule *et al.* 2014). Likewise, high trait chocolate cravers demonstrated more positive attitudes towards chocolate, higher reward- associated brain stimulation during thoughts about chocolate, and had difficulties disengaging their attention from chocolate cues (Kemps and Tiggemann 2009).

Furthermore, these cravings were often followed by consumption (Hill and Heaton-Brown 1994). In a more recent study, both trait level and state-level cravings were accompanied by consumption (Forman *et al*. 2013), demonstrating the behavioural a consequence of food cravings as well as the presence of inter individual differences. Equally, total energy intake was higher in female trait food cravers than in non-cravers in a study using a three-day food record (Lafay *et al*. 2001).

However, several situational and individual features can affect whether craved foods are truly consumed (Hill 2007). For example, the moderating effect of trait food craving on the relationship between state food craving and subsequent consumption has received little attention. Thus, additional research is required on how closely state cravings, feelings about foods, and food intake are interconnected as a function of trait food craving in normal life (Richard *et al*. 2017).

1.3.8 Food craving, weight gain and obesity

Food craving is clinically significant because it is potentially accompanied by, and predicts, over-eating and subsequent body weight increase (Boswell and Kober 2016). The rise in food cues in the environment is a society-level mechanism whereby craving stimulates obesity, which, as consequence, increases craving and eating at the population-level. Certainly, the rising rates of overweight and obesity have been linked with increases in the accessibility and advertisement of unhealthy/high caloric foods (Swinburn *et al.* 2011). Therefore, individuals who live in an environment that contains calorie rich foods (e.g., fast food, such as McDonalds) eat those foods more regularly, which results in a higher BMI (Brownell and Horgen 2004). Furthermore, the presence of “junk food” advertisements serve as a salient food cue, leading to even more

regular unhealthy food eating (Harris *et al*. 2009). Some have called this an "obesogenic" or "toxic" food environment, wherein ultra-prevalent food and food cues lead to increased craving, food consumption, and weight gain (Morris *et al*. 2015, Wadden *et al*. 2002). While this environment affects everyone to some degree, some individuals may be more sensitive to food-related cues or experience more craving, which may be related to weight-gain (Ferriday and Brunstrom 2011, Tetley *et al*. 2009). Individuals who report tonic food cravings show higher caloric intake than those who report infrequently undergoing food craving (Hill *et al*. 1991), however it is not possible to determine whether this is due to cause or effect.

Tonic craving for specific foods or food groups also predicts consumption of these certain foods (Martin *et al*. 2008). Tonic and trait food craving are associated with long-term weight consequences such as more weight gain over time and lifetime high BMI (Cushing *et al*. 2014, Demos *et al.* 2012, Gilhooly *et al.* 2007). Likewise, food cues and cue-induced food craving are also accompanied with food intake. For example, exposure to food cues causes a craving response that leads to consequent eating, such that higher cue-induced craving levels are accompanied with greater food consumption (Fedoroff *et al*. 1997). Additionally, cue-induced food craving predicts overeating in overweight children (Jackson *et al.* 2003) and adults (Ng and Davis 2013).

In a nonclinical population, one study found that both neural food cue reactivity and self-reported craving predicted subsequent eating over a period of one week (Lopez *et al.* 2014). Furthermore, in a quantitative meta-analysis; both tonic and cue-induced food craving were found to be prospectively predictive of eating and long-term weight increase across 45 studies, with a medium effect size. Significantly, these craving measures accounted for 11 percent of the variance in eating -related outcomes, which

is higher than any other single predictor of eating and weight (Boswell and Kober 2016). Given that food craving is strongly associated with increased food intake and eating, weight gain, its investigation is key to understanding obesity, and may inform prevention and treatment approaches (Potenza and Grilo 2014).

1.3.9 Food craving and weight loss

As high food cravings for certain foods have been related to previous dieting failures (Meule *et al.* 2011) and prospectively predict increased food intake and weight gain (Boswell and Kober 2016) data about the characteristics of food cravings is important for health behaviours in several fields. Moreover, it has been proposed that cravings may increase with dietary monotony without energy restriction (ER) (Pelchat *et al.* 2004), however, such suggestions seem to be contradicted by other studies using monotonous diets to achieve ER that have detected reductions in cravings (Martin *et al.*2006).

The importance of food cravings in achievement, or lack of success, with dieting is also unclear. Earlier data have proposed that a short-term reduction of energy intake may raise the reinforcing value of food (Raynor and Epstein 2003). However, varied results have been found when observing the effect of longer-term weight loss diet programs on food cravings (Martin *et al.* 2006), Some studies have stated that following low-energy diets, particularly monotonous programmes leads to a reduction in food cravings (Harvey *et al*. 1993). However, this opinion is at odds with the separate finding that missing favourite foods is a commonly cited cause of giving up a weight loss diet (LaPorte and Stunkard 1990) but there are differences in study design, some used cross-sectional and the other used longitudinal data which may have contributed to the inconclusive results obtained to date (Gilhooly *et al.* 2007).

Other studies have examined both actual dietary intake and stated food cravings, however, the results have not been able to determine whether foods reported as craved foods are truly consumed in the diet and whether the intake of craved foods changes with weight loss (Gilhooly *et al.* 2007). Some interventional studies have mentioned that both surgical and non-surgical weight loss treatment studies have often found decrease in food cravings, with greater decreases being related to greater weight loss (Batra *et al.* 2013, Leahey *et al*. 2012). However, no strong associations have been found between baseline levels of food cravings and weight loss (Martin *et al.* 2011). While higher trait food craving scores at baseline were related to higher weight loss in a behavioural weight-loss treatment study (Batra *et al*. 2013), pre-surgical trait food craving scores did not predict post-surgical weight loss in bariatric patients (Leahey *et al.* 2012). More frequent cue-elicited food cravings before surgery predicted higher weight loss after surgery, but more frequent feelings of guilt resulting from cravings before surgery predicted lower weight loss after surgery (Crowley *et al.* 2012).

1.4 The genetics of common obesity

A significant proportion of obesity is heritable. Family and twin studies have highlighted that genetic factors contributes 40-70% of the variation in common obesity (Maes *et a*l. 1997). Many of the physiological processes underlying energy homeostasis such as eating behavior, physical energy expenditure, appetite regulation, satiety signaling are under genetic influence (Cheung and Mao 2012, Ramachandrappa and Farooqi 2011). The initial understanding of genetic factors was primarily in relation to monogenic forms of obesity. The rapid advancement of the field of genetics has

started to reveal much about the genetic makeup of many previously poorly understood complex traits such as obesity and diabetes.

1.4.1 Genetics, dietary habits and obesity

A probable occurrence of obesity is due to the interaction between environmental variables and obesity related genes. It has been suggested that the response to the environmental changes and weight increase is different between people and this highlights the hereditary variables that prompt this variety in their response (Zhao *et al.* 2014). A significant role of genetics in the pathogenesis of obesity has been identified. Indications for a strong heritable link between the influence of genes and human obesity is consistently recognized by twin, family and adoption studies (Maes *et al*.1997). Twin studies in children frequently create strong assessments for food intake such as regularity of eating specific foods, satiety and enjoyment of food (Cecil *et al*. 2012).

Other studies that use a family approach have indicated a modest genetic impact on energy intake and food preference, though when food intake is observed under controlled laboratory circumstances, familial aggregation of energy intake and favouring for fat, protein and carbohydrates is significant (Faith *et al.* 2004). Particularly, a modern family-based study using a genome-wide screening approach has discovered significant heritability assessments for dietary intake (fat, protein, carbohydrate) in children, ranging from 47 – 69% (Cai *et al*. 2006). Eating in the absence of hunger (EAH) linked positively to increase weight is one of the hyperphagic dietary behavioural characters that is used in children to measure adaptable eating, and eating levels, this is also recognized as being under significant genetic control in children (Ceci*l et al.* 2012).

Supporting evidence from Rankinen & Bouchard (2006) demonstrated that appetite and eating behaviour connected with susceptibility to weight increase are also under significant genetic control (Rankinen and Bouchard 2006). Much of this work has been focused in adults, where heritability assessments of the order of 65% have been detected for energy intake (de Castro 1993); macronutrient consumption, meal frequency, meal size, and dietary behavioural phenotypes such as emotional, restraint, hunger, and disinhibited eating which are also under genetic influence (Keskitalo *et al*. 2008).

1.4.2 Single nucleotide polymorphisms as markers of disease

The single nucleotide polymorphism (SNP) is the simplest and most common form of genetic variation observed in humans and results from a single nucleotide change in the DNA sequence of an individual. A SNP is defined as occurring at a frequency of greater than 1% in a population. Over 3 million SNPs are thought to occur in the human genome, occurring approximately once every 1000 bps though the density of such variation depends on the chromosome region. SNPs are responsible for genetic variation for population diversity, susceptibility to disease and response to medications. SNPs are distributed throughout the genome and occur in coding regions, non-coding regions as well as intergenic regions. Polymorphisms which do not result in a change in protein sequence are termed synonymous SNPs. In contrast non-synonymous SNPs result in a change in amino acid sequence which may lead to a functionally different protein.

More than 500 genetic loci for a range of adiposity traits have been identified. More than 80% of loci were first identified in populations that were exclusively or

predominantly of European ancestry. Despite much smaller sample sizes, GWAS of exclusively Asian or African ancestry populations have identified at least 64 additional loci for BMI, and 18 for WHR that had not been identified in much larger European ancestry GWAS (Akiyama et al. 2017, Ng et al. 2017, Locke et al. 2015).

The most recent GWAS meta-analysis for body fat percentage (BFP), (Nmax 100,000) identified five novel loci that had not been reported by much larger GWAS for BMI or WHR adjusted BMI (Lu *et al.* 2016). Most notable is a locus near IRS1, of which the BFP-increasing allele protects against type 2 diabetes and cardiovascular disease – an unexpected association, mediated through an effect on fat deposition (Lu *et al.*2016). Several other BFP-associated loci (in/near COBLL1, TOMM40, and PLA2G6) stand out because of cross trait associations similar to the near-IRS1 locus (Lu *et al.*2016). For most loci, associations are directionally consistent across ancestries, but allele frequencies and/or effect sizes may differ. Loci discovered in the earliest, and thus smallest, meta analyses tend to have the largest (albeit modest) effect sizes. As sample sizes increase with each new meta-analysis, the power to identify variants with smaller effect sizes and/or lower minor allele frequencies (MAFs) increases and the variance explained by each new locus becomes incremental. Current GWAS-identified loci combined explain 4% of the phenotypic variation of BMI. For WHR adj BMI, effect sizes and variance explained tend to be larger for women (2.7%) than for men (1.4%) (Loos *et al.* 2018).

The current study focuses on one of the early gene variants that was shown to contribute to human obesity and dietary habits namely the fat mass and obesity-associated gene (*FTO*).

1.4.3 The fat mass and obesity–associated gene, *FTO*

The first obesity risk gene recognised by genome wide association studies (GWAS) was the fat mass and obesity–associated gene *FTO.* The discovery of the *FTO* rs9939609 SNP through GWAS in 2007 by Frayling and colleagues was a key milestone in obesity genetics (Frayling *et al.* 2007). Initially discovered in UK type 2 diabetics and replicated in a larger cohort of Europeans, further identification of *FTO* variants in two further studies within the same year established *FTO* as a leading locus in common obesity (Dina *et al.* 2007, Scuteri *et al.* 2007). *FTO* is composed of nine exons that span more than 400 kb on chromosome 16 and is a member of the Fe (II) and 2 oxoglutarate-dependent oxygenase superfamily (Larder *et al.* 2011). According to bioinformatics analysis members of this family are involved in post translational modification, DNA repair and fatty acid metabolism (Gerken *et al.* 2007). *FTO* has been found to be strongly expressed in the brain particularly in the hypothalamic nuclei governing energy balance (Gerken *et al.* 2007), a key region for control of appetite behaviour (Stratigopoulos *et al.* 2008). Furthermore, *FTO* mRNA levels in the arcuate nucleus were found to be regulated by fasting and feeding (Gerken *et al.* 2007). Several SNPs are located in the first intron of the gene, a region where the sequence is strongly maintained across species (Frayling et al. 2007). The SNPs not only affect expression at molecular level, but also affect body mass, food intake, and energy homeostasis; all factors that give rise to polygenic obesity. Genomic variants in the FTO gene have also been linked to a number of diseases such as type 2 diabetes (Frayling et al. 2007), increased hypertension(Pausova et al. 2009), Alzhemier disease (Reitz et al. 2012), risk of acute coronary syndrome (Hubacek et al. 2010) increased adiposity (Church et al. 2009) and metabolic abnormalities (Gerken et al. 2007).

1.4.4 *FTO* SNPs and Obesity Risk

Frayling *et al.* (2007) found homozygous carriers of the *FTO* rs9939609 variant `A' minor allele recorded greater mean weight of 3 kg and had a 1.7 fold risk of obesity compared to the non-variant homozygous `T' allele carriers. This correlation has been detected in children aged 7 years and upward and represents a specific rise in fat mass (Frayling *et al.* 2007). A supporting study by Scuteri *et al*. (2007), found variants in *FTO* and PFKP (platelet type phosphofructokinase) genes showing strong association with increased BMI and weight. On average, each copy of the A-allele raises BMI by around 0.4-0.5 (Yang *et al.* 2012). Additionally, Scuteri et al also noted that the frequency of *FTO* risk allele (AA) was high in European ancestry population, 63% heterozygotes (AT) and 16% homozygotes (AA) (Scuteri *et al*. 2007). Moreover, the A-allele of this SNP relates to increased BMI in age 7 years and older (Cecil *et al. 2*008). Each additional copy of the minor allele was associated with a 0.39 $kg.m^{-2}$ increase in BMI in Europeans (Speliotes *et al.* 2010).

Whilst *FTO* rs9939609 fast became an established biomarker of obesity and obesity related anthropometric traits in Caucasian populations, initial inconsistencies were observed in replication in non-Caucasian populations. However larger studies conducted over the years have been successful in replicating the association of *FTO* with obesity in multiple ethnic populations including Chinese (Wu *et al.* 2014, Tan *et al.* 2008), Asian Indians (Vasan *et al.* 2012) and Africans (Peters *et al.* 2013). The calculated effect of each copy of the rs9939609 risk 'A' allele was 0.26 $kg.m^{-2}$ BMI which was a smaller effect than the value observed in Europeans (0.39 $kg.m^{-2}$). The variation of effect of *FTO* across different ancestries can be attributable to varying frequencies of the variant `A' allele and linkage disequilibrium patterns. The minor allele frequency (MAF) of *FTO* rs9939609 is greatest in Europeans and approximately 40% (Li *et al.* 2012).

Despite the significance of *FTO* as a marker of obesity, the mechanisms underlying this association are not fully understood. Evidence from animals and humans strongly indicates effects on brain food intake and energy regulation. Earlier studies demonstrated that *FTO* gene encodes a 2-oxoglutarate Fe (II) dependant nucleic acid demethylase and is highly expressed in the hypothalamus (Gerken *et al*. 2007). *FTO* reaches the maximum level in the hypothalamic site of brain tissue that controls food consumption. Carriers of the *FTO* rs9939609 risk allele showed changed food intake, with 505 kJ and 1,231 kJ per day more in A allele carriers and AA allele carriers than TT homozygotes, respectively (Yang *et al*. 2012). Selective deletion of the analogous gene in mice, *FTO,* results in post-natal growth retardation with loss of adipose tissue, hypophagia and increased energy expenditure indicating a role of the gene in energy homeostasis (Fischer *et al.* 2009).

In contrast, mice engineered to over-express *FTO* show increased body mass and hyperphagia (Church *et al.* 2010). Recent evidence associates *FTO* with the expression of iroquois-related homeobox (*IRX3*) gene, which has direct effects on body mass and metabolism in mice (Smemo *et al.* 2014). In humans, the study of *FTO* on eating behaviours has generated great interest and growing evidence supports a role of *FTO* in food intake and eating behaviour. For instance the *FTO* SNPs risk alleles have been associated with increased energy intake (Haupt *et al.* 2009, Speakman 2008) and eating behaviours (Harbron *et al.* 2014). Therefore, the investigation of the relationship between *FTO* variants and various eating behaviour dimensions can help in understanding how *FTO* predisposes to obesity.

In addition to the A allele of rs9939609, other *FTO* SNPs have been showed to be related to obesity, for example, the *FTO* SNP rs8050136 has also been considered as an obesity risk factor through regulating energy intake rather than energy expenditure

(Haupt *et al.* 2009). Supporting evidence from Park et al. (2013) showed that the risk allele for *FTO* SNP rs8050136 was also associated with BMI increasing (Park *et al.* 2013). Another SNP rs3751812 is in complete linkage disequilibrium with SNP rs9939609, with the genotypes of these two SNPs in concordance with each other. Okuda et al in a case control study indicated that T-allele of rs3751812 raises risk for obesity by 120-170% in Japanese (Okuda *et al*. 2011). In addition, SNP (rs1558902) is also in linkage disequilibrium with SNP rs9939609. The minor allele (A-allele) was associated with 41% increased risk for obesity with each copy of the C-allele contributing a BMI rise of 0.22-0.38 in the general population (Hotta *et al*. 2008). In addition, T-allele of rs3751812 increases risk for obesity by 27% in Caucasians and 31% in African Americans (Grant *et al*. 2008).

1.4.5 *FTO*, eating behaviours and food craving

It has also been proposed that *FTO* influences food reward mechanisms. Individuals with at least one A allele of *FTO* rs9939609 (the first *FTO* single nucleotide polymorphism associated with obesity) have been reported to show greater externally driven eating (Velders *et al.* 2012), lowered satiety (Wardle *et al.* 2008), enhanced fMRI response to food (Karra *et al.* 2013) and report more frequent loss of control over eating than those having two T alleles (Tanofsky-Kraff *et al.* 2009). The latest study indicates that *FTO* controls ghrelin concentration through the methylation of ghrelin mRNA. Increased *FTO* activity in the risk allele carriers leads to decreased ghrelin mRNA methylation and enhanced ghrelin expression (Karra *et al.* 2013). In fact, reduced satiety of risk variant carriers has been suggested to be the main reason for increased food consumption and subsequently increased BMI by several epidemiological studies.

Cecil and colleagues in 2008 were the first researchers who established the reduced satiety of risk variant carriers in a study including 2,726 Scottish school children, where the role of the risk variant in metabolism and eating behaviour was examined (Cecil *et al.* 2008). Other studies using different procedures established the linkage between *FTO* risk variant and diminished satiety. For example, the relation between A-allele of the SNP rs9939609 and considerably reduced satiety was confirmed by a study based on psychometric measurement of eating behaviours through questionnaires in 3,337 participants in the UK (Cecil *et al.* 2012, Wardle *et al.* 2008).

Another study including 103 adults of Western European descent used visual analogue scales, a psychometric measurement using questionnaires, to determine the postprandial (after meal) response to hunger and satiety, after the participants were given test meals according to their energy needs. The results revealed that individuals with low postprandial responses in satiety were highly represented among the risk allele carriers compared to the non-carriers. This information established the link between risk variants and reduced satiety from another angle (den Hoed *et al*. 2009). In addition, risk variant carriers tend to eat foods containing more total calories, have a preference for energy-rich fatty foods, enjoying tasty food after having eaten a meal, and eat more repeatedly during the day. On average, adult risk variant carriers consume between 125 and 280 calories more each day compared to non-carriers (Sandholt *et al*. 2012).

In a study that examined the link between the *FTO* variants and food preference (among 27 food groups), the result showed that A-allele carriers of rs9939609 consumed considerably more biscuits, pastries, fatty meats, ice cream, fruit, cereal, cheese and significantly less soft drinks and salty snacks (Brunkwall *et al*. 2013). The

study mentioned that the food groups consumed more by the A-allele carriers were usually appetizers, desserts, or snacks. Another study also showed that increased snacking is associated with the A-allele carriers (McCaffery *et al.* 2012). Supporting evidence was provided by Park *et al.,* who investigated whether there was a link between *FTO* and food choices and found a higher percentage of calories came from fat (Park *et al.* 2013).

Furthermore, a study conducted with different groups of people established the association between *FTO* variant carriers and preference for high calorie-dense foods and other correlated eating behaviours, such as enjoying palatable foods and snacking more frequently (Timpson *et al.* 2008). In agreement with Timpson *et al*., evidence by Harbron *et al* (2014) found risk alleles of the *FTO* polymorphisms were associated with higher intake of high fat food and refined starches accompanied with depressive symptoms in Caucasian adults (Harbron *et al.* 2014).

The control of eating is particularly hard in the context of heightened food cravings (Hill 2007), but few studies have addressed whether *FTO* rs9939609 is related to alterations in food cravings. One study (Huang *et al.* 2014) observed no relationship between *FTO* and participants' responses to one question about how often they experienced cravings in the previous week, but there was an indication of a possible interaction between *FTO* and diet on the change in craving from baseline to 6 months after participating in a weight loss program, with evidence of an *FTO* effect only arising in those with high protein intake. In evaluating such a result, it is worth noting that food craving is a multidimensional construct (Cepeda-Benito *et al.* 2000). It is not clear which aspects of craving this single-question test captured and how different aspects of cravings relate to *FTO*. It is also unclear whether the restriction of the sample to

overweight and obese subjects impacted the ability to observe effects (Dang *et al.* 2018).

Given the importance of dopamine to reward and addictive behaviour (Di Chiara and Bassareo 2007), it is striking that at the neurochemical level, mice with deficient *FTO* expression exhibit characteristics similar to mice lacking midbrain dopamine D2 receptors (DRD2) (Hess *et al.* 2013, Bello *et al.* 2011). Moreover, inactivation of the *FTO* gene impaired DRD2-dependent neuronal and reward responses in mice, though the study did not observe a significant difference in body weight or DRD2 expression between *FTO*-deficient and control mice (Hess *et al*. 2013). Further evidence of *FTO's* effects on dopamine-dependent reward learning (Sevgi *et al.* 2015) and resting state functional connectivity in dopaminergic circuitries (Olivo *et al.* 2016) has led to the recent proposal that *FTO* alters DRD2 function in the presence of an obesogenic diet to confer risk of obesity (Sun *et al*. 2017). Evidence of an association between *FTO* and DRD2 function in humans would further support this hypothesis (Dang *et al.* 2018).

Potential relationships between *FTO,* cravings, and DRD2 availability must unfold in the context of life-span development. Fat mass is well-known to increase across adulthood (St-Onge 2005) and at least one *FTO* risk gene (rs1421085) has been reported to impact the trajectory of weight gain as well as personality traits and ventral and medial prefrontal brain functions (Chuang *et al.* 2015). At the neurochemical level, the most replicated finding in the dopamine imaging literature is the robust decline in DRD2 availability across adulthood (Dang *et al.* 2018), recently reported that associations between DRD2 and BMI change with age. Both the intensity of craving and the number of foods craved decline with age (Antonini *et al.* 1993). It is not yet known whether *FTO* influences the age-related decline in either food cravings or DRD2. However, given the developmental trajectories of these phenotypic variables, it is important to

determine whether any potential relations with *FTO* vary or interact with age (Dang *et al.* 2018).

1.5 Motivation to exercise

Healthy eating and participation in regular exercise are important components of a healthy lifestyle, and both are recommended for promoting physical wellbeing (Fisher *et al.* 2011). However, given the widespread availability of indulgent, high-calorie food and drink options (e.g., confectionary, junk food, soda/soft drinks), overcompensating with these types of foods and drinks prior to, or following, exercise may undermine health and weight loss/management goals (King *et al.* 2007, Werle *et al*. 2015).

The consumption of unhealthy foods and drinks following an exercise session as a compensatory behaviour could counter some of the benefits of exercise, and explain, at least in part, the variation in weight-loss responses to exercise regimes (Finlayson *et al*. 2011, King *et al*. 2008). Recently, researchers have proposed that an individual's motivation for exercise may be important in determining post-exercise intake from hedonically pleasurable snack foods and drinks (Dimmock *et al*. 2015, Fenzl *et al*. 2014).

1.5.1 Self-determination Theory

The Self-determination Theory is a macro-theory of human motivation that has a connection with the development and functioning of the personality within social contexts. The theory analyses the extent to which human behaviour is volitional or self-determined, in other words, the degree to which people achieve their activities at

the highest level of reflection and are involved in the actions with a sense of choice (Deci and Ryan 1985).

The self-determined subscales (the intrinsic motivation, the integrated and identified regulation subscales) were grouped to form a global score of autonomous regulation (Pelletier 2002, Sheldon and Elliot 1998). Autonomous motivation, by definition, is characterised by a sense of agency, volition, and identity (Dimmock *et al.* 2015); similarly, the non-self-determined subscales (the introjected and external regulation subscales as well as the amotivation subscale) were grouped to form a global score of controlled regulation (Pelletier 2002, Sheldon and Elliot 1998). Controlled motivation is reflected in a sense of inauthenticity and pressure, autonomously motivated exercisers, as opposed to those possessing controlled motivation, are more likely to embrace a goal commitment focus during/post exercise, and this focus should dampen their desire to pursue the contradictory goal of unhealthy snack consumption (Dimmock *et al.* 2015).

One of the theories in the Self-determination Theory is the Organismic Integration Theory by Ryan and Deci which postulates the different forms of motivation to exercise and the related factors that either encourage or avoid their internalisation and integration in behavioural regulation (Ryan and Deci 2000) . These writers create a taxonomy where motivation is organised in the form of a continuum that covers the different degrees of self-determination of behaviour, from the non-self-determined, to the self-determined, establishing three types of motivation (amotivation, extrinsic motivation and intrinsic motivation) and a series of behavioural regulation stages (amotivation, external regulation, introjected regulation, identified regulation and intrinsic regulation). Every one of the motivation types is determined by a series of

regulatory processes, which can be values, rewards, self-control, interests, fun, satisfaction, etc (Murcia *et al*. 2007).

1.5.2 The Behavioural Regulation in Exercise Questionnaire (BREQ)

The Behavioural Regulation in Exercise Questionnaire (BREQ) was created to measure self-determined motivation in physical exercise (Mullan *et al*. 1997), the original questionnaire was established to measure external, introjected, identified and intrinsic regulation which was after that reviewed and finalised by Markland and Tobin and validating it as BREQ-2. This study adds another factor to these four: amotivation (Markland and Tobin 2004).

1.5.3 Exercise motivation and food intake and eating behaviours

Most of the previous studies in this field focused on effect of exercise on post exercise food intake and most of them used exercise motivation as predictor to post exercise food intake. Fenzl *et al.* invited participants with varying types of exercise motivation to complete a 20 min cycle session labelled as either “fat-burning” or “endurance” training, and then offered participants unhealthy snacks (a large bowl of pretzels). The researchers found an interaction effect between exercise framing and contextual motivation, but in general, autonomously motivated exercisers consumed less of the unhealthy snack food than those exhibiting controlled motivation (Fenzl *et al*.2014).

Many individuals have difficulty maintaining an equilibrium between fulfilling immediate desires (e.g., consuming pleasurable snacks) and satisfying long-term goals (e.g., for health) (Muraven and Baumeister 2000, Ramanathan and Menon 2006). It has been proposed that one cognitive strategy people employ to reach this equilibrium is to activate compensatory beliefs (Knäuper *et al.* 2004). These compensatory beliefs

reflect the idea that the negative effects of one behaviour can be neutralised or compensated for by the positive effects of another. According to the compensatory beliefs model (Knäuper *et al*. 2004) when goals associated with pleasure and harm come into conflict (e.g., "this cake will be tasty but it is unhealthy"), a negative intrapersonal state of cognitive dissonance is created. Cognitive dissonance reflects an aversive motivational state that occurs when an individual holds two cognitions that are inconsistent with each other (Dimmock *et al.* 2015).

Conceptual work indicates that compensatory health beliefs are more likely to be active when individuals experience controlled motivation for a task (Rabia *et al.*2006). Compensatory beliefs become active when people face a conflict between goals to maximize pleasure and to minimize harm. In the case of controlled exercisers, the experience of physical activity satisfies the goal to minimize harm—most individuals are likely to recognize at least some health benefits of physical exercise. However, these individuals are less likely to simultaneously satisfy their desire to experience pleasure while undertaking physical activity, so the potential for conflict between maximizing pleasure and avoiding harm is salient for these people.

Goal conflict is less problematic for those who are autonomously motivated for exercise, because their experience of autonomous functioning is likely to satisfy both positive instrumental and affective goals (Nix *et al.* 1999). As such, individuals who are controlled in their exercise regulation are more likely to activate compensatory beliefs to satisfy their multiple goals, and preliminary empirical work by Miquelon *et al*. (2012) has supported this premise. These authors found that autonomous motivation toward weight loss lessened participants' activation of dietary compensatory beliefs, and that compensatory beliefs weakened consistency in adherence to dieting rules.

1.6 Alexithymia

While there have been numerous studies examining the role of mood, emotions, and emotional regulation and the links to gaining weight in people with obesity, the particular process by which emotions affect eating behaviour remains elusive (Silva 2015). Research has provided evidence in support of theories that favour an emotion regulation model of eating behaviours (Anestis *et al*. 2009). These theories speculate that individuals become involved in dysregulated eating behaviours to improve negative affect. Some individuals may eat as an emotion regulation strategy thereby developing problematic eating behaviours.

Consequently, problems with emotional regulation may contribute to the development and maintenance of difficult eating behaviour. In addition, it has been suggested that patients use maladaptive eating behaviours (e.g., bingeing, purging, dietary restriction) and excessive exercise as a way to avoid or cope with their emotions (Cooper 2005). Specifically, an early childhood environment in which emotions are viewed as unacceptable or frightening leads to the development of the belief that emotions are bad and should not be experienced or expressed. These beliefs become activated each time that an emotion is experienced, which then leads to a secondary emotion (i.e., an emotion in response to another emotion) such as shame, guilt, or disgust about experiencing an emotion. These secondary emotions increase the patient's distress and decrease his/her coping abilities, thus leading to engagement in eating disorder behaviours in an attempt to avoid or cope with the emotion (Corstorphine 2006).

1.6.1 Definition of Alexithymia

The concept of alexithymia was first identified by Sifneos who described a set of characteristics originally observed in people with psychological problems that included difficulties identifying feelings and differentiating between feelings and bodily sensations, difficulties communicating feelings, lack of fantasy, and a concrete cognitive style focused on the external environment (Sifneos 1996). Alexithymia is defined as an inability to describe and/or recognise one's own emotions and is considered a common feature in eating disorders. Alexithymia is likely associated with problems in modulating affects and with difficulties in the interpersonal and social realm (Taylor *et al.* 2016).

Research has focused on both understanding alexithymia and on measuring it in both clinical and general populations. Alexithymia is known to be present in several psychiatric disorders, including depression (Li *et al.* 2015); Obsessive-Compulsive Disorder (Roh *et al*. 2011); Schizophrenia (O'Driscoll *et al.* 2014); Post-Traumatic Stress Disorder; Autism Spectrum Disorder (Berthoz and Hill 2005) and eating disorders (Gramaglia *et al.* 2016).

Prevalence estimates of alexithymia within the general population, as measured by the twenty-item Toronto Alexithymia Scale [TAS-20] (Pinna *et al*. 2014), range from 5.2 to 18.8%, with a prevalence of 18% being reported in a British undergraduate sample (Mason *et al.* 2005). In this study, alexithymia was found be to be more prevalent in females than in males. Alexithymia is also associated with higher levels of sub-clinical disordered eating in undergraduate females (Ridout *et al*. 2010), mirroring what has been found in eating disorder populations (Courty *et al.* 2015, Beadle *et al.* 2013, Nowakowski *et al.* 2013).

1.6.2 Assessment of Alexithymia

Alexithymia is assessed by the Toronto Alexithymia Scale (TAS-20) which is a well-validated self-report scale composed of 20 items (Bagby *et al.* 1994). In addition, it has been found to be stable and replicable across clinical and nonclinical populations (Bagby *et al*. 1994), on which participants rate their level of agreement to statements on a five-point Likert scale, yielding a total score as well as subscale scores designed to measure: difficulty identifying feelings (DIF) and to distinguish them from somatic sensations accompanying emotional arousal (e.g. 'I am often confused about what emotion I am feeling' and 'I have feelings that I can't quite identify'), difficulty describing feelings (DDF), the ability to describe feelings to other people (e.g. 'I am able to describe my feelings easily' and 'It is difficult for me to reveal my innermost feelings, even to close friends') and externally-oriented thinking (EOT). (e.g. 'I prefer to analyze problems rather than just describe them' and 'looking for hidden meanings in movies or plays distracts from their enjoyment').

The maximum possible score on the TAS-20 is 100, a cut-off score of 60 is used to classify as having alexithymia, with a score of 61 or above indicative of high levels of alexithymia (Taylor *et al*. 1999). The TAS-20 demonstrates good reliability and factorial validity (Wise *et al.* 2000). In addition, it is a useful screening instrument for both English and non-English speaking populations (Taylor *et al*. 2003).

1.6.3 Alexithymia and Eating Behaviour

While alexithymia is described as a stable personality trait (Martínez-Sánchez *et al.* 2003) it correlates highly with symptoms of both depression and anxiety and may be a predisposing factor for the development of other psychopathologies (Taylor and Bagby

2004). In addition, alexithymia is thought to underlie emotional difficulties in individuals with eating disorders (Brewer *et al.* 2015) and has been implicated in both the development and maintenance of disorders (Treasure and Schmidt 2013). It is also related to poorer treatment outcome, making it a relevant treatment target (Pinna *et al.* 2014).

The involvement of alexithymia in eating disorders has been shown (Cochrane et al. 1993, Schmidt *et al.* 1993). In a critical review of the literature on alexithymia in eating disorders, Nowakowski *et al* (2013) report that individuals with EDs consistently report higher levels of alexithymia on the TAS than controls (Nowakowski *et al* 2013). However, as this review did not include a meta-analysis of studies, it is not known whether the effect size is the same across the spectrum of EDs, e.g., in Anorexia Nervosa (AN), Bulimia Nervosa (BN) or Binge eating disorder (BED), or whether a diagnosis is associated with higher levels of alexithymia. They report that individuals with EDs score higher on two of the TAS-20 subscales: Difficulty describing feelings and difficulty identifying feelings, but not on externally orientated thinking. Performing meta-analyses of subscale scores will help synthesise this literature further and to determine whether significant differences exist between groups on all sub-scale scores (Nowakowski *et al.* 2013).

The relationships between alexithymia and eating behaviour in obesity have been sparsely studied and poorly understood. There is empirical evidence suggesting a relationship between alexithymia and obesity (Clerici *et al*. 1992). Although some studies do not support this hypothesis, alexithymia is present in obese or eating-disorder subjects with psychopathological characteristics. These studies suggest that

alexithymia could be associated with eating disorders in people with obesity (Pinaquy et al. 2003). It has been suggested that, in patients with severe obesity, alexithymia traits might reflect an underlying eating disorder, such as binge eating disorder (de Zwaan *et al.* 1995), or cause emotional eating as a result of difficulties in reading internal cues (Pinaquy *et al.* 2003).

Little is known about the relationship between alexithymia and eating behaviour in non-clinical populations. Further research is needed in non-clinical populations to understand the contribution of alexithymia to general eating behaviour. Therefore, the association between eating behaviour and alexithymia needs to be inferred from studies utilising clinical samples. Alexithymia and eating behaviour have mainly been studied in eating disordered populations beginning with observations of patients with eating disorders having difficulty recognising and describing emotions that predated the formulation of the alexithymia construct (Bruch 1962, Bruch 1974). De Berardis *et al.,* (2007) hypothesised that alexithymia plays an indirect role in the pathogenesis and maintenance of abnormal eating behaviors and in encouraging depressive symptoms and lower self-esteem. Abnormal eating behaviours may worsen self-esteem and the feelings about one's body (De Berardis *et al.* 2007).

There are a few studies that investigate the relationships between alexithymia in emotional eating. Pinaquy *et al.* (2003) examined the relationship between alexithymia and emotional eating in 169 women with obesity, with and without binge eating disorder, emotional and external eating was significantly higher in binge eating disorder BED participants; there was no difference in restrained eating. Alexithymia was revealed to be a significant predictor of emotional eating only for the BED group,

BED women scored higher on the difficulty identifying feelings subscale and the difficulty describing feelings subscale; the women did not differ on the externally orientated thinking subscale. For the BED women only, the difficulty identifying feelings subscale was a predictor of emotional eating. The results of this study support Bruch's idea of difficulty identifying feelings being central to emotional eating (Bruch 1973).

Larsen et al (2006) investigated the relationship between alexithymia and emotional eating in a sample of 413 obese men and women. Males and females showed no difference in the TAS-20 total score, the difficulty identifying feelings subscale or the difficulty describing feelings subscale. However, men scored higher on the externally orientated thinking subscale than women. Alexithymia was associated with more emotional eating with only the subscales difficulty identifying feelings and difficulty describing feelings being significant. Sex effects were examined and the correlations between alexithymia and emotional eating were stronger for men than women. (Larsen *et al.* 2006).

Results from both, Larsen *et al.* 2006, Pinaquy *et al.* 2003 propose that alexithymia is linked with emotional eating, particularly the difficulty identifying subscale of alexithymia. Opposing results have been reported by Noli et al. (2010), these writers studied 150 individuals with obesity undergoing bariatric surgery and 132 individuals at least 1-year after biliopancreatic diversion (BPD) (Noli *et al.* 2010). Emotional eating was measured by organised interview and alexithymia with the TAS-20. High rates of alexithymia were found in those patients with obesity undergoing bariatric surgery and in the BPD patients. This conclusion confirms other findings of high incidence rates of alexithymia in people with obesity (Legorreta *et al* 1988, Elfhag and Lundh 2007) and suggests that alexithymia is not secondary to having a chronic state as in the BPD

group body weight had normalised; while the mean BMI of 34.4 kg/m² for this group is still considered overweight. Nevertheless, opposing earlier research (Pinaquy *et al.* 2003) comparison between alexithymics and non-alexithymics revealed no difference in reported emotional eating.

The research from clinical samples indicates that alexithymia may be related to emotional eating, in particular the difficulty identifying feelings subscale of the TAS-20; results for the difficulty describing feelings subscale have been mixed, while externally orientated thinking does not seem to be related to emotional eating. A limitation of these studies is that the populations were obese and were motivated to lose weight, having been engaged in weight management clinics research which may influence the findings and limit their application to the general population (Larsen *et al.* 2006).

This overview has provided only a brief account of some studies conducted on the association of common obesity-associated factors, genetics and BMI. This study focused on *FTO,* one of the most studied genes related to obesity. However, there are a number of genes and other factors that have been shown to also be related to obesity. Providing information on these factors and the interactions that happen between them will help in identifying individual therapy for obesity in the future.

1.7 Objectives of PhD

1.7.1 Overall aim

Obesity is an increasing problem, globally. Previous studies have explored relationships between eating behaviours, BMI and obesity. However there are a number of factors that interact with eating behaviours that could influence these relationships such as food cravings, alexithymia, motivation, age, sex and genetics. Therefore, the

programme of research as part of this PhD was conducted with the aim of investigating the interactions between BMI, age, sex and *FTO* genotype.

1.7.2 Specific objectives

The specific objectives of this programme of study as part of the PhD are as follows:

1) Investigate the association between eating behaviours, determined by TFEQ, food craving and BMI and identify the influence of age, sex, BMI and *FTO* genotype on these relationships.
2) Investigate the association between eating behaviours, alexithymia and BMI and identify the influence of age, sex and *FTO* genotype on these relationships.
3) Investigate the association between motivation to exercise; eating behaviours and BMI and identify the influence of age, sex, BMI and *FTO* genotype on these relationships.

It is hoped that further understanding of all these interactions and the factors that influence them will help in addressing the obesity epidemic.

The programme of study as part of this PhD recruited volunteers from Sheffield Hallam University students and staff and the surrounding area as well as participants from local weight loss intervention programmes. Chapter 2 describes the general methods used in each study.

2 CHAPTER 2: Materials and methods

2.1 Ethics approval and informed consent

Ethical clearance for all studies was granted by the Faculty of Health and Wellbeing Ethics Committee, Sheffield Hallam University and from NHS research ethics committee (RECs) IRAS number 17/NE/0018, Sheffield Hallam Number CD 9-2-2015 - NJM. Participant information sheets (Appendix 5 and 7) and consent forms (Appendix 4 and 6) were also approved by the committee on research and ethical review, Biomedical Research Centre (BMRC), Sheffield Hallam University. All participants recruited read the participant information sheet and provided written informed consent. Samples and questionnaires were allocated a code number to ensure no identifying details could be linked with the names of the participants. All consent forms were sealed and separated from the participants study packs to ensure everything was kept anonymous and confidential. Participants had the right to withdraw at any time.

2.2 Participants

SHU participants

Participants for the Cross-Sectional study (Chapter 3) were recruited through word of mouth and posters surrounding Sheffield Hallam University campus. A study pack that included all the questionnaires and the Flinders Technology Associates (FTA cards) for DNA sample were provided for all participants. All participants completed all the questionnaires and anthropometric measurements were taken as will be described below.

Rotherham institute for Obesity (RIO - Tier 3 weight management service) Participants

RIO is a privately-run specialist centre for weight management focusing on one-to-one or group sessions delivered by exercise therapists in an on-site gym, a dietician, and specialist nursing team. The team also includes specialist psychological support.

RIO is a unique and specialist centre for the management of weight problems with a multidisciplinary approach to reducing and maintaining weight loss for both adults and children. RIO does not claim to have invented the cure for weight problems, and cannot guarantee weight loss for patients, but it brings together all the NHS approved and evidence-based methods for weight loss into one primary care based centre in the hope that they can maximise the chances for weight loss.

Participants were recruited for this study before they entered the weight management programme, with assistance from the staff at RIO. On arrival they met the nurse and completed a medical history screen questionnaire (medical, body weight, diet and psychological) and anthropometric measurements were taken. Thereafter, the study objectives were explained to each participant in more detail, the questions asked by the participants were answered. A consent form was signed by all the participants who agreed to take part in the study. A DNA sample was collected using an FTA card the same day.

During the second session the researcher met the participants and the study pack containing the questionnaires was collected, anthropometric measurements, body weight and height were provided by RIO from specialists trained to collect this data.

Rotherham's leisure centres – Shapeup (Tier 2 community weight management intervention) Participants

The Shape Up initiative is available for people who feel they need extra support to lose weight, gain fitness and improve their overall health and wellbeing. Experts provide several Shape Up programmes at venues across Rotherham. Following an initial assessment, people are given advice, guidance and practical solutions to help them find the best way to lose weight and access support. The Shape Up service for adults includes a free 12-week gym membership at one of Rotherham's leisure centres alongside 10 structured sessions in a group of 12-15, 2 hours for each group session focusing on weight management, developing healthy eating habits and enjoying being more active, more often.

Participants from shape up were recruited by visiting the centre and meeting each group during their first session. The study objectives were explained to each group in more detail, the questions asked by the participants were answered, and the consent form was signed by all participants who volunteered to participate. A study pack including all the questionnaires, the participant information sheet, consent form and FTA card was provided. During the second session the principal investigator met the participants and the study pack was collected. Anthropometric measurement (body weight and height) were provided by shapeup from specialists trained to collect these measures.

The community-based exercise and diet intervention programme – Concorde Leisure Centre Participants

Participants were referred to the programme by their general practitioner via a Physical Activity Referral Scheme (PARS), which adheres to the National Quality

Assurance Framework (NQAF) for PARS. The programme was delivered by accredited physical activity professionals (Register of Exercise Professionals: REPS), and the scheme is independently accredited by the City of Sheffield Physical Activity referral group.

A total of 100 adults with overweight or obesity who were participating in a community-based exercise and diet intervention programme took part in the study prior to starting a 12-week weight management intervention programme based on lifestyle modification, in line with NFAQ standards for PARS. The programme included both physical activity and diet and nutrition advice and involved a combination of home-based and PARS centre-based activities, with ongoing support from accredited physical activity professionals. All participants had their weight, height to determine BMI.

Table 2-1 summarises the participants included in this study by chapter. Some data and FTA cards for groups 1 and 2 had previously been collected by the candidate's supervisor, however the raw data from all questionnaires was re-inputted for all participants and all samples were re-genotyped.

Table 2-1 The place and the number of the participants included in each study and the relevant chapter

Group number	Location and participant groups	Numbers of participants	Chapter
1	Sheffield Hallam University - Staff and students	424	3 and 4
2	Community-based exercise and diet intervention programme based at Concorde Leisure centre	100	4
3	Rotherham Institute for Obesity – patients referred to a Tier 3 weight change programme	32	4 and 5
4	Rotherham's leisure centres Shape up programme – Tier 2 group intervention	51	3, 4 and 5

2.3 Anthropometry

Anthropometric measurements were conducted in all studies described in this thesis as follows:

2.3.1 Height

Height was measured using a wall-mounted stadiometer (Seca, Hamburg, Germany). Participants stood barefoot with their heels together against a wooden back plate. Subjects kept their arms loosely by their side. The head was placed in the Frankfort Plane i.e. a horizontal line between the lower orbits of the eyes and the external auditory meatus. The stadiometer head plate was lowered onto the top of the head and then the height was recorded to the nearest 0.1 cm

2.3.2 Weight

Weight was measured to the nearest 0.01 kg using a balance beam scale (Avery, Birmingham, U.K.). Subjects wore light clothing, removed their shoes and jewellery and

were told to remove anything from their pockets while being weighed.

2.3.3 Body mass index (BMI).

BMI was calculated as weight in kilograms divided by the square of height in metres. Table 1.1 in chapter 1 shows the international definitions of generalised and central obesity.

2.4 Eating Behaviours

The Three-Factor Eating Questionnaire-R18 is a shortened version of the original 51-item TFEQ (Stunkard and Messick 1985) (Appendix 1). The questionnaire measures three different aspects of eating behaviour: (a) restrained eating (b) uncontrolled eating and (c) emotional eating. The questionnaire comprises of 18 items that are measured on a 4-point response scale (definitely true: 4, mostly true: 3, mostly false: 2, definitely false: 1) and items scores are summated into subscale scores: CR, UE and EE..

2.5 Food Craving

The food cravings inventory (FCI) developed by (White *et al.* 2002) see Appendix 2, is a valid self- report measure of specific food cravings in a subjective manner within the past month. The questionnaire consists of 28 items measuring the frequency of cravings for a specific food item on a scale of 0-never to 4-almost every day. Each food item belongs to a subscale as shown in table 2.2. A total score for each subscale is calculated by the summation of each food item score for each participant.

The FCI has established content validity, concurrent validity with the Conceptual Craving Scale (Hill *et al*. 1991) and disinhibition and hunger scales of the TFEQ (Stunkard and Messick 1985b) and discriminant validity with the restraint scale of the TFEQ. The FCI has demonstrated acceptable internal consistency reliability and test-

retest reliability in adults. The inventory shows adequate internal consistency (Cronbach's ά of 0.86 for the fats and sweets subscales, 0.84 for the starches/complex carbohydrates subscale, 0.76 for the fast-food subscale, and 0.93 for the inventory as a whole (White *et al.* 2002). Further psychometric support for the FCI has been established in diverse community and clinical samples (White and Grilo 2005, Barnes and Tantleff-Dunn 2010).

Table 2-2 Food craving inventory questionnaire consists of 4 subscales

SUBSCALE			
HIGH FAT	SWEETS	CARBOHYDRATES	FAST FOOD
Fried chicken	Brownies	Breads	Hamburger
Sausages	Cookies	Pancakes	French fries
Gravy	Chocolate	Biscuits	Pizza
Fried fish	Doughnuts	Sandwich bread	
Bacon	Cakes	Rice	
Steak	Ice-cream	Baked potato	
Sausage rolls	Sweets	Pasta	
	Sponge cake	Cereal	
		Danish pastry	
		Crisps	

Note. Each food item listed is summated accordingly to provide total subscale score.

2.6 Motivation to exercise.

Participants rated their motivation for exercise using the Behavioural Regulation in Exercise Questionnaire-2 BREQ-2 (Markland and Tobin 2004) Appendix 3. The 19-item BREQ-2 assesses an individual's reasons for engaging in exercise using a 5-point response scale anchored at 0 (not at all true for me) to 4 (very true for me). These scores were added together to provide a total score for each subscale. The BREQ-2 consists of five subscales: amotivation is formed by four items, it covers the subject's

non-intentional behaviour. There is no clear reason for exercising. It includes items, such as “I don’t see why I should have to exercise” or “I can’t see why I should bother exercising”. External regulation, formed by 4 items, refers to the subject performing the behaviour as a means of obtaining an external reward or due to influence by external subjects or factors. The behaviour is performed but controlled by external contingencies. It has items such as “Because others say I should”, “Because my friends/family/partner say I should” or “To please other people”. Introjected regulation refers to the way the subject performs the behaviour so as not to feel guilty or uneasy about not having exercised, it is formed by 3 items , such as “because I feel guilty when I don’t exercise” and “because I feel ashamed when I miss a session”. Identified regulation is formed by 3 items and refers to the subject thinking that the behaviour is valuable, but it is done as it is considered to be beneficial for the subject. It includes items such as “Because I value the benefits of exercise” or “Because it is important to me to exercise regularly”, and intrinsic motivation formed by 4 items, refers to the type of behavioural regulation in which it is chosen freely. The reward is the behaviour itself and it is something pleasant. It includes items such as “Because I think exercise is fun” or “Because I enjoy the exercise sessions” (Murcia *et al* 2007).

Validity and reliability evidence to support the use of scores derived from the BREQ-2 has been reported in previous studies (Fenzl *et al*. 2014, Markland and Tobin 2004).The BREQ-2 was completed by 194 former GP exercise referral scheme participants and subjected to confirmatory factor analyses The model had an excellent fit to the data (Satorra-Bentler Scaled Chi Sq = 136.49, df = 125, p = .23; CFI = .95; RMSEA = .02, 90% CI = .00 - .04; SRMR = .05). Cronbach's alpha reliabilities were as follows: Amotivation .83 External regulation .79, Introjected regulation .80, Identified regulation .73, Intrinsic regulation .86 (Markland and Tobin 2004).

2.7 Alexithymia

Alexithymia refers to people who have trouble identifying and describing emotions and minimise emotional experience and focus attention externally. The Toronto Alexithymia Scale (TAS) is a 20-item instrument that is the most commonly used tool to measure alexithymia (Appendix 4) (Bagby *et al.* 1994).

The TAS-20 has 3 subscales:

• Difficulty Describing Feelings subscale is used to measure difficulty describing emotions. 5 items – 2, 4, 11, 12, 17.

• Difficulty Identifying Feeling subscale is used to measure difficulty identifying emotions. 7 items – 1, 3, 6, 7, 9, 13, 14.

• Externally-Oriented Thinking subscale is used to measure the tendency of individuals to focus their attention externally. 8 items – 5, 8, 10, 15, 16, 18, 19, 20.

To score items are rated using a 5-point Likert scale whereby 1 = strongly disagree and 5 = strongly agree. There are 5 items that are negatively keyed (items 4, 5, 10, 18 and 19). The total alexithymia score is the sum of responses to all 20 items, while the score for each subscale factor is the sum of the responses to that subscale. The TAS-20 uses cut-off scoring: equal to or less than 51 = non-alexithymia, equal to or greater than 61 = alexithymia. Scores of 52 to 60 = possible alexithymia.

The tool demonstrates good internal consistency (Cronbach's alpha = .81) and test-retest reliability (.77, $p<.01$). TAS-20 validity demonstrates adequate levels of convergent and concurrent validity. The 3-factor structure was found to be theoretically congruent with the alexithymia construct. In addition, it has been found

to be stable and replicable across clinical and nonclinical populations (Bagby *et al.* 1994).

2.8 Genetics

2.8.1 Extraction of DNA:

Samples for genotyping were collected using Whatman Easy Collect buccal swabs. Buccal swabs compromised of an FTA card containing chemicals which allowed the cells to be immediately processed, the sample could then be considered as DNA not relevant material under the HTA act. DNA was extracted from the FTA using a QIAamp DNA mini kit (QIAGEN, Manchester). Pieces of the FTA card was submerged in 200µl of PBS, 20µl of QIAGEN protease stock solution and 200 µl buffer AL and vortexed for 15s.

The spin column method for DNA purification was followed guided by the manufacturer's protocol as follows.

1) 20 µl of proteinase K was pipetted into 1.5 ml microcentrifuge tube.
2) 200 µl of whole blood was added to the microcentrifuge tube.
3) 200 µl of buffer AL was added to the sample followed by vortexing for 15 seconds to obtain a homogenous solution.
4) The mixture was incubated in a pre-heated water bath at 56°C for 10 minutes.
5) The mixture was centrifuged briefly.
6) 200 µl of 100% ethanol was added to the sample followed by vortexing for 15 s and brief centrifuge.
7) The mixture was applied to the QIAamp mini spin column provided and centrifuged at 6000 x g (8000 rpm) for 1 minute. The spin column was placed in a fresh 2 ml collection tube and the tube containing the filtrate was discarded. In cases where

incomplete passage of the filtrate through the spin column was observed, the sample was re-centrifuged at a higher speed.

8) 500 µl of prepared AW1 buffer was added to the spin column and centrifuged at 6000 x g (8000 rpm). The collection tube with filtrate was discarded and the spin column placed in a new collection tube.

9) 500 µl of prepared AW2 buffer was added to the spin column and centrifuged at full speed (13000 rpm) for 3 minutes. The spin column was placed in a new collection tube and centrifuged for a further 1 minute.

10) The spin column was placed in a 1.5 ml microcentrifuge tube and 200 µl Buffer AE added. The sample was incubated at room temperature (25°C) for 5 minutes and centrifuged for 1 minute.

11) The final sample of purified DNA in AE buffer was capped and stored at -20°C.

2.8.2 TaqMan® SNP genotyping

The TaqMan® method of SNP genotyping utilises the 5'- exonuclease activity of *Taq* DNA polymerase combined with allele specific hybridization for fluorescence based allele detection (Syvänen 2001, Kim and Misra 2007). The TaqMan® Predesigned Genotyping Assays contain two forward and reverse oligonucleotide primers and two oligonucleotide probes. Each probe consists of a sequence specific oligonucleotide with a fluorescent reporter dye at the 5' end and a quencher molecule at the 3' end. Two probes, one which is complementary to the variant allele and the other complimentary to the wild type allele are labelled with two separate VIC™ and FAM™ reporter dyes.

The TaqMan® probes also consist of a minor groove binder (MBG) which increases the efficiency of allelic discrimination. The MBG strengthens the binding of the probe to

the DNA template and increases the melting temperature without increasing the probe length. Shorter probes result in greater differences in melting temperature between matched and unmatched probes thus increasing efficiency of allelic discrimination. In the intact state of the probe, the fluorescence emitted by the fluorophore is quenched by the quencher molecule. This phenomenon is named fluorescence resonance energy transfer (FRET). When the fluorophore is separated from the oligonucleotide chain during the PCR reaction and is thus not in proximity to the quencher, FRET does not occur resulting in emission of light signal from the reporter dye (Figure 2.1).

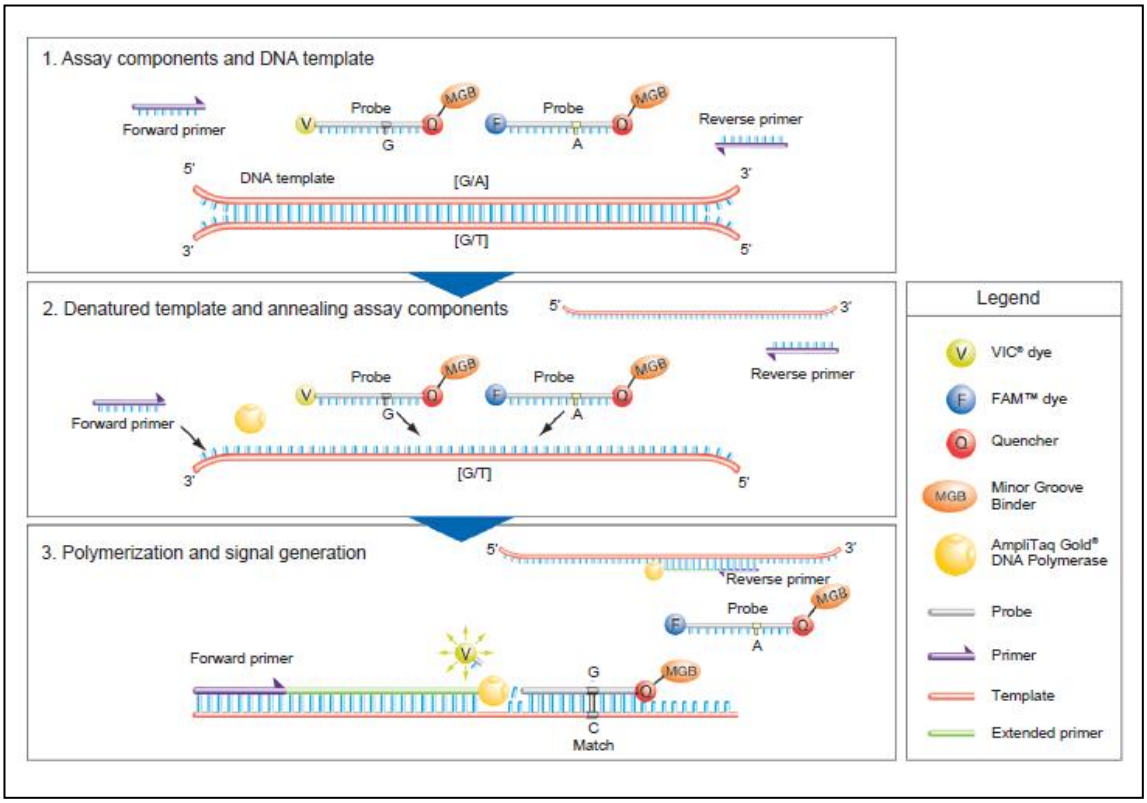


Figure 2-1 TaqMan® MGB probe-based method of allelic discrimination = (Source: Product Bulletin, TaqMan® SNP Genotyping Assays)

During the PCR reaction, the double stranded genomic DNA is separated during the denaturation process. During the annealing phase, the intact probe is hybridized onto the complementary sequence between the forward and reverse primers. During the extension phase, *Taq* DNA polymerase extends the DNA strand from the primers which

results in displacement of the 5' end of the tightly bound probe (Figures 2.2). As the fluorophore is cleaved, a laser emitted by the real-time PCR machine excites the fluorescence dye which now emits fluorescence freely. If the probe is only weakly bound to the DNA template the entire probe is displaced without separation of the reporter and quencher. As the amplification proceeds, the fluorescence accumulation is captured by the instrument after each cycle. The amount of fluorescence emitted is the thus directly proportional to the amount of PCR product produced. The VIC™ and FAM™ dyes have distinctly different wavelengths which can be detected separately by the RT- PCR machine.

In genotyping experiments, the endpoint fluorescence detection is used as opposed to a real-time detection. Here the quantity of the target sequence at the end of PCR is valued. The fluorescence intensity of the reporter dye is normalized against the passive reference ROX™ dye by the machine depicted as 'Rn'. The difference in Rn before and after PCR is calculated to obtain the endpoint normalized increase in fluorescence intensity (ΔRn) as follows; ΔRn = Rn (post-PCR read) – Rn (pre-PCR read). The real-time data collected are beneficial in interrogating the causes of genotype failure and other anomalies that may occur during the experiment.

2.8.3 Quantification of DNA

Quantification of extracted DNA was performed on the NanoDrop™ 2000 UV spectrophotometer (Thermo Scientific Fisher, USA).

2.8.4 Genotyping protocol

Genotyping was performed using TaqMan® Predesigned Genotyping Assays on the StepOnePlus© Real-Time PCR system platform (Applied Biosystems, Foster City, CA,

USA). The TaqMan® genotyping assay contains the two SNP specific forward and reverse primers and two VIC™ and FAM™ dye labelled TaqMan® MGB allelic probes. The TaqMan® Genotyping Master Mix was used for standard time genotyping and the TaqMan® GTXpress™ Master Mix was utilized for fast genotyping. The TaqMan® Genotyping Master Mix contains AmpliTaq Gold® DNA polymerase whereas the TaqMan® GTXpress™ Master Mix contains AmpliTaq® Fast DNA polymerase. In addition, both mixes contain the required dNTPs, the ROX™ as a passive reference dye and buffer components. Real-Time PCR was performed in a 96-well plate format in a total 10µl reaction volume prepared as per manufacturer's guidelines as follows:

1) Template genomic DNA was brought to room temperature from refrigeration at 4°C.
2) The TaqMan® GTXpress™ Master Mix was thoroughly mixed.
3) The TaqMan® Genotyping Assays was mixed and centrifuged.
4) The PCR reaction mixture was prepared for 110 samples for a 96 well reaction plate to allow for excesses. The reaction components were added guided by manufacturer's recommendations (Table 2.3).
5) A reduced genotyping assay volume of 0.25µl was used instead of the manufacturer recommended volume of 0.5µl to conserve the assays.

Table 2-3 Components and volumes of PCR mix for genotyping

PCR component	Volume per well (µl)
Master Mix	5.00
Genotyping Assay	0.25
DNase-free water	2.75
Genomic DNA	2.00

Total	10

6) All samples were analysed in duplicate with two no template controls (NTC) per plate.

7) A volume of 2µl of DNA template was added to each well to make a total reaction volume of 10µl.

8) The plate was sealed with adhesive film and centrifuged briefly to eliminate bubbles.

9) The plate was loaded onto the real-time PCR system and the reaction mixture was subjected to the manufacturer recommended thermal protocols depending on the standard or fast method as follows.

Table 2-4 Thermal protocols for standard and fast TaqMan® Real-time PCR genotyping

	Temperature (°C)	Duration	Cycles
Standard method			
Enzyme activation	95	10 minutes	Hold
Denature	95	15 seconds	40
Anneal/Extend	60	30 seconds	
Fast method			
Enzyme activation	95	20 seconds	Hold
Denature	95	3 seconds	40
Anneal/Extend	60	30 seconds	

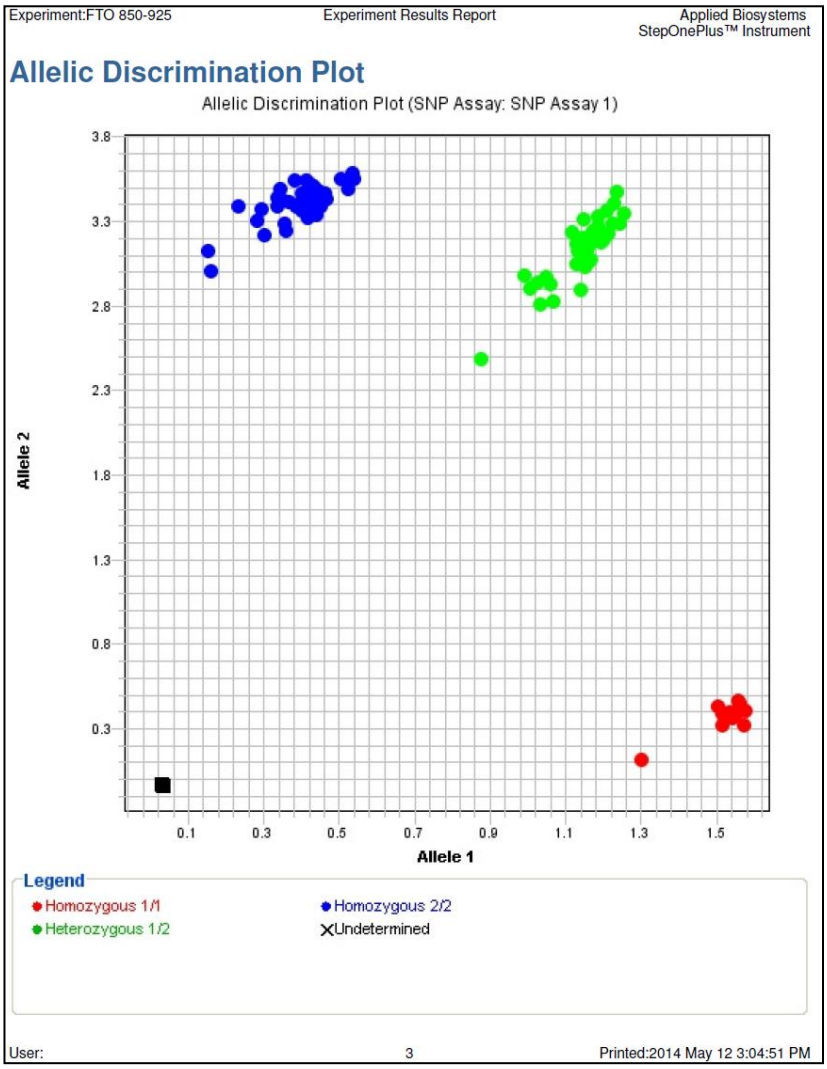


Figure 2-2 Sample allelic discrimination plot from *FTO* rs9939609 genotyping

The red cluster of dots represents fluorescence from VIC™ dye resulting from the probe binding to allele 1 only (The 'A' allele of the *FTO* rs9939609) and therefore indicates homozygosity for the allele 1. Similarly, the blue clusters represent FAM™ dye fluorescence and therefore homozygosity for allele 2 (The 'T' allele of *FTO* rs9939609). The green cluster represents the emission of both fluorescence signals and therefore indicates the heterozygous state (AT).

2.9 Statistical analysis

The Statistical Package for the Social Sciences (SPSS software version 24, IBM) was used for the statistical analysis with significance accepted if $p < 0.05$. Distribution of data was checked using the Kolmogorov-Smirnov Test and descriptive statistics were calculated. Pearson correlation was undertaken to explore associations between variables including age, BMI, eating behaviours, food craving, exercise motivation and alexithymia. T-tests were performed to assess sex and genotype differences in age, BMI, eating behaviours, food cravings, exercise motivation and alexithymia.

In order to examine the effects of age, sex and *FTO* genotype on these relationships, participants were split according to their sex (F and M) and according to their genotype group (AA+AT and TT). Participants were also split according to their age into (≤25 Y and > 25 Y), the aim of this analysis was to investigate differences between people who were still at an age where they are known to be developing eating patterns and an older group who are more likely to have settled eating patterns'. As shown in previous studies such as settling down with a partner (Mata *et al.* 2018, Anderson *et al*.,2004), getting a job (Au and Hollingsworth 2011), having children (Laroche *et al.* 2012) are all known to be associated with changes in eating habits and behaviours Therefore, the population was split according to their age into two groups before and after the likely ages where these life events take place.

The Bonferroni correction was used to reduce the chances of obtaining false-positive results (type I errors) when multiple pair wise tests are performed on a single set of data. The probability of identifying at least one significant result due to chance increases as more hypotheses are tested.

The Bonferroni correction is an adjustment made to *P* values when several dependent or independent statistical tests are being performed simultaneously on a single data set. To perform a Bonferroni correction, divide the critical *P* value (α) by the number of comparisons being made. For example, if 10 hypotheses are being tested, the new critical *P* value would be α/10. The statistical power of the study is then calculated based on this modified *P* value.

Multiple regression analysis was performed to assess the multivariate relationships between the independent variables and BMI. In the regression model, the selected predictors (variables which were significant or approached significance in the bivariate analysis) were forced into the model and the semi partial correlation coefficient was calculated to quantify the unique contribution of each predictor to the variance in the dependent measure(Cohen *et al*. 2014) Considering the relatively small subject-parameter ratio (24:1) and in the absence of strong theoretical support for a hierarchical entering of predictors into the model, this *a priori* (forced) model is preferable to a stepwise model as it minimizes instability in the selection of variables into the model (and in parameter estimation) caused by potential sampling biases (Biddle *et al.* 2001).

Mediation analysis was undertaken to explore relationships between variables. This is a method to help explain how one variable influences an outcome variable. Mediation represents the consideration of how a third variable affects the relationship between these two other variables. The application of such analysis is in prevention and treatment research, where interventions are designed to change the outcome of interest by targeting mediating variables that are hypothesized to be causally related to the outcome (MacKinnon *et al*. 2007). Mediation in its simplest form represents the

addition of a third variable to an X → Y relationship, whereby X is related to the mediator, M, and M is related to Y, implying X → M → Y. The PROCESS programme within SPSS calculates the extent of mediation and allows for the inclusion of covariates and confounders in the analysis. After analysis if the effect of X on Y completely disappears, M fully mediates between X and Y (full mediation). If the effect of X on Y still exists, but in a smaller magnitude, M partially mediates between X and Y (partial mediation).

Mediation analysis with bootstrapping was undertaken as recommended (Preacher and Hayes 2008); the SPSS macro provided by Hypotheses were tested in SPSS using PROCESS Model 59 (Hayes and Preacher 2014), when using model 4, 10,000 bootstrapped estimates and a 95 confidence interval. This model estimates a moderated indirect effect by evaluating the impact of the moderator on the indirect effect, as well as the predictive relationship to the direct effect.

For outcome data, effect sizes were calculated using Cohens d. Thresholds were set at 0.0-0.19 for a trivial effect, 0.2-0.49 for a small effect, 0.5-0.79 for a medium effect and 0.8 and above for a large effect (Cohen 1992, Sullivan and Feinn 2012). All data are presented as mean ± standard deviation unless otherwise stated.

3 CHAPTER 3: Eating behaviours and food cravings; influence of age, sex, BMI and *FTO* genotype

3.1 Introduction

Behaviours related to food intake which influence the frequency, meal size, meal content, and attitude to meals are described as 'Eating Behaviours'. Eating behaviours can influence the amount of energy consumed by an individual and thus predispose to an increased risk of obesity (Blundell and Cooling 2000). Previous studies have shown an association of eating behaviours with weight gain and increasing BMI which are directly related to food intake (van Strien *et al.* 2016, Burton *et al.* 2007).

Food craving is defined as a strong, irresistible desire to consume a specific type of food (Cherpitel *et al.* 2010) which is extremely common with some studies estimating that it is experienced by more than 90% of the population (Hallam *et al.* 2016, Hill 2007).. Increased food cravings have been shown to be associated with increased BMI (Chao *et al*. 2014, Burton *et al.*2007).

An influence of *FTO* on eating behaviours has also been shown, although the results are contradictory, Habron *et al* showed that the *FTO* risk allele was associated with differences in eating behaviours in adults with overweight or obesity (Harbron *et al.* 2014), and similar findings have been shown in normal weight controls(Cornelis *et al.* 2014). In contrast, in a group of adolescents and children *FTO* genotype was associated with BMI but did not influence eating behaviour (Ibba *et al.* 2013).The *FTO* gene has been reported to influence food cravings, with individuals carrying the obesity-susceptible A allele having higher total food cravings compared to TT homozygotes which correlated with higher BMI (Dang *et al.* 2018).

Sex and age also influence eating behaviours and food cravings, previous studies highlight that females had higher scores for cognitive restraint than males but inconsistent sex effects for uncontrolled eating or emotional eating (Chearskul *et al.* 2010, Hainer *et al.* 2006, Drapeau *et al.* 2003, Weingarten and Elston 1991). Other studies found significant differences between sexes with females scoring higher on emotional eating and cognitive restraint but equal mean scores for uncontrolled eating (Karlsson *et al.* 2000, Lluch *et al*. 2000) De Lauzon *et al.* 2004). Löffler *et al* found that females scored significantly higher than males in all subscales of eating behaviours and also found older individuals had significantly higher mean scores than younger people for cognitive restraint, but lower mean scores for other factors measured by TFEQ 51 (Löffler *et al.* 2015).

Regarding the effects of sex and age on food cravings, Imperatori et al found that females with overweight or obesity were more likely to experience cravings than males (Imperatori *et al.* 2013). Chao *et al* (2015) found that females had significantly higher cravings for sweets than males (Chao *et al.* 2015). A previous study also stated that women reported significantly more cravings for chocolate and for sweets than did men. However, craving for sweets declined with age among women (Pelchat 1997). These findings are in agreement with another two studies that included older females in reporting a negative association between food cravings and age, although neither of these studied controlled for BMI (Basdevant *et al*. 1993, Hill*et al.* 1991).

Food cravings declined with age, but this age effect differed across variants of *FTO* rs 9939609: while TT homozygotes showed the typical age-related decline in food cravings, there was no such decline among A carriers, suggesting that they are at risk for larger weight gain over the course of aging as fat mass often increases with age

(Dang *et al.* 2018). The decline in food cravings with age may also be related to age-dependent changes in taste sensitivity that have been reported (Narukawa *et al.* 2018, Sergi *et al*. 2017) and may also be responsible for age-related declines in food intake.

3.2 Objectives of the study

The current study investigates the interactions between eating behaviours, food cravings and BMI. As previously highlighted, there are interactions between eating behaviours and food cravings that influence BMI, these findings indicate that when considering the influence of eating behaviours and food cravings on obesity it is important to consider other variables that are known to also influence these measures including genetics, age, sex and BMI. It is also important consider which associations are mediated by other relevant variables. The objectives of this study were:

1) To investigate the interactions between eating behaviours, food cravings and BMI.

2) To determine the influence of *FTO* genotype, sex and age on these interactions.

3) To use mediation analysis to explore the role of these mediators in these interactions.

3.3 Experimental section

3.3.1 Study Participants

Participants were recruited through word of mouth and posters surrounding Sheffield Hallam University, Sheffield, UK and from participants of the Shape Up programme, Rotherham, UK. To be included in the study participants needed to be ≥ 18 years. People who were pregnant or breastfeeding, who had a history of serious psychiatric

illness or were taking medication known to affect appetite or metabolism were excluded. A total of 475 participants (N=252 F, N=223 M) volunteered.

Total sample BMI (25.82±6.14) Kg/m², age (30.65±14.20) years were included in this study. 249 of the participants were aged 25 years or younger (≤ 25 years), with 226 participants aged over 25 years (> 25 years). We were interested in studying eating behaviours at a stage in life before patterns had become fully established. We considered previous work which shows that life events such as co-habiting, marriage, securing a job and having children are associated with changes in eating patterns and weight gain (Mata *et al.* 2018, Laroche *et al.* 2012, Au and Hollingsworth 2011).

The 25 years as the cut-off were chosen because for many in the study group up to this age would be prior to the aforementioned life events,(although this is making assumptions about the participants). All participants completed two questionnaires 1) revised three factor eating questionnaire TFEQ – R18 and Food Craving Inventory (FCI), anthropometric measurements (height and weight were taken) a buccal swab was collected for genotyping for *FTO* gene, SNP ID: rs9939609.

3.3.2 Anthropometry

Body weight and height was measured as described in chapter 2. BMI was calculated as body mass in kilograms divided by the square of height in meters.

3.3.3 Eating Behaviours

Eating behaviours were measured using the revised 18 items 'Three Factor Eating Questionnaire (TFEQ-R18, (Karlsson *et al.* 2000)) as described in chapter 2

3.3.4 Food cravings

Food cravings were measured using the Food Craving Inventory (FCI), (White *et al*. 2002) as described in chapter 2.

3.3.5 Genotyping

FTO gene, SNP ID: rs9939609 was investigated in this study. Buccal samples for genotyping were collected using easy collect devices (Whatman). DNA was extracted from the FTA card contained in the device using QIAamp DNA mini kit (QIAGEN) according to the manufacturer's instructions. Genotyping was performed using Taqman SNP genotyping assays (Applied Biosystems) as described in chapter 2.

3.3.6 Statistical analysis

Statistical Package for the Social Sciences (SPSS software version 24, IBM) was used for the statistical analysis with significance accepted if $p < 0.05$. Distribution of data was checked using the Kolmogorov-Smirnov Test and descriptive statistics were calculated. Pearson correlation was undertaken to explore association between variables including age, BMI, eating behaviours and food craving. T-tests were performed to assess gender and genotype differences in age, BMI, eating behaviours and food cravings after Bonferroni correction *p* value of <0.005 was considered significant.

Multiple regression analysis was performed to assess the multivariate relationships between the independent variables and BMI. In this regression model, the selected predictors (age, TFEQ -18 subscales and FCI) were forced into the model and the semi partial correlation coefficient was calculated to quantify the unique contribution of each predictor to the variance in the dependent measure (Cohen *et al*. 2014).

For the mediation model (Figures 3.4 and 3.5), BMI was the independent variable, eating behaviours was the mediator variable, and food craving was the dependent variable. Age, sex and *FTO* genotype were the covariates. For outcome data, effect sizes were calculated using Cohens d.

3.4 Results

3.4.1 Descriptive statistics

The descriptive statistics for the primary variables for the overall sample and by sex are shown in table 3.1 and by genotype are shown in table 3.2. There were no significant differences in mean BMI between men and women but there was a significant difference between carriers of the *FTO* TT genotype compared to those with AT+AA genotype (24.62±5.29 vs 26.52±6.55 kg/m², p=0.001). The data were analysed for deviation from Hardy-Weinberg equilibrium, X^2=1.48 so it did not significantly deviate from the expected values. The *FTO* MAF of the risk allele A was 0.42, compared to the published global MAF of 0.34.

Table 3.1 also shows the results of mean food craving scores; women had higher mean scores for carbohydrate cravings compared to men (14.73±5.99 vs 13.59±5.74 p=0.036), however, after Bonferroni correction this is not significant. There were no differences in eating behaviour scores between men and women and no difference in scores for food cravings or eating behaviours between the different genotypes.

Table 3-1 Descriptive statistics for primary variables for overall sample, by sex.

	Overall (N = 475)		Women (N = 252)		Men (N = 223)				
	M	SD	M	SD	M	SD	*t*	*p*	*D*
Age (years)	30.6	14.2	30.35	13.8	30.9	14.6	-0.462	0.64	0.04
BMI (kg/m^2)	25.8	6.14	25.73	6.72	25.8	5.40	-0.285	0.77	0.03
Fat craving	10.0	5.4	9.73	5.72	10.3	4.91	-1.283	0.20	0.12
Sweet craving	18.3	7.8	18.84	9.15	17.7	10.2	1.244	0.21	0.12
Carbohydrate craving	14.2	5.89	14.73	5.99	13.5	5.74	2.099	0.03	0.19
Fast Food craving	9.57	5.1	9.47	5.06	9.64	5.06	-.0359	0.72	0.03
Total food craving	52.1	20.4	52.78	20.3	51.3	20.3	0.779	0.43	0.07
Cognitive restraint	12.8	3.5	12.83	3.51	12.8	3.46	-0.222	0.82	0.01
Uncontrolled eating	20.7	5.4	20.82	5.35	20.6	5.63	0.405	0.68	0.04
Emotional eating	6.68	3.1	6.87	3.11	6.45	3.07	1.487	0.13	0.14

Note. All significance tests were two-tailed. M= mean score; SD =standard deviation; t =t-test; *p*= p-value; d=Cohen's d.

Table 3-2 Descriptive statistics for primary variables for overall sample, by genotype.

	TT genotype (N = 153) 32%		AT+AA genotype (N = 322) 67%				
	M	SD	M	SD	*t*	*p*	*d*
Age (years)	29.19	12.94	31.05	14.46	-1.249	0.212	0.135
BMI (kg/m^2) *	24.62	5.29	26.52	6.55	-3.266	0.001	0.319
Fat craving	10.71	5.33	9.75	5.28	1.827	0.068	0.180
Sweet craving	18.16	9.10	18.86	10.04	-0.636	0.525	0.073
Carbohydrate craving	14.55	6.194	14.33	5.61	0.388	0.698	0.037
Fast Food craving	9.31	4.48	9.82	5.32	-1.010	0.313	0.103
Total food craving	52.73	18.78	52.71	20.72	0.050	0.960	0.001
Cognitive restraint	12.79	3.29	13.06	3.557	-0.764	0.445	0.078
Uncontrolled eating	20.31	5.59	20.98	5.387	-1.288	0.198	0.122
Emotional eating	6.71	3.05	6.7	3.07	-.300	0.764	0.003

Note. All significance tests were two-tailed. M= mean score; SD =standard deviation; t =t-test; *p*= p-value; d=Cohen's d. * Denotes a significant difference between genotypes

3.4.2 Relationships between age, BMI, eating behaviours and food cravings

Correlations between age, BMI, eating behaviours and food cravings have been calculated and categorised for the overall population in tables 3.3 and 3.4, by sex (male and female) in table 3.5 by genotype (TT genotype and AT+AA genotype) table 3.6, and by age (≤25 Y and >25 years) in table 3.7.

Table 3.3 shows that there is a positive relationship between age and BMI (r=0.509**) and an inverse relationship between age and fatty food cravings (r=-0.107*),

uncontrolled eating (r=-0.222**) and emotional eating (r=-0.184*) for the whole sample. There is an inverse relationship between BMI and fatty food cravings (r=-0.180**), and a positive relationship between BMI and cognitive restraint (r= 0.128**).

Table 3-3 Relationships between age, BMI, eating behaviours and food cravings

	BMI	Fatty foods	Sweet	Carbohydrates	Fast foods	Cognitive restraint	Uncontrolled eating	Emotional eating
Age (years)	0.509**	-0.107*	-0.041	-0.071	-0.037	-0.024	-0.222**	-0.184**
BMI (kg/m²)		-0.180**	-0.075	-0.078	0.026	0.128**	0.014	0.082

Note. Correlations of primary variables for overall population. All significance tests were two-tailed (*$p < .05$; **$p < .01$).

Table 3.4 shows that there is an inverse relationship between cognitive restraint and fatty food cravings (r= -0.259**), sweet food cravings (r=-0.138**) and fast food cravings (r=-0.167**). There is a positive relationship between uncontrolled eating and carbohydrate cravings (r=0.164**) and there is an inverse relationship between emotional eating and fatty food cravings (r=-.197**), and fast food cravings (r=0-.125**).

Table 3-4 Relationships between eating behaviours and food cravings

	Fatty foods	Sweet food	Carbohydrates	Fast foods
Cognitive restraint	-0.259**	-0.138**	0.005	-0.167**
Uncontrolled eating	.000	0.059	0.164**	0.004
Emotional eating	-0.197**	-0.029	0.043	-0.125**

Note. Correlations of primary variables for overall population. All significance tests were two-tailed (*p < .05; **p < .01).

In table 3.5 the results show that when exploring the differences between men and women, table 3-5 shows that in women there is an inverse relationship between age and fat cravings (r=-0.157*) and carbohydrate cravings (r=-0.195**), in contrast to men where these relationships are not seen. In men there is an inverse relationship between BMI and cognitive restraint (r=0.210**) in contrast to women where there is no relationship. In men there were also inverse relationships between cognitive restraint, emotional eating and fast food cravings which were not seen in women.

Table 3-5 Relationships of primary variable by sex.

	1-Age	2-BMI	3 - Fat craving	4 - Sweet craving	5- carbohydrates	6 - fast foods	7 - Cognitive restraint	8 - Uncontrolled eating	9- Emotional eating
1-Age	XX	.544**	-.157*	-.107	-.195**	-.117	-.073	-.233**	-.140*
2-BMI	.473**	XX	-.186**	-.102	-.122	.000	.081	-.028	.122
3-Fat craving	-.050	-.185**	XX	.494**	.533**	.525**	-.225**	-.097	-.241**
4-Sweet craving	.020	-.063	.357**	XX	.330**	.664**	-.121	.020	-.028
5-Carbohydrates	.071	-.016	.418**	.430**	XX	.331**	.011	.183**	.038
6-Fast Food	.045	.050	.435**	.686**	.379**	XX	-.117	-.049	-.083
7-Cognitive restraint	.032	.210**	-.301**	-.139*	.003	-.156*	XX	.303**	.400**
8-Uncontrolled eating	-.215**	.059	.113	.078	.140*	.047	.173**	XX	.499**
9-Emotional eating	-.232**	.020	-.144*	-.055	.033	-.184**	.376**	.464**	XX

Note. Correlations of primary variables among women N=252 presented above the diagonal, and correlations of primary variables among men N=223 are presented below the diagonal. All significance tests were two-tailed (*p < .05; **p < .01).

Table 5 shows that *FTO* genotype has no effect on the relationships between age, BMI, eating behaviours and food cravings, with all correlations similar for each genotype.

	1-Age	2-BMI	3-Fat craving	4- Sweet craving	5- carbohydrates	6 - fast foods	7- Cognitive restraint	8- Uncontrolled eating	9- Emotional eating
1-Age	XX	.412**	-.082	.014	-.089	-.021	-.034	-.215*	-.144
2-BMI	.548*	XX	-.078	-.032	-.077	.076	.154	-.038	.145
3-Fat craving	-.103	-.206**	XX	.326**	.497**	.449**	-.283**	.020	-.154
4-Sweet craving	-.035	-.098	.465**	XX	.280**	.599**	-.308**	-.068	-.075
5-Carbohydrates	-.042	-.083	.451**	.381**	XX	.304**	-.080	.135	.024
6-Fast Food	-.024	.016	.501**	.690**	.333**	XX	-.219**	.063	-.108
7-Cognitive restraint	-.020	.101	-.278**	-.114*	.001	-.133*	XX	.233**	.445**
8-Uncontrolled eating	-.220**	.029	-.046	.065	.147**	-.075	.255**	XX	.442**
9-Emotional eating	-.201**	.053	-.223**	-.050	.011	-.161**	.354**	.504**	XX

Table 3-6 Relationships of primary variable by genotype

Note. Correlations of primary variables among TT genotype N=153 presented above the diagonal, and correlations of primary variables among AA+AT genotype N= 322 are presented below the diagonal. All significance tests were two-tailed (*$p < .05$; **$p < .01$).

As there was such a strong effect of age on eating behaviours and food cravings, we investigated the participant group split by age. The results show differences between the < 25 years and > 25 years age groups. There is an inverse relationship between sweet cravings and emotional eating in the younger group, whereas in the older group this relationship is positive. A similar difference is seen for the relationship between fat cravings and emotional eating. In the younger group there are relationships between fast food cravings and cognitive restraint and emotional eating which are not present in the older group.

	1-Age	2-BMI	3-Fat craving	4- Sweet craving	5- carbohydrates	6 - fast foods	7- Cognitive restraint	8- Uncontrolled eating	9- Emotional eating
1-Age	XX	0.009	-0.05	-0.094	0.024	-0.095	.032	.103	.038
2-BMI	0.322**	XX	-0.119	-0.058	-0.095	0.046	.174**	.022	.185**
3-Fat craving	0.059	-0.111	XX	.490**	.430**	0.513**	-.326**	-.047	-.314**
4-Sweet craving	-0.116	-0.127	.365**	XX	0.371**	0.710**	-.227**	-.004	-.176**
5-Carbohydrates	0.002	0.012	.489**	.397**	XX	0.300**	-.032	.133*	-.045
6-Fast Food	-0.186**	-0.045	.512**	.646**	.428**	XX	-.262**	-.059	-.242**
7-Cognitive restraint	.005	.127	-.105	-.003	.102	.044	XX	.264**	.474**
8-Uncontrolled eating	-.272**	.143	-.049	.144*	.138	.086	.211**	XX	.405**
9-Emotional eating	-.239**	.127	-.071	.159*	.127	.032	.217**	.565**	XX

Table 3-7 Relationships of primary variable by age.

Note. Correlations of primary variables among ≤ 25years N=249 presented above the diagonal, and correlations of primary variables among > 25 years N=226 are presented below the diagonal. All significance tests were two-tailed (*p<.05; **p<.01).

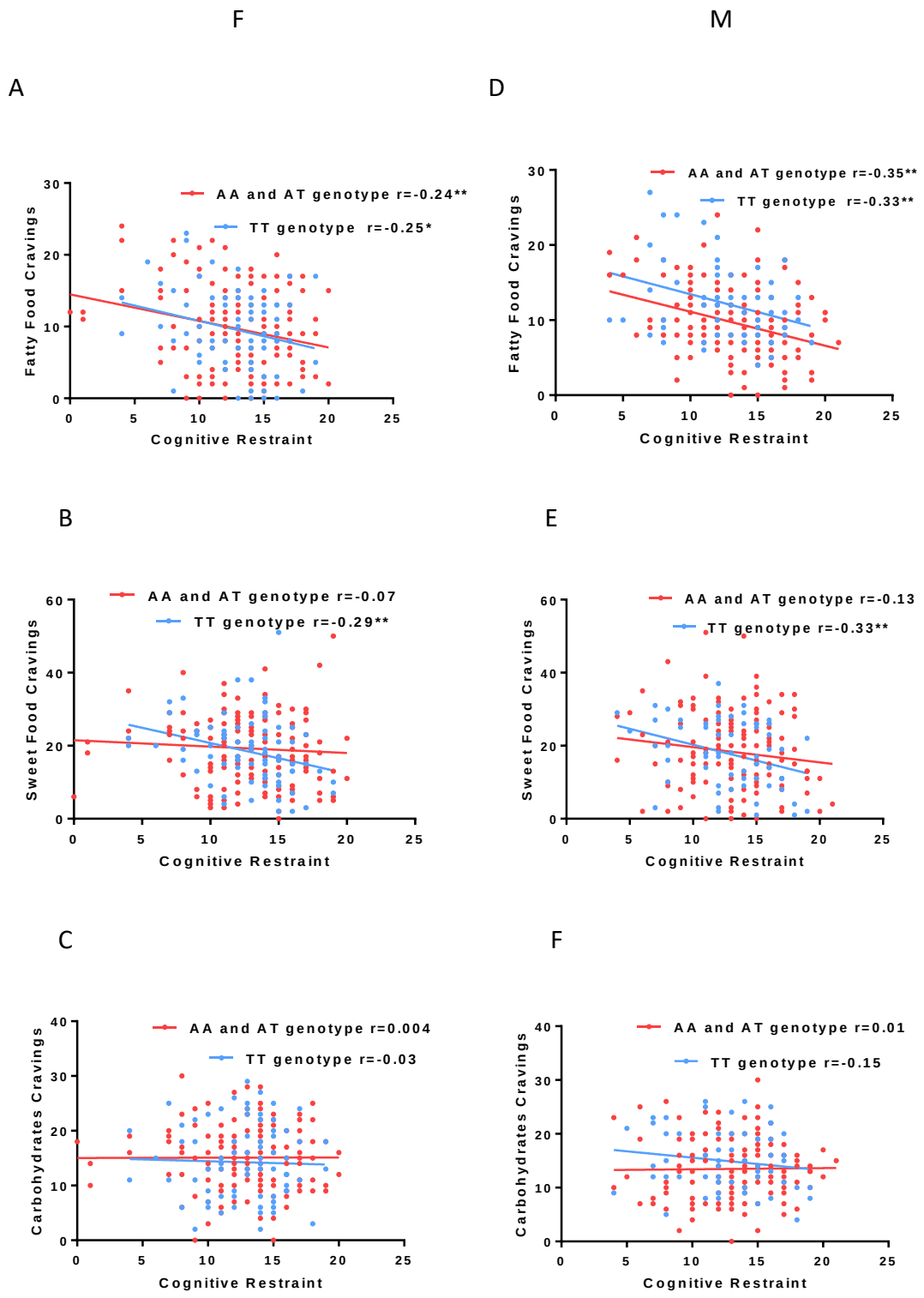


Figure 3-1 The relationships between cognitive restraint and fatty foods craving, sweet craving and carbohydrates craving. Panels A, B and C are for females and panels D, E and F are males. There were significant inverse relationships between cognitive restraint and fatty food craving in both genotype groups and in both sexes, and significant inverse relationships between cognitive restraint and sweet food craving in the TT genotype group in both sexes.

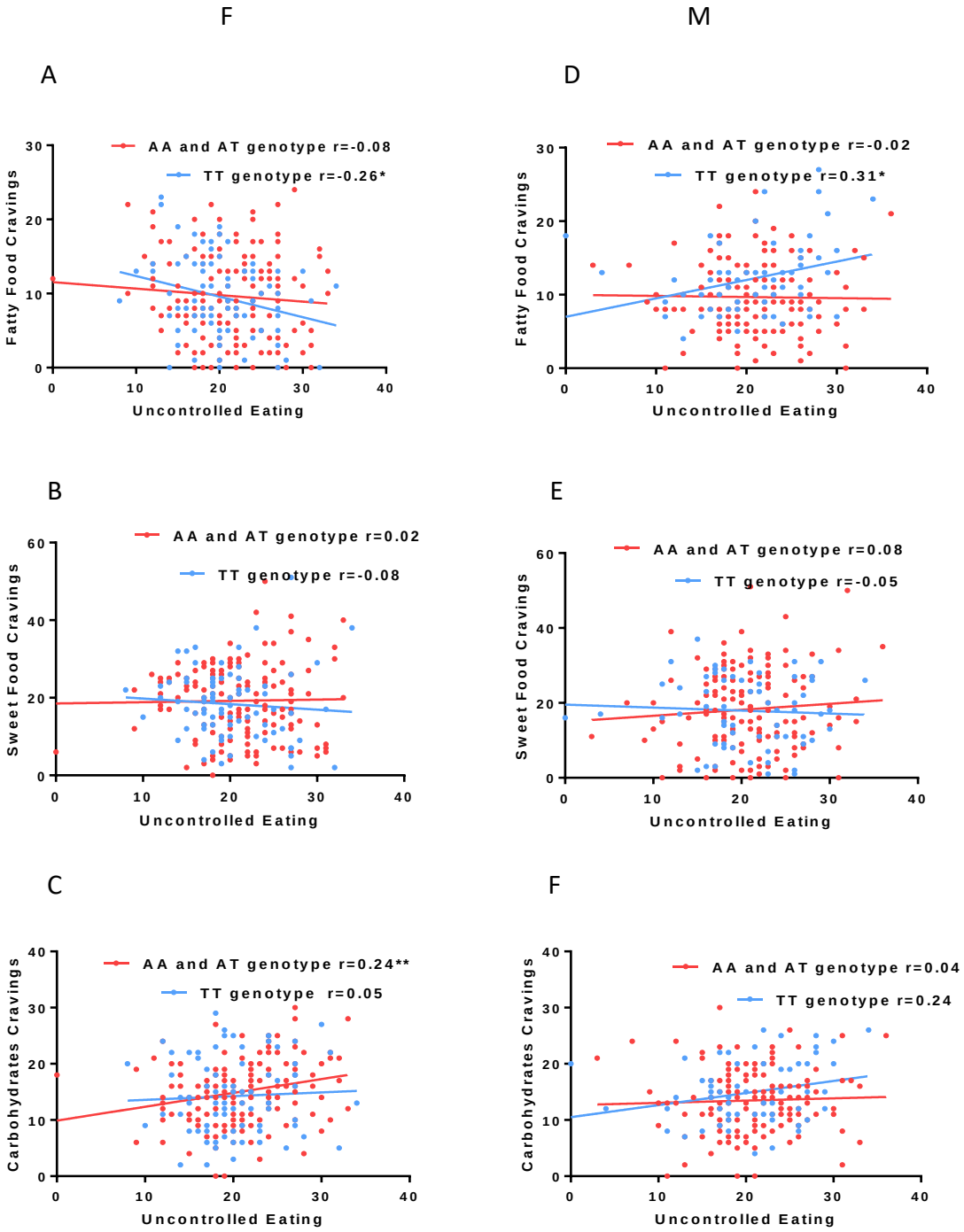


Figure 3-2 The relationships between uncontrolled eating and fatty foods craving, sweet craving and carbohydrates craving. Panels A, B and C are for females and panels D, E and F are for males. There was a significant inverse relationship between uncontrolled eating and fatty food craving in the TT genotype group in females; in contrast, there was a significant positive relationship between uncontrolled eating and fatty food craving in the TT genotype group in males. There was also a significant positive relationship between uncontrolled eating and carbohydrate craving in the AA+AT genotype group in females.

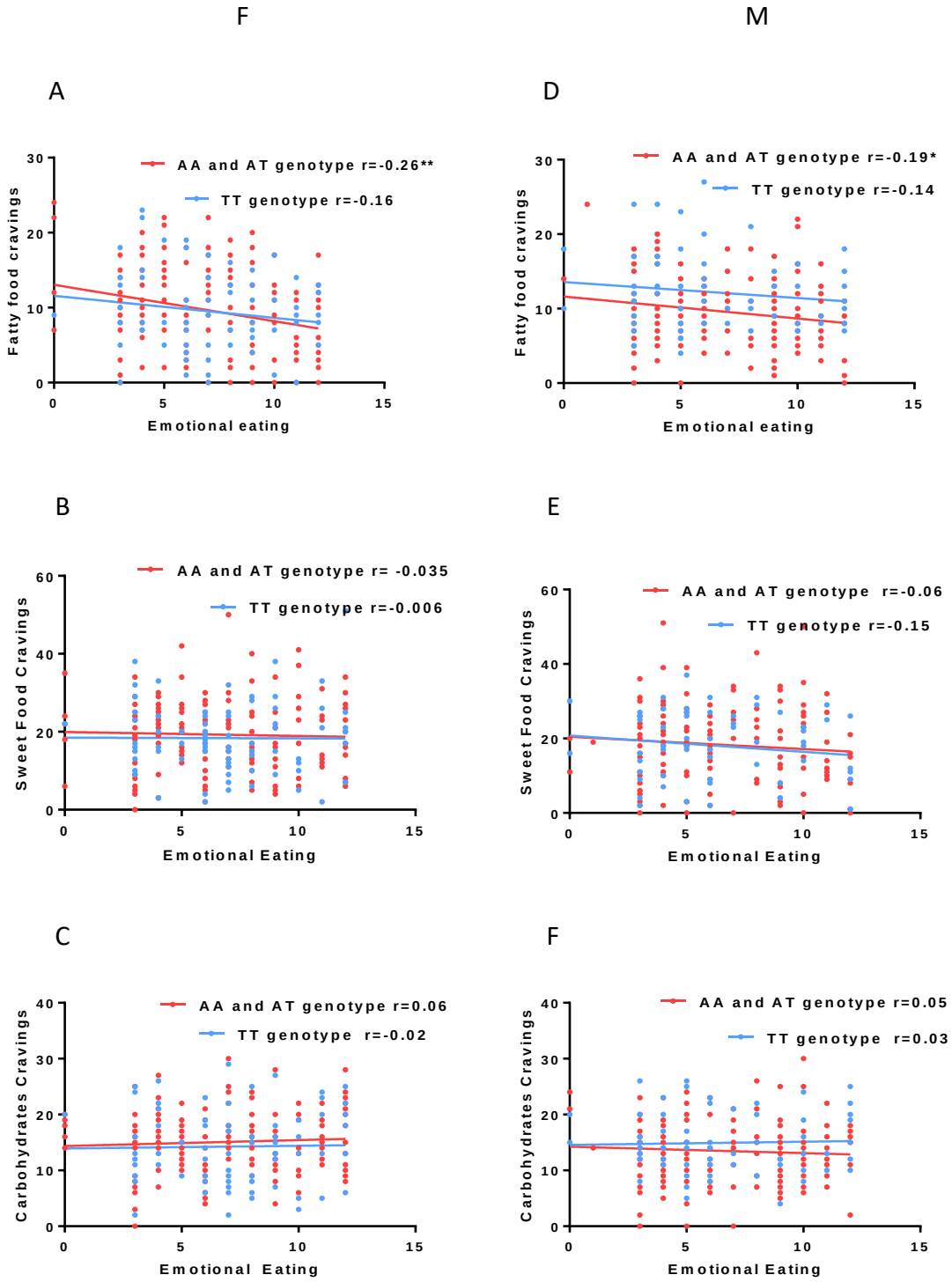


Figure 3-3 The relationships between emotional eating and fatty foods craving, sweet craving and carbohydrates craving. Panels A, B and C are for females and panels D, E and F are males. There were significant inverse relationships between emotional eating and fatty food craving in the AA+AT genotype group in both sexes.

3.4.3 Regression analysis for influence of age, eating behaviours and food craving on BMI

The results of the final model, which included TFEQ-R18, FCI and age, are presented in Table 3.8. Results of the regression analysis indicated that the adjusted R^2 indicates a high predictive value for the model of = 31.3. Age was significantly associated with BMI and increases by .43 for every point increase in age (p <.0001). Fast food craving was significantly associated with BMI. Specifically, BMI increased by .27 for every point increase in fast food craving score (p <.0001). After that emotional eating with p=.005, sweet food craving p=.007, and then fatty food craving which negatively associated with BMI, BMI decreased by (-.136) for every point increase in fatty food craving score (p <.02).

Table 3-8 Multiple Regression Analysis for factors influence BMI

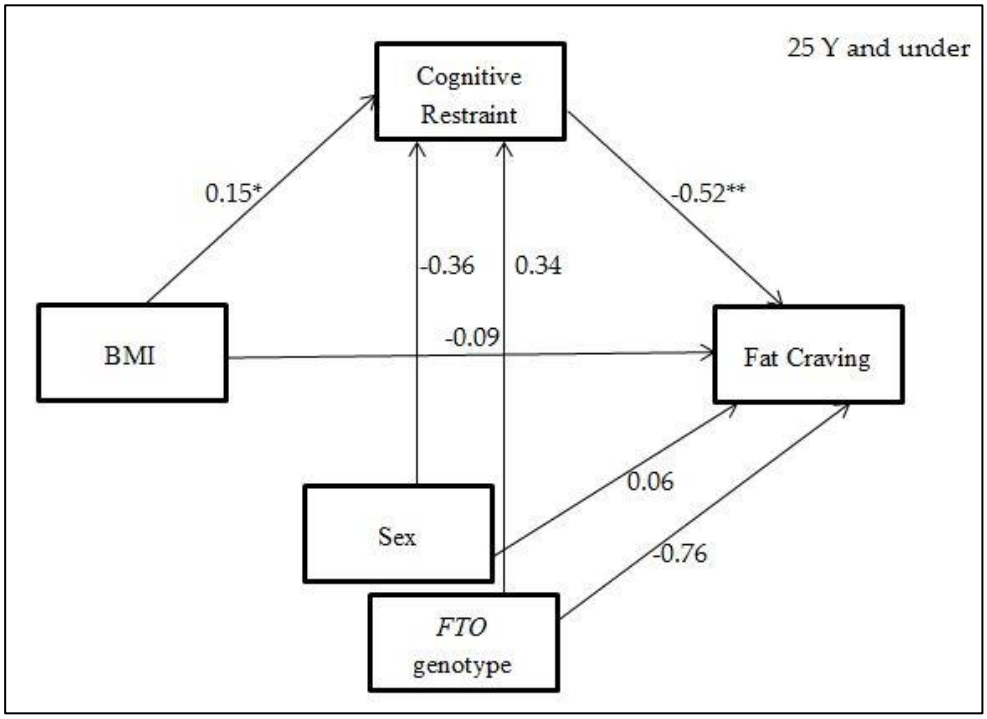
	B	*t*	*p*	Semi partial correlation
Age	.235	13.256	.000	.516
Fatty food craving	-.136	-2.333	.020	-.091
Sweet food craving	-.094	-2.696	.007	-.105
Carbohydrates craving	-.021	-.428	.669	-.017
Fast food craving	.275	4.091	.000	.159
Cognitive Restraint	.202	2.301	.442	.030
Uncontrolled eating	.070	1.378	.169	.054
Emotional eating	.270	2.791	.005	.109

$R^2 \times 100$= 32.5 (adjusted R^2 =31.3), SEE= 5.11, F (df, 8.45) = 28, 63 (p<0.0001).

3.4.4 Mediation analysis

Results of the mediation analysis are shown in (Figures 3.4 and 3.5) and cognitive restraint mediates the relationships between BMI and fatty food and sweet food craving in 25 years and under.

A



B

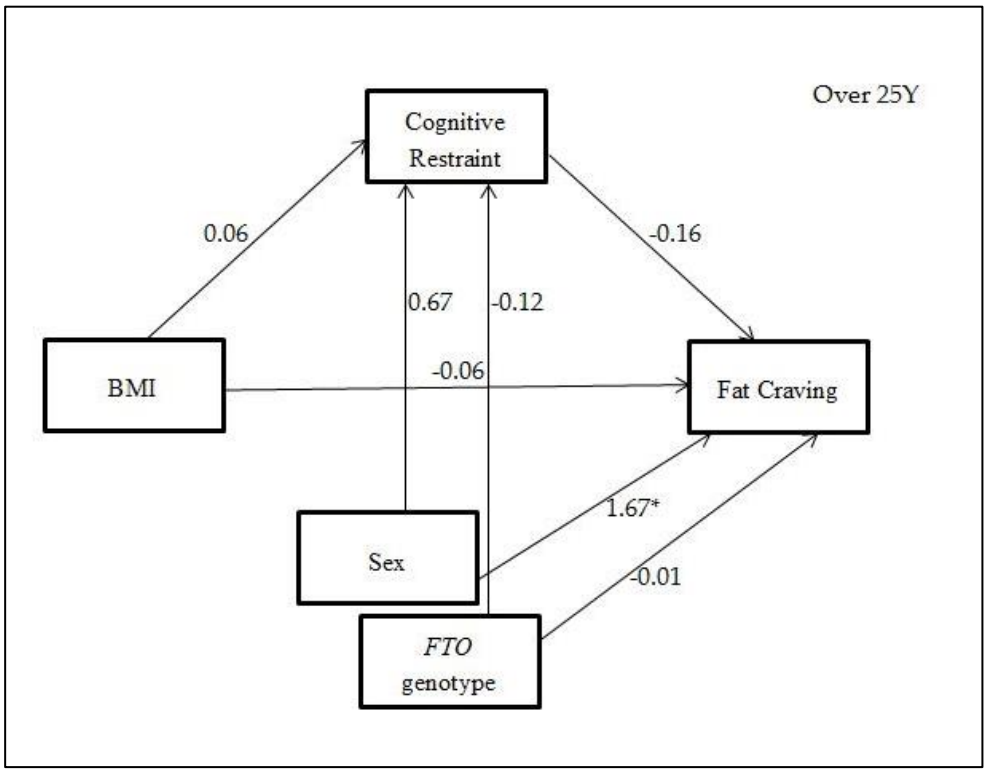
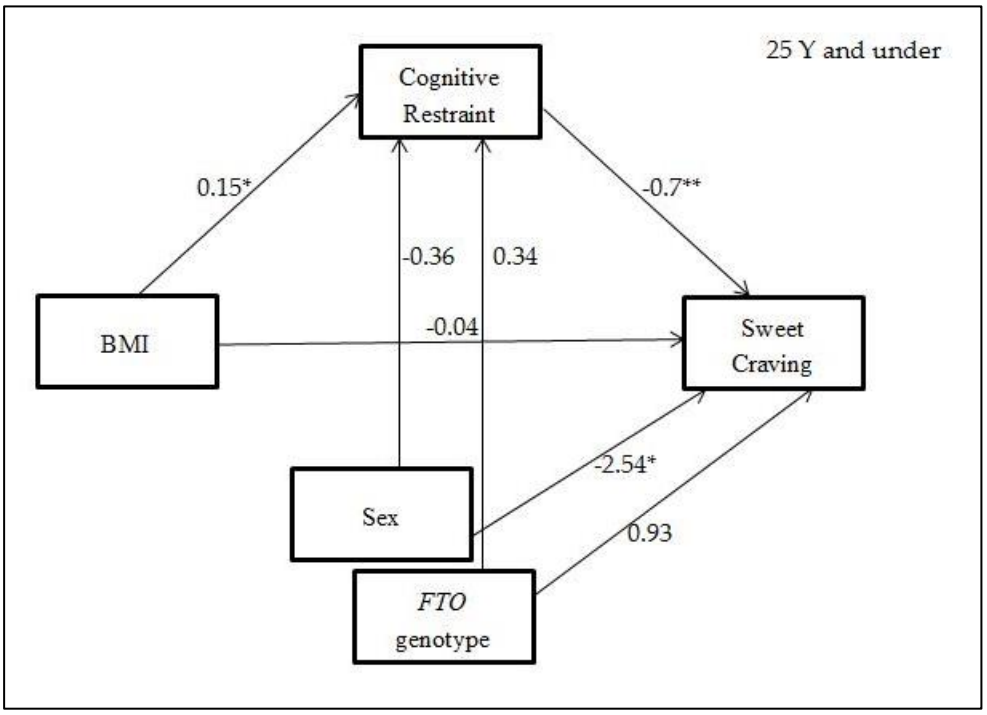


Figure 3-4 Mediation analysis model for the relationship between BMI, cognitive restraint and fatty food craving. Panel A in ≤25 years and panel B in >25 years group. The model indicates that cognitive restraint may mediate the relationship between BMI and cravings for fatty food in the ≤25 years group but not in the > 25 years group ($^{*}p < .05$; $^{**}p < .01$).

A



B

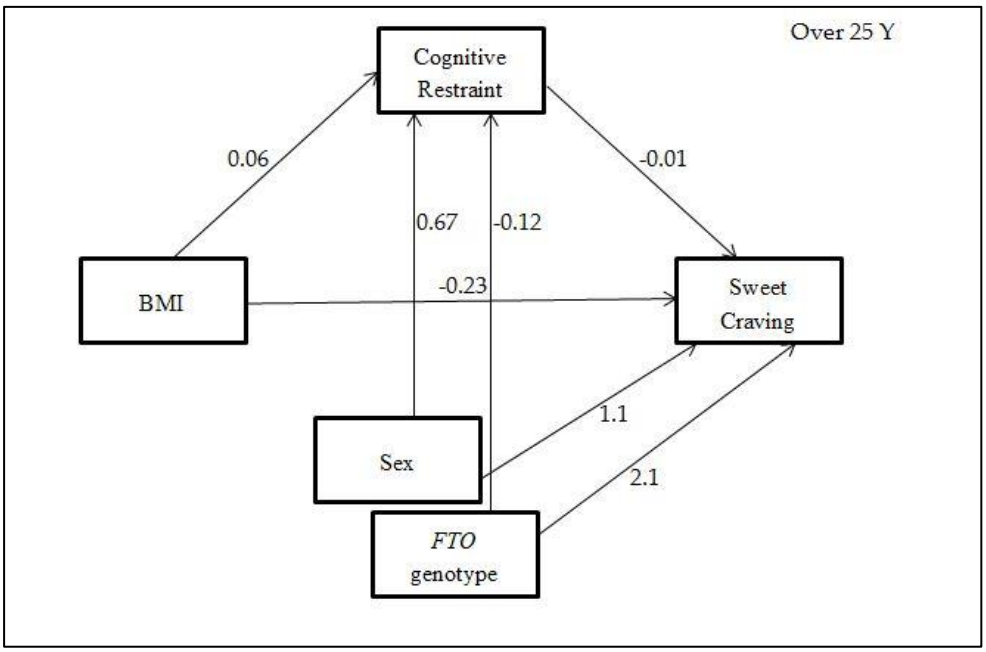


Figure 3-5 Mediation analysis model for the relationship between BMI, cognitive restraint and sweet food craving. Panel A in ≤ 25 years group and panel B in > 25 years group. The model indicates that cognitive restraint may mediate the relationship between BMI and cravings for sweet food in the ≤ 25 years group but not in the > 25 years group ($^{*}p < .05$; $^{**}p < .01$).

In table 3.9 the results show that when exploring the differences between students, staff and weight managers, there were significant positive relationships between BMI and cognitive restraint (r=.174**)and emotional eating (r=.185**) in the student group only and an inverse relationships between age and uncontrolled eating and emotional eating in SHU staff and weight managers groups. There were also positive relationships between BMI and fatty food cravings, and an inverse relationship between age and sweet craving in the weight managers only. And inverse relationships between age and fast food craving in SHU staff and weight managers.

Table 3-9 Relationships between age, BMI, eating behaviours and food cravings between different population

	Age			BMI		
	Students	SHU Staff	Weight managers	Students	SHU Staff	Weight managers
Cognitive restraint	.032	.005	.181	.174**	.127	-.110
Uncontrolled eating	.103	-.272**	-.290**	.022	.143	.206
Emotional eating	.038	-.239**	-.265**	.185**	.127	.215
Fat craving	-.05	.059	-.046	-.119	-.111	.312*
Sweet craving	-.094	-.116	-.433**	-.058	-.127	.046
Carbohydrates craving	.024	.002	-.249	-.095	.012	.304
Fast food craving	-.095	-.186**	-.508**	.046	-.045	.297

All significance tests were two-tailed (*p < .05; **p < .01).

In table 3.10 the results showed that there were inverse relationships between cognitive restraint and fat, sweet and fast food craving in the student group, In contrast, there was a positive relationship between cognitive restraint and fast food craving in the weight manager group. Amongst the students, there was a positive relationship between uncontrolled eating and carbohydrates only and in SHU staff between uncontrolled eating and sweet food craving, in contrast in the weight

manager group there was a relationship between uncontrolled eating and sweet, carbohydrates and fast food cravings. There were also inverse relationships between emotional eating and fat, carbohydrates and fast food craving in the students group; in contrast, there were positive relationships between emotional eating and sweet food craving in SHU staff and emotional eating and sweet, carbohydrates and fast food in weight manager group.

Table 3-10 Relationships between eating behaviours and food cravings between different population

	Cognitive restraint			Uncontrolled eating			Emotional eating		
	Students	SHU Staff	Weight managers	Students	SHU Staff	Weight managers	Students	SHU Staff	Weight managers
Fat craving	-.326**	-.105	.197	-.047	-.049	.228	-.314**	-.071	.231
Sweet craving	-.227**	-.003	.133	-.004	.144*	.412**	-.176**	.159*	667**
Carbohydrates craving	-.032	.102	.237	.133*	.138	.468**	-.045	.127	.310*
Fast food craving	-.262**	.044	.352*	-.059	.086	.484**	-.242**	.032	.341*

All significance tests were two-tailed (*p < .05; **p < .01).

3.5 Discussion

The main objective of this study was to explore the relationships between eating behaviours and food cravings, and examine the influence of sex, BMI, age and *FTO* genotype on these relationships. The TFEQ-R18, the FCI, and genotyped for the rs9939609 *FTO* polymorphism were used to study 475 individuals. The data was analysed for the group as well as split by sex, *FTO* genotype and age (< 25 years vs > 25 years old). The *FTO* MAF of the risk allele A was 0.42, compared to the published global MAF of 0.34, indicating that the risk allele was slightly more common in our population. Mediation analysis was used to investigate possible mechanisms underlying the association between some of the relationships observed. The main findings are as follows.

3.5.1 BMI, TFEQ -R18 subscales and FCI subscales

Results of this study showed that mean scores for BMI, the three subscales of the TFEQ-R18 and the four subscales of the FCI were consistent with values previously reported (Zavattari *et al.* 2011) (Table 3. 1).

- **Influence of sex on BMI, TFEQ -R18 subscales and FCI subscales**

There were no differences between mean scores for BMI, eating behaviours or food cravings when the group split by sex except for cravings for carbohydrate which were higher in women but not significant after Bonferroni correction. This agrees with previous studies which showed approximately equal mean scores for uncontrolled eating (Cappelleri *et al.* 2009, Lluch *et al.* 2000). However, Löffler *et al* (2015) found significant gender effects on the results in all three factors of TFEQ with generally

higher mean scores in females than in males (Löffler *et al*. 2015). In addition, other studies proposed that women showed more emotional eating than men (Van Strien *et al.* 2005). Other studies reported significant differences between genders with females scoring higher on the emotional eating and cognitive restraint scales (Lluch *et al.* 2000, Cappelleri *et al.* 2009, Karlsson *et al*. 2000). Higher restraint scores in women may be related to a tendency for dieting (de Lauzon *et al.* 2004). This difference may be due to the age of the groups studied; the average age of our group was 31 years, whereas the average age of the participants in these two studies was 50 and 48 years indicating that sex differences in eating behaviours may become more apparent with increasing age.

- **Influence of *FTO* genotype on BMI, TFEQ -R18 subscales and FCI subscales**

When the group was analysed by genotype (Table 3.2) the AA+AT group had a mean BMI of 26.52 kg/m² compared to the TT genotype group who had a mean BMI of 24.62 kg/m², this is consistent with the findings of previous studies which also found that carriers of the risk allele A had higher BMI scores compared to people with the TT genotype (Frayling *et al.* 2007, Zavattari *et al.* 2011).

No differences in TFEQ-R18 or FCI scores were found when the groups were split by genotype; this is in agreement with a recent study of children by Rivas *et al*., (2018), which also did not find differences in subscale scores for the TFEQ-R18 (Rivas *et al.* 2018). But contrasts with other findings which describe higher food cravings associated with the A allele in a group with average age of 50 years (Dang *et al.* 2018). These differences agree with the findings presented in table 3.6 which demonstrate an influence of *FTO* genotype on age-related eating behaviours. The difference due to the A allele in our population of 2 BMI units is very similar to the older cohort in the

Frayling *et al.,* study which had an average age of around 60 years (Frayling *et al.* 2007); however, our cohort is younger with an average age of 31 years. Frayling *et al.,* also included younger cohorts and the effect of the risk allele was less in this group with an effect of 1 BMI unit. In the 10 years since the Frayling *et al.,* study was published the obesogenic environment has increased so our data may indicate that a greater effect of the allele can be seen at a younger age. Various studies have claimed an effect of genotype on food cravings and eating behaviours (Cecil *et al.* 2008, Dang *et al.* 2018, Timpson *et al.* 2008), but our results do not show this. Most of these studies were in people who all were either overweight or had obesity, in contrast to the majority of our population.

3.5.2 Interaction of age with eating behaviours and food craving

Age had a significant effect on BMI, food cravings and eating behaviours (Table 3.3), with high BMI associated with age, whilst low cravings for fatty food, and uncontrolled eating and emotional eating were associated with age, in agreement with earlier studies (Hill *et al.*1991, Basdevant *et al*. 1993, Pelchat 1997). Consistent with the extant literature, food cravings declined across adulthood (Dang *et al.* 2018). This may reflect changes in eating patterns associated with stages of life; with younger people tending to consume less healthy food (Bull 1992, Munt *et al*.2017). It may also be due in part to age-related changes in taste sensitivity (Narukawa *et al.* 2018, Sergi *et al.* 2017).

3.5.3 Interactions between BMI, eating behaviours and food craving

The data also illustrated that high BMI was associated with low cravings for fatty foods but high cognitive restraint, confirming previous results by Johnson *et al* who

proposed that high cognitive restraint in normal weight individuals increases the risk of overeating tendencies when restraint is relaxed, thus leading to further increases in BMI (Johnson *et al.* 2012).

3.5.4 Interactions between eating behaviours and food craving

Highly significant relationships between eating behaviours and food cravings were found (Table 3.4); high cognitive restraint correlated with lower cravings for fatty foods, sweet foods and fast foods, high uncontrolled eating was associated with high cravings for carbohydrates, and high emotional eating was associated with lower cravings for fatty foods and fast foods. This is consistent with previous findings; decreased food cravings are associated with high fMRI-FCR of brain regions that regulate executive control over ingestion (Kahathuduwa *et al.* 2018) and with cognitive reappraisal strategies, in particular those focusing on the benefits of not eating unhealthy foods, this could potentially increase the ability of individuals with obesity to inhibit appetitive motivation and reduce unhealthy food intake (Yokum and Stice 2013).

- **Influence of sex on the interactions between age, BMI, eating behaviours and food craving**

When the group were analysed split by sex (Table 3.5) the relationships between age and low food cravings were stronger in women compared to men. However, the relationships between eating behaviours and food cravings were not affected by sex.

- **Influence of *FTO* genotype on the interactions between age, BMI, eating behaviours and food craving**

FTO genotype influenced some of the relationships between BMI, age, eating behaviours and food cravings; in particular the relationship between BMI and fatty food craving was stronger in the TT genotype group compared to the AA+AT group. An effect of the *FTO* genotype on the relationship between age and emotional eating has been seen, with age-related decline in this behavior only present in the AA+AT genotype group.

- **Influence of age on the interactions between age, BMI, eating behaviours and food craving**

When the group was split into a younger and older age group based on assumptions of life changes that may influence eating behaviours clear differences between the < 25 years group compared to the > 25 years group were observed. The inverse relationships between cognitive restraint and emotional eating with food cravings for fatty, sweet and fast foods were much stronger in the < 25 years group compared to the > 25 years group. In the case of the relationship between sweet food cravings and emotional eating there was a negative correlation in the < 25 years group, but in the > 25 years group there was a significant positive correlation. There was also a strong relationship between age and BMI in the > 25 years group but not in the < 25 years group.

When the group was split into student, staff and weight managers, we found that higher BMI was related to high cognitive restraint and emotional eating in the student group only, which is may be as explained before by younger people with increased BMI using restraint to try to lose weight, perhaps leading increased emotional eating as they become under stress due to their higher BMI, However, in people engaged in a weight loss intervention there were also positive relationships between BMI and fatty

food cravings, and this matches the literature where increased intake of high fat food is associated with increases in BMI.

Age was associated with low fast food craving, uncontrolled eating and emotional eating in SHU staff and weight manager groups, and with low sweet craving in the weight managers only. This may be because they are older than the student group and we show that age is associated with lower eating behaviours scores. In addition, high cognitive restraint was associated with low fat, sweet and fast food craving in the student group and with high fast food craving in the weight manager group. High uncontrolled eating was associated with high carbohydrates craving in the student group and SHU staff group, in weight managers it was associated with sweet, carbohydrates and fast food cravings. High emotional eating was associated with high fat, carbohydrates and fast food craving in the students group, high emotional eating was associated with high sweet food craving only in SHU staff and with high sweet, carbohydrates and fast food in the weight manager group

3.5.5 Regression analysis and mediation analysis

To better understand the role of age, eating behaviours and food craving, Regression analysis was used to examine the influence of TFEQ subscales, FCI and age on BMI, to investigate the relationships of all of these factors together and to determine which of these factors has the strongest effect on BMI (table 3.7). This shows that age and fast food craving have significant influence on BMI, after that emotional eating and sweet food craving and then fatty foods inversely related to BMI. Sweet foods craving, carbohydrates and fatty food craving are negative correlated with BMI while the others are positive.

Mediation analysis was used to investigate these relationships (Figures 3.4 and 3.5). The figures are a graphical summary of the data from the mediation analysis model see appendix 8.9, table 8.1 for an example of the SPSS PROCESS output. Figure 3.4 compares the ≤ 25 years group with the > 25 years group, and models the relationship between BMI and fat craving in these groups. This type of analysis can be used when there is a significant relationship between two variables, in this case BMI and fat craving as shown in table 3.7. If a relationship is mediated by a third variable (in this case cognitive restraint) this will be evident in the significant correlations shown between the third variable and the other variables.

The mediation analysis in figure 3.4 for the ≤ 25 years group shows a significant correlation between BMI and cognitive restraint (r=0.15), and between cognitive restraint and fat craving (r=-0.52), but the correlation between BMI and fat craving is no longer significant, demonstrating mediation by cognitive restraint. This analysis also allows for the investigation of the effect of other variables (in this case sex and *FTO* genotype). In the case of the > 25 years group, the mediating effect of cognitive restraint is not present (as the correlations between BMI and cognitive restraint, and cognitive restraint and fat craving are not significant). Also, in contrast with the ≤ 25 years group, the effect of sex on fat craving is much stronger, and in this group, this has the greatest effect in contrast to the effect of BMI.

Therefore, in the ≤ 25 years group for both cravings for fatty food and cravings for sweet food, cognitive restraint mediated almost all the relationships with BMI, demonstrating that it is very likely that the people in this group with higher BMI are using cognitive restraint to suppress food cravings.

This contrasted with the > 25 years group where this pattern was not seen. In the < 25 years group fat and sweet cravings were strongly influenced by sex, with a more pronounced inverse relationship between BMI and these cravings seen in women. When cognitive restraint was first investigated as an eating behavior the strong correlation observed between cognitive restraint and BMI led to the conclusion that cognitive restraint was a type of unhealthy eating behavior (Hays and Roberts 2008), and that people who restrained were more susceptible to binge eating, thereby leading to increased BMI.

Thus, cognitive restraint as an eating behavior was seen to drive a high BMI. However, many early studies were carried out in participants with overweight or obesity and in older demographic groups; in these groups cognitive restraint may indeed be driving a high BMI. In contrast the data presented here supports that in younger age groups BMI may drive cognitive restraint rather than the other way round, a suggestion which has also been made in other papers (de Lauzon-Guillain *et al.* 2006, Yokum and Stice 2013).

The association between cognitive restraint and BMI was observed in previous studies, but in the ≤ 25 years group this was particularly associated with low food cravings. Therefore, in people ≤ 25 years, who are perhaps more self-conscious about their weight, cognitive restraint is used to suppress food cravings, particularly in people with high BMI, hence the association between BMI and cognitive restraint. This may instil habitual eating behaviours which later in life increase the susceptibility to the cycles of restraint and binge-eating associated in some older populations with increased BMI (Stice *et al.* 1996). Evidence to support this theory is provided by Rocks *et al.* who studied undergraduate students and found that this group, with a similar age and background to the ≤ 25 years group, demonstrated high dissatisfaction with body

weight and high rates of disordered eating behaviours (Rocks *et al.* 2017). An additional possibility is that BMI also mediates the effect of age on eating behaviours and food cravings.

3.6 Limitations

This study has limitations; although many of the participants were drawn from the same geographical area there may be demographic differences between the ≤ 25 years group who were mostly undergraduate students, and the > 25 years group who were a mixture of staff, students and participants from Shape up, a weight-management course. In addition, the lifestyle and eating habits of the ≤25 years group in this study may not be fully representative of the general population in this age category. As some of the participants were friends and family of the students at the university, they may share similar tastes, food preferences and cultural background which may also have influenced the results due to sampling bias.

Detailed data on socio-economic status, education, marriage status or ethnicity was not collected in the current study so in future studies these potential confounders could be considered. The division into two age groups with a cut-off of 25 years was based on previous work that shows that life events such co-habiting, employment and having children are associated with changes in eating behaviour (Mata *et al.* 2018, Laroche *et al.* 2012, Au and Hollingsworth 2011); in the study group the age of 25 reflects a point after which these life events start to have an effect, in future studies data on these variables could allow for their inclusion in the analysis. The effect of *FTO* genotype were chosen for examination as this has been reported to be the most influential gene on BMI, in the future investigating a wider range of target genes would potentially reveal more information about the influence of genetics on the variables

studied. A limitation of the use of self-reported questionnaires is that participants may not always be honest when answering, and the degree to which this is an issue may vary with weight status. In future studies food frequency questionnaires and DEXA analysis could be incorporated into the study protocol.

3.7 Conclusions

In conclusion whilst the findings regarding the strong association between increasing BMI and age confirm previous reports, the mediation analysis shows that sex, *FTO* genotype and BMI have an influence on the relationships between eating behaviours and food cravings and that these variables interact with notable differences between young and older age groups. Examining these interactions along with further polymorphisms linked to obesity could help identify those at risk of increasing BMI.

4 Chapter 4: Motivation to exercise, eating behaviours and BMI, influence of age, sex and *FTO* genotype

4.1 Introduction

Motivation is central to many social psychological theories that aim to explain behaviour, including self-determination theory, one of the most influential theories of human motivation developed in the last three decades (Hagger and Chatzisarantis 2007).

Self-determination Theory is a macro-theory of human motivation that has a connection with the development and functioning of the personality within social contexts. The theory analyses the extent to which human behaviour is volitional or self-determined, in other words, the degree to which people achieve their activities at the highest level of reflection and are involved in the actions with a sense of choice (Deci and Ryan 1985).

According to self-determination theory (SDT) autonomous motivation refers to goal pursuit due to personal importance of the activity (i.e., identified regulation), alignment of the activity with one's core values (i.e., integrated regulation), and/or due to inherent enjoyment of the activity (i.e., intrinsic motivation). Controlled motivation, refers to goal pursuit that is driven by internally imposed pressures (e.g., avoiding guilt; introjected regulation) or externally imposed pressures (e.g., to obtain reward or avoid punishment; external regulation) (Ryan and Deci 2000).

The Behavioural Regulation in Exercise Questionnaire (BREQ) was created to measure self-determined motivation in physical exercise (Mullan *et al.* 1997). The original questionnaire was established to measure external, introjected, identified and intrinsic regulation which was then reviewed and finalised by Markland and Tobin and

validated as BREQ-2. The BREQ-2 questionnaire adds another factor to these four: amotivation (Markland and Tobin 2004).

Previous studies focused on the relationships between motivation to exercise and food intake. Researchers have proposed that an individual's motivation for exercise may be important in determining post-exercise food intake (Fenzl *et al*. 2014, Dimmock *et al.* 2015). Little is known about the potential relationship between motivation for exercise and eating behaviours and BMI. Studies that have examined eating style and physical activity motivation have found a positive relationship between an intrinsic motivation to engage in physical activity and a self-regulated style of eating (Mata *et al.* 2009, Teixeira 2006), indicating that similar patterns of regulation may influence both these types of behaviour.

4.2 Objectives of the study

The current study investigates the interactions between motivation to exercise, eating behaviours and BMI. As previously reported in chapter 3, there are interactions between eating behaviours and food cravings and BMI, and it is important to consider other variables that are known to also influence these measures including genetics, age, sex and BMI. In this study we propose that an individual's motivation to exercise might interact with their eating behaviours, thereby influencing BMI. Thus, objectives of this study were:

1) To examine the relationships between motivation to exercise, eating behaviours and BMI.

2) To identify the influence of age, sex, BMI and *FTO* genotype on these relationships.

3) To use mediation analysis to explore the role of these mediators in these interactions.

4.3 Experimental Section

4.3.1 Study Participants

A total of 320 participants (as the BREQ2 data were collected only from 320 participants) were included in this study from Sheffield Hallam University students and staff , as well as 183 adults with overweight or obesity studied prior to participating in weight loss intervention programmes at Shape Up, RIO and Concorde (see table 2.1 in chapter 2). The study group from the university was a subgroup of those studied in Chapter 3 as not all of the participants in Chapter 3 were asked to complete the questionnaires for this part of the study.

Ethical clearance for the study was granted by the local NHS and the Ethics Committee of the Biomolecular Research Centre, Sheffield Hallam University, all participants provided written informed consent before taking part in the study.

4.3.2 Anthropometry

Body weight and height for the participants was measured by the method described in chapter 2. BMI was calculated as body mass in kilograms divided by the square of height in meters.

4.3.3 Eating Behaviours

Eating behaviours were measured using the TFEQ-R18 (Karlsson *et al.* 2000) as previously described in chapter 2.

4.3.4 Exercise motivation.

Participants self-rated their motivation for exercise using the Behavioural Regulation in Exercise Questionnaire-2 (BREQ-2; (Markland and Tobin 2004). As previously described in chapter 2.

4.3.5 Genotyping

Was undertaken as previously described in chapter 2.

4.3.6 Statistical analysis

The Statistical Package for the Social Sciences (SPSS software version 24, IBM) was used for the statistical analysis with significance accepted if $p < 0.05$. Distribution of data was checked using the Kolmogorov-Smirnov Test and descriptive statistics were calculated. Pearson correlation was undertaken to explore association between variables including age, BMI, eating behaviours and motivation to exercise. T-tests were performed to assess sex and genotype differences in age, BMI, eating behaviours and motivation to exercise. in order to examine effect of age, sex, *FTO* genotype and BMI, the population split by age in ≤ 25 years vs > 25 years, by sex to male and female, by genotype into AA+AT vs TT genotype and by their BMI into obese BMI ≥30kg/m² vs non-obese <30kg/m². After Bonferroni correction p value need to be 0.005 to consider as significant.

Multiple regression analysis was performed to assess the multivariate relationships between the independent variables and BMI. In this regression model, the selected predictors (age, TFEQ-R18 subscales and BREQ2 subscales) were forced into the model and the semi-partial correlation coefficient was calculated to quantify the unique

contribution of each predictor to the variance in the dependent measure (Cohen *et al.* 2014).

To test our primary hypothesis, a mediation analysis with bootstrapping was undertaken (Preacher and Hayes 2008). For the mediation model (Figures 4.10 and 4.11), exercise motivation is the independent variable, eating behaviours are the mediator variable, and BMI is the dependent variable. Age, sex and *FTO* genotype are the covariates. For outcome data, effect sizes were calculated using Cohens d.

4.4 Results

4.4.1 Descriptive statistics

The descriptive statistics for the primary variables for the overall sample, by sex, genotype and by BMI are shown in tables 4.1, 4.2 and 4.3. The subjects had a mean ± SD age of 36.6±16.8 years, and BMI of 29.7±8.9 kg/m^2. In this sample there were significant differences in mean BMI between men (28.5±7.9) kg/m^2 and women (30.8±9.4) kg/m^2. Also, between carriers of the *FTO* TT genotype (28.1±8.6) kg/m^2, compared to those with AT+AA genotype (30.5±8.9) kg/m^2. TFEQ-R18 scores and BREQ-2 results show no significant difference between the genotypes. However, there were significant differences between males and females in cognitive restraint and identified regulation, with males having a higher mean score than women. However, this is not significant after Bonferroni correction. The results also shows that people with obesity in table 4.3 were older than non-obese people and had higher mean score for emotional eating, had higher score of amotivation and external regulation and lower score of identifying regulation and intrinsic regulation than non-obese people, these significant relationships were still present when age was controlled for.

Table 4-1 Descriptive statistics for primary variables for total sample and, by sex.

	Overall		Female		Male				
	N=503		N=285		N=218				
	M	SD	M	SD	M	SD	*t*	*p*	*d*
Age	36.6	16.8	36.9	16.6	35.6	17.1	.88	.376	.077
BMI*	29.7	8.9	30.8	9.4	28.5	7.9	2.9	.004	.264
Cognitive restraint	12.9	3.3	12.7	3.5	13.3	3.0	-2.05	.041	.184
Uncontrolled eating	20.3	5.6	20.2	5.7	20.5	5.5	-.67	.498	.053
Emotional eating	7.1	3.2	7.4	3.3	6.9	3.1	1.69	.091	.156
Amotivation	1.5	2.6	1.4	2.5	1.7	2.8	-1.0	.304	.113
External regulation	2.6	3.1	2.6	3.0	2.8	3.1	-.48	.630	.065
Introjected regulation	4.8	3.5	4.8	3.6	4.9	3.5	-.24	.804	.028
Identified regulation	9.9	4.2	9.6	4.3	10.4	4.0	-1.9	.047	.192
Intrinsic regulation	9.6	4.7	9.4	4.8	10.1	4.6	-1.7	.073	.149

Note. All significance tests were two-tailed. M= mean score; SD =standard deviation; t =t-test; *p*= p-value; d=Cohen's d;* significant p≤0.005 (after Bonferroni correction).

Table 4-2 Descriptive statistics for primary variables, by genotype.

	TT		AT+AA				
	N=155 30%		N=348 69%				
	M	SD	M	SD	t	p	d
Age	32.7	15.1	37.0	16.9	-2.67	.008	0.27
BMI	28.1	8.6	30.5	8.9	-2.64	.008	0.27
Cognitive restraint	12.8	3.3	13.1	3.3	-.640	.522	0.09
Uncontrolled eating	19.7	5.8	20.6	5.4	-1.58	.113	0.16
Emotional eating	7.15	3.1	7.2	3.2	-.208	.836	0.02
Amotivation	1.4	2.7	1.5	2.6	-.513	.608	0.03
External regulation	2.5	2.9	2.7	3.1	-1.04	.300	0.06
Introjected regulation	4.9	3.6	4.8	3.5	-.076	.939	0.03
Identified regulation	9.5	4.3	10.1	4.2	-1.46	.145	0.14
Intrinsic regulation	9.2	4.6	9.8	4.7	-1.26	.209	0.13

Note. All significance tests were two-tailed. M= mean score; SD =standard deviation; t=t-test; p=p-value; d=Cohen's d.

Table 4-3 Descriptive statistics for primary variables, by BMI.

Note. (Non-obese BMI < 30Kg/m², people with obesity BMI ≥ 30kg/m². All significance tests were two-tailed. M= mean score; SD =standard deviation; t =t-test; p= p-value; d=Cohen's d ;* significant p≤0.005 (after Bonferroni correction).

	Non-obese N=290		People with with obesity N=213				
	M	SD	M	SD	*t*	*p*	*d*
Age*	28.2	13.3	47.3	14.8	-14.54	.000	1.357
BMI*	23.5	3.1	38.7	6.4	-31.38	.000	3.022
Cognitive restraint	13.1	3.5	12.9	2.9	.140	.889	0.062
Uncontrolled eating	20.6	5.7	19.8	5.4	1.54	.125	0.144
Emotional eating*	6.8	3.2	7.7	3.3	-2.97	.003	0.276
Amotivation*	1.2	2.4	1.9	2.8	-3.25	.001	0.268
External regulation*	2.2	2.6	3.4	3.5	-4.165	.000	0.389
Introjected regulation	4.9	3.4	4.8	3.7	.283	.777	0.028
Identified regulation*	10.9	3.8	8.7	4.4	5.682	.000	0.535
Intrinsic regulation*	10.8	4.2	8.1	5.1	6.169	.000	0.577

4.4.2 Relationships between age, BMI, eating behaviours and motivation to exercise

Correlations between age, BMI, eating behaviours and motivation to exercise were calculated and categorised for the overall population in table 4.4, by sex (male and female) in table 4.5, by genotype (TT genotype and AT+AA genotype) in table 4.6, and by age (≤ 25 years and >25 years) in table 4.7.

Table 4.4 shows that age has a significant inverse relationship with introjected regulation (r=-0.160**), identified regulation (r=-0.138**) and intrinsic regulation (-0.189**). BMI has a significant positive relationship with amotivation (r=0.175**), and external regulation (r=0.226**) and significant inverse relationships with identified regulation (r=-0.229**) and intrinsic regulation (r=-0.267**). Uncontrolled eating has significant positive relationships with introjected regulation (r=0.135**), identified regulation (r=0.152**) and intrinsic regulation (r=0.119**) Emotional eating has significant positive relationships with external regulation (r=0.144**) and introjected regulation (r=0.106*).

Table 4-4 Relationships between age, BMI, eating behaviours and motivation to exercise for the overall sample

	Amotivation	External regulation	Introjected regulation	Identified regulation	Intrinsic motivation
Age	.079	.013	-.160**	-.138**	-.189**
BMI	.175**	.226**	.008	-.229**	-.267**
Cognitive restraint	-.028	-.009	.085	.053	.048
Uncontrolled eating	-.029	.044	.135**	.152**	.119**
Emotional eating	-.001	.144**	.106*	-.001	-.026

Note. Correlations of primary variables for overall population. All significance tests were two-tailed (*p < .05; **p < .01).

In table 4.5 the results show the relationships between age, BMI, eating behaviours and motivation to exercise. In women there is a significant positive relationship between age and amotivation, (r=0.120*), in contrast with men where no such relationship is seen. BMI has significant positive relationship with amotivation (r=0.220**) in women, in contrast with men where no such relationship is seen. For cognitive restraint, in women there is a significant positive relationship between cognitive restraint and introjected regulation (r=0.149*). In men, the relationship is not significant.

Considering uncontrolled eating with exercise motivation, there is a significant positive relationship between uncontrolled eating and introjected regulation (r=0.233**), identified regulation (r=0.200**) and intrinsic regulation (r=0.123*) in women. In men, the relationships are not significant. For emotional eating with motivation to exercise,

there is a significant positive relationship between emotional eating and external regulation (r=0.243**) and introjected regulation (r=0.206**) in women, the relationships are not significant in men.

Table 4-5 Relationships between primary variables by sex

	Amotivation		External regulation		Introjected regulation		Identified regulation		Intrinsic regulation	
	F	M	F	M	F	M	F	M	F	M
Age	.120*	.035	-.059	.103	-.199**	-.109	-.151*	-.115	-.167**	-.214**
BMI	.220**	.129	.192**	.291**	-.063	.127	-.266**	-.143*	-.299**	-.195**
Cognitive restraint	-.020	-.051	.027	-.055	.149*	-.017	.083	-.019	.073	-.010
Uncontrolled eating	-.014	-.057	.126*	-.080	.233**	-.007	.200**	.090	.123*	.125
Emotional eating	.035	-.047	.243**	.005	.206**	-.040	.053	-.053	-.020	-.005

Note. M=male, F=female. All significance tests were two-tailed (*p < .05; **p < .01).

In table 4.6 the results show that age has positive relationship with amotivation (r=0.240**) and an inverse relationship with introjected regulation (r=-0.321**), identified regulation (r=-0.321**) among the TT genotype group only. With uncontrolled eating there are significant positive relationships between uncontrolled eating and introjected regulation (r=0.212*) identified regulation (r=0.305**), and intrinsic regulation (r=0.290*) in the TT genotype group. In contrast with the AA genotype group where no such relationship exists. Considering emotional eating, there is a significant positive relationship with external regulation (r=0.237**) in the TT genotype group which contrasts with men where no such relationship is seen.

Table 4-6 Relationships between primary variables by genotype.

	Amotivation		External regulation		Introjected regulation		Identified regulation		Intrinsic regulation	
	TT	AA+AT	TT	AA+AT	TT	AA+AT	TT	AA+AT	TT	AA+AT
Age	.240**	.028	-.084	.048	-.321**	-.099	-.321**	-.092	-.325**	-.187**
BMI	.239**	.150**	.188*	.234**	-.139	.061	-.393**	-.176**	-.399**	-.237**
Cognitive restraint	-.152	.004	-.097	.014	.068	.085	.100	.026	.140	.004
Uncontrolled eating	-.128	-.001	-.012	.047	.212*	.080	.305**	.066	.290**	.046
Emotional eating	-.034	.012	.237**	.098	.120	.082	.037	-.026	.089	-.072

Note. TT= TT genotype group, AA+AT= AA+AT genotype group. All significance tests were two-tailed ($^{*}p < .05$; $^{**}p < .01$).

In table 4.7 the results show that there are significant inverse relationships between age and introjected regulation (r=-0.293**), identified regulation (r=-0.167**) and in the > 25 years. In contrast with ≤ 25 Y where no such relationship is seen. For BMI with motivation to exercise, there are significant positive relationships between BMI and amotivation (r=0.240**), and significant inverse relationships between BMI and identified regulation (r=-0.352**) and intrinsic regulation (r=-0.330**) in the group > 25 years. In the ≤ 25 years group, these relationships are not significant.

Considering uncontrolled eating with motivation to exercise, there is a significant positive relationship between uncontrolled eating and identified regulation (r=0.242**) and intrinsic regulation (r=0.191**) in the ≤ 25 years group, in contrast in the above 25 years group the relationship is significant with introjected regulation (r=0.151*). For emotional eating with motivation to exercise, there are significant positive relationships between emotional eating and external regulation (r=0.192**) and introjected regulation (r=0.175**) in the > 25 years group, the relationship is not significant in the ≤ 25 years group. Regarding cognitive restraint, there were no relationships with motivation to exercise.

Table 4-7 Relationships between primary variables by age.

	Amotivation		External regulation		Introjected regulation		Identified regulation		Intrinsic regulation	
	≤25 Y	>25Y	≤25 Y	>25Y	≤25 Y	>25Y	≤25 Y	>25Y	≤25 Y	>25 Y
Age	-.102	.039	-.051	-.033	-.017	-.293**	.061	-.167**	.042	-.121
BMI	-.005	.240**	.207**	.303**	.130	-.024	-.008	-.352**	.00	-.330**
Cognitive restraint	-.034	-.005	-.037	.022	.015	.133*	.034	.037	.095	-.025
Uncontrolled eating	-.041	.012	-.022	.048	.065	.151*	.242**	.056	.191**	.036
Emotional eating	-.035	.028	.034	.192**	-.036	.175**	.004	-.032	.059	-.088

Note. ≤25 Y= 25 Years and under, >25 = Over 25 Years. All significance tests were two-tailed (*p < .05; **p < .01).

Table 4.8 shows there are significant inverse relationships between age and external regulation (r=-0.151**) and introjected regulation (r=-0.172**) in the non-obese group. These relationships are not significant in people with obesity. For BMI with motivation to exercise, there are significant positive relationships between BMI and external regulation (r=0.198**) in people with obesity but not in non-obese people.

With regards to uncontrolled eating with motivation to exercise, there is a significant positive relationship between uncontrolled eating and identified regulation (r=0.165**) in the non-obese group only. Considering emotional eating with motivation to exercise, there are significant positive relationships between emotional eating and external regulation (r=0.212**) and introjected regulation (r=0.173**) in the people with obesity, in contrast with the non-obese group where no such relationship is seen.

Table 4-8 Relationships between primary variables by BMI

	Amotivation		External regulation		Introjected regulation		Identified regulation		Intrinsic regulation	
	non obese	obese	non obese	obese	non obese	obese	non obese	obese	non obese	obese
Age	-.035	.028	-.151*	-.099	-.172**	-.192**	.091	-.066	.034	-.098
BMI	.023	.139	-.039	.198**	.067	.016	.115	-.112	.057	-.133
Cognitive restraint	-.037	-.022	-.032	.010	.075	.097	.019	.092	.035	.062
Uncontrolled eating	-.015	-.030	.016	.117	.119*	.165*	.165**	.114	.093	.134
Emotional eating	-.040	-.024	.020	.212**	.055	.173*	.010	.068	.008	.027

Note. (Non-obese BMI <30Kg/m² and obese BMI ≥30Kg/m²). All significance tests were two-tailed (*p < .05; **p < .01).

In table 4.9 descriptive statistics for the primary variables by sex and genotype. The males with AA+AT genotype have a higher BMI of (29.3±8.3) kg/m^2 than males with TT genotype (25.8±5.7) kg/m^2. There was significant differences between females with different genotype group in identifying regulation. Females with the AA+AT genotype had higher identified regulation (10.1±4.2 vs 8.5±4.2) than those with TT genotype group.

Table 4-9 Descriptive statistics for females and males split by genotype.

	Female					Male				
	N= 285					N= 218				
	TT N=89 31.2%	AA+AT N=196 68.7%				TT N=68 31.1%	AA+AT N= 150 68.8%			
	M±SD	M±SD	*t*	*p*	*d*	M±SD	M±SD	*t*	*p*	*d*
Age	33.6±15.6	38.0±16.8	-2.02	.04	0.27	31.4±14.4	35.7±17.1	-1.79	.07	0.27
BMI	29.7±9.9	31.3±9.3	-1.28	.2	0.166	25.8±5.7	29.3±8.3	-3.46	.00	0.49
Cognitive restraint	12.8±3.3	12.8±3.5	-.073	.94	0	12.9±3.3	13.4±2.9	-.117	.90	0.16
uncontrolled eating	19.2±5.4	20.6±5.5	-1.86	.06	0.256	20.5±6.4	20.6±5.3	.769	.44	0.017
Emotional eating	7.1±3.1	7.5±3.3	-.84	.39	0.124	7.2±3.4	6.8±3.1	-1.90	.05	0.122
A motivation	1.7±2.7	1.3±2.4	1.04	.29	0.156	1.1±2.5	1.9±2.8	-1.909	.05	0.3
External regulation	2.6±3.0	2.7±3.2	-.23	.82	0.032	2.3±2.7	2.9±3.2	-1.223	.22	0.202
Introjected regulation	4.7±3.6	4.9±3.6	-.32	.75	0.055	5.0±3.6	4.9±3.5	.311	.75	0.028
Identified regulation*	8.5±4.2	10.1±4.2	-2.93	.004	0.38	10.9±3.9	10.2±4.1	1.266	.20	0.17
Intrinsic regulation	8.5±4.5	9.7±4.9	-1.99	.048	0.255	10.3±4.7	10.0±4.5	.403	.68	0.065

Note. All significance tests were two-tailed. M= mean score; SD =standard deviation; t =t-test; p= p-value; d=Cohen's d ;* significant p≤0.005 (after Bonferroni correction).

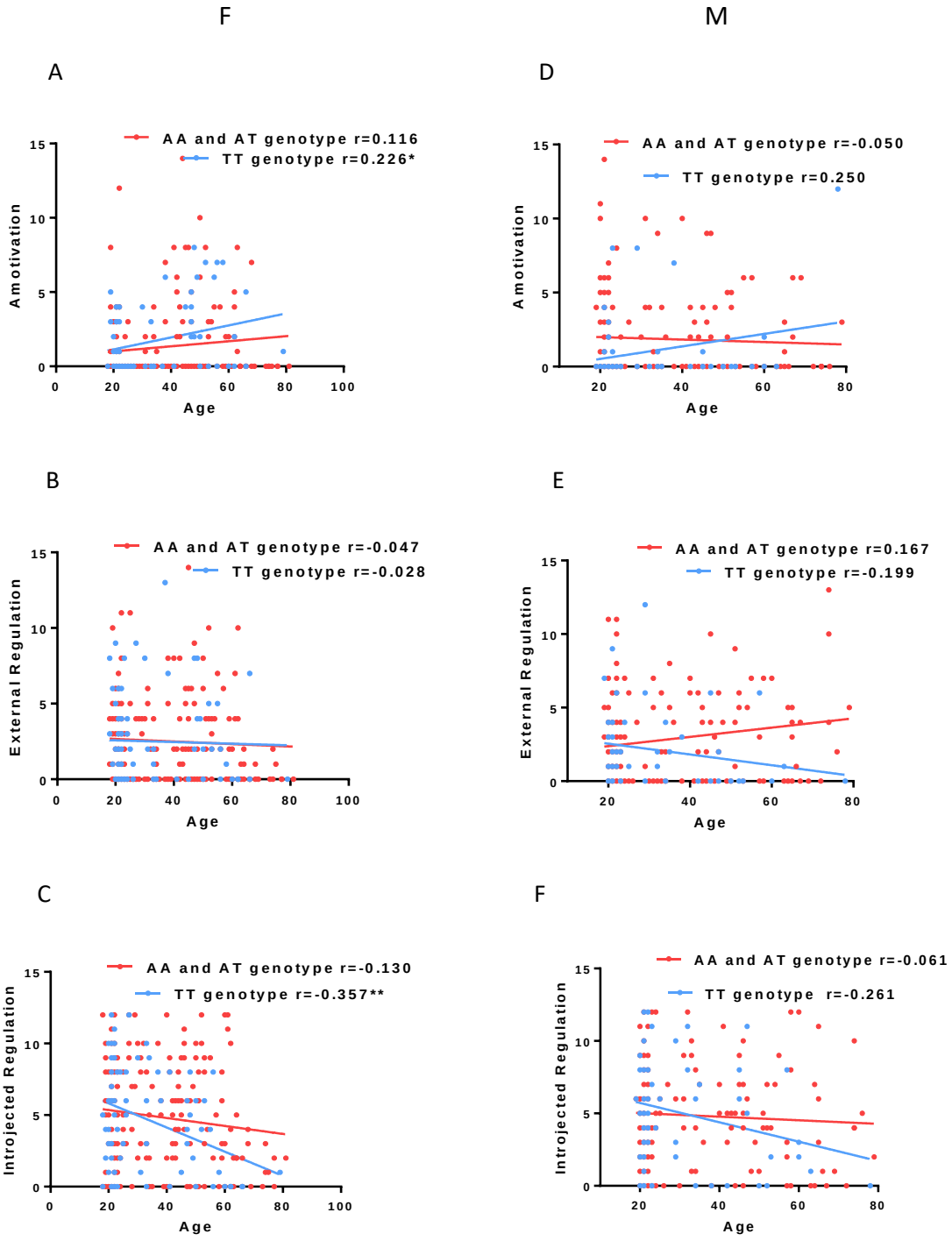


Figure 4-1 The relationships between age and amotivation, external regulation and introjected regulation. Panels A, B and C are for females and panels D, E and F are males. There were significant positive relationships between age and amotivation in the TT genotype group in females. and a significant inverse relationship between age and introjected regulation in the TT genotype group also in females.

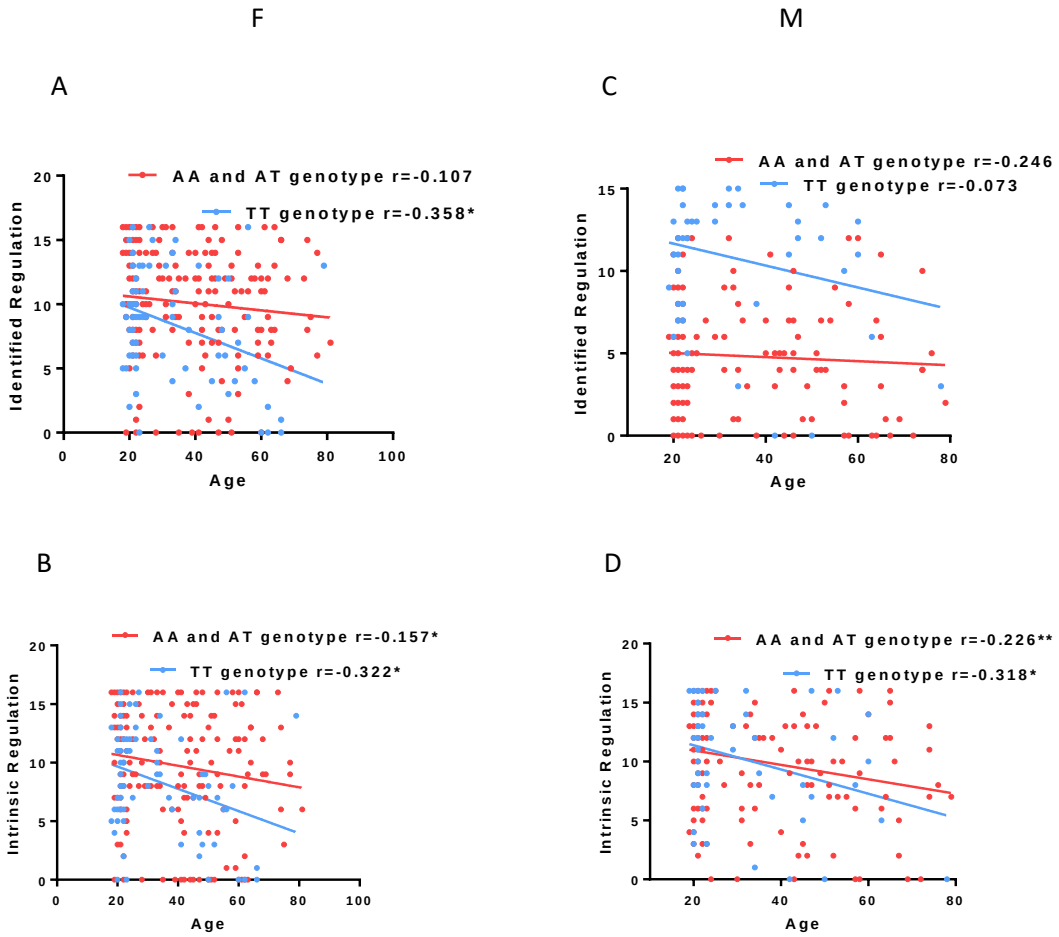


Figure 4-2 The relationships between age and identified regulation and intrinsic regulation. Panels A, B and for females and panels C and D are males. There was a significant inverse relationship between age and identified regulation in the TT genotype group in females and significant inverse relationships between age and intrinsic regulation in both genotype groups in both sexes.

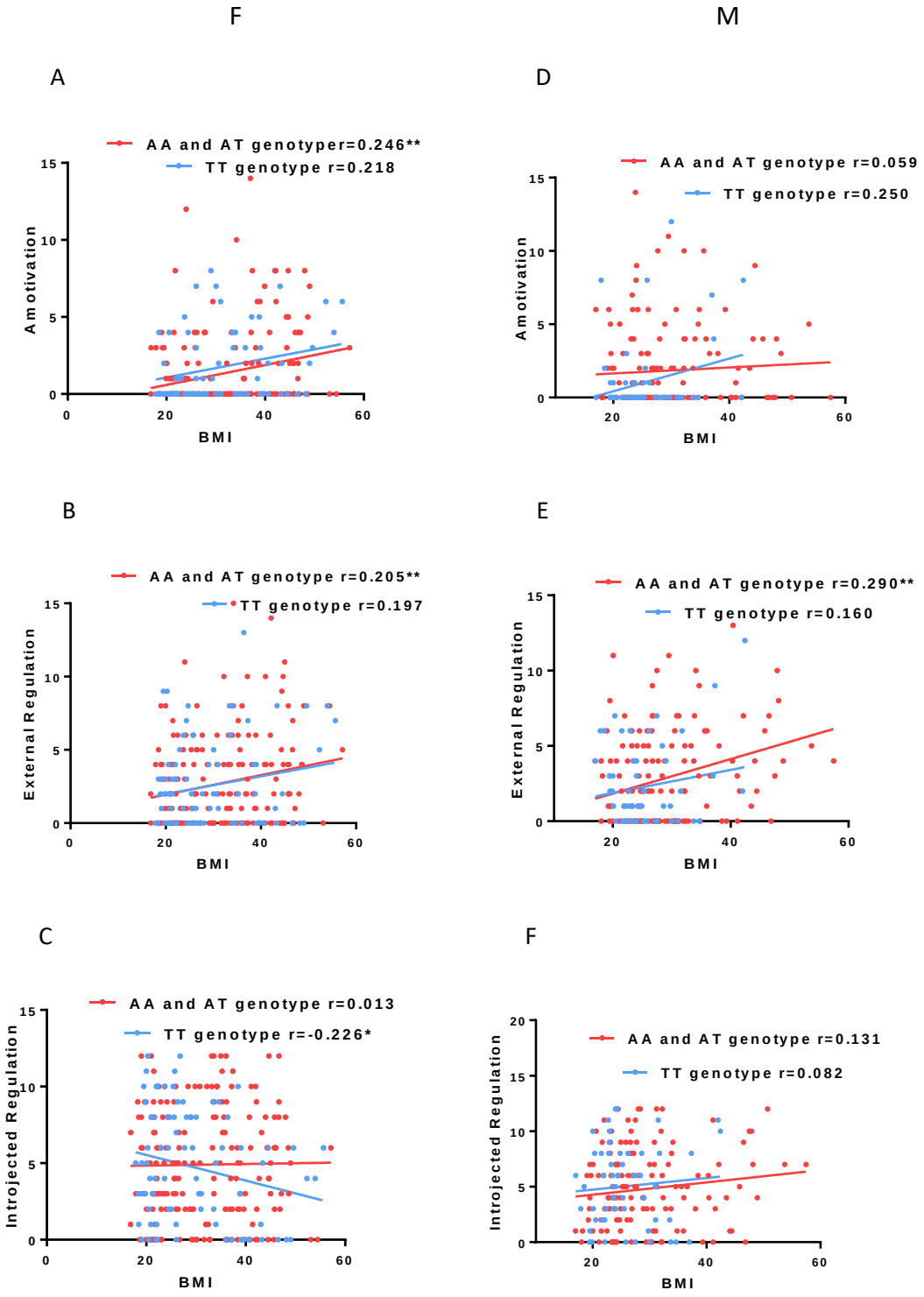


Figure 4-3 The relationships between BMI and amotivation, external regulation and introjected regulation. Panels A, B and C are for females and panels D, E and F are males. There was a significant positive relationship between amotivation and BMI in the AA+AT genotype group in females only and positive relationships between BMI and external regulation in the AA+AT group in both sexes. There was also an inverse relationship between BMI and introjected regulation in the TT genotype group in females.

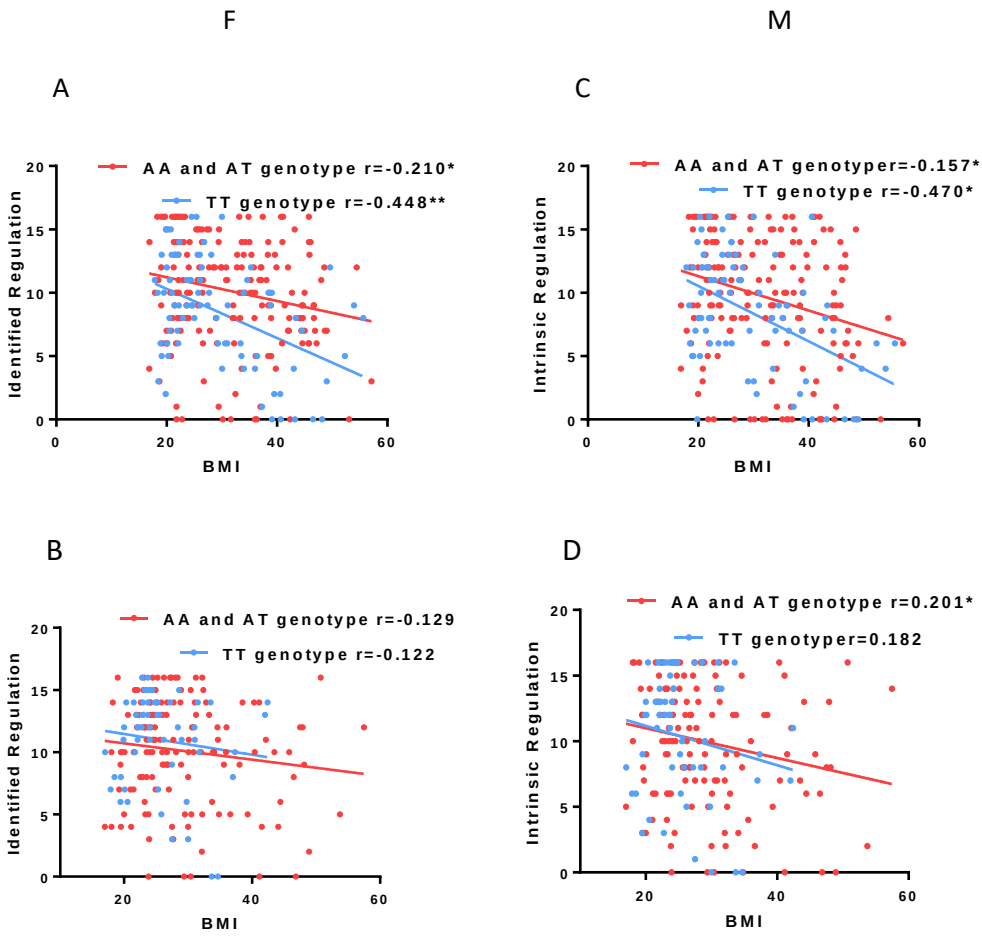


Figure 4-4 The relationships between BMI and identified regulation and intrinsic regulation. Panels A, B and for females and panels C and D are males. There were inverse relationships between identified regulation and BMI in both genotype groups in both sexes and an inverse relationship between intrinsic regulation and BMI in the AA+AT genotype group in males only.

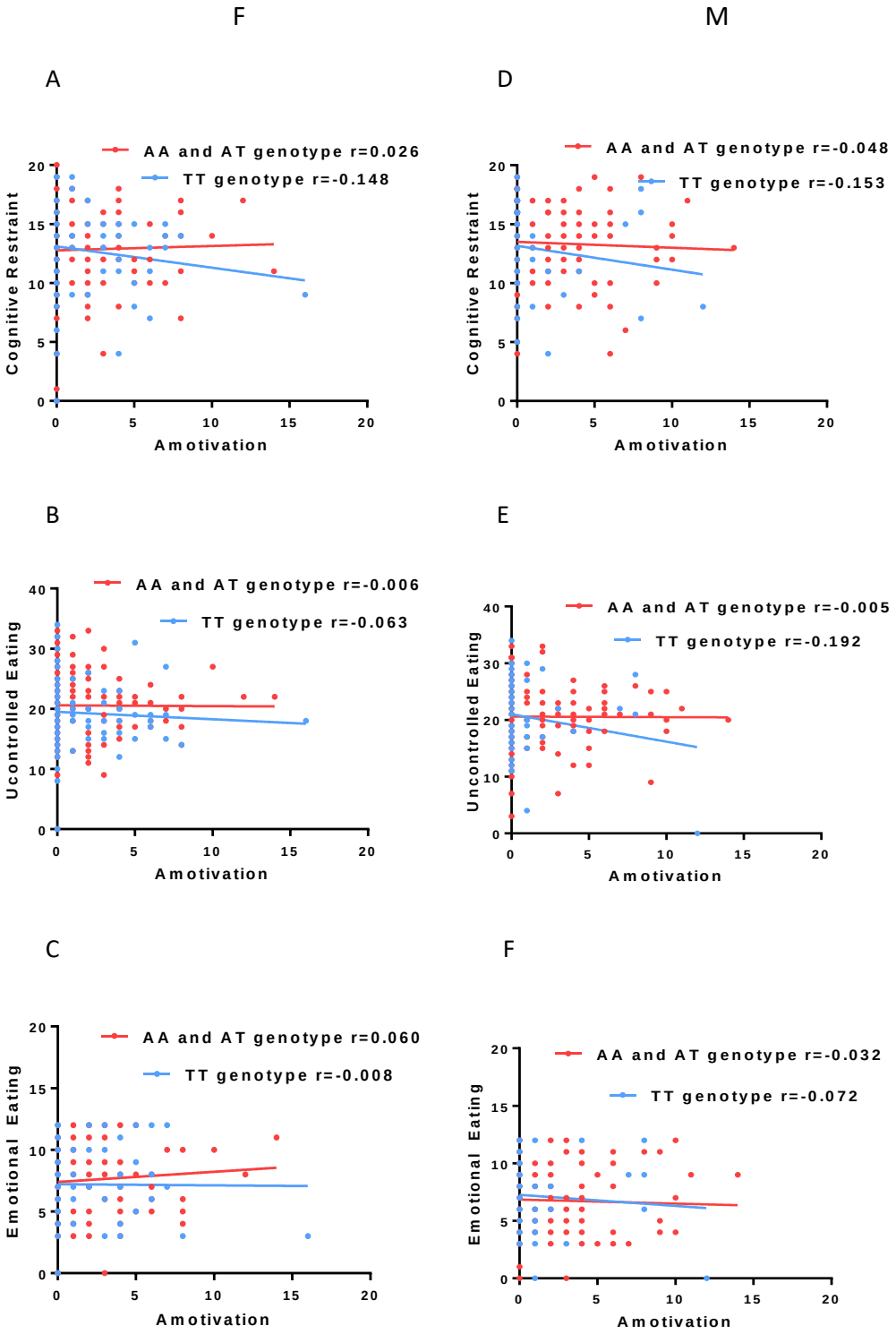


Figure 4-5 The relationships between amotivation and cognitive restraint, uncontrolled eating and emotional eating. Panels A, B and C for females and panels D, E and F are males. There were no significant relationships between amotivation and eating behaviours in both genotype groups in both sexes.

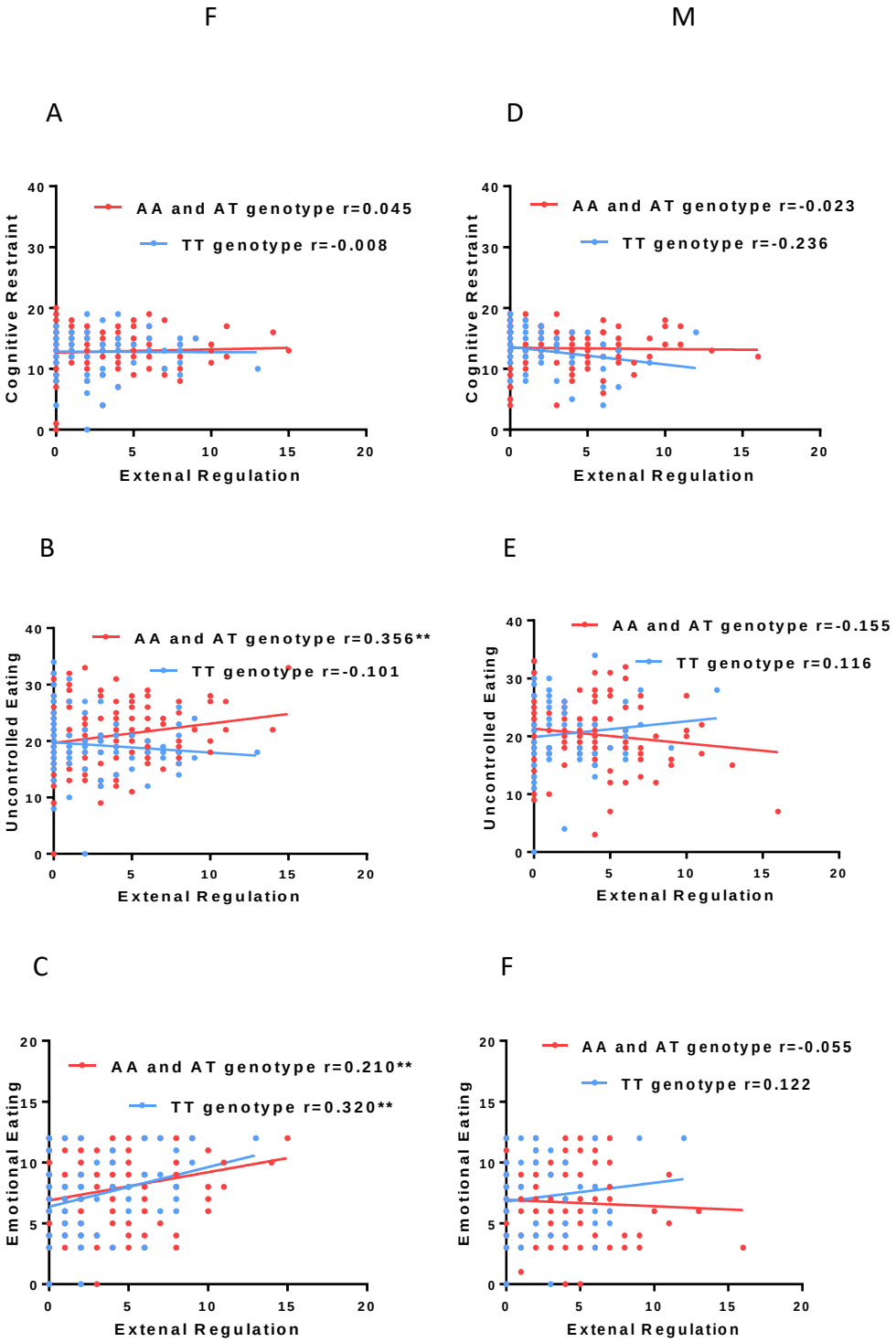


Figure 4-6 The relationships between external regulation and cognitive restraint, uncontrolled eating and emotional eating. Panels A, B and C for females and panels D, E and F are for males. There was a significant positive relationship between external regulation and uncontrolled eating in the AA+AT genotype group and positive relationships between emotional eating and external regulation in both genotype groups in females only.

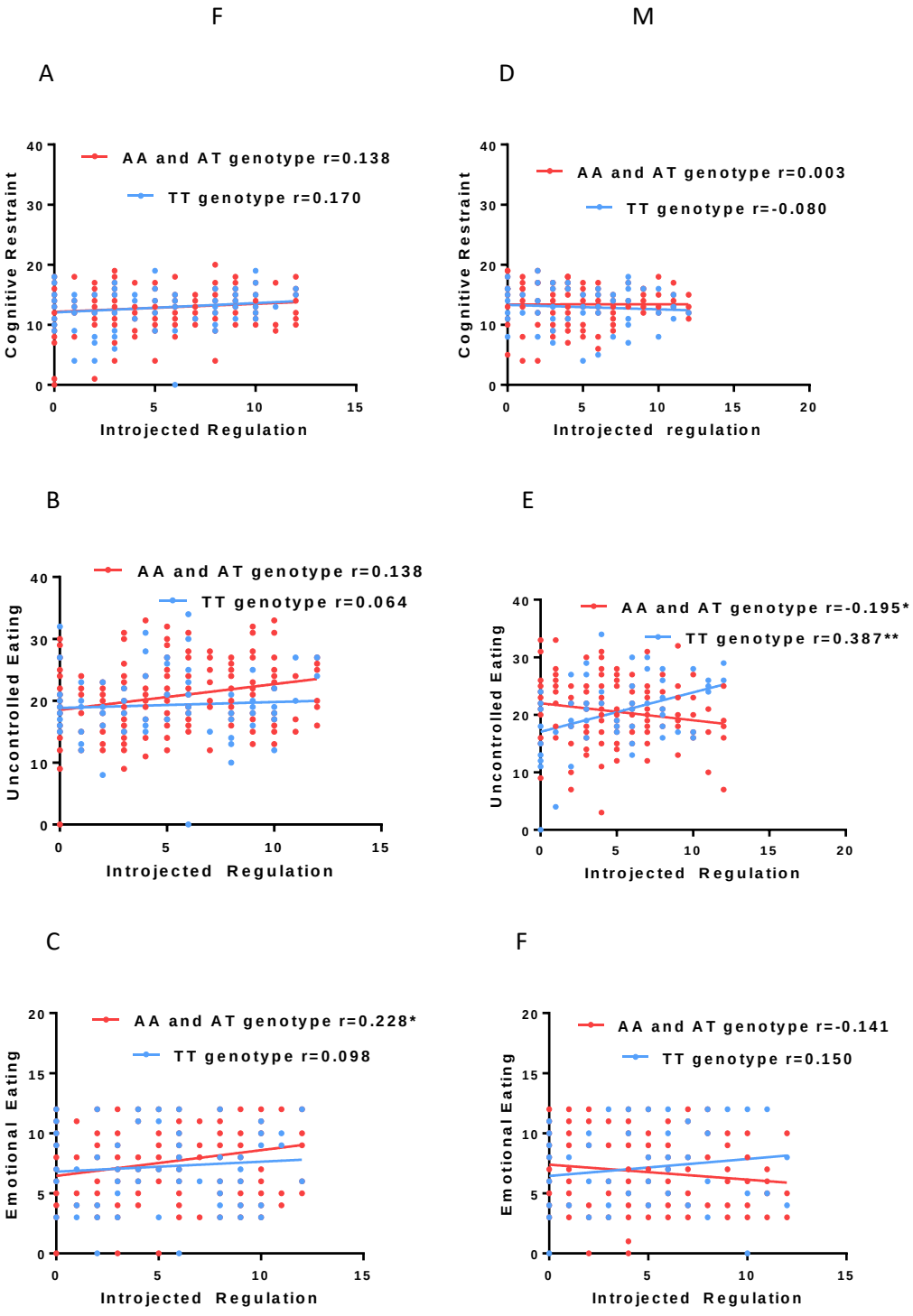


Figure 4-7 The relationships between introjected regulation and cognitive restraint, uncontrolled eating and emotional eating. Panels A, B and C for females and panels D, E and F are males. There was a significant inverse relationship between uncontrolled eating and introjected regulation in the AA+AT genotype group and a significant positive relationship in the TT genotype group, there was also a significant positive

relationship between emotional eating and introjected regulation in the AA+AT genotype group.

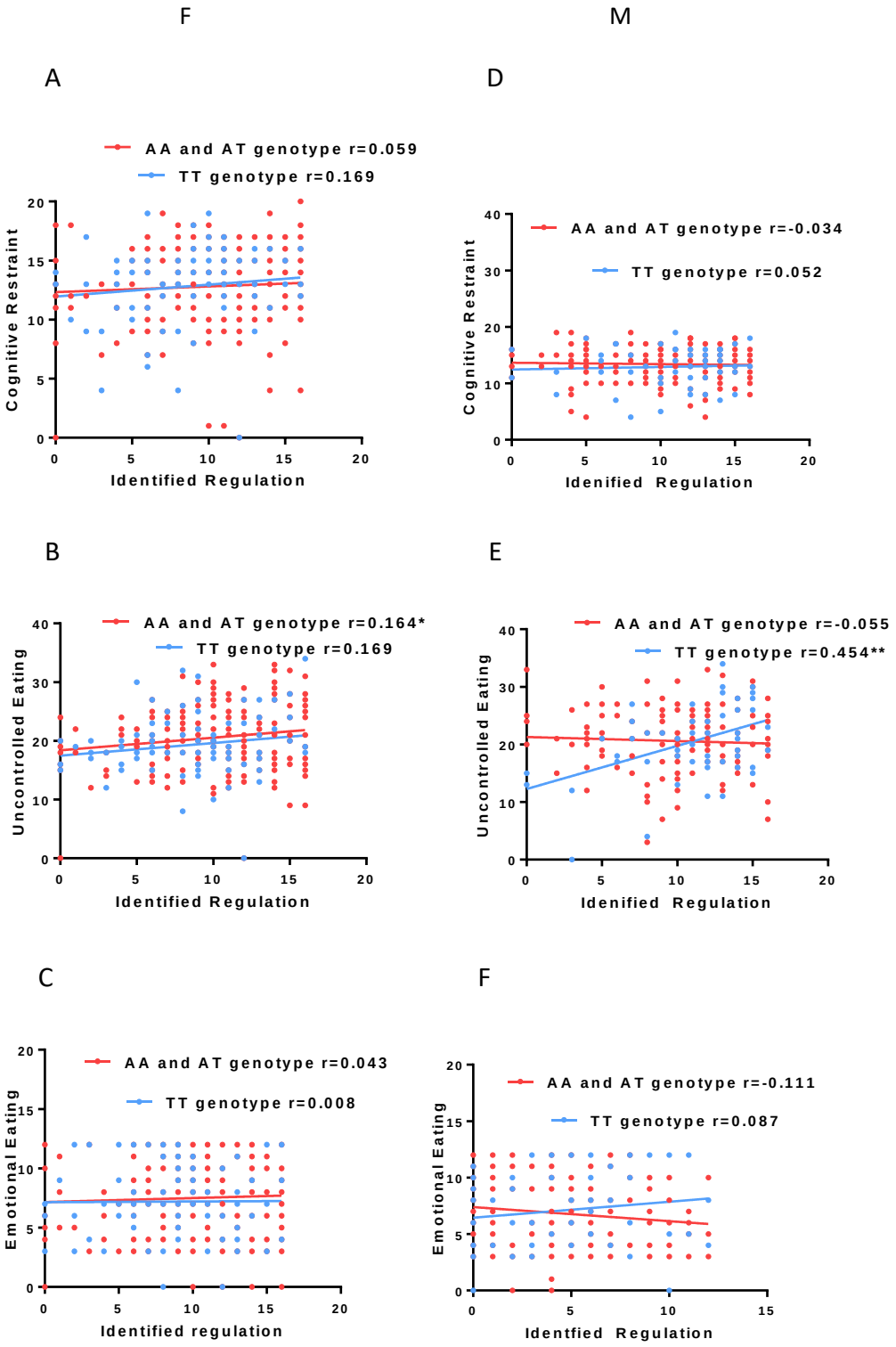


Figure 4-8 The relationships between identified regulation and cognitive restraint, uncontrolled eating and emotional eating. Panels A, B and C for females and panels D, E and F are males. There were significant positive relationships between uncontrolled eating and identified regulation in the TT genotype group in both sexes.

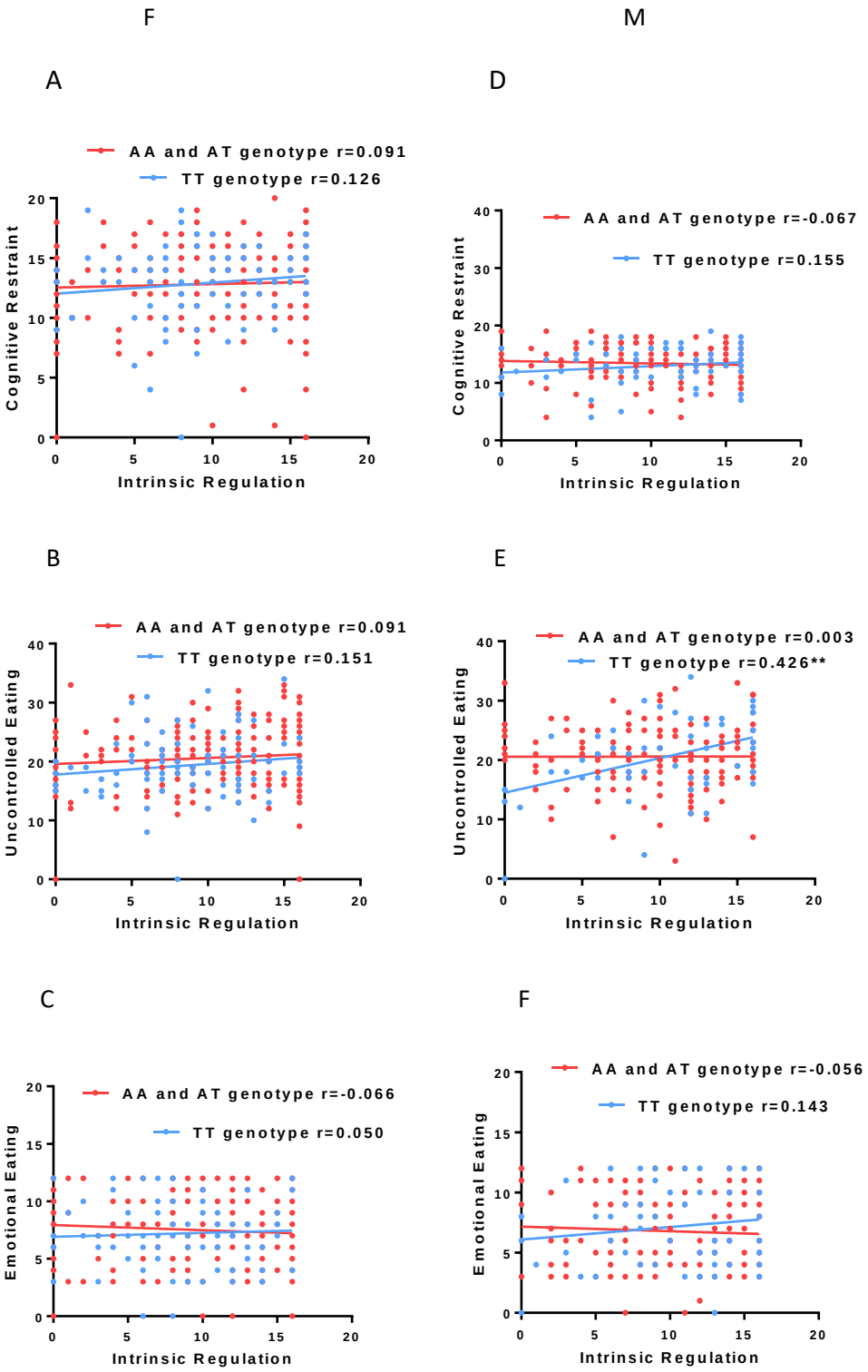


Figure 4-9 The relationships between intrinsic regulation and cognitive restraint, uncontrolled eating and emotional eating. Panels A, B and C for females and panels D, E and F are males. There was a significant positive relationship between uncontrolled eating and identified regulation in the TT genotype group in males only.

4.4.3 Regression analysis for influence of age, TFEQR18 subscales and BREQ2 subscales on BMI

The results of the final model, which included TFEQ-R18, BREQ-2 and age, are presented in Table 4.10, Regression analysis results highlights that the adjusted R^2 of 42.8 indicates a high predictive value for the model. Age was significantly associated with BMI. Specifically, BMI increased by .304 for every point increase in age (p <.0001). External regulation was also significantly associated with BMI. Specifically, BMI increased by .461 for every point increase in External regulation score (p <.0001). The variables which had the greatest effect after that were emotional eating (p=.001), and introjected regulation (p=.003). Identified regulation was negatively associated with BMI which decreased by -.428 for every point increase in Identified regulation score (p=.001).

Table 4-10 Multiple Regression Analysis for factors influencing BMI

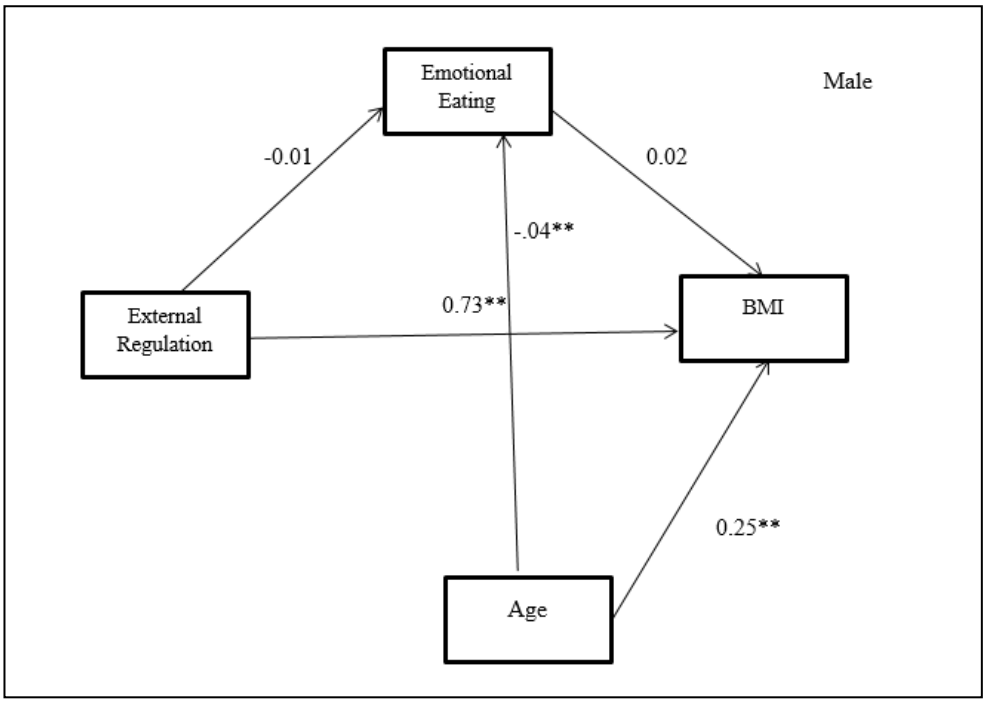
	B	*t*	*p*	Semi partial correlation
Age	.304	15.358	.000	.537
Cognitive restraint	.016	.154	.878	.005
uncontrolled eating	.007	.109	.914	.004
Emotional eating	.387	3.390	.001	.118
A motivation	.129	.990	.323	.035
External regulation	.461	3.860	.000	.135
Introjected regulation	.345	3.007	.003	.105
Identified regulation	-.428	-3.298	.001	-.115
Intrinsic regulation	-.071	-.678	.498	-.024

R^2×100= 43.9 (adjusted R^2 =42.8), SEE= 6.7 F (df, 9.46) = 39.9 (p<0.0001).

4.4.4 Mediation analysis

The regression analysis showed that external regulation was the subscale most associated with BMI, but in the AA+AT genotype group only; emotional eating was strongly correlated with external eating in females only. According to these findings the mediation analysis was run. Results of mediation analysis are shown in figures 4.10 and 4.11. Emotional eating mediates the relationships between external regulation and BMI in females, but not in males, and to a small extent in people with obesity, compared to people of normal weight.

A



B

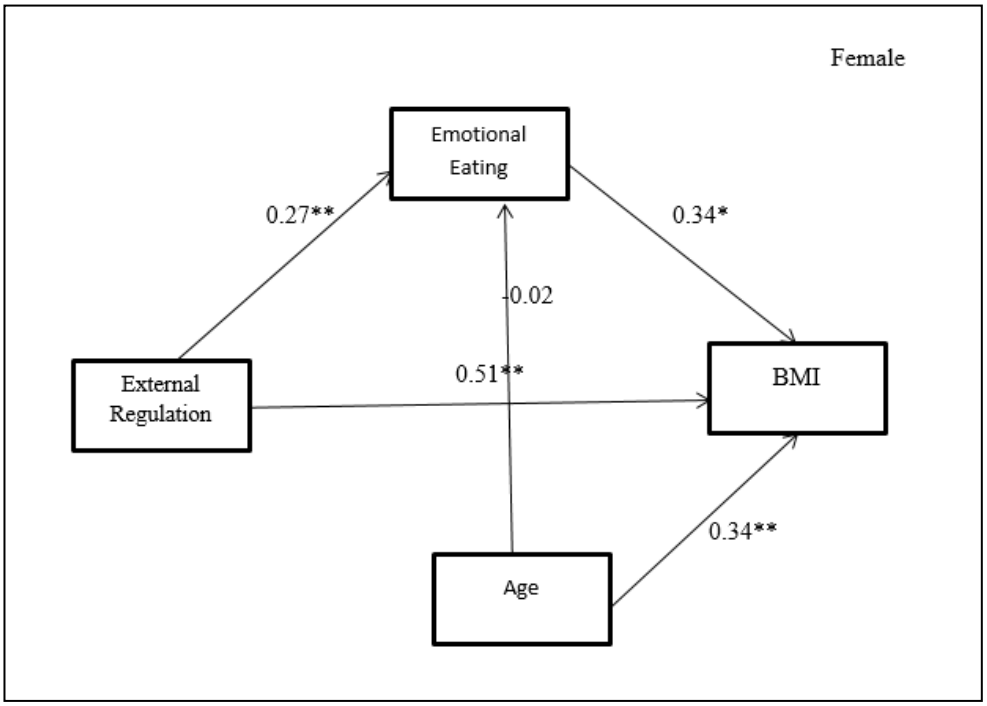
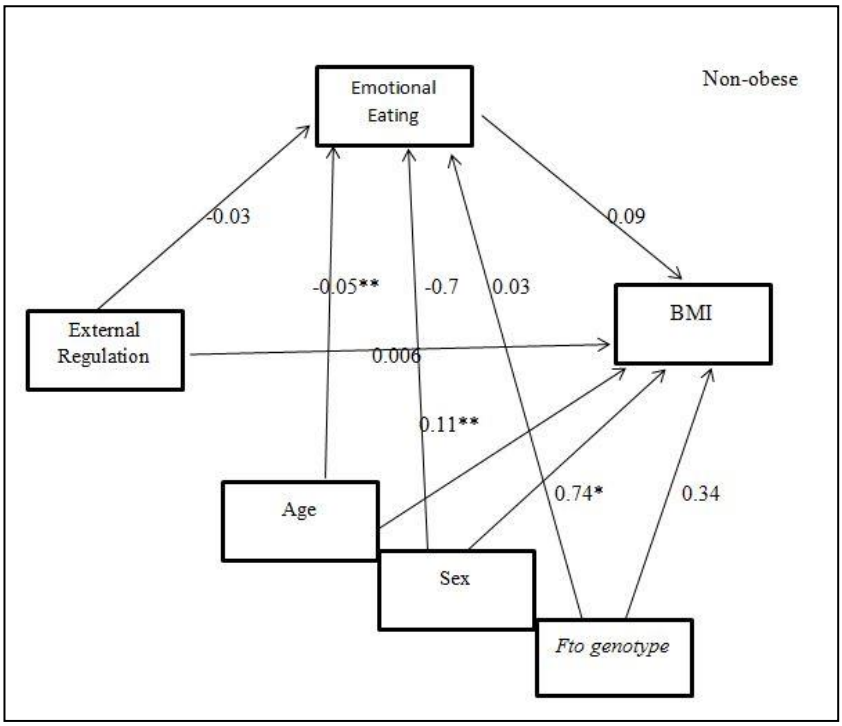


Figure 4-10 Mediation analysis model for the relationship between BMI, emotional eating and external regulation. Panel A males and panel B females. The model indicates that Emotional eating may partially mediate the relationship between external regulation and BMI in the female group but not in the male group ($^{*}p < .05$; $^{**}p < .01$).

A



B

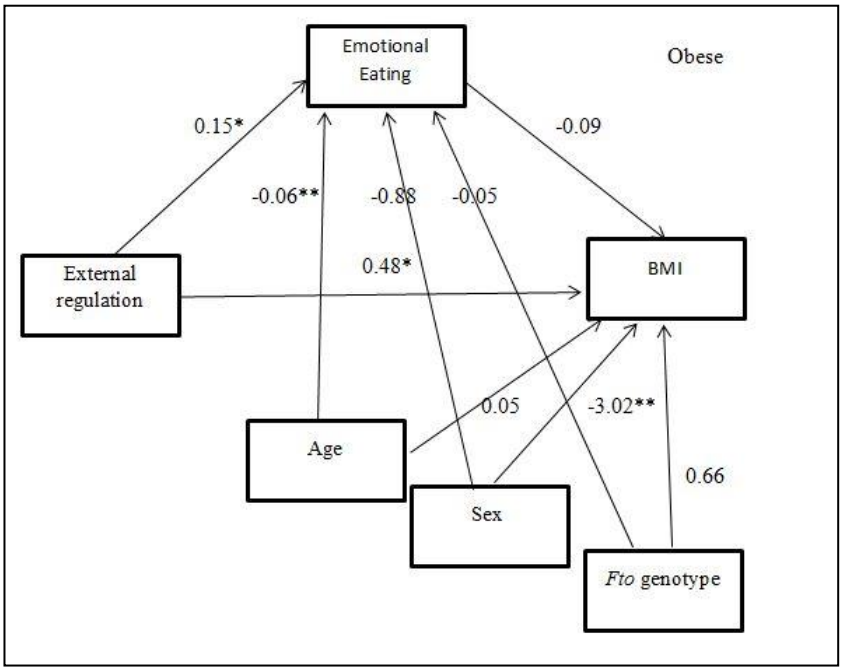


Figure 4-11 Mediation analysis model for the relationship between BMI, emotional eating and external regulation. Panel A non-obese and panel B people with obesity. There is an indication that there may be some partial mediation of the relationship between external regulation and BMI by emotional eating in people in the obesity group, but this is not seen in the non-obese group ($^{*}p < .05$; $^{**}p < .01$).

Table 4.11 shows there are significant inverse relationships between age and external regulation (r=-.235*) and introjected regulation (r=-.420**) in the weight manager group. There are also inverse relationships between age and introjected regulation (r=-.293**) and identified regulation (r=-.167**) in the SHU staff group. For BMI with motivation to exercise, there was significant positive relationships between BMI and amotivation (r=.207**) there were also significant positive relationships between BMI and amotivation there are significant positive relationships between BMI and amotivation (r=.240**) and external regulation (r=.303**) and inverse relationships with identified regulation (r=-.352**) and intrinsic regulation (r=-.330**) in SHU staff.

Table 4-11 Relationships between age, BMI and motivation to exercise by between different population

	Age			BMI		
	Student	SHU staff	weight manager	Student	SHU staff	weight manager
Amotivation	-.102	.039	-.019	-.005	.240**	.125
External regulation	-.051	-.033	-.235*	.207**	.303**	.190
Introjected regulation	-.017	-.293**	-.420**	.130	-.024	.002
Identified regulation	.061	-.167**	.023	-.008	-.352**	-.294*
Intrinsic regulation	.042	-.121	-.077	.00	-.330**	-.325**

All significance tests were two-tailed (*p < .05; **p < .01).

In table 4.12 there is a significant positive relationship between cognitive restraint and introjected regulation in SHU staff group, considering the uncontrolled eating; there

are positive relationships between uncontrolled eating and introjected regulation in SHU staff group and positive relationships between uncontrolled eating and identified regulation and intrinsic regulation in the students group. Turning to, emotional eating there are positive relationships between emotional eating and external regulation and introjected regulation in SHU staff groups and negative relationships between emotional eating identified regulation in the weight manager group.

Table 4-12 Relationships between eating behaviours and motivation to exercise between different population

	Cognitive restraint			Uncontrolled eating			Emotional eating		
	Students	SHU Staff	Weight managers	Students	SHU Staff	Weight managers	Students	SHU Staff	Weight managers
Amotivation	-.034	-.005	.071	-.041	.012	.012	-.035	.028	.163
External regulation	-.037	.022	-.024	-.022	.048	.132	.034	.192**	.222
Introjected regulation	.015	.133*	.101	.065	.151*	.087	-.036	.175**	.091
Identified regulation	.034	.037	.179	.242**	.056	-.135	.004	-.032	-.277*
Intrinsic regulation	.095	-.025	.085	.191**	.036	-.049	.059	-.088	-.135

All significance tests were two-tailed (*p < .05; **p < .01).

4.5 Discussion

The aim of this study was to explore the association between motivation to exercise and eating behaviours as well as BMI and to examine the influence of age, sex, BMI and *FTO* genotype on these relationships. TFEQ-R18, the BREQ2, and genotype for the rs9939609 *FTO* polymorphism were used to study 503 individuals. The data were analysed and the population split by sex, *FTO* genotype, age and BMI. Regression analysis was used to examine the effect of all of these factors on BMI and to identify which one has the strongest effect. Mediation analysis was used to investigate possible mechanisms underlying the association between some of the relationships observed. The main findings are as follows:

4.5.1 Behaviour regulation exercise questionnaire (BREQ2) subscales

- **Influence of sex on (BREQ-2) subscales**
- When the population was split by sex, (table 4.1) the only difference between mean scores for BREQ-2 was for identified regulation (which is when a person thinks the behaviour is valuable) which were higher in men than women However, it is not significant after Bonferroni correction. A study by Mahony *et al.* 2018, found sex differences in BREQ-2 subscales with regards to intrinsic motivation, which is the type of behavioural regulation which is chosen freely (Murcia *et al.* 2007), with males scoring higher than females (Mahony *et al.* 2018). However this study was carried out in a specific population of healthcare professionals who may be more aware of the benefits of exercise. Another study has been carried out by Arbinaga and García who found higher scores in introjected regulation in females and higher scores in external regulation in males (Arbinaga Ibarzábal and García García 2003). The mean scores for BMI

were higher than presented in chapter 3, because this study included an additional 132 participants with obesity. The females had a higher mean BMI of 30.8±9.4 kg/m² than the males who had a mean BMI of 28.5±7.9 kg/m²;

Influence of *FTO* genotype on BREQ-2 subscales.

When the population was split by genotype (table 4.2), the results showed that there were no significant differences in BREQ-2 subscales between the genotype groups, although people in the AA+AT group had higher a mean score for identified regulation and intrinsic regulation, but there were no significant differences between the mean scores. The AA+AT group had a mean BMI of 30.5±8.9 kg/m² compared to the TT genotype group who had a mean BMI of 28.1±8.6 kg/m², which agreed with the data in the previous chapter. The result also showed that the TT genotype group had a lower mean age of (32.7±15.1) compared to the AA+AT group (37.0±16.9), the difference in BMI between the genotype groups may be due to the influence of *FTO* genotype or age as we also showed that age was associated with increased BMI.

- **Influence of BMI on BREQ-2 subscales**

When the population was split by BMI, the results showed that there are significant differences between the groups, the non-obese group (BMI<30 kg/m²) had a higher mean in identified regulation and intrinsic regulation compared to people with obesity group (BMI≥30 kg/m²). People with obesity had higher score-controlled motivation (amotivation and external regulation) than non-obese people.

The Health Survey for England reported that physical activity levels are typically lower in people with obesity (Health Survey for England, 2016) and these results show that motivation may have an important influence on this. However, it is not possible to determine from these results whether lower motivation to exercise is a causal factor in

high BMI, or whether people with a higher BMI are less motivated to exercise due to other factors, for example weight stigma, physical difficulty or discomfort.

4.5.2 Interactions between age on BREQ-2 subscales

Age has a significant inverse relationship with introjected regulation, identified regulation and intrinsic regulation. These results are not in line with a previous study which found no significant relationship between age and introjected regulation, intrinsic regulation, external regulation, and identified regulation subscales (Gast *el al.* 2015). A possible reason is the lack of variance of the age of the sample in Gast's study; most of the sample consisted of freshman college students, with a mean age of 19 years (SD=2.42) (Gast *et al.* 2015). In contrast the population used in our study is larger with a wider variation in age groups and in population type.

The Health Survey for England also reported that there is a decrease in physical activity levels as people age (Health Survey for England, 2016) and our data support this finding, implying that this decrease in exercise may be associated with a low motivation to exercise. This finding is important for the design of programmes to encourage greater participation in exercise, particularly in older adults, as it suggests that targeting motivation may be an effective strategy.

- **Influence of sex on the relationships between age and motivation to exercise**

When the population was split by sex, the result showed low motivation to exercise (introjected regulation, identified regulation and intrinsic regulation) with age in both sexes but a high in amotivation with age for women only. This difference may be due to the effect of life style changes, such as settling down with a partner (Mata *et al.* 2018, Anderson *et al.* 2004), getting a job (Au and Hollingsworth 2011), and

particularly having children (Laroche *et al.* 2012) which may sometimes disproportionately influence the opportunity to exercise in women compared to men. .

- **Influence of genotype on the relationships between age and exercise motivation**

When the results were split by genotype, low scores of introjected regulation, identified regulation and intrinsic regulation in the TT genotype group were associated with age, and intrinsic regulation with age in the AA+AT genotype group.

4.5.3 Interactions between BMI and exercise motivation

The result of the correlation between BMI and motivation to exercise showed that, BMI has a significant positive relationship with amotivation and external regulation and a significant inverse relationship with identified regulation and intrinsic regulation. These findings partially agree with another study which found significant positive relationships between BMI and external regulation and introjected regulation and significant inverse relationships between BMI and internal regulation (Gast *et al.* 2015).

This means that higher motivation to exercise is associated with lower BMI. This may be due to these people doing regular physical activity compared to people with higher BMI who don't do exercise due to lack of motivation (Health Survey for England, 2016). Or it may be that higher BMI leads people to lose their motivation to exercise due to stress or as they become heavier they find it harder to do physical activity, and are more self-conscious when participating. Addressing weight-stigma and providing welcoming environments to exercise may help to address this lack of motivation.

- **Influence of sex on the relationships between BMI and motivation to exercise**

When the group was split by sex, the results showed that the relationships between BMI and amotivation and external regulation were significant only in women, low motivation to exercise was associated with high BMI in women, which may be because women disproportionately become less motivated to exercise and/or have a lack of opportunity to exercise due to other responsibilities such as childcare. And as a result their body weight may increase; increasing BMI may also make women unhappy and lose their motivation to exercise, although it is difficult to determine the cause and effect of these variables.

- **Influence of genotype on the relationships between BMI and exercise motivation**

When the results are split by genotype, the relationships between BMI and external regulation are significant only in the AA+AT genotype group. This may be because this genotype is associated with increased BMI and external motivation may interact with the effects of the gene or it may be due to compensatory beliefs and an increase in food intake before and after exercise due to increased appetite associated with the AA+AT genotype, although this was not measured in this study.

- **Influence of age on the relationships between BMI and motivation to exercise**

When the results were split by age, there was an inverse relationship between BMI and introjected regulation, identified regulation and intrinsic regulation in people > 25 years only and there were positive relationships between BMI and external regulation in people ≤25 years. This means that in older people internal motivation was associated with low BMI, which may be due to people undertaking exercise regularly

or eating healthily (although neither of these factors were measured in the current study), in the younger group external motivation was associated with high BMI, which may be due to compensatory beliefs or may be due to having unhealthy eating habits that make their weight increase.

4.5.4 Interactions between exercise motivation and uncontrolled eating

Results of this study showed that uncontrolled eating has a significant positive relationship with introjected regulation, identified regulation and intrinsic regulation. A higher score for these types of motivation was associated with high uncontrolled eating, this may be due to compensatory beliefs that happen after exercise, people feel they have done plenty of exercise and they will lose weight, so eat too much food as a reward compared to the actual number of calories they have used, but this hypothesis was not tested in the current study. When the group was split by sex, there were significant relationships between external regulation, introjected regulation, identified regulation and intrinsic regulation in women only. When the population was split by age these relationships become significant in ≤ 25 years group only. When the group was split by genotype these relationships become significant in TT genotype group only.

According to the compensatory beliefs model (Knäuper *et al.* 2004) when goals associated with pleasure and harm come into conflict (e.g., "this cake will be tasty but it is unhealthy"), a negative intrapersonal state of cognitive dissonance is created. Cognitive dissonance reflects an aversive motivational state that occurs when an individual holds two cognitions that are inconsistent with each other (Festinger 1957). Conceptual work indicates that compensatory health beliefs are more likely to be active when individuals experience controlled motivation for a task (Rabia *et al*. 2006).

Compensatory beliefs become active when people face a conflict between goals to maximize pleasure and to minimize harm. In the case of controlled exercisers, the experience of physical activity satisfies the goal to minimize harm—Most individuals are likely to recognize at least some health benefits of physical exercise. However, these individuals are less likely to simultaneously satisfy their desire to experience pleasure while undertaking physical activity, so the potential for conflict between maximizing pleasure and avoiding harm is salient for these people. Our results indicate that these effects may be stronger in women, in the younger age group and in the TT genotype group.

4.5.5 Interactions between motivation to exercise and emotional eating

The results showed that external regulation and introjected regulation had significant positive relationships with emotional eating. This means that when people are motivated to exercise due to external regulation from friends or family members not due to internal motivation it may lead to an increase in emotional eating. Only a few studies have examined the association between exercise motivation and eating behaviours. Mata *et al.* 2009 found positive relationships between measures of autonomy and eating variables typically associated with successful weight management (cognitive restraint and eating self-efficacy) and negative relationships for hindering eating variables (disinhibition, emotional and external eating) (Mata *et al.* 2009).

When the group was split by sex these relationships were significant in women only, When the group split by age there were significant positive relationships between introjected regulation, external regulation and emotional eating in the >25 years groups.

This means an increase in emotional eating associated with external regulation was observed in women only and only in the > 25 years group, compared to the older group. It is possible that these people respond to external motivation cues to exercise, and they feel that they cannot undertake exercise due to responsibilities like going to work and looking after children. This puts them under more under stress, increasing feelings of unhappiness and resulting in an increase in emotional eating taking place. However the current study did not collect data to test this hypothesis which may be conjecture. When the group was split by genotype there were significant positive relationships between external regulation and emotional eating in the TT genotype group only.

4.5.6 Interactions between motivation to exercise and cognitive restraint

For cognitive restraint, in women there is a significant positive relationship between cognitive restraint and introjected regulation only. This is mean receiving external motivation to exercise may make women restrain more to try to lose weight where their weight has increased due to not doing exercise. Previous studies examined the increase in food intake after exercise and used exercise motivation to predict post exercise food intake (Dimmock *et al.* 2015, Fenzl *et al.* 2014). It has been proposed that one cognitive strategy people employ to reach this equilibrium is to activate compensatory beliefs (Knäuper *et al.* 2004). These compensatory beliefs reflect the idea that the negative effects of one behaviour can be neutralised or compensated for by the positive effects of another.

4.5.7 Regression analysis and mediation analysis

To better understand the role of age, eating behaviors and exercise motivation, regression analysis was used to investigate how all of these factors (TFEQ subscales, BREQ2 and age on BMI), interact together, and interact with BMI, to determine which of these factors has the strongest effect on BMI (table 4.10). The results show that age, external regulation and emotional eating have significant positively-associated influences on BMI; identified regulation and after that introjected regulation also has an effect.

Mediation analysis was used to investigate these relationships (Figures 4.10 and 4.11). Figure 4.10 compares the female group with the male group and models the relationship between external regulation and BMI in these groups. This type of analysis can be used when there is a significant relationship between two variables, in this case external regulation and BMI as shown in table. If a relationship is mediated by a third variable (in this case emotional eating) this will be evident in the significant correlations shown between the third variable and the other variables.

The mediation analysis in figure 4.10 for the females group shows a significant correlation between external regulation and emotional eating (r=0.27), and between emotional eating and BMI (r=0.34), and the correlation between external regulation BMI is also significant. This analysis also allows for the investigation of the effect of other variables (in this case age). In the case of male group, the mediating effect of emotional eating is not present (but the correlation between external regulation and BMI is significant). Therefore, in the female group for high BMI, emotional eating mediated almost all of the relationships with external regulation, demonstrating a

possibility that the female group with higher external regulation are using emotional eating to suppress stress.

The mediation analysis in figure 4.11 for people with obesity group shows a significant correlation between external regulation and emotional eating (r=0.15), and the correlation between external regulation and BMI is also significant (r=0.48). This analysis also allows for the investigation of the effect of other variables (in this case age, sex and *FTO* genotype). In the case of non-obese people group, the mediating effect of emotional eating is not present and the correlation between external regulation and BMI is not significant). Therefore, in people with obesity, emotional eating may be partially mediating the relationships with external regulation, demonstrating a possibility that in people with obesity and higher external regulation are using emotional eating to suppress stress.

4.6 Strengths of the study

A strength of this study is the novel findings; to our knowledge this study is the first to examine the association between motivation to exercise and eating behaviour and BMI, and this study is the first study to look at the effect of *FTO* genotype (the first gene associated with obesity) on motivation to exercise and how it influences the association between motivation to exercise and eating behaviour and BMI. This study was also conducted on a large group of participants with a wide range of age groups and different body weights, although this group was heterogeneous and this may limit the validity of the findings.

4.7 Limitations of the study

A limitation of this study is that we did not measure physical activity levels; the relationships between BREQ-2 scores and physical activity are well-established in the literature and we were already using a large number of questionnaires with the participants so tried to avoid overloading them leading to participant fatigue. Regardless physical activity questionnaires are prone to bias. A more robust way of monitoring physical activity is to use devices such as the ACTi heart combined accelerometer and heart rate monitor; however, this was not feasible with the size of the population being studied due to cost and availability of equipment.

Another limitation is the use of self-reported answers to questionnaires; people may choose answers which reflect how they wish things were rather than being honest, and this effect may be influenced by the variables we studied including sex and BMI, potentially having a disproportionate effect on some aspects of the findings. Finally, we chose to only study one polymorphism, again due to time and cost limitations, genome-wide screening of the samples may identify variants which are equally or more important in influencing the relationships studied here.

4.8 Conclusion

In conclusion, this study revealed that motivation to exercise interacts with eating behaviours and these interactions are influence by age, sex, BMI and *FTO* genotype. Emotional eating is a partial mediator between external regulation and high BMI, explaining a proportion of this relationship. These findings will help address the epidemic of obesity, providing a way for the specialists in obesity treatment to help people to lose weight by giving them personalised interventions such as support to

motivate them to do exercise regularly and follow healthy eating style depending on the aforementioned factors.

5 CHAPTER 5: Eating behaviour, alexithymia and BMI in people with obesity

5.1 Introduction

Alexithymia is a personality trait that may affect the development and course of obesity, concomitant mental disorders, and the effectiveness of weight reduction therapy (Sifneos 1996). Alexithymia, which means “no words for emotions,” is a set of cognitive–emotional deficits that includes the inability to identify and express emotions and affects, an impoverished fantasy life, preference for concrete concerns, and avoidance in coping with conflicts or reporting emotions (Sifneos 1996). Alexithymia is also associated with the development of eating disorders, such as anorexia and bulimia nervosa (Cochrane *et al.* 1993). Nevertheless, the results of studies evaluating the relationship between alexithymia and eating behaviours are conflicting (Franco Adami *et al.* 2001), and only a few studies have looked at the relationships between alexithymia and eating behaviour in people with obesity.

Dated empirical evidence suggests a relationship between alexithymia and obesity (Clerici *et al.* 1992), although some studies do not support this hypothesis, suggesting that alexithymia is only present in people with obesity who have eating disorders (Pinaquy *et al.* 2003). It has also been suggested that in patients with severe obesity, alexithymia traits might reflect an underlying eating disorder, such as binge eating disorder (de Zwaan *et al.* 1995), or cause emotional eating because of difficulties in reading internal cues (Pinaquy *et al.* 2003).

In addition, results of some studies propose a bilateral relationship between alexithymia and obesity (Clerici *et al.* 1992). Some authors have stated that obesity favours the development of secondary alexithymia, (Grabe *et al.* 2010), whereas

others consider alexithymia a primary trait, influencing binge eating and obesity (Larsen *et al.* 2003). The high frequency of alexithymia in people with obesity has also been stated to be a potential consequence of depression (de Groot *et al*.1995). The Toronto Alexithymia Scale (TAS-20) is a 20-item instrument that is frequently used to measure alexithymia (Bagby *et al.* 1994).

Alexithymia and eating behaviour have been studied in people with eating disorders. Initial observations highlighted that patients with eating disorders have difficulty recognising and describing emotions; which predated the formulation of the alexithymia construct (Bruch 1962, Bruch 1973). Pinaquy *et al.* (2003) examined the relationship between alexithymia and emotional eating in 169 women with obesity, with and without binge eating disorder (BED); emotional and external eating was significantly higher in BED participants but there was no difference in restrained eating.

Sex can influence eating behaviours and BMI as detailed in chapter 3 and its influence on alexithymia and when investigated in large-scale studies in the general population, results highlight that men score significantly higher than women on the TAS-20 scale (Taylor *et al*. 2003). In addition, in 2007, Moriguchi et al reported that the investigation of the effect of sex on alexithymia revealed no sex difference in the total alexithymia scores but mentioned some different in alexithymia subscales (Moriguchi *et al.* 2007).

The effect of genetics on alexithymia have been shown in previous studies with one study finding a substantial contribution of genetic factors to individual differences in alexithymia and all its facets as measured by theTAS-20 (Picardi *et al.* 2011). This finding is consistent with another large study which suggests that genetic factors have a noticeable and similar impact on all facets of alexithymia (Jorgensen *et al.* 2007). The effect of *FTO* genotype on eating behaviours and BMI has been shown in previous

studies, which is supported in the previous study in chapter 3, but to the principal investigators knowledge no study has examined the effect of age and *FTO* genotype on alexithymia.

As we age, body weight typically increases. In chapter 3 we found age has a strong inverse relationship with uncontrolled eating and emotional eating and there is increasing in BMI with age. A previous study also showed an association between age and alexithymia. Moriguchi *et al.* reported that the total score of the TAS-20 is negatively correlated with age and showed that TAS-20 scores were high in teenagers, decreased with age until the age of about 30 years and then remained relatively unchanged (Moriguchi *et al.* 2007).

5.2 Objectives of the study

The current study investigates the interactions between eating behaviours, alexithymia and BMI. Based on previous literature, there are interactions between emotional eating and alexithymia that influence BMI in people with eating disorders and people with obesity. The characteristics of the population included in this study (1) they are overweight or have obesity BMI of 39.21±6.11 kg/m2 (2) the average age is older, age of 51.94±13.8 years (in contrast to the average age in the previous 2 chapters).

The previous findings indicate that when considering the relevance of eating behaviours to obesity it is important to consider other variables that are known to influence these measures such as genetics, age, sex. It is also important consider which associations are mediated by other relevant variables. Thus, objectives of this study were:

1) To investigate the interactions between eating behaviours, alexithymia and BMI. 2) To determine the influence of *FTO* genotype, sex and age on these interactions. 3) To use mediation analysis to explore role of potential mediators in these relationships.

5.3 Experimental Section

5.3.1 Study Participants

Participants for this study were recruited from the Rotherham Institute for Obesity (RIO) and from the Shape Up programme at Rotherham's leisure centres. See chapter 2 for details. A total of 83 participants (59 female, 24 male) were included in this study.

5.3.2 Anthropometry

Body weight and height were collected by trained specialists at the RIO and from Rotherham's leisure centres see chapter 2 for details. BMI was calculated as body mass in kilograms divided by the square of height in metres.

5.3.3 Eating Behaviours

Eating behaviours were measured as described previously.

5.3.4 Alexithymia

Alexithymia was measured using the Toronto Alexithymia Scale (TAS-20) (see appendix 4), the widely used measure of alexithymia.TAS-20 Demonstrates good internal consistency (Cronbach's alpha = .81) and test-retest reliability (.77, p<.01) (Bagby *et al.* 1994). The TAS-20 consists of three subscales. Factor 1 assesses the difficulty of identifying feelings and consists of 5 items; factor 2 assesses the difficulty of describing feelings and consists of 7 items; factor 3 assesses externally oriented

thinking and consists of 8 items. Possible answers to each item on the TAS-20 and their scores were strongly disagree = 1, disagree = 2, neither agree nor disagree = 3, agree = 4, strongly agree= 5, so that the total score ranged from 20 to 100 points. Following Taylor *et al.,* scores of 61 and above were judged as indicating the person had an alexithymic state (Taylor *et al.* 1999) (See chapter 2 for details).

5.3.5 Genotyping

Was undertaken as previously described in chapter 2.

5.3.6 Data analysis.

The Statistical Package for the Social Sciences (SPSS software version 24, IBM) was used for the statistical analysis with significance accepted if $p \leq 0.05$, or $p \leq 0.005$ after Bonferroni correction where appropriate. Distribution of data was checked using the Kolmogorov-Smirnov Test and descriptive statistics were calculated. Pearson correlation was undertaken to explore association between variables including age, BMI, eating behaviours and alexithymia. The population was split by sex, *FTO* genotype and according to total alexithymia score in (alexithymic = TAS-20 scores were > 60 and non alexithymic TAS-20 scores were $\leq$ 60), T-tests were performed to assess sex, genotype differences and according to alexithymia score in age, BMI, eating behaviours and alexithymia.

Multiple regression analysis was performed to assess the multivariate relationships between the independent variables and BMI and weight loss. In this regression model, the selected predictors (variables which were significant or approached significance in the bivariate analysis) were forced into the model and the semi-partial correlation coefficient was calculated to quantify the unique contribution of each predictor to the

variance in the dependent measure (Cohen *et al*. 2014). Considering the relatively small subject-parameter ratio (24:1) and in the absence of strong theoretical support for a hierarchical entering of predictors into the model, this a priori (forced) model is preferable to a stepwise model as it minimises instability in the selection of variables into the model (and in parameter estimation) caused by potential sampling biases (Biddle *et al.* 2001). To further explore relationships between variables, mediation analysis with bootstrapping was used (Preacher and Hayes 2008). For the mediation model (Figures 5.3, 5.4, 5.5 and 5.6), difficulty identifying feelings was the independent variables, eating behaviours were the mediator variables, and BMI the dependent variable. Age, sex and *FTO* genotype were the covariates. For outcome data, effect sizes were calculated using Cohens d.

5.4 Results

5.4.1 Participant characteristics

Descriptive statistics for the primary variables for the overall population, by sex, by genotype and by alexithymic scores are shown in tables 5.1, 5.2 and 5.3. The participants had a mean ± SD age of 51.94±13.8 years, and BMI of 39.21±6.11 kg/m^2.

In Table 5.1, the findings are shown for the overall population and result for males are compared with the females. BMI values in the female participants were slightly higher than males; there was also significant difference in age between the sexes I.e. males were older (57.19±11.09 years) than females (50.0±14.20 years). For TFEQ-R18 scores, males had higher cognitive restraint scores (14.05±1.75) than females (12.12±2.66), TAS-20 scores revealed that females had a higher score in total alexithymia and

alexithymia subscales than males, but the differences were not significant (after Bonferroni correlation). .

Table 5-1 Descriptive statistics for primary variables for overall sample and by sex.

	All		Female		Male				
Number	N=83		N=59		N=24				
	M	SD	M	SD	M	SD	*p*	*t*	*d*
Age	51.94	13.8	50.0	14.20	57.19	11.09	.036	-2.136	0.564
BMI	39.21	6.11	39.37	6.29	38.78	5.72	.712	.370	0.098
Cognitive restraint*	12.65	2.57	12.12	2.66	14.05	1.75	.000	-3.731	0.857
Uncontrolled eating	19.96	3.64	19.72	3.59	20.24	3.48	.573	-.566	0.147
Emotional eating	7.00	3.29	7.19	3.29	6.24	3.18	.256	1.144	0.294
Difficulty Describing Feelings	13.78	4.99	14.03	4.66	13.00	5.95	.412	.824	0.193
Difficulty Identifying Feeling	17.48	8.58	17.95	8.45	16.05	9.12	.379	.885	0.216
Externally-Oriented Thinking	24.41	7.17	24.9	5.81	23.00	10.14	.293	.831	0.229
Total alexithymia score	55.6	18.36	56.88	16.57	52.05	22.91	.296	1.052	0.242

Note. All significance tests were two-tailed. M= mean score; SD =standard deviation; t =t-test; p= p-value; d=Cohen's d; significant if p≤0.005 (after Bonferroni correction).

In table 5.2, the data shows the result for different *FTO* genotype groups AA+AT and TT). There were no differences in BMI, TFEQ-R18, and TAS-20 between the two groups.

Table 5-2 Descriptive statistics for primary variables by genotype

	TT		AT+AA				
Number	N= 28 (8M/20F) 33%		N=55(16M/39F) 66%				
	M	SD	M	SD	*p*	*t*	*d*
Age	47.70	9.48	52.22	15.07	.131	-1.533	0.359
BMI	39.12	7.17	39.76	5.72	.696	-.392	0.098
Cognitive Restraint	12.20	2.67	12.76	2.47	.395	-.855	0.217
Uncontrolled Eating	19.65	4.09	20.07	3.57	.665	-.435	0.109
Emotional Eating	7.45	3.14	6.91	3.38	.535	.624	0.165
Difficulty Describing Feelings	14.30	2.75	14.33	4.88	.976	-.030	0.007
Difficulty Identifying Feeling	18.65	7.31	18.18	8.48	.827	.219	0.059
Externally-Oriented Thinking	25.45	4.31	25.22	6.01	.875	.158	0.044
Total alexithymia score	58.40	10.50	57.73	16.92	.869	.166	0.078

Note. All significance tests were two-tailed. M= mean score; SD =standard deviation; t =t-test; p= p-value; d=Cohen's d.

Table 5.3 highlights 41 participants (49%) demonstrated alexithymic traits, whereas, in the other individuals, TAS-20 scores were lower than 60. Average BMI values of the alexithymic group were higher (40.9±5.6) than the other group (37.6±6.2), people with alexithymia were younger (48.3±10.9) than people without alexithymia (48.3±10.9). The TFEQ score values of the alexithymic patients were significantly higher than those

observed in their non-alexithymic group in uncontrolled eating and emotional eating, but cognitive restraints score was similar in both groups. However, it is not significant after Bonferroni correction as p value needs to be < 0.005 to consider as statistically significant.

Table 5-3 Descriptive statistics for primary variables according to total alexithymia score

	Non alexithymic + possibile alexithymic N=42 (14M/28F)		Alexithymic N=41 (10M/31F)				
	M	SD	M	SD	p	t	d
Age	55.3	15.3	48.3	10.9	.019	2.41	0.53
BMI	37.6	6.2	40.9	5.6	.017	-2.43	0.56
Cognitive restraint	12.8	2.5	12.5	2.6	.688	.402	0.09
Uncontrolled eating	19.0	3.4	20.8	3.6	.024	-2.31	0.52
Emotional eating	6.1	2.9	7.9	3.4	.011	-2.61	0.59
Difficulty Describing Feelings*	10.4	4.5	17.2	2.6	<.001	-8.54	1.87
Difficulty Identifying Feeling*	10.9	6.2	24.2	4.5	<.001	-11.04	2.44
Externally-Oriented Thinking*	21.4	8.5	27.5	3.5	<.001	-4.21	0.93
Total alexithymia score*	42.7	17.2	68.9	5.9	<.001	-9.19	2.03

Note. Alexithymic (TAS-20 score > 60) and in non-alexithymic individuals. All significance tests were two-tailed. M= mean score; SD =standard deviation; t =t-test; p= p-value; d=Cohen's d; significant if p≤0.005 (after Bonferroni correction).

5.4.2 Relationships between age, BMI, eating behaviours and alexithymia

Correlations between age, BMI, eating behaviours and food cravings are categorised for the overall population in tables 5.4 and 5.5, by sex in table 5.6, by genotype in table 5.7 and by alexithymia score in table 5.8.

Table 5.4 shows that there is a significant inverse relationship between age and uncontrolled eating (r=-0.290**), emotional eating(r=-0.265*), difficulty describing feelings(r=-0.268*), difficulty identifying feelings (r=-0.332**) and total alexithymia score (r=-0.302**), BMI has significant positive relationship with difficulty identifying feelings (r=0.285*).

Table 5-4 Relationships between age, BMI, eating behaviours and alexithymia for overall

N=83	Cognitive restraint	Uncontrolled eating	Emotional eating	Difficulty Describing Feelings	Difficulty Identifying Feeling	Externally-Oriented Thinking	Total alexithymia score
Age	.181	-.290**	-.265*	-.268*	-.332**	-.189	-.302**
BMI	-.110	.206	.215	.152	.285*	-.017	.167

Note. Correlations of primary variables for overall population. All significance tests were two-tailed (*p < .05; **p < .01).

Table 5.5 Shows that uncontrolled eating has significant positive relationships with difficulty identifying feelings (r=0.290**) and total alexithymia score (r=0.251*), emotional eating has positive relationships with difficulty describing feelings (r=0.241*), difficulty identifying feelings (r=0.378**), externally-oriented thinking (r=0.221*) and total alexithymia score (r=0.349**).

Table 5-5 Relationships between eating behaviours and alexithymia for the overall population

N=83	Difficulty Describing Feelings	Difficulty Identifying Feelings	Externally-Oriented Thinking	Total alexithymia score
Cognitive restraint	-.043	-.003	.050	.004
Uncontrolled eating	.185	.290**	.122	.251*
Emotional eating	.241*	.378**	.221*	.349**

Note. Correlations of primary variables for overall population. All significance tests were two-tailed (*p < .05; **p < .01).

In table 5.6 the results show that in women there are significant positive relationships between BMI and alexithymia scores including difficulty identifying feelings (r=0.334*) and total alexithymia score (r=0.289*), in contrast these relationships are not seen in men.

Relationships between uncontrolled eating and difficulty identifying feeling and total alexithymia were significant only in women, but not in men. Also relationships between emotional eating and difficulty identifying feeling and total alexithymia were only significant in women but not in men.

Table 5-6 Relationships between primary variable by sex.

	Difficulty Describing Feelings		Difficulty Identifying Feeling		Externally-Oriented Thinking		Total alexithymia score	
	F	M	F	M	F	M	F	M
Age	-.265*	-.247	-.273*	-.487*	-.166	-.209	-.272*	-.351
BMI	.249	-.086	.334*	.143	.135	-.306	.289*	-.101
Cognitive restraint	-.018	-.014	-.009	.184	.200	-.010	.044	.070
Uncontrolled eating	.172	.224	.347**	.166	.013	.306	.268*	.265
Emotional eating	.225	.245	.368**	.377	.125	.358	.327*	.383

Note. All significance tests were two-tailed (*p < .05; **p < .01).

In table 5.7 the results show that age has an inverse relationship with difficulty identifying feelings (r=-0.356**) and total alexithymia score (r=-0.301*) in AA+AT genotype group. In contrast, these relationships are not significant in the TT genotype group. With regards to BMI and alexithymia, in the AA+AT genotype group there was significant relationship between BMI and Difficulty Identifying Feelings (r=0.344*). Comparing with the TT genotype group, the relationships between BMI with alexithymia were not significant.

Considering the relationship between eating behaviours and alexithymia, there was a significant relationship between cognitive restraint and Externally-Oriented Thinking (r=.459*) in the TT genotype group. However, the relationships are not significant in AA+AT genotype group. There were also significant positive relationships between uncontrolled eating and externally-oriented thinking (r=0.490*) and total alexithymia

score (r=0.494*) in the TT genotype group only. Again, the relationships are not significant in the AA+AT genotype group. A significant positive relationship between emotional eating with difficulty describing Feelings (r=0.288*) and difficulty identifying feeling (r=0.368**) and total alexithymia score (r=0.350**) were noted in the AA+AT genotype group, but the relationships are not significant in TT genotype group.

Table 5-7 Relationships of primary variable by genotype.

	Difficulty Describing Feelings		Difficulty Identifying Feelings		Externally-Oriented Thinking		Total alexithymia score	
	TT	AA+AT	TT	AA+AT	TT	AA+AT	TT	AA+AT
Age	-.228	-.235	.050	-.356**	.041	-.156	-.008	-.301*
BMI	-.277	.253	.073	.344*	.094	-.164	.017	.184
Cognitive restraint	-.123	-.029	-.002	.029	.459*	-.044	.155	-.010
Uncontrolled eating	.271	.157	.319	.265	.490*	-.003	.494*	.177
Emotional eating	-.023	.288*	.303	.368**	.128	.231	.258	.350**

Note. All significance tests were two-tailed (*p < .05; **p < .01).

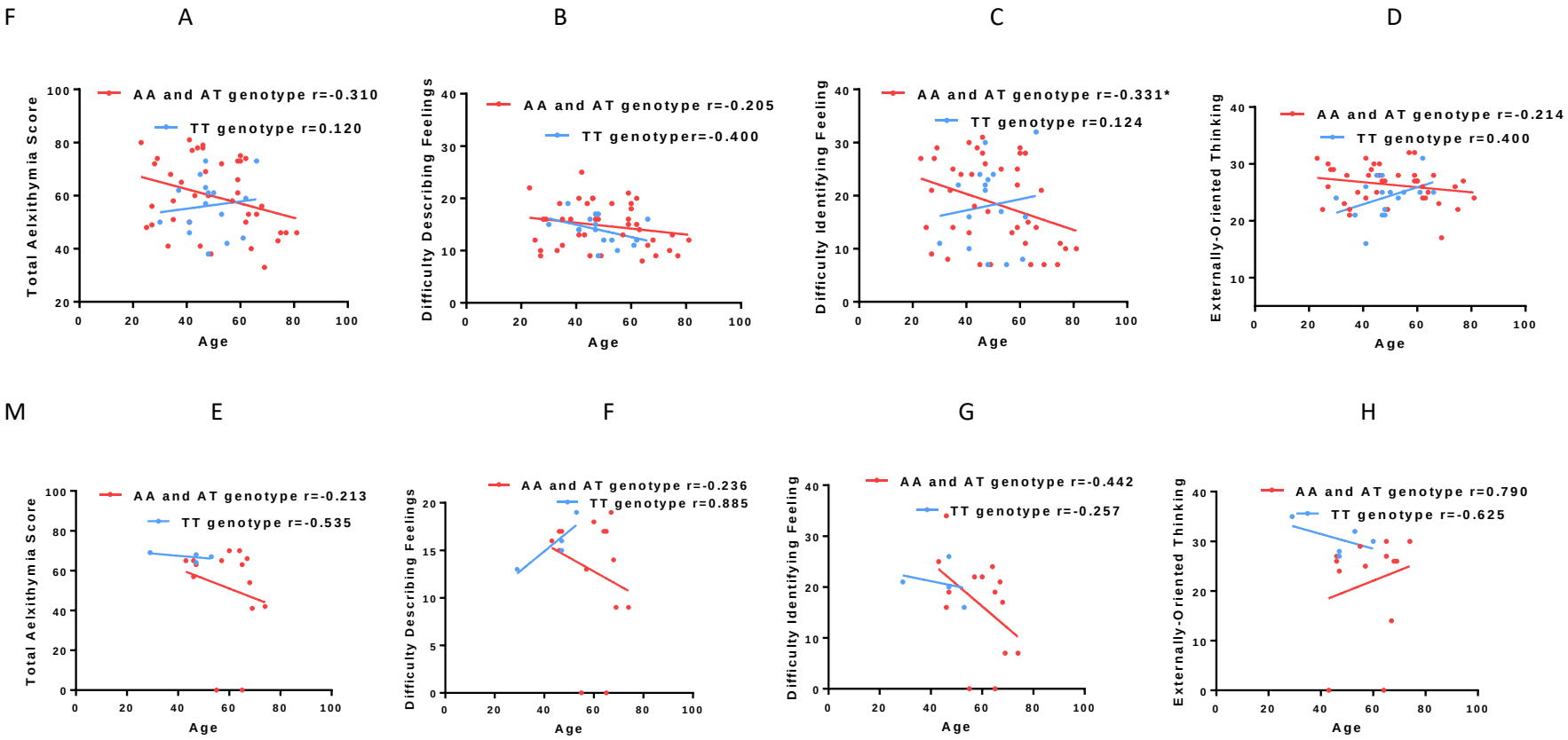


Figure 5-1 The relationships between age and total alexithymia score, difficulty describing feeling, difficulty identifying feeling and external oriented thinking. Panels A, B, C and D are for females and panels E, F, G and H are males. There was a significant inverse relationship between age and difficulty identifying feeling in the AA+AT genotype group in females.

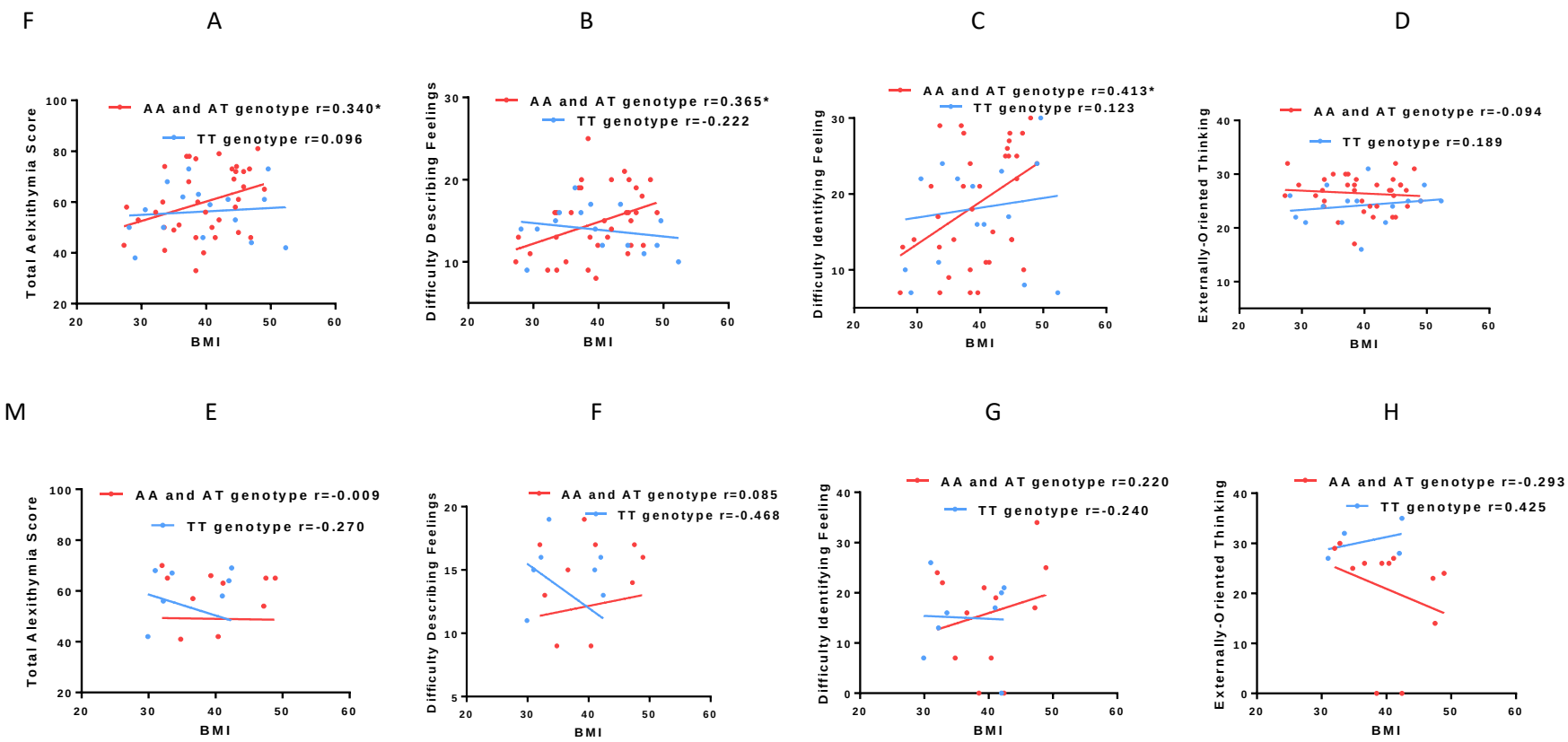


Figure 5-2 The relationships between BMI and total alexithymia score, difficulty describing feeling, difficulty identifying feeling and external oriented thinking. Panels A, B, C and D are for females and panels E, F, G and H are males. There were significant positive relationships between BMI and total alexithymia, difficulty identifying feeling and difficulty describing feeling in the AA+AT genotype group in females.

5.4.3 Regression analysis for influence of age, eating behaviours and alexithymia on BMI

The results of the final model, which included TFEQ, TAS-20 and age, are presented in Table 5.8. Regression analysis results indicated that the adjusted R^2 indicates a medium predictive value for the model, adjusted R^2=11.5. Difficulty identifying feelings was significantly associated with BMI. Specifically, BMI increased by 0.297 kg/m² for every point increase in difficulty identifying feelings score (*p*=.038). Age was positively associated with BMI, but the effect was non-significant. Specifically, BMI increased by .102 for every point increase in age *(p* <.077). The overall model is significant (*p*=0.036).

Table 5-8 Multiple Regression Analysis for factors influence BMI

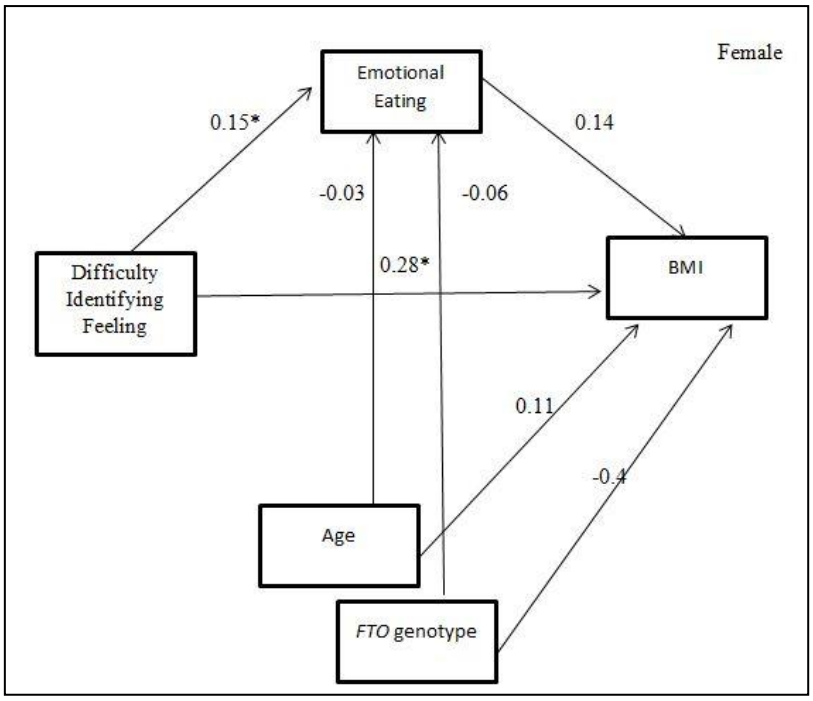
	B	t	p	Semi-partial correlation
Age	.102	1.795	.077	.200
Uncontrolled eating	-.402	-1.449	.152	-.162
Cognitive restraint	.262	1.152	.254	.129
Emotional eating	.203	.800	.427	.089
Difficulty describing feeling	-.061	-.226	.822	-.025
Difficulty identifying feeling	.297	2.117	.038	.236
External orientation	-.234	-1.577	.120	-.176

R^2×100= 20.2 (adjusted R^2 =11.5), SEE= 5.78, F (df, 6.56) = 2,34 (p=0.036)

5.4.4 Mediation analysis results

The results of the mediation analysis are shown in (Figures 5.3 to 5.8). The regression analysis showed that difficulty identifying feelings was the subscale most associated with BMI. Uncontrolled eating and emotional eating were strongly correlated with difficulty identifying feelings and total alexithymia; according to these findings the mediation analysis was run. The results indicate that emotional eating and uncontrolled eating may partially mediate the relationships between difficulty identifying feelings and BMI in females.

A



B

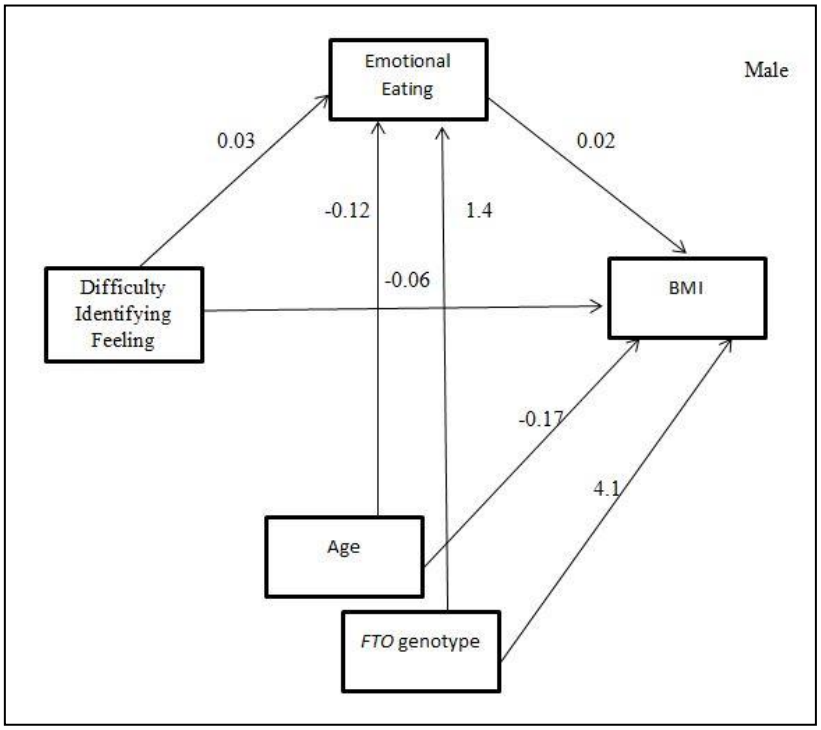
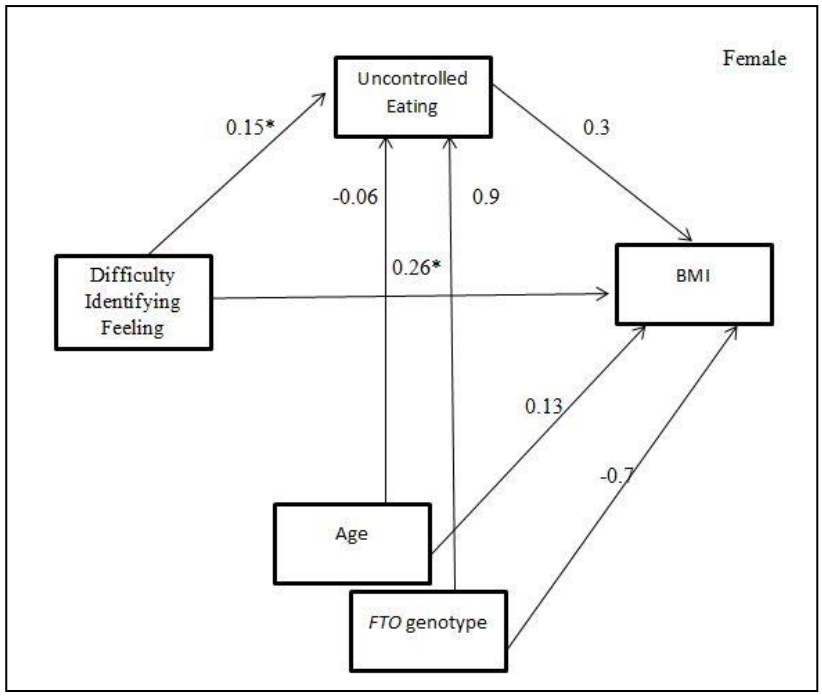


Figure 5-3 Mediation analysis model for the relationship between difficulty identifying feelings, emotional eating and BMI. Panel A female and panel B male. Difficulty identifying feelings was associated with high BMI and high emotional eating in females, The model indicates that emotional eating may partially mediate the relationship between difficulty identifying feelings and BMI in females but not in males ($^{*}p < .05$; $^{**}p < .01$).

A



B

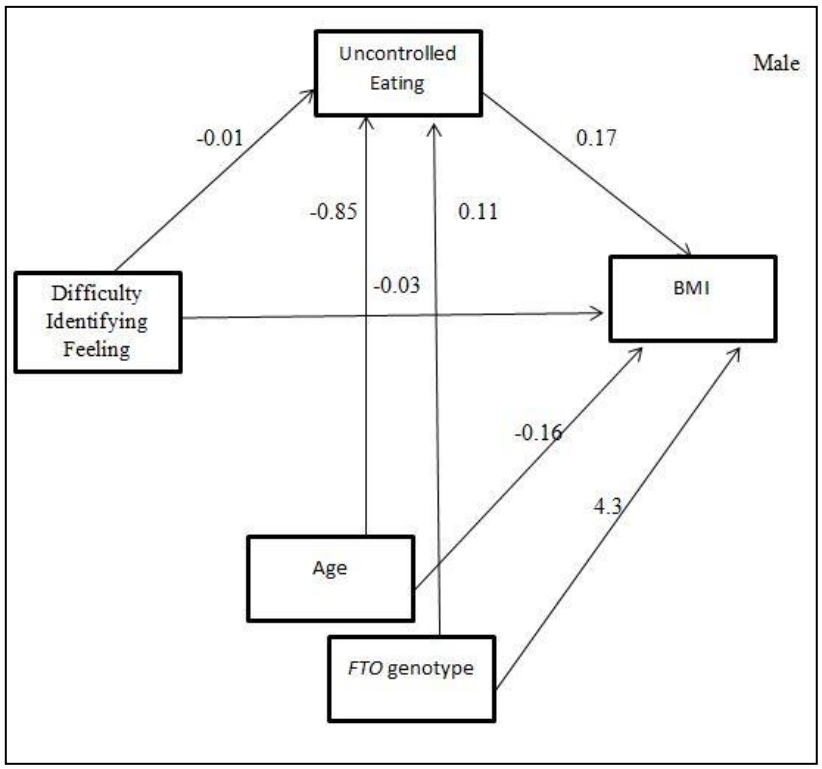
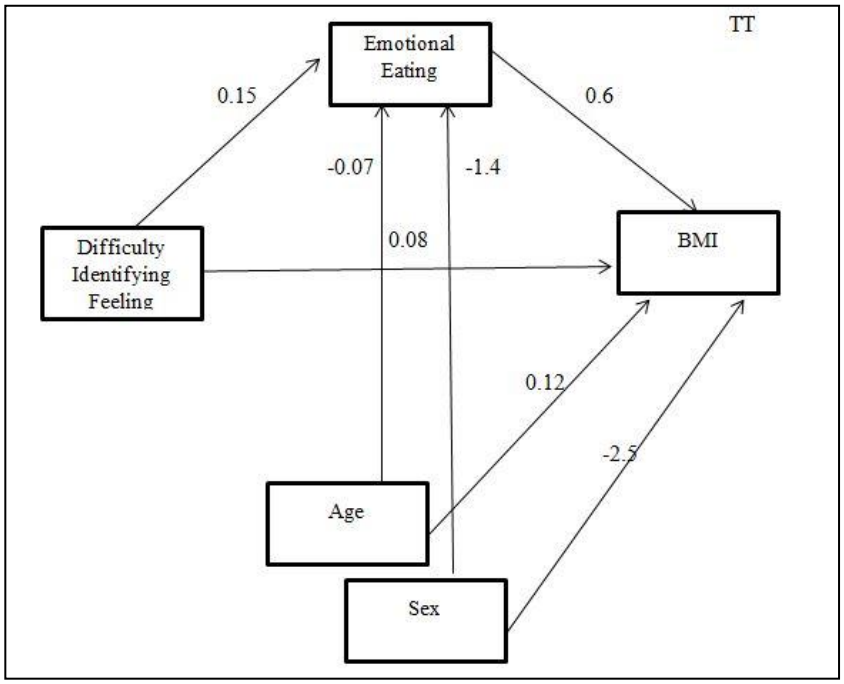


Figure 5-4 Mediation analysis model for the relationship between difficulty identifying feelings, uncontrolled eating and BMI. Panel A female and panel B male. Difficulty identifying feelings was associated with high BMI and high uncontrolled eating in females. The model indicates that uncontrolled eating mediates the relationship between difficulty identifying feelings and BMI in females but not in males ($^{*}p < .05$; $^{**}p < .01$).

A



B

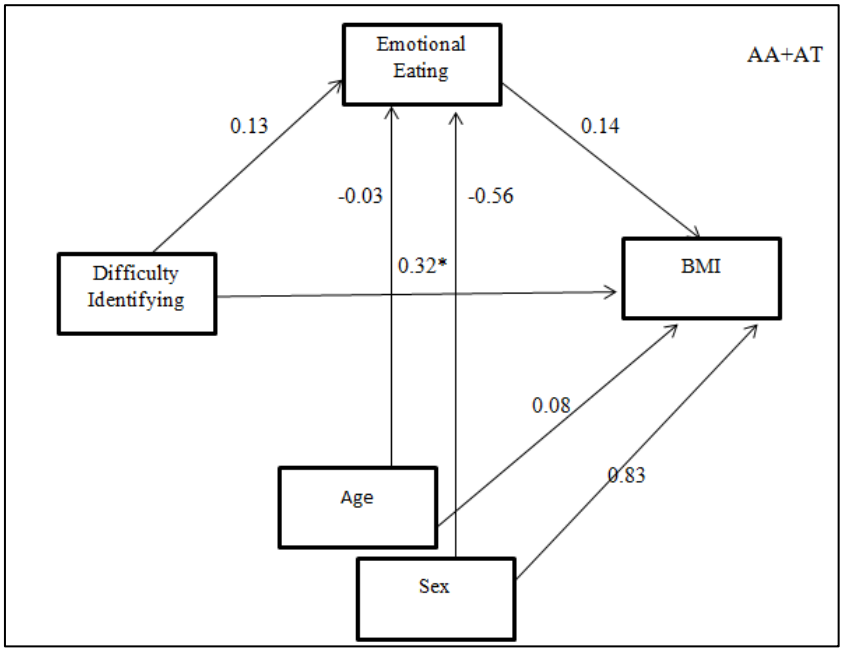
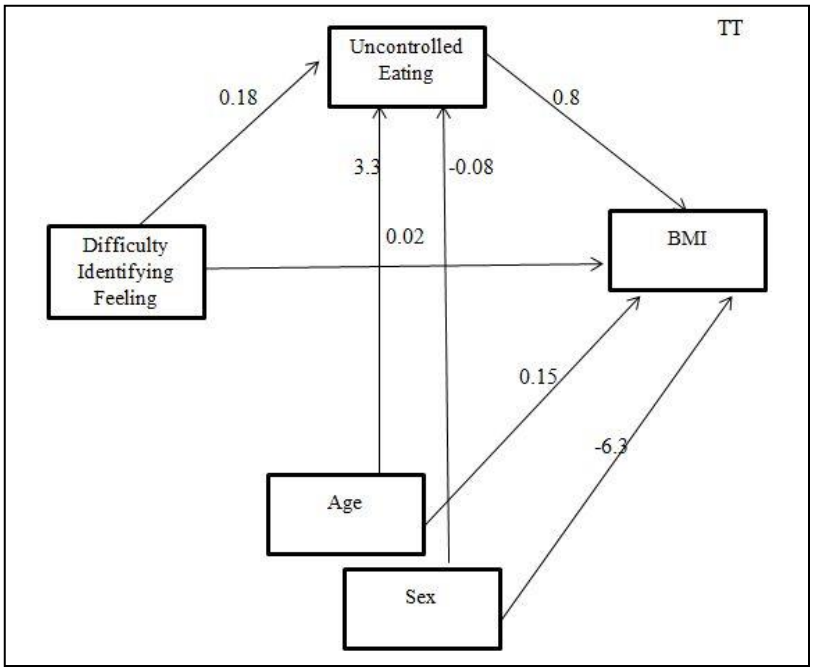


Figure 5-5 Mediation analysis model for the relationship between difficulty identifying feeling, emotional eating and BMI. Panel A in TT genotype group and panel B in AA+AT genotype group. Difficulty identifying feeling was associated with high BMI in the AA+AT genotype group. Emotional eating did not mediate the relationship between difficulty identifying feeling and BMI in either genotype group ($^{*}p < .05$; $^{**}p < .01$).

A



B

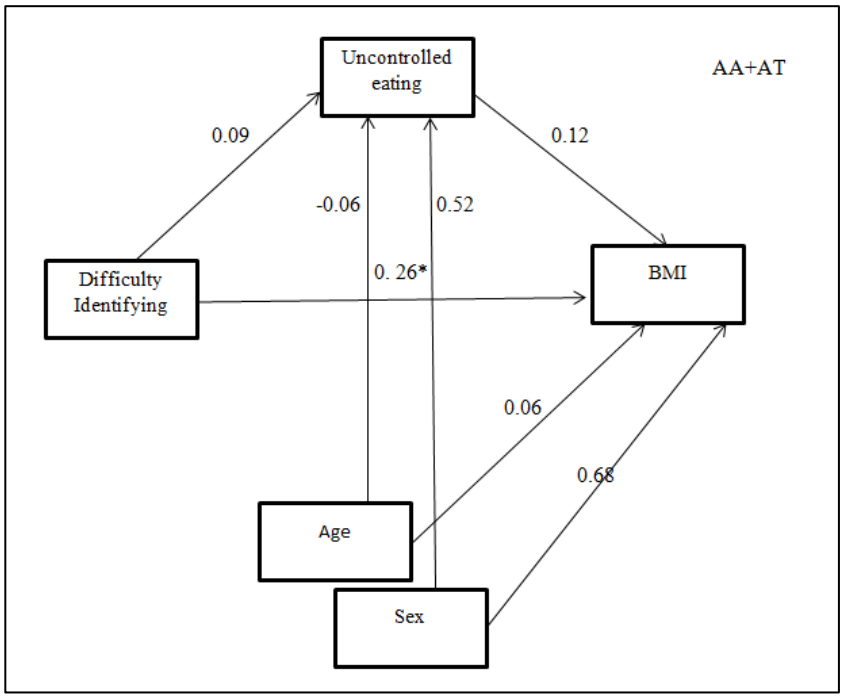


Figure 5-6 Mediation analysis model for the relationship between difficulty identifying feeling, Uncontrolled eating and BMI. Panel A in TT genotype group and panel B in AA+AT genotype group. Difficulty identifying feeling was associated with high BMI in the AA+AT genotype group. Uncontrolled eating did not mediate the relationship between difficulty identifying feeling and BMI in either genotype group ($^{*}p < .05$; $^{**}p < .01$).

5.5 Discussion

The aim of this study was to explore the association of alexithymia with eating behaviours and BMI and to examine the influence of age, sex and *FTO* genotype on these relationships. Results of TFEQ-R18, TAS-20 and rs9939609 *FTO* polymorphism were used to study 83 individuals with overweight and obesity prior to participating in weight loss interventions. The data were analysed and the population split by sex (59 F and 24 M), *FTO* genotype (55 AA+AT 66% and 28 TT 33%) and according to alexithymia score (42 non alexithymic and 41 alexithymic). The TAS-20 uses cutoff scoring: equal to or less than 51 = non-alexithymia, equal to or greater than 61 = alexithymia. Scores of 52 to 60 = possible alexithymia. Because the number of participant in this chapter is small, the participants were split into two groups alexithymic and non alexithymic to avoid doing the analysis with too small number and it will not be possible get accurate results. The proportions of AA+AT and TT genotype group similar to that in chapter 3 and 4. However when the group by sex and then by genotype the number were too small, especially, the proportion for TT genotype group in male population was too small and the group are not representative to general population. Regression analysis was used to examine the effect of all of these factors on BMI and to identify which one has the strongest effect. Mediation analysis was used to investigate possible mechanisms underlying the association between some of the relationships observed.

The key finding of this study is a significant relationship between alexithymia and eating behaviours; and difficulty identifying feelings subscale was associated with high BMI. The main findings are as follows:

5.5.1 TAS-20 subscales

The result of mean scores of BMI, eating behaviours and TAS-20 reported in (Table 5.1). The result of this study showed that mean scores TAS-20 observed in the study group were consistent with values previously reported (Noli *et al.* 2010, Pinaquy *et al.* 2003).

- **Influence of sex on alexithymia**

There was no difference between mean scores for alexithymia subscales when the group was split by sex (table 5.1). In agreement with this, Larsen *et al* (2006) did not observe significant sex differences on total TAS-20 scores and on the factor difficulty describing feelings and found men only scored significantly higher than women did on externally oriented thinking (Larsen *et al.* 2006). However, large-scale studies in general population samples have found that men score significantly higher than do women on the total TAS-20 scale and on the factors assessing difficulty describing feelings and externally oriented thinking (Taylor *et al.* 2003). In addition, in 2007, Moriguchi *et al*. reported that the investigation of the effect of sex on alexithymia revealed a significantly higher difficulty identifying feeling in females and external oriented thinking in males, these findings mean that females are not as good at identifying inner emotions as males, and males tend to be more externally-oriented in their thinking, there was no sex difference in difficult describing feelings scores, these sex differences on these two factors resulted in no sex difference in the total scores (Moriguchi *et al.* 2007).

- **Influence of *FTO* genotype on TAS-20 subscales.**

When the group was analysed by *FTO* genotype (Table 5.2) there was no difference in alexithymia subscales. So far, no previous study has looked at the effect of *FTO* genotype on alexithymia.

- **Influence of alexithymia on eating behaviour**

When the group was split according to total alexithymia score, approximately half of the participants were classified as alexithymic according to TAS-20 cut of 61 or more. The alexithymic people were younger than non alexithymic people, these people are attending the centre because of obesity so this implies that people with alexithymia may experience obesity earlier, as it may be that alexithymia leads to changing eating behaviour as the results show that alexithymic people have higher scores in emotional eating and uncontrolled eating and BMI than non alexithymic people. However, the effect is not significant after to Bonferroni correction as p value needs to be < 0.005 to consider as statistically significant. These results are in line with another study conducted in 2010 by Noli, *et al.*, who reported that, in people with obesity with alexithymic traits, all TFEQ scores were higher than that of their non-alexithymic counterparts, and this could suggest a relationship between alexithymia and the presence of disordered eating (Noli *et al.* 2010). The high score of emotional eating and uncontrolled eating in people with alexithymia may be associated with high BMI and the risk of getting obesity. Previous studies showed that alexithymia has been linked to obesity (Karukivi *et al.* 2016, Pinna *et al.* 2014).

5.5.2 Interactions between age and alexithymia

Regarding the relationship between age and alexithymia, the results of this study showed that age has a significant inverse relationship with difficulty identifying feelings, difficulty describing feeling and total alexithymia score, which means there is a decline in alexithymia as people get older. These results are in agreement with another study by Moriguchi *et al.* who reported that the total score of the TAS-20 is negatively correlated with age and showed that the TAS-20 total scores, difficulties in identifying and describing feelings scores were high in teenagers, decreased with age until the age of about 30 and then remained relatively unchanged (Moriguchi *et al.* 2007). Heterogeneous data have been obtained from earlier studies; one study (Bagby *et al.* 1994b) showed a low correlation between alexithymia and age ($r=-0.13$, $p < 0.01$), while other studies did not show a significant correlation (Bressi *et al.* 1996, Pandey *et al.* 1996).

- **Influence of sex and *FTO* genotype on the interaction between age and alexithymia**

The results also showed no sex effect on the relationship between age and alexithymia, but there is a genotype effect since there were significant inverse relationships between age and alexithymia only in people with AA+AT genotype group, *FTO* genotype may influence the relationships between alexthymia and other variables, but not have a direct effect on alexithymia scores as the results showed no different in alexithymia between different genotype groups.

When the female and male groups were split by genotype into two groups (TT and AA+AT) (figure 5.1) and relationships between age and alexithymia were examined,

the result showed that, in females, alexithymia declined with age in the TT genotype group only with no change in AA+AT genotype group, while in the male group alexithymia decreased with age in the TT group and increased in the AA+AT genotype group. This may mean that the AA+AT genotype is associated with low alexithymia in males only and the TT genotype associated with low alexithymia in both sexes. However, to confirm the effect of *FTO* genotype on the interaction between age and alexithymia the study needs to be conducted on a larger group.

5.5.3 Interaction between BMI and alexithymia

There was a positive relationship between BMI and difficulty identifying feeling in the overall sample. These findings were in line with another study that showed BMI was significantly and positively associated with TAS-20 scores in the adult population (Ramzi *et al*. 2018) which may mean that people with alexithymia have a risk of higher BMI and developing obesity due to difficulties in identifying their feelings. The findings suggest that treatment of obesity requires more attention, not just to the eating behaviours that people with obesity people have, but also their emotional and psychological state.. Taking this into account before any intervention will help to improve the effectiveness of weight loss strategies.

- **Influence of sex and *FTO* genotype on the interaction between BMI and alexithymia**

When the participants were split by sex, the results showed that there are positive relationships between BMI and difficulty identifying feeling and total alexithymia score in females only indicating that alexithymia is associated with high BMI in females.

When the sample was split by *FTO* genotype a significant relationship between BMI and difficult identifying feeling in AA+AT genotype group was found, which means that alexithymia is associated with high BMI in this genotype group.

FTO genotype is associated with increasing BMI and obesity (Frayling *et al.* 2007) . Variants of *FTO* affect dopamine-dependent midbrain brain responses and learning from negative outcomes in humans during a reward learning task. Furthermore, *FTO* variants modulate the connectivity in a basic reward circuit of meso-striato-prefrontal regions, suggesting a mechanism by which genetic vulnerability in reward processing can increase predisposition to obesity. Previous studies found that the DRD2/ANKK1 Taq1A polymorphism associated with alexithymia, Walter *et al* (2011) found that carriers of at least one DRD2/ANKK1 A1 allele showed the highest scores in the total Toronto Alexithymia Scale and in the subscale "Difficulties Identifying Feelings (Walter *et al.* 2011). Heni *et al* (2016) reported an interaction between variations in *FTO* and the DRD2/ANKK1 polymorphism which associates with dopamine (D2) receptor density. In cases of reduced D2 receptor availability, as indicated by the DRD2/ANKK1 polymorphism, *FTO* variation was associated with increased body fat and waist circumference and reduced peripheral insulin sensitivity. Similarly, altered central insulin sensitivity was observed in the caudate nucleus in individuals with the *FTO* obesity-risk allele and diminished D2 receptors (Heni *et al.* 2016). *FTO* and DRD2/ANKK1 TaqIA polymorphism may have a role in driving gene × environment interactions promoting obesity, metabolic dysfunction, and cognitive change by their influence on DA receptor subtype 2 (DRD2) signalling (Sun *et al.* 2017). In addition, there is an association between the COMT Val108/158Met gene polymorphism, which influences dopamine levels and alexithymia (Ham *et al.* 2005). Therefore, we

hypothesise that the *FTO* polymorphism is interacting with alexithymia via dopamine to influence BMI.

When the female and male groups were split separately by genotype into two groups (TT and AA+AT) (Figure 5.2) and the relationship between BMI and alexithymia was explored, the results showed that in females there was a relationship between total alexithymia score and BMI in AA+AT genotype groups, while in males it was correlated with low BMI in the TT genotype group and not related to BMI in the other group. In females, difficulty describing feelings associates with low BMI in the TT genotype group and high BMI in the AA+AT genotype group. In males difficulty identifying feelings associates with BMI in TT genotype group. In females, difficulty identifying feelings was related to high BMI in both genotype groups, while in males it was associated with high BMI in the AA+AT genotype group and low BMI in the other group. In females external orientation was related to low BMI in the TT group only, while in males it was associated with low BMI in AA+AT genotype groups and high BMI in the TT genotype group. However it is not possible to determine causality from these data. The number of participants in this chapter is too small and splitting them by sex and then by genotype, as we did in the previous chapter did not give good results and it is not appropriate, and this analysis needs to be conducted with large group number.

5.5.4 Interactions between uncontrolled eating and alexithymia

Considering the relationships between the eating behaviours and alexithymia, the results showed that there were positive relationships between uncontrolled eating and difficulty identifying feeling and total alexithymia score. To our knowledge no studies have previously showed any correlation between uncontrolled eating and alexithymia.

- **Influence of sex and *FTO* genotype on the interactions between uncontrolled eating and alexithymia**

When the group was split by sex, the results showed that females have stronger relationships between difficulty identifying feelings and total alexithymia and uncontrolled eating. When the group was split by genotype, there was a strong association between uncontrolled eating and external orientated thinking and total alexithymia score in people in the TT genotype group only.

5.5.5 Interaction between emotional eating and alexithymia

The results of this study showed that there were positive relationships between emotional eating and total alexithymia and alexithymia subscales. High BMI in people with alexithymia may be due to changes in their eating behaviours. These results were in agreement with other studies that showed that total alexithymia and all alexithymia subscales were positively associated with emotional eating (Pike 2013) and this corroborates the findings of previous research in clinical populations (Larsen *et al.* 2006, Pinaquy *et al.* 2003). Pinquay *et al.* suggested that alexithymia was only related to emotional eating in eating disordered populations, with their results showing a relationship between emotional eating and alexithymia only in participants with BED (Pinaquy *et al.* 2003).

It has been argued that alexithymia is related to the psychological characteristics of eating disorders rather than to eating behaviour itself (Cochrane *et al.* 1993, Taylor *et al.* 1999). However, Pike, (2013) shows that the alexithymia/emotional eating association is also applicable to non-eating disordered populations (Pike 2013). Furthermore, Pike (2013) also found that the component of alexithymia that was most

strongly associated with emotional eating was difficulty identifying feelings which were also found by Larsen et al. and Pinaquy et al. (Larsen *et al.* 2006, Pinaquy *et al.* 2003). Pike (2013) reported that finding the same relationship between the alexithymia, its components and emotional eating in a normal sample as clinical samples, points to difficulty identifying feelings as a possible underlying component of emotional eating. This finding is theoretically consistent with psychosomatic theory which emphasises the concept of interoceptive awareness. Difficulty with identifying feelings could lead to confusion between internal feelings of hunger and emotions with individuals misattributing emotions as hunger (Pike 2013).

- **Influence of sex and *FTO* genotype on the Interaction between emotional eating and alexithymia**

When the group was split by sex the results showed that females have stronger relationships between difficulty identifying feelings and total alexithymia and emotional eating compared to males. However, the relationships between emotional eating and difficulty identifying feelings, difficulty describing feelings and total alexithymia score were also stronger in people with AA+AT genotype than the TT genotype group.

In agreement with this, a previous study has found a relationship between interoceptive awareness and emotional eating among females (Van Strien *et al.* 2005). In addition, difficulty in identifying feelings has been shown to be associated with emotional eating among females with obesity with binge eating disorder, but not among those without binge eating disorder (Pinaquy *et al.* 2003). However, Larsen *et al* found sex differences in the relationship of alexithymia with emotional eating in people with obesity with men showing stronger associations between alexithymic

characteristics and emotional eating than did the women (Larsen *et al.* 2006). These findings suggest that alexithymia may influence eating behaviours leading to raised BMI, particularly in females. The results imply that interventions that address difficulties in identifying feelings may help people to maintain a healthy weight or assist in success on weight-loss programmes.

5.5.6 Interactions between cognitive restraint and alexithymia

The result showed that cognitive restraint was strongly associated with external orientation in people with TT genotype group but not in the other group. So far, no studies have examined the relationship between alexithymia and cognitive restraint and looked at the genotype effect.

5.5.7 Regression and mediation analysis

To better understand the role of age, eating behaviors and alexithymia, regression analysis was used to investigate the effect of TFEQ subscales, TAS-20 subscales and age on BMI, to investigate how all of these factors interact together and with BMI and which of these factors has the strongest effect on BMI (table 5.9). This shows that difficulty identifying feelings and age have a significant influence on BMI.

Mediation analysis was used to investigate these relationships (Figures 5.3, 5.4, 5.5 and 5.6). Figure 5.3 and 5.4 compare the male group with the female group, figures 5.5 and 5.6 compare the TT genotype group with the AA+AT genotype group and models the relationship between difficulty identifying feelings and BMI in these groups. This type of analysis can be used when there is a significant relationship between two variables, in this case difficulty identifying feelings and BMI as shown in table 5.9 If a relationship is mediated by a third variable (in this case emotional eating) this will be

evident in the significant correlations shown between the third variable and the other variables.

The mediation analysis in figures 5.3 and 5.4 for the female group shows a significant correlation between difficulty identifying feelings and BMI, and between emotional eating and uncontrolled eating and difficulty identifying feelings, demonstrating mediation by these eating behaviours. In the case of the male group, the mediating effect of emotional eating or uncontrolled eating is not present (as the correlations between difficulty identifying feelings and emotional eating or uncontrolled eating are not significant).

5.6 Strengths of the study

The strength of this study is the novel findings, as to our knowledge only a few studies looked at the association between alexithymia and eating behaviours. However, these were in clinical samples and this study is the first study to look at the effect of *FTO* genotype (the first gene associated with obesity) on alexithymia and how it influences the association between alexithymia and eating behaviour and BMI.

5.7 Limitations of the study

A limitation of this study is that it is not clinically designed; completion of the TAS-20 is self-reported and people may choose answers which reflect feelings at that point in time and how they wish things were rather than being honest. This effect may be influenced by the variables we studied including sex and BMI, potentially having a disproportionate effect on some aspects of the findings. Another limitation is that only studied one polymorphism due to time and cost limitations. Genome-wide screening of the samples may identify variants which are equally or more important in influencing the relationships studied here.

5.8 Conclusion

In conclusion this study showed strong associations between alexithymia and eating behaviours, and BMI and these relationships were influenced by sex and *FTO* genotype. Particularly in females with the AA+AT risk genotype alexithymia leads to an increase in uncontrolled eating and emotional eating and so may lead to higher BMI. Males and/or people with the TT genotype may be less at risk of this influence of alexithymia on BMI. Difficulty identifying feelings was associated with an increase in BMI, these findings will help in the treatment of obesity by informing personal intervention programmes for each person according to his or her situation and it should be considered whether the TAS-20 should be used in routine practice.

6 Chapter 6: General discussion and conclusions

6.1 General Discussion

The programme of research for the PhD was conducted with the aim of investigating the interactions between obesity associated behaviours, BMI, age, sex and *FTO* genotype. The participants for the cross-sectional study in chapter 3 were from university students and staff with a range of age groups as well as a group of participants about to start a community weight-management programme. Participants for the cross-sectional study in chapter 4 were also university students and staff with the addition of participants with obesity recruited from different obesity management centres; finally, participants in chapter 5 were only from obesity management centres.

The main finding from this programme of research is there are strong interactions between obesity-related behaviours and age, BMI, sex and *FTO* genotype. These interactions influence body weight that may lead to obesity.

6.1.1 Eating behaviours and food craving

The study of the interactions between age, BMI, eating behaviours and food cravings as discussed in Chapter 3, revealed statistically significant associations between these factors. High cognitive restraint was associated with low cravings for fatty foods, sweet foods and fast foods, high uncontrolled eating was correlated with high cravings for carbohydrates, and high emotional eating was associated with lower cravings for fatty foods and fast foods. The association between high cognitive restraint and low food craving is possibly because the people who exhibit higher restraint are trying to control their food intake by reducing the consumption of fatty and sweet food.

Kahathuduwa *et al.* reported that decreased food cravings are associated with increased fMRI-food cue reactivity in brain regions that regulate executive control over ingestion (Kahathuduwa *et al.* 2018), and with cognitive reappraisal strategies, in particular those focusing on the benefits of not eating unhealthy foods, could potentially increase the ability of individuals with obesity to inhibit appetitive motivation and reduce unhealthy food intake (Yokum and Stice 2013).

The present study found a positive relationship between cognitive restraint and BMI; previous studies showed that eating behaviours and food craving were associated with an increase in BMI and also showed that the relationship between cognitive restraint and BMI was U shaped with some people with high cognitive restraint having a high BMI and some people with high cognitive restraint having a low BMI. Westenhoefer *et al*., (1999) further divided cognitive restraint into two subscales depending on its relationships with both BMI and disinhibition or UE (Westenhoefer *et al.* 1999). The subscales were flexible control, a more relaxed version of restraint associated with both low UE and low BMI, and rigid control, a more severe restrictive state associated with both high UE and high BMI (Westenhoefer *et al.* 1999). But it is not clear whether cognitive restraint leads to increased BMI or high BMI make people want to lose weight so they restrain more. The present study showed that high cognitive restraint was associated with low food craving scores in the ≤ 25 years group. Mediation analysis demonstrated that in this group the association between BMI and reduced food cravings was mediated by cognitive restraint indicating that in this age group individuals are using cognitive restraint to control their food cravings. This may explain why in the previous study Westenhoefer *et al*., (1999) people with high cognitive restraint and high BMI tend to be people over 25 years and people with high cognitive restraint and low BMI were ≤ 25 years.

Banna *et al* (2018) reported that the association between cognitive restraint and high BMI may be explained by the overeating that may result from dietary restraint, leading to a cycle of weight gain and restriction and unsuccessful restraint that fosters storing of excess energy. Those who are overweight or obese may also be more likely to be on a diet and restricting intake for weight loss. In the current study, there may be other factors that explain the positive correlation between restrained eating and BMI. For example, the responses to the items on restrained eating may not be an accurate reflection of behaviour if overweight and obese participants considered restrained eating to be a socially acceptable means of controlling weight and responded accordingly regardless of whether they were actually behaving in this manner (Banna *et al.* 2018).

The study also showed that the *FTO* risk AA+AT genotypes were associated with high BMI and age was associated with high BMI, low emotional eating and uncontrolled eating and low food craving scores. This effect was stronger in women compared to men. In this study regression analysis showed that age, emotional eating and fast food cravings have a significant effect on BMI. The positive correlation between age and BMI is unsurprising but the findings of this study clearly show that age, sex, *FTO* genotype and BMI have an influence on eating behaviours and food cravings and that these variables interact.

People with obesity find it difficult to control their food intake which may be due to obesity related factors that are associated with increased in body weight.

A complete understanding of the association between BMI, food craving and eating behaviours and how age, sex and *FTO* genotype influence these interactions may

explain why these factors are associated with body weight and obesity as shown in previous studies. This may help in developing a good weight loss strategy that makes people aware about their eating habits and how they interact with other factors which make them more likely to put on weight.

6.1.2 Eating behaviours and behaviour regulation

The aim of chapter 4 was to examine the association between of motivation to exercise on eating behaviours. The study used the BREQ-2 questionnaire and was conducted with 320 participants from the university and 183 volunteers with obesity from obesity management centres. The analysis was conducted for the overall population, by sex, *FTO* genotype, by age (≤25 years vs > 25 years) and by BMI (<30 Kg/m^2 vs ≥30Kg/m^2).

It is well established that regular exercise plays an important role in achieving a number of health and wellbeing outcomes. However, certain post-exercise behaviours, including the consumption of unhealthy high-calorie foods, can counteract some of the benefits of physical activity. There are at least three overlapping pathways through which exercise may increase the likelihood of consuming pleasurable but unhealthy foods: through impulsive cognitive processes, reflective cognitive processes, and/or physiological responses (Dimmok *et al.* 2015). Previous studies have shown that controlled motivation to exercise was associated with increased food intake before or after exercise (Fenzl *et al*. 2014, Dimmock *et al.* 2015). The association between physical activity and motivation to exercise were showed in the previous study, people with high motivation to exercise do the physical activity regularly, this study aimed to examine the association between motivation to exercise and eating behaviours and BMI.

The present study showed significant differences in BREQ-2 subscales between people with obesity and non-obese people; non-obese people were more motivated to exercise than people with obesity with higher scores of internal regulation subscales (identified regulation and intrinsic regulation). BMI was also positively associated with high scores for internal regulation (identified regulation and intrinsic regulation) and low scores for external regulation subscales. However, it is difficult to determine cause and effect of that, maybe people with obesity lose motivation to exercise due to physical restriction or other extrinsic reasons, or may be people with low motivation to exercise don't do exercise regularly and this make them put on more weight which leads to obesity.

People with obesity who were included in this study were older than the equivalent non-obese people which could be another explanation why people with obesity were less motivated than non-obese people. The study showed that there is an inverse relationship between motivation to exercise and age; because people lose their motivation to exercise as they age due to the time constraints of having children and getting jobs or may be loss of their ability to do physical activity, and this may happen due to increases in their body weight or any other medical condition that they may have.

This study examined the interaction between eating behaviours and motivation to exercise and showed a significant association between uncontrolled eating and introjected regulation, identified regulation and intrinsic regulation. This may be due to compensatory beliefs, when people who do a lot of exercise they believe that they will lose weight due to the exercise, and so reward themselves by eating additional food, which leads to an overall increase in energy intake (Rabia *et al*. 2006).

There was also a positive relationship between emotional eating and external regulation; people with high scores for external regulation are motivated to exercise in response to prompts from friends and family rather than being intrinsically motivated. The data indicate that the relationship between emotional eating and motivation to exercise may be associated with hedonic feeding behaviours and an increase in emotional eating.

The study also found that age, sex, *FTO* genotype and BMI influenced these interactions. However, only a few studies have investigated the interaction between motivation to exercise and eating behaviours. Most of the previous studies focused on the interactions between motivation to exercise and post-exercise food intake. Werle *et al.,* (2015) reported that participants who possessed controlled forms of motivation for exercise consumed more unhealthy snacks than those possessing intrinsic regulation (Werle *et al.* 2015). Influencing one's motivation for exercise through framing a walk as 'exercise' rather than 'fun' a component of intrinsic motivation, and the most autonomous form of motivation (Deci and Ryan 1985) has also been associated with greater post-exercise food intake from hedonically pleasurable foods (Werle *et al.* 2015).

The result of the regression analysis for this study showed that age, emotional eating, external regulation, introjected regulation are associated with high BMI while identified regulation associated with low BMI. Mediation analysis showed that emotional eating may partially mediate the relationship between external regulation and high BMI in the female group, but not in males, and also in people with obesity, but not in non-obese people. These findings indicate that, particularly in women and in people with obesity, if people are not intrinsically motivated to exercise, but instead

are only externally motivated, they are more likely to engage in emotional eating, which may lead to weight gain, although it is not possible to determine cause and effect in these relationships.

The findings of this study highlight the importance of motivation to exercise and how it is associated with eating behaviours and BMI. There are only a few studies that have examined the association between motivation to exercise and eating behaviours and BMI. Future study should focus on how people's motivation to exercise influences other behaviours and any weight loss strategy should take this into account to encourage people and support them to increase their motivation to exercise.

6.1.3 Eating behaviours and alexithymia

The study of the interactions between alexithymia and eating behaviours as described in chapter 5 aimed to examine the relationships between alexithymia and eating behaviours and BMI, and also to identify the influence of age, sex and *FTO* genotype on any relationship. Alexithymia is defined as an inability to identify and describe emotions in the self (Sifneos 1996). Previous studies showed that alexithymia was associated with obesity (Clerici *et al.* 1992) eating disorders (Nowakowski *et al.* 2013b) and eating behaviours (Noli *et al.* 2010).

The study presented in chapter 5 shows that people with alexithymia had higher scores than people without alexithymia in BMI, emotional eating and uncontrolled eating but the differences were not significant after Bonferroni correction. The study also showed that age was associated with low alexithymia. This was supported by the finding that, in the study group attending obesity interventions, the average age of

people with alexithymia was younger (48.3±10.9) years than the group of people without alexithymia (55.3±15.3) years.

There were also significant positive associations between alexithymia scores and uncontrolled eating and emotional eating. There were also significant positive associations between difficulty identifying feelings and BMI. However, these associations were only seen in females and people with the AA+AT genotype. Regression analysis also showed that difficulty identifying feelings has a significant effect on increased BMI, and emotional eating and uncontrolled eating may mediate the relationship between difficulties identifying feelings and increasing BMI. These findings suggest that alexithymia may influence eating behaviours leading to raised BMI, particularly in females and people with AA+AT genotype group. A clear strength of this study is to the authors' knowledge we are the first to explore any such relationship however there is no previous literature to support or disagree with the findings.

A possible contribution to the increasing rate of adult obesity is poor emotion handling, which may negatively influence healthy behaviour and lifestyle. The results imply that interventions that address difficulties in identifying feelings may help people to maintain a healthy weight or assist in success on weight-loss programmes and the TAS-20 should be used in routine practice. Previous findings also suggest that consideration of alexithymia diagnosis may help in design of treatment strategies for morbidly obese patients (Bull *et al*.1991) since alexithymic individuals have been shown to have poorer nutritional intake and decreased immune functioning (Lumley *et al.* 2008).

6.2 Limitations of the programme of study

This body of work as part of this PhD has some limitations which mean the results need to be interpreted with caution;

- There may be demographic differences between the age groups that were chosen to split the population, younger group were mainly students. However, many of the student participants were drawn from the same geographical area as most of the older participants, so this effect may not be that strong.
- Detailed data on socio-economic status, education, marriage status or ethnicity was not collected, and these variables may influence the results which cannot be ascertained.
- The *FTO* genotype was chosen for examination as this has been reported to be the most influential gene on BMI. However; we chose to only study one polymorphism, due to time and cost limitations. Genome-wide screening of the samples may identify variants which are equally or more important in influencing the relationships studied here.
- The use of self-reported questionnaires is a limitation because people may not always be honest when answering, and the degree to which this is an issue may vary with weight status. However the reliability and validity of all the questionnaires used has been established in in the literature which goes some way to mitigate this effect.
- We did not measure physical activity levels which will form a future line of enquiry.
- The study may not be sufficiently powered to observe all the effects studied to a significant level, especially when the group is split into subgroups; the

number in each group may not be enough to confirm the effects on the variables or the relationships.

- In addition when the groups were split by sex and then by genotype, the number of participants may become too small to confirm the influence of sex or genotype, especially in the smaller TT genotype group.
- Regarding the study conducted in chapter 5, the number of participants is only 83, and when split them by sex or *FTO* genotype the number of participants in each group was too small, therefore the results cannot confirm the association or the difference between the groups, further studies should include a larger number of participants.

6.3 Strengths of the programme of study

This body of work as part of this PhD has a number of strengths;

- It was conducted on a reasonably large group of participants with a range of age groups and different body weights. These are novel findings; only a few studies have examined the association between alexithymia and eating behaviours and BMI in non-clinical populations. This study is the first study to look at the effect of *FTO* genotype on alexithymia and how it influences the association between alexithymia and eating behaviour and BMI.
- We are the first to look at the association of *FTO* genotype (The first gene associated with obesity) on motivation to exercise and how it influences the association between motivation to exercise and eating behaviour and BMI.

6.4 Future research recommendations

Future studies should be conducted:

- To determine the interaction between other behaviours related to obesity, such as food intake and exercise.

- To study more genes those are related to obesity including *MC4R* for example. Investigating a wider range of target genes would potentially reveal more information about the influence of genetics on the variables studied in future studies.

- Gather data on socio-economic status, education, marriage status or ethnicity which could also have an influence and may further influence the mediation analysis.

- Food frequency questionnaires and DEXA analysis could be incorporated into the study protocols along with measuring the physical activity levels; by using other questionnaires or the more robust way of monitoring physical activity by using objective devices such as ACTihearts.

- It is also recommended that future studies need to be conducted on larger groups to confirm the influence of genetics on the associations and variables studied here, in particular looking at other genes that may be associated with BMI according to GWAS studies.

- It is also recommended to study the association between alexithymia and eating behaviour on a larger group. Since depression has been separately associated with obesity and with alexithymia (Dehaan et al. 2012, Honkalampi et al. 2004) future studies will be needed to investigate TAS-20 score in subjects with and without depression, and specifically how this interacts with BMI status and weight change. In addition, the observation of changed individual TAS-20 score (previously considered to

reflect a stable personality trait) over the test period, raises the possibility of designing specific strategies to improve emotion-handling capacity, for inclusion in interventions for obesity or to promote healthy regulation of eating behaviours.

- Future studies regarding the association between changes in BMI/weight and emotion-processing are needed, for the direction of causality to be fully determined. To date, there has been no information in the literature exploring the phenotypic and genetic profile of alexithymia and BMI simultaneously over the life course in general populations. Mendelian randomisation and other causal studies could be conducted to determine the directions of causality between alexithymia, depression and obesity. The development of obesity in some cases may be associated with undiagnosed alexithymia. Deficits in emotion-processing should, therefore, be considered in the design of weight-management programmes.

6.5 Conclusion

In this thesis, important interactions between obesity related behaviours, age, sex, *FTO* genotype and BMI were found. Identifying these interactions may help in utilising dietary and behavioural interventions to counteract unhealthy eating behaviours along with other lifestyle interventions such as promoting physical activity and healthy living in general. The aim would be that the effect of these interactions on common obesity may be minimised, reversed or hopefully even prevented someday in the future. This paradigm should motivate researchers and health care professionals to continue act to meet the challenges posed by the global epidemic of obesity in the years to come.

7 References

ABILÉS, V., RODRÍGUEZ-RUIZ, S., ABILÉS, J., MELLADO, C., GARCÍA, A., DE LA CRUZ, A PÉREZ and FERNÁNDEZ-SANTAELLA, M.C., 2010. Psychological characteristics of morbidly obese candidates for bariatric surgery. Obesity Surgery, 20(2), pp. 161-167.

ADAMS, J., GOFFE, L., BROWN, T., LAKE, A.A., SUMMERBELL, C., WHITE, M., WRIEDEN, W. AND ADAMSON, A.J., 2015. Frequency and socio-demographic correlates of eating meals out and take-away meals at home: cross-sectional analysis of the UK national diet and nutrition survey, waves 1–4 (2008–12). International Journal of Behavioral Nutrition and Physical Activity, 12(1), p.51.

ADAN, R., TIESJEMA, B., HILLEBRAND, J., LA FLEUR, S., KAS, M. and DE KROM, M., 2006. The MC4 receptor and control of appetite. British journal of pharmacology, 149(7), pp. 815-827.

AKIYAMA, M., OKADA, Y., KANAI, M., TAKAHASHI, A., MOMOZAWA, Y., IKEDA, M., IWATA, N., IKEGAWA, S., HIRATA, M., MATSUDA, K. AND IWASAKI, M., 2017. Genome-wide association study identifies 112 new loci for body mass index in the Japanese population. Nature genetics, 49(10), p.1458.

ALBERTS, H.J., MULKENS, S., SMEETS, M. and THEWISSEN, R., 2010. Coping with food cravings. Investigating the potential of a mindfulness-based intervention. Appetite, 55(1), pp. 160-163.

ANDERSON, A.S., MARSHALL, D.W. and LEA, E.J., 2004. Shared lives-an opportunity for obesity prevention? Appetite, 43(3), pp. 327-329.

ANESTIS, M.D., SMITH, A.R., FINK, E.L. and JOINER, T.E., 2009. Dysregulated eating and distress: Examining the specific role of negative urgency in a clinical sample. Cognitive Therapy and Research, 33(4), pp. 390-397.

ANGLÉ, S., ENGBLOM, J., ERIKSSON, T., KAUTIAINEN, S., SAHA, M., LINDFORS, P., LEHTINEN, M. and RIMPELÄ, A., 2009. Three factor eating questionnaire-R18 as a measure of cognitive restraint, uncontrolled eating and emotional eating in a sample of young Finnish females. International Journal of Behavioral Nutrition and Physical Activity, 6(1), pp. 41.

ANTONINI, A., LEENDERS, K.L., REIST, H., THOMANN, R., BEER, H. and LOCHER, J., 1993. Effect of age on D2 dopamine receptors in normal human brain measured by positron emission tomography and 11C-raclopride. Archives of Neurology, 50(5), pp. 474-480.

APFELDORFER, G. and ZERMATI, J.P., 2001. Cognitive restraint in obesity. History of ideas, clinical description. Presse medicale (Paris, France : 1983), 30(32), pp. 1575-1580.

APPELHANS, B.M., FRENCH, S.A., PAGOTO, S.L. and SHERWOOD, N.E., 2016. Managing temptation in obesity treatment: A neurobehavioral model of intervention strategies. Appetite, 96, pp. 268-279.

ARAMBEPOLA, C., ALLENDER, S., EKANAYAKE, R. and FERNANDO, D., 2008. Urban living and obesity: is it independent of its population and lifestyle characteristics? Tropical medicine & international health, 13(4), pp. 448-457.

ARBINAGA IBARZÁBAL, F. and GARCÍA GARCÍA, J., 2003. Motivación para el entrenamiento con pesas en gimnasios: un estudio piloto.

AU, N. and HOLLINGSWORTH, B., 2011. Employment patterns and changes in body weight among young women. Preventive medicine, 52(5), pp. 310-316.

BAGBY, R.M., PARKER, J.D. and TAYLOR, G.J., 1994. The twenty-item Toronto Alexithymia Scale—I. Item selection and cross-validation of the factor structure. Journal of psychosomatic research, 38(1), pp. 23-32.

BAIK, J., 2013. Dopamine signaling in reward-related behaviors. Frontiers in neural circuits, 7, pp. 152.

BALL, K., BROWN, W. and CRAWFORD, D., 2002. Who does not gain weight? Prevalence and predictors of weight maintenance in young women. International journal of obesity, 26(12), pp. 1570.

BANNA, J., PANIZZA, C., BOUSHEY, C., DELP, E. AND LIM, E., 2018. Association between Cognitive Restraint, Uncontrolled Eating, Emotional Eating and BMI and the Amount of Food Wasted in Early Adolescent Girls. *Nutrients*, *10*(9), p.1279

BARNARD, N.D., NOBLE, E.P., RITCHIE, T., COHEN, J., JENKINS, D.J., TURNER-MCGRIEVY, G., GLOEDE, L., GREEN, A.A. and FERDOWSIAN, H., 2009. D2 dopamine receptor Taq1A polymorphism, body weight, and dietary intake in type 2 diabetes. Nutrition, 25(1), pp. 58-65.

BARNES, R.D., FISAK JR, B. and TANTLEFF-DUNN, S., 2010. Validation of the food thought suppression inventory. Journal of Health Psychology, 15(3), pp. 373-381.

BARNES, R.D. and WHITE, M.A., 2010. Psychometric properties of the Food Thought Suppression Inventory in men. Journal of health psychology, 15(7), pp. 1113-1120.

BASDEVANT, A., CRAPLET, C. and GUY-GRAND, B., 1993. Snacking patterns in obese French women. Appetite, 21(1), pp. 17-23.

BATRA, P., DAS, S.K., SALINARDI, T., ROBINSON, L., SALTZMAN, E., SCOTT, T., PITTAS, A.G. and ROBERTS, S.B., 2013. Relationship of cravings with weight loss and hunger. Results from a 6 month worksite weight loss intervention. Appetite, 69, pp. 1-7.

BATTERHAM, R.L. and BLOOM, S.R., 2003. The gut hormone peptide YY regulates appetite. Annals of the New York Academy of Sciences, 994(1), pp. 162-168.

BEADLE, J.N., PARADISO, S., SALERNO, A. and MCCORMICK, L.M., 2013. Alexithymia, emotional empathy, and self-regulation in anorexia nervosa. Annals of Clinical Psychiatry : Official Journal of the American Academy of Clinical Psychiatrists, 25(2), pp. 107-120.

BEFORT, C.A., NAZIR, N. and PERRI, M.G., 2012. Prevalence of obesity among adults from rural and urban areas of the United States: findings from NHANES (2005 ‐ 2008). The Journal of Rural Health, 28(4), pp. 392-397.

BEISEIGEL, J.M. and NICKOLS-RICHARDSON, S.M., 2004. Cognitive eating restraint scores are associated with body fatness but not with other measures of dieting in women. Appetite, 43(1), pp. 47-53.

BELL, L.M., BYRNE, S., THOMPSON, A., RATNAM, N., BLAIR, E., BULSARA, M., JONES, T.W. and DAVIS, E.A., 2006. Increasing body mass index z-score is continuously associated with complications of overweight in children, even in the healthy weight range. The Journal of Clinical Endocrinology & Metabolism, 92(2), pp. 517-522.

BELLO, E.P., MATEO, Y., GELMAN, D.M., NOAÍN, D., SHIN, J.H., LOW, M.J., ALVAREZ, V.A., LOVINGER, D.M. and RUBINSTEIN, M., 2011. Cocaine supersensitivity and enhanced motivation for reward in mice lacking dopamine D 2 autoreceptors. Nature neuroscience, 14(8), pp. 1033.

BENTON, D., GREENFIELD, K. and MORGAN, M., 1998. The development of the attitudes to chocolate questionnaire. Personality and Individual Differences, 24(4), pp. 513-520.

BERRIDGE, K.C., 1996. Food reward: brain substrates of wanting and liking. Neuroscience & Biobehavioral Reviews, 20(1), pp. 1-25.

BERTHOUD, H., 2007. Interactions between the “cognitive” and “metabolic” brain in the control of food intake. Physiology & Behavior, 91(5), pp. 486-498.

BERTHOUD, H. and MORRISON, C., 2008. The brain, appetite, and obesity. Annu.Rev.Psychol., 59, pp. 55-92.

BERTHOZ, S. and HILL, E.L., 2005. The validity of using self-reports to assess emotion regulation abilities in adults with autism spectrum disorder. European psychiatry, 20(3), pp. 291-298.

BIDDLE, S.J., MARKLAND, D., GILBOURNE, D., CHATZISARANTIS, N.L. and SPARKES, A.C., 2001. Research methods in sport and exercise psychology: Quantitative and qualitative issues. Journal of sports sciences, 19(10), pp. 777-809.

BLAIR, A., LEWIS, V. and BOOTH, D.A., 1990. Does emotional eating interfere with success in attempts at weight control? Appetite, 15(2), pp. 151-157.

BLUNDELL, J., GIBBONS, C., CAUDWELL, P., FINLAYSON, G. and HOPKINS, M., 2015. Appetite control and energy balance: impact of exercise. Obesity reviews, 16, pp. 67-76.

BLUNDELL, J.E. and COOLING, J., 2000. Routes to obesity: phenotypes, food choices and activity. British Journal of Nutrition, 83(S1), pp. S33-S38.

BLUNDELL, J.E. and GILLETT, A., 2001. Control of food intake in the obese. Obesity research, 9(S11), pp. 263S-270S.

BOLIN, J.H., 2014. Hayes, Andrew F.(2013). Introduction to Mediation, Moderation, and Conditional Process Analysis: A Regression‐Based Approach. New York, NY: The Guilford Press. Journal of Educational Measurement, 51(3), pp. 335-337.

BOND, M., MCDOWELL, A. and WILKINSON, J., 2001. The measurement of dietary restraint, disinhibition and hunger: an examination of the factor structure of the Three Factor Eating Questionnaire (TFEQ). International journal of obesity, 25(6), pp. 900.

BOOTH, C., SPRONK, D., GROL, M. and FOX, E., 2018. Uncontrolled eating in adolescents: The role of impulsivity and automatic approach bias for food. Appetite, 120, pp. 636-643.

BOSCHI, V., IORIO, D., MARGIOTTA, N., D'ORSI, P. and FALCONI, C., 2001. The three-factor eating questionnaire in the evaluation of eating behaviour in subjects seeking participation in a dietotherapy programme. Annals of Nutrition & Metabolism, 45(2), pp. 72-77.

BOSWELL, R.G. and KOBER, H., 2016. Food cue reactivity and craving predict eating and weight gain: a meta‐analytic review. obesity reviews, 17(2), pp. 159-177.

BRESSI, C., TAYLOR, G., PARKER, J., BRESSI, S., BRAMBILLA, V., AGUGLIA, E., ALLEGRANTI, I., BONGIORNO, A., GIBERTI, F. and BUCCA, M., 1996. Cross validation of the factor structure of the 20-item Toronto Alexithymia Scale: an Italian multicenter study. Journal of psychosomatic research, 41(6), pp. 551-559.

BREWER, R., COOK, R., CARDI, V., TREASURE, J. and BIRD, G., 2015. Emotion recognition deficits in eating disorders are explained by co-occurring alexithymia. Royal Society open science, 2(1), pp. 140382.

BROBERGER, C., 2005. Brain regulation of food intake and appetite: molecules and networks. Journal of internal medicine, 258(4), pp. 301-327.

BROWNELL, K.D. and HORGEN, K.B., 2004. Food fight: The inside story of the food industry, America's obesity crisis, and what we can do about it. Contemporary books Chicago, IL.

BRUCH, H., 1974. Eating disorders. Obesity, anorexia nervosa, and the person within. Routledge & Kegan Paul.

BRUCH, H., 1973. Eating disorders. Obesity, anorexia and the person within. New York. Basic Books, 357.

BRUCH, H., 1962. Perceptual and conceptual disturbances in anorexia nervosa. Psychosomatic medicine, 24(2), pp. 187-194.

BRUINSMA, K. and TAREN, D.L., 1999. Chocolate: food or drug? Journal of the American Dietetic Association, 99(10), pp. 1249-1256.

BRUNER, M.W., LAWSON, J., PICKETT, W., BOYCE, W. and JANSSEN, I., 2008. Rural Canadian adolescents are more likely to be obese compared with urban adolescents. International Journal of Pediatric Obesity, 3(4), pp. 205-211.

BRUNKWALL, L., ERICSON, U., HELLSTRAND, S., GULLBERG, B., ORHO-MELANDER, M. and SONESTEDT, E., 2013. Genetic variation in the fat mass and obesity-associated gene (FTO) in association with food preferences in healthy adults. Food & nutrition research, 57(1), pp. 20028.

BUCHER, T., COLLINS, C., ROLLO, M.E., MCCAFFREY, T.A., DE VLIEGER, N., VAN DER BEND, D., TRUBY, H. AND PEREZ-CUETO, F.J., 2016. Nudging consumers towards healthier choices: a systematic review of positional influences on food choice. British Journal of Nutrition, 115(12), pp.2252-2263.

BULL, R.H. AND LEGORRETA, G., 1991. Outcome of gastric surgery for morbid obesity: weight changes and personality traits. Psychotherapy and psychosomatics, 56(3), pp.146-156.

BURTON, P., SMIT, H.J. and LIGHTOWLER, H.J., 2007. The influence of restrained and external eating patterns on overeating. Appetite, 49(1), pp. 191-197.

CAI, G., COLE, S.A., BUTTE, N., BACINO, C., DIEGO, V., TAN, K., GÖRING, H.H., O'RAHILLY, S., FAROOQI, I.S. and COMUZZIE, A.G., 2006. A quantitative trait locus on chromosome 18q for physical activity and dietary intake in Hispanic children. Obesity, 14(9), pp. 1596-1604.

CALLE, E.E., THUN, M.J., PETRELLI, J.M., RODRIGUEZ, C. and HEATH JR, C.W., 1999. Body-mass index and mortality in a prospective cohort of US adults. New England Journal of Medicine, 341(15), pp. 1097-1105.

CAMILLERI, G.M., MÉJEAN, C., KESSE-GUYOT, E., ANDREEVA, V.A., BELLISLE, F., HERCBERG, S. and PÉNEAU, S., 2014. The Associations between Emotional Eating and

Consumption of Energy-Dense Snack Foods Are Modified by Sex and Depressive Symptomatology, 2. The Journal of nutrition, 144(8), pp. 1264-1273.

CANETTI, L., BERRY, E.M. and ELIZUR, Y., 2009. Psychosocial predictors of weight loss and psychological adjustment following bariatric surgery and a weight‐loss program: The mediating role of emotional eating. International Journal of Eating Disorders, 42(2), pp. 109-117.

CAPPELLERI, J., BUSHMAKIN, A., GERBER, R., LEIDY, N., SEXTON, C., LOWE, M. and KARLSSON, J., 2009. Psychometric analysis of the Three-Factor Eating Questionnaire-R21: results from a large diverse sample of obese and non-obese participants. International journal of obesity, 33(6), pp. 611.

CAPPELLERI, J.C., BUSHMAKIN, A.G., GERBER, R.A., LEIDY, N.K., SEXTON, C.C., KARLSSON, J. and LOWE, M.R., 2009. Evaluating the Power of Food Scale in obese subjects and a general sample of individuals: development and measurement properties. International journal of obesity, 33(8), pp. 913.

CARTWRIGHT, F. and STRITZKE, W.G., 2008. A multidimensional ambivalence model of chocolate craving: construct validity and associations with chocolate consumption and disordered eating. Eating Behaviors, 9(1), pp. 1-12.

CASPI, C.E., SORENSEN, G., SUBRAMANIAN, S.V. AND KAWACHI, I., 2012. The local food environment and diet: a systematic review. Health & place, 18(5), pp.1172-1187.

CECIL, J.E., TAVENDALE, R., WATT, P., HETHERINGTON, M.M. and PALMER, C.N., 2008. An obesity-associated FTO gene variant and increased energy intake in children. New England Journal of Medicine, 359(24), pp. 2558-2566.

CECIL, J., DALTON, M., FINLAYSON, G., BLUNDELL, J., HETHERINGTON, M. and PALMER, C., 2012. Obesity and eating behaviour in children and adolescents: contribution of common gene polymorphisms, .

CEPEDA-BENITO, A., FERNANDEZ, M.C. and MORENO, S., 2003. Relationship of gender and eating disorder symptoms to reported cravings for food: construct validation of state and trait craving questionnaires in Spanish. Appetite, 40(1), pp. 47-54.

CEPEDA-BENITO, A., GLEAVES, D.H., WILLIAMS, T.L. and ERATH, S.A., 2000. The development and validation of the state and trait food-cravings questionnaires. Behavior therapy, 31(1), pp. 151-173.

CHANTAL, Y., GUAY, F., DOBREVA-MARTINOVA, T. and VALLERAND, R.J., 1996. Motivation and elite performance: An exploratory investigation with Bulgarian athletes.

CHAO, A., GRILO, C.M., WHITE, M.A. and SINHA, R., 2014. Food cravings, food intake, and weight status in a community-based sample. Eating Behaviors, 15(3), pp. 478-482.

CHEARSKUL, S., PUMMOUNG, S., VONGSAIYAT, S., JANYACHAILERT, P. and PHATTHARAYUTTAWAT, S., 2010. Thai version of three-factor eating questionnaire. Appetite, 54(2), pp. 410-413.

CHERPITEL, C.J., BORGES, G., YE, Y., BOND, J., CREMONTE, M., MOSKALEWICZ, J. and SWIATKIEWICZ, G., 2010. Performance of a craving criterion in DSM alcohol use disorders. Journal of studies on alcohol and drugs, 71(5), pp. 674-684.

CHEUNG, C.C., CLIFTON, D.K. and STEINER, R.A., 1997. Proopiomelanocortin neurons are direct targets for leptin in the hypothalamus. Endocrinology, 138(10), pp. 4489-4492.

CHEUNG, W.W. and MAO, P., 2012. Recent advances in obesity: genetics and beyond. ISRN endocrinology, 2012.

CHUANG, Y., TANAKA, T., BEASON-HELD, L.L., AN, Y., TERRACCIANO, A., SUTIN, A.R., KRAUT, M., SINGLETON, A.B., RESNICK, S.M. and THAMBISETTY, M., 2015. FTO genotype and aging: pleiotropic longitudinal effects on adiposity, brain function, impulsivity and diet. Molecular psychiatry, 20(1), pp. 140.

CHURCH, C., LEE, S., BAGG, E.A., MCTAGGART, J.S., DEACON, R., GERKEN, T., LEE, A., MOIR, L., MECINOVIĆ, J. and QUWAILID, M.M., 2009. A mouse model for the metabolic effects of the human fat mass and obesity associated FTO gene. PLoS genetics, 5(8), pp. e1000599.

CHURCH, C., MOIR, L., MCMURRAY, F., GIRARD, C., BANKS, G.T., TEBOUL, L., WELLS, S., BRÜNING, J.C., NOLAN, P.M. and ASHCROFT, F.M., 2010. Overexpression of Fto leads to increased food intake and results in obesity. Nature genetics, 42(12), pp. 1086.

CLEOBURY, L. and TAPPER, K., 2014. Reasons for eating 'unhealthy'snacks in overweight and obese males and females. Journal of Human Nutrition and Dietetics, 27(4), pp. 333-341.

CLERICI, M., ALBONETTI, S., PAPA, R., PENATI, G. and INVERNIZZI, G., 1992. Alexithymia and obesity. Study of the impaired symbolic function by the Rorschach test. Psychotherapy and psychosomatics, 57(3), pp. 88-93.

COBB, L.K., APPEL, L.J., FRANCO, M., JONES-SMITH, J.C., NUR, A. AND ANDERSON, C.A., 2015. The relationship of the local food environment with obesity: a systematic review of methods, study quality, and results. Obesity, 23(7), pp.1331-1344.

COCHRANE, C.E., BREWERTON, T.D., WILSON, D.B. and HODGES, E.L., 1993. Alexithymia in the eating disorders. International Journal of Eating Disorders, 14(2), pp. 219-222.

COHEN, P., WEST, S.G. and AIKEN, L.S., 2014. Applied multiple regression/correlation analysis for the behavioral sciences. Psychology Press.

COOPER, M.J., 2005. Cognitive theory in anorexia nervosa and bulimia nervosa: Progress, development and future directions. Clinical psychology review, 25(4), pp. 511-531.

CORNELIS, M.C., RIMM, E.B., CURHAN, G.C., KRAFT, P., HUNTER, D.J., HU, F.B. and VAN DAM, R.M., 2014. Obesity susceptibility loci and uncontrolled eating, emotional eating and cognitive restraint behaviors in men and women. Obesity, 22(5), pp. E135-E141.

CORSTORPHINE, E., 2006. Cognitive–emotional–behavioural therapy for the eating disorders: Working with beliefs about emotions. European Eating Disorders Review: The Professional Journal of the Eating Disorders Association, 14(6), pp. 448-461.

COURTY, A., GODART, N., LALANNE, C. and BERTHOZ, S., 2015. Alexithymia, a compounding factor for eating and social avoidance symptoms in anorexia nervosa. Comprehensive psychiatry, 56, pp. 217-228.

CROWLEY, N.M., LEPAGE, M.L., GOLDMAN, R.L., O'NEIL, P.M., BORCKARDT, J.J. and BYRNE, T.K., 2012. The food craving questionnaire-trait in a bariatric surgery seeking population and ability to predict post-surgery weight loss at six months. Eating Behaviors, 13(4), pp. 366-370.

CUMMINGS, D.E., 2006. Ghrelin and the short-and long-term regulation of appetite and body weight. Physiology & Behavior, 89(1), pp. 71-84.

CURRIE, P.J., COIRO, C.D., NIYOMCHAI, T., LIRA, A. and FARAHMAND, F., 2002. Hypothalamic paraventricular 5-hydroxytryptamine: receptor-specific inhibition of NPY-stimulated eating and energy metabolism. Pharmacology Biochemistry and Behavior, 71(4), pp. 709-716.

CUSHING, C.C., BENOIT, S.C., PEUGH, J.L., REITER-PURTILL, J., INGE, T.H. and ZELLER, M.H., 2014. Longitudinal trends in hedonic hunger after Roux-en-Y gastric bypass in adolescents. Surgery for Obesity and Related Diseases, 10(1), pp. 125-130.

DANG, L.C., SAMANEZ-LARKIN, G.R., SMITH, C.T., CASTRELLON, J.J., PERKINS, S.F., COWAN, R.L., CLAASSEN, D.O. and ZALD, D.H., 2018. FTO affects food cravings and interacts with age to influence age-related decline in food cravings. Physiology & Behavior, 192, pp. 188-193.

DAS, U.N., 2010. Obesity: genes, brain, gut, and environment. Nutrition, 26(5), pp. 459-473.

DE BERARDIS, D., CARANO, A., GAMBI, F., CAMPANELLA, D., GIANNETTI, P., CECI, A., MANCINI, E., LA ROVERE, R., CICCONETTI, A. and PENNA, L., 2007. Alexithymia and its relationships with body checking and body image in a non-clinical female sample. Eating Behaviors, 8(3), pp. 296-304.

DE CASTRO, J.M., 2002. Independence of heritable influences on the food intake of free-living humans. Nutrition, 18(1), pp. 11-16.

DE CASTRO, J.M., 1993. Genetic influences on daily intake and meal patterns of humans. Physiology & Behavior, 53(4), pp. 777-782.

DE GROOT, J.M., RODIN, G. and OLMSTED, M.P., 1995. Alexithymia, depression, and treatment outcome in bulimia nervosa. Comprehensive psychiatry, 36(1), pp. 53-60.

DE LAUZON-GUILLAIN, B., BASDEVANT, A., ROMON, M., KARLSSON, J., BORYS, J., CHARLES, M.A. and FLVS STUDY GROUP, 2006. Is restrained eating a risk factor for weight gain in a general population?–. The American Journal of Clinical Nutrition, 83(1), pp. 132-138.

DE WITT HUBERTS, JESSIE C, EVERS, C. and DE RIDDER, D.T., 2014. "Because I Am Worth It" a theoretical framework and empirical review of a justification-based account of self-regulation failure. Personality and Social Psychology Review, 18(2), pp. 119-138.

DE ZWAAN, M., MITCHELL, J.E., SEIM, H.C., SPECKER, S.M., PYLE, R.L., RAYMOND, N.C. and CROSBY, R.B., 1994. Eating related and general psychopathology in obese females with binge eating disorder. International Journal of Eating Disorders, 15(1), pp. 43-52.

DE ZWAAN, M., BACH, M., MITCHELL, J.E., ACKARD, D., SPECKER, S.M., PYLE, R.L. and PAKESCH, G., 1995. Alexithymia, obesity, and binge eating disorder. International Journal of Eating Disorders, 17(2), pp. 135-140.

DECI, E.L. and RYAN, R.M., 1985. The general causality orientations scale: Self-determination in personality. Journal of research in personality, 19(2), pp. 109-134.

DEMOS, K.E., HEATHERTON, T.F. and KELLEY, W.M., 2012. Individual differences in nucleus accumbens activity to food and sexual images predict weight gain and sexual behavior. The Journal of neuroscience : the official journal of the Society for Neuroscience, 32(16), pp. 5549-5552.

DE HAAN, H., JOOSTEN, E., WIJDEVELD, T., BOSWINKEL, P., VAN DER PALEN, J. AND DE JONG, C., 2012. Alexithymia is not a stable personality trait in patients with substance use disorders. Psychiatry research, *198*(1), pp.123-129.

DEN HOED, M., WESTERTERP-PLANTENGA, M.S., BOUWMAN, F.G., MARIMAN, E.C. and WESTERTERP, K.R., 2009. Postprandial responses in hunger and satiety are associated with the rs9939609 single nucleotide polymorphism in FTO–. The American Journal of Clinical Nutrition, 90(5), pp. 1426-1432.

DI CHIARA, G. and BASSAREO, V., 2007. Reward system and addiction: what dopamine does and doesn't do. Current opinion in pharmacology, 7(1), pp. 69-76.

DIETRICH, A., FEDERBUSCH, M., GRELLMANN, C., VILLRINGER, A. and HORSTMANN, A., 2014. Body weight status, eating behavior, sensitivity to reward/punishment, and gender: relationships and interdependencies. Frontiers in psychology, 5, pp. 1073.

DIMMOCK, J.A., GUELFI, K.J., WEST, J.S., MASIH, T. and JACKSON, B., 2015. Does motivation for exercise influence post-exercise snacking behavior? Nutrients, 7(6), pp. 4804-4816.

DINA, C., MEYRE, D., GALLINA, S., DURAND, E., KÖRNER, A., JACOBSON, P., CARLSSON, L.M., KIESS, W., VATIN, V. and LECOEUR, C., 2007. Variation in FTO contributes to childhood obesity and severe adult obesity. Nature genetics, 39(6), pp. 724.

DOBBS, R., SAWERS, C., THOMPSON, F., MANYIKA, J., WOETZEL, J., CHILD, P., MCKENNA, S. AND SPATHAROU, A., 2014. How the world could better fight obesity. McKinsey Global Institute.

DRAPEAU, V., PROVENCHER, V., LEMIEUX, S., DESPRÉS, J., BOUCHARD, C. and TREMBLAY, A., 2003. Do 6-y changes in eating behaviors predict changes in body weight? Results from the Quebec Family Study. International journal of obesity, 27(7), pp. 808.

ELFHAG, K. and LINNÉ, Y., 2005. Gender differences in associations of eating pathology between mothers and their adolescent offspring. Obesity research, 13(6), pp. 1070-1076.

ELFHAG, K. and LUNDH, L., 2007. TAS‐20 alexithymia in obesity, and its links to personality. Scandinavian Journal of Psychology, 48(5), pp. 391-398.

ELFHAG, K. and RÖSSNER, S., 2005. Who succeeds in maintaining weight loss? A conceptual review of factors associated with weight loss maintenance and weight regain. Obesity reviews, 6(1), pp. 67-85.

FAIRBURN, C.G. and COOPER, P.J., 1982. Self-induced vomiting and bulimia nervosa: an undetected problem. British medical journal (Clinical research ed.), 284(6323), pp. 1153-1155.

FEDOROFF, I.D., POLIVY, J. and HERMAN, C.P., 1997. The effect of pre-exposure to food cues on the eating behavior of restrained and unrestrained eaters. Appetite, 28(1), pp. 33-47.

FENZL, N., BARTSCH, K. and KOENIGSTORFER, J., 2014. Labeling exercise fat-burning increases post-exercise food consumption in self-imposed exercisers. Appetite, 81, pp. 1-7.

FERRIDAY, D. and BRUNSTROM, J., 2011. 'I just can't help myself': effects of food-cue exposure in overweight and lean individuals. International journal of obesity, 35(1), pp. 142.

FESTINGER, L., 1957. A theory of cognitive dissonance: Stanford Univ Pr. Fornell, C., & Larcker, DF (1981).Evaluating structural equation models with, .

FINLAYSON, G., CAUDWELL, P., GIBBONS, C., HOPKINS, M., KING, N. and BLUNDELL, J., 2011. Low fat loss response after medium-term supervised exercise in obese is associated with exercise-induced increase in food reward. Journal of obesity, 2011, pp. 10.1155/2011/615624. Epub 2010 Sep 20.

FINUCANE, M.M., STEVENS, G.A., COWAN, M.J., DANAEI, G., LIN, J.K., PACIOREK, C.J., SINGH, G.M., GUTIERREZ, H.R., LU, Y. and BAHALIM, A.N., 2011. National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9· 1 million participants. The Lancet, 377(9765), pp. 557-567.

FISCHER, J., KOCH, L., EMMERLING, C., VIERKOTTEN, J., PETERS, T., BRÜNING, J.C. and RÜTHER, U., 2009. Inactivation of the Fto gene protects from obesity. Nature, 458(7240), pp. 894.

FISHBACH, A. and SHAH, J.Y., 2006. Self-control in action: implicit dispositions toward goals and away from temptations. Journal of personality and social psychology, 90(5), pp. 820.

FISHER, E.B., FITZGIBBON, M.L., GLASGOW, R.E., HAIRE-JOSHU, D., HAYMAN, L.L., KAPLAN, R.M., NANNEY, M.S. and OCKENE, J.K., 2011. Behavior matters. American Journal of Preventive Medicine, 40(5), pp. e15-e30.

FLEURBAIX LAVENTIE VILLE SANTE (FLVS) STUDY GROUP BLANDINE DE LAUZON DELAUZON@ VJF. INSERM. FR ROMON MONIQUE DESCHAMPS VALÉRIE LAFAY LIONEL BORYS JEAN-MICHEL KARLSSON JAN DUCIMETIÈRE PIERRE CHARLES M. ALINE, 2004. The Three-Factor Eating Questionnaire-R18 is able to distinguish among different eating patterns in a general population. The Journal of nutrition, 134(9), pp. 2372-2380.

FORMAN, E.M., HOFFMAN, K.L., JUARASCIO, A.S., BUTRYN, M.L. and HERBERT, J.D., 2013. Comparison of acceptance-based and standard cognitive-based coping strategies for craving sweets in overweight and obese women. Eating Behaviors, 14(1), pp. 64-68.

FORTIER, M.S., VALLERAND, R.J., BRIERE, N.M. and PROVENCHER, P.J., 1995. Competitive and recreational sport structures and gender: A test of their relationship with sport motivation. International journal of sport psychology, 26, pp. 24-24.

FRANCO ADAMI, G., CAMPOSTANO, A., RAVERA, G., LEGGIERI, M. and SCOPINARO, N., 2001. Alexithymia and body weight in obese patients. Behavioral Medicine, 27(3), pp. 121-126.

FRANK, S., LAHARNAR, N., KULLMANN, S., VEIT, R., CANOVA, C., HEGNER, Y.L., FRITSCHE, A. and PREISSL, H., 2010. Processing of food pictures: influence of hunger, gender and calorie content. Brain research, 1350, pp. 159-166.

FRAYLING, T.M., TIMPSON, N.J., WEEDON, M.N., ZEGGINI, E., FREATHY, R.M., LINDGREN, C.M., PERRY, J.R., ELLIOTT, K.S., LANGO, H., RAYNER, N.W., SHIELDS, B., HARRIES, L.W., BARRETT, J.C., ELLARD, S., GROVES, C.J., KNIGHT, B., PATCH, A.M., NESS, A.R., EBRAHIM, S., LAWLOR, D.A., RING, S.M., BEN-SHLOMO, Y., JARVELIN, M.R., SOVIO, U., BENNETT, A.J., MELZER, D., FERRUCCI, L., LOOS, R.J., BARROSO, I., WAREHAM, N.J., KARPE, F., OWEN, K.R., CARDON, L.R., WALKER, M., HITMAN, G.A., PALMER, C.N., DONEY, A.S., MORRIS, A.D., SMITH, G.D., HATTERSLEY, A.T. and MCCARTHY, M.I., 2007. A common variant in the FTO gene is associated with body mass index and predisposes to childhood and adult obesity. Science (New York, N.Y.), 316(5826), pp. 889-894.

FREEDMAN, M., 1998. Iodine-123-Iodobenzofuran SPECT. J Nucl Med, 39, pp. 1511-1518.

FRENCH, S.A., EPSTEIN, L.H., JEFFERY, R.W., BLUNDELL, J.E. and WARDLE, J., 2012. Eating behavior dimensions. Associations with energy intake and body weight. A review. Appetite, 59(2), pp. 541-549.

FREWEN, P.A., DOZOIS, D.J., NEUFELD, R.W. and LANIUS, R.A., 2008. Meta‐analysis of alexithymia in posttraumatic stress disorder. Journal of Traumatic Stress: Official Publication of The International Society for Traumatic Stress Studies, 21(2), pp. 243-246.

GANLEY, R.M., 1988. Emotional eating and how it relates to dietary restraint, disinhibition, and perceived hunger. International Journal of Eating Disorders, 7(5), pp. 635-647.

GARFIELD, A.S. and HEISLER, L.K., 2009. Pharmacological targeting of the serotonergic system for the treatment of obesity. The Journal of physiology, 587(1), pp. 49-60.

GAST, J., MADANAT, H. and NIELSON, A.C., 2012. Are men more intuitive when it comes to eating and physical activity? American journal of men's health, 6(2), pp. 164-171.

GAST, J., NIELSON, A.C., HUNT, A. and LEIKER, J.J., 2015. Intuitive eating: associations with physical activity motivation and BMI. American Journal of Health Promotion, 29(3), pp. e91-e99.

GELIEBTER, A. and AVERSA, A., 2003. Emotional eating in overweight, normal weight, and underweight individuals. Eating Behaviors, 3(4), pp. 341-347.

GERKEN, T., GIRARD, C.A., TUNG, Y.C., WEBBY, C.J., SAUDEK, V., HEWITSON, K.S., YEO, G.S., MCDONOUGH, M.A., CUNLIFFE, S., MCNEILL, L.A., GALVANOVSKIS, J., RORSMAN,

P., ROBINS, P., PRIEUR, X., COLL, A.P., MA, M., JOVANOVIC, Z., FAROOQI, I.S., SEDGWICK, B., BARROSO, I., LINDAHL, T., PONTING, C.P., ASHCROFT, F.M., O'RAHILLY, S. and SCHOFIELD, C.J., 2007. The obesity-associated FTO gene encodes a 2-oxoglutarate-dependent nucleic acid demethylase. Science (New York, N.Y.), 318(5855), pp. 1469-1472.

GIBSON, E.L., 2001. Learning in the development of food craving. Food Cravings and Addiction.Leatherhead Publishing: Leatherhead, , pp. 193-234.

GILHOOLY, C., DAS, S., GOLDEN, J., MCCRORY, M., DALLAL, G., SALTZMAN, E., KRAMER, F. and ROBERTS, S., 2007. Food cravings and energy regulation: the characteristics of craved foods and their relationship with eating behaviors and weight change during 6 months of dietary energy restriction. International journal of obesity, 31(12), pp. 1849.

GRABE, H.J., SCHWAHN, C., BARNOW, S., SPITZER, C., JOHN, U., FREYBERGER, H.J., SCHMINKE, U., FELIX, S. and VÖLZKE, H., 2010. Alexithymia, hypertension, and subclinical atherosclerosis in the general population. Journal of psychosomatic research, 68(2), pp. 139-147.

GRAMAGLIA, C., RESSICO, F., GAMBARO, E., PALAZZOLO, A., MAZZARINO, M., BERT, F., SILIQUINI, R. and ZEPPEGNO, P., 2016. Alexithymia, empathy, emotion identification and social inference in anorexia nervosa: A case-control study. Eating Behaviors, 22, pp. 46-50.

GRANT, S.F., LI, M., BRADFIELD, J.P., KIM, C.E., ANNAIAH, K., SANTA, E., GLESSNER, J.T., CASALUNOVO, T., FRACKELTON, E.C. and OTIENO, F.G., 2008. Association analysis of the FTO gene with obesity in children of Caucasian and African ancestry reveals a common tagging SNP. PloS one, 3(3), pp. e1746.

GRIMM, E.R. and STEINLE, N.I., 2011. Genetics of eating behavior: established and emerging concepts. Nutrition reviews, 69(1), pp. 52-60.

HAGGER, M.S. and CHATZISARANTIS, N.L., 2007. Intrinsic motivation and self-determination in exercise and sport. Human Kinetics.

HAINER, V., KUNESOVA, M., BELLISLE, F., PARIZKOVA, J., BRAUNEROVA, R., WAGENKNECHT, M., LAJKA, J., HILL, M. and STUNKARD, A., 2006. The Eating Inventory, body adiposity and prevalence of diseases in a quota sample of Czech adults. International journal of obesity, 30(5), pp. 830.

HAKANEN, M., RAITAKARI, O.T., LEHTIMÄKI, T., PELTONEN, N., PAHKALA, K., SILLANMÄKI, L., LAGSTRÖM, H., VIIKARI, J., SIMELL, O. and RÖNNEMAA, T., 2009. FTO genotype is associated with body mass index after the age of seven years but not with energy intake or leisure-time physical activity. The Journal of Clinical Endocrinology & Metabolism, 94(4), pp. 1281-1287.

HALAAS, J.L., GAJIWALA, K.S., MAFFEI, M., COHEN, S.L., CHAIT, B.T., RABINOWITZ, D., LALLONE, R.L., BURLEY, S.K. and FRIEDMAN, J.M., 1995. Weight-reducing effects of the plasma protein encoded by the obese gene. Science (New York, N.Y.), 269(5223), pp. 543-546.

HALL, K.D., HEYMSFIELD, S.B., KEMNITZ, J.W., KLEIN, S., SCHOELLER, D.A. and SPEAKMAN, J.R., 2012. Energy balance and its components: implications for body weight regulation–. The American Journal of Clinical Nutrition, 95(4), pp. 989-994.

HALLAM, J., BOSWELL, R.G., DEVITO, E.E. and KOBER, H., 2016. Gender-related Differences in Food Craving and Obesity. The Yale journal of biology and medicine, 89(2), pp. 161-173.

HAM, B.J., LEE, M.S., LEE, Y.M., KIM, M.K., CHOI, M.J., OH, K.S., JUNG, H.Y., LYOO, I.K. and CHOI, I.G., 2005. Association between the catechol O-methyltransferase Val108/158Met polymorphism and alexithymia. Neuropsychobiology, 52(3), pp. 151-154.

HARBRON, J., VAN DER MERWE, L., ZAAHL, M.G., KOTZE, M.J. and SENEKAL, M., 2014. Fat mass and obesity-associated (FTO) gene polymorphisms are associated with physical activity, food intake, eating behaviors, psychological health, and modeled change in body mass index in overweight/obese Caucasian adults. Nutrients, 6(8), pp. 3130-3152.

HARRIS, J.L., POMERANZ, J.L., LOBSTEIN, T. and BROWNELL, K.D., 2009. A crisis in the marketplace: how food marketing contributes to childhood obesity and what can be done. Annual Review of Public Health, 30, pp. 211-225.

HARVEY, J., WING, R.R. and MULLEN, M., 1993. Effects on food cravings of a very low calorie diet or a balanced, low calorie diet. Appetite, 21(2), pp. 105-115.

HASSELBALCH, A.L., ANGQUIST, L., CHRISTIANSEN, L., HEITMANN, B.L., KYVIK, K.O. and SØRENSEN, T.I., 2010. A Variant in the Fat Mass and Obesity-Associated Gene (FTO) and Variants near the Melanocortin-4 Receptor Gene (MC4R) Do Not Influence Dietary Intake–3. The Journal of nutrition, 140(4), pp. 831-834.

HASSELBALCH, A.L., HEITMANN, B.L., KYVIK, K.O. and SØRENSEN, T.I., 2008. Studies of twins indicate that genetics influence dietary intake. The Journal of nutrition, 138(12), pp. 2406-2412.

HAUPT, A., THAMER, C., STAIGER, H., TSCHRITTER, O., KIRCHHOFF, K., MACHICAO, F., HAERING, H., STEFAN, N. and FRITSCHE, A., 2009. Variation in the FTO gene influences food intake but not energy expenditure. Experimental and Clinical Endocrinology & Diabetes, 117(04), pp. 194-197.

HAUTALA, L.A., JUNNILA, J., HELENIUS, H., VÄÄNÄNEN, A., LIUKSILA, P., RÄIHÄ, H., VÄLIMÄKI, M. and SAARIJÄRVI, S., 2008. Towards understanding gender differences in

disordered eating among adolescents. Journal of Clinical Nursing, 17(13), pp. 1803-1813.

HAYES, A.F. and PREACHER, K.J., 2014. Statistical mediation analysis with a multicategorical independent variable. British Journal of Mathematical and Statistical Psychology, 67(3), pp. 451-470.

HEISLER, L.K., JOBST, E.E., SUTTON, G.M., ZHOU, L., BOROK, E., THORNTON-JONES, Z., LIU, H.Y., ZIGMAN, J.M., BALTHASAR, N. and KISHI, T., 2006. Serotonin reciprocally regulates melanocortin neurons to modulate food intake. Neuron, 51(2), pp. 239-249.

HENI, M., KULLMANN, S., AHLQVIST, E., WAGNER, R., MACHICAO, F., STAIGER, H., HÄRING, H., ALMGREN, P., GROOP, L.C. and SMALL, D.M., 2016. Interaction between the obesity-risk gene FTO and the dopamine D2 receptor gene ANKK1/TaqIA on insulin sensitivity. Diabetologia, 59(12), pp. 2622-2631.

HERMAN, C.P. and MACK, D., 1975. Restrained and unrestrained eating 1. Journal of personality, 43(4), pp. 647-660.

HERRERA, B.M., KEILDSON, S. and LINDGREN, C.M., 2011. Genetics and epigenetics of obesity. Maturitas, 69(1), pp. 41-49.

HESS, M.E., HESS, S., MEYER, K.D., VERHAGEN, L.A., KOCH, L., BRÖNNEKE, H.S., DIETRICH, M.O., JORDAN, S.D., SALETORE, Y. and ELEMENTO, O., 2013. The fat mass and obesity associated gene (Fto) regulates activity of the dopaminergic midbrain circuitry. Nature neuroscience, 16(8), pp. 1042.

HETHERINGTON, M.M. and MACDIARMID, J.I., 1993. " Chocolate addiction": A preliminary study of its description and its relationship to problem eating. Appetite, .

HILL, A.J., 2007. The psychology of food craving*: Symposium on 'Molecular mechanisms and psychology of food intake'. Proceedings of the Nutrition Society, 66(2), pp. 277-285.

HILL, A.J. and HEATON-BROWN, L., 1994. The experience of food craving: a prospective investigation in healthy women. Journal of psychosomatic research, 38(8), pp. 801-814.

HILL, A.J., WEAVER, C.F. and BLUNDELL, J.E., 1991. Food craving, dietary restraint and mood. Appetite, 17(3), pp. 187-197.

HOFKER, M. and WIJMENGA, C., 2009. A supersized list of obesity genes. Nature genetics, 41(2), pp. 139.

HONKANEN, P., OLSEN, S.O., VERPLANKEN, B. and TUU, H.H., 2012. Reflective and impulsive influences on unhealthy snacking. The moderating effects of food related self-control. Appetite, 58(2), pp. 616-622.

HONKALAMPI, K., KOIVUMAA-HONKANEN, H., ANTIKAINEN, R., HAATAINEN, K., HINTIKKA, J. AND VIINAMÄKI, H., 2004. Relationships among alexithymia, adverse childhood experiences, sociodemographic variables, and actual mood disorder: a 2-year clinical follow-up study of patients with major depressive disorder. psychosomatics, *45*(3), pp.197-204.

HORSTMANN, A., KOVACS, P., KABISCH, S., BOETTCHER, Y., SCHLOEGL, H., TÖNJES, A., STUMVOLL, M., PLEGER, B. and VILLRINGER, A., 2013. Common genetic variation near MC4R has a sex-specific impact on human brain structure and eating behavior. PLoS One, 8(9), pp. e74362.

HOTTA, K., NAKATA, Y., MATSUO, T., KAMOHARA, S., KOTANI, K., KOMATSU, R., ITOH, N., MINEO, I., WADA, J. and MASUZAKI, H., 2008. Variations in the FTO gene are associated with severe obesity in the Japanese. Journal of human genetics, 53(6), pp. 546.

HUANG, T., QI, Q., LI, Y., HU, F.B., BRAY, G.A., SACKS, F.M., WILLIAMSON, D.A. and QI, L., 2014. FTO genotype, dietary protein, and change in appetite: the Preventing Overweight Using Novel Dietary Strategies trial–. The American Journal of Clinical Nutrition, 99(5), pp. 1126-1130.

HUBACEK, J.A., STANĚK, V., GEBAUEROVÁ, M., PILIPČINCOVÁ, A., DLOUHÁ, D., POLEDNE, R., ASCHERMANN, M., SKALICKÁ, H., MATOUŠKOVÁ, J. and KRUGER, A., 2010. A FTO variant and risk of acute coronary syndrome. Clinica chimica acta, 411(15-16), pp. 1069-1072.

HYLAND, M.E., IRVINE, S.H., THACKER, C., DANN, P.L. and DENNIS, I., 1989. Psychometric analysis of the Stunkard-Messick Eating Questionnaire (SMEQ) and comparison with the Dutch Eating Behavior Questionnaire (DEBQ). Current Psychology, 8(3), pp. 228-233.

IBBA, A., PILIA, S., ZAVATTARI, P., LOCHE, A., GUZZETTI, C., CASINI, M.R., MINERBA, L. and LOCHE, S., 2013. The role of FTO genotype on eating behavior in obese Sardinian children and adolescents. Journal of Pediatric Endocrinology and Metabolism, 26(5-6), pp. 539-544.

IMPERATORI, C., INNAMORATI, M., TAMBURELLO, S., CONTINISIO, M., CONTARDI, A., TAMBURELLO, A. and FABBRICATORE, M., 2013. Gender differences in food craving among overweight and obese patients attending low energy diet therapy: a matched case–control study. Eating and Weight Disorders-Studies on Anorexia, Bulimia and Obesity, 18(3), pp. 297-303.

JACKSON, M., WALKER, S., FORRESTER, T., CRUICKSHANK, J. and WILKS, R., 2003. Social and dietary determinants of body mass index of adult Jamaicans of African origin. European journal of clinical nutrition, 57(4), pp. 621.

JANSEN, A., 1998. A learning model of binge eating: cue reactivity and cue exposure. Behaviour research and therapy, 36(3), pp. 257-272.

JANSEN, A., THEUNISSEN, N., SLECHTEN, K., NEDERKOORN, C., BOON, B., MULKENS, S. and ROEFS, A., 2003. Overweight children overeat after exposure to food cues. Eating Behaviors, 4(2), pp. 197-209.

JANSSEN, H.G., DAVIES, I.G., RICHARDSON, L.D. AND STEVENSON, L., 2018. Determinants of takeaway and fast food consumption: a narrative review. Nutrition research reviews, 31(1), pp.16-34.

JAWOROWSKA, A., BLACKHAM, T., DAVIES, I.G. AND STEVENSON, L., 2013. Nutritional challenges and health implications of takeaway and fast food. Nutrition reviews, 71(5), pp.310-318.

JOHNSON, F., PRATT, M. and WARDLE, J., 2012. Dietary restraint and self-regulation in eating behavior. International journal of obesity, 36(5), pp. 665.

JOHNSON, L., VAN JAARSVELD, C.H., EMMETT, P.M., ROGERS, I.S., NESS, A.R., HATTERSLEY, A.T., TIMPSON, N.J., SMITH, G.D. and JEBB, S.A., 2009. Dietary energy density affects fat mass in early adolescence and is not modified by FTO variants. PloS one, 4(3), pp. e4594.

JORGENSEN, M.M., ZACHARIAE, R., SKYTTHE, A. and KYVIK, K., 2007. Genetic and environmental factors in alexithymia: a population-based study of 8,785 Danish twin pairs. Psychotherapy and psychosomatics, 76(6), pp. 369-375.

KADOWAKI, T., YAMAUCHI, T. and KUBOTA, N., 2008. The physiological and pathophysiological role of adiponectin and adiponectin receptors in the peripheral tissues and CNS. FEBS letters, 582(1), pp. 74-80.

KAPLAN, H.I. and KAPLAN, H.S., 1957. The psychosomatic concept of obesity. Journal of Nervous and Mental Disease, .

KARLSSON, J., PERSSON, L., SJÖSTRÖM, L. and SULLIVAN, M., 2000. Psychometric properties and factor structure of the Three-Factor Eating Questionnaire (TFEQ) in obese men and women. Results from the Swedish Obese Subjects (SOS) study. International journal of obesity, 24(12), pp. 1715.

KARRA, E., O'DALY, O.G., CHOUDHURY, A.I., YOUSSEIF, A., MILLERSHIP, S., NEARY, M.T., SCOTT, W.R., CHANDARANA, K., MANNING, S. and HESS, M.E., 2013. A link between FTO, ghrelin, and impaired brain food-cue responsivity. The Journal of clinical investigation, 123(8), pp. 3539-3551.

KARUKIVI, M., JULA, A., HUTRI-KÄHÖNEN, N., JUONALA, M. and RAITAKARI, O., 2016. Is alexithymia associated with metabolic syndrome? A study in a healthy adult population. Psychiatry research, 236, pp. 58-63.

KASS, A.E., KOLKO, R.P. and WILFLEY, D.E., 2013. Psychological treatments for eating disorders. Current opinion in psychiatry, 26(6), pp. 549-555.

KAVANAGH, D.J., ANDRADE, J. and MAY, J., 2005. Imaginary relish and exquisite torture: the elaborated intrusion theory of desire. Psychological review, 112(2), pp. 446.

KELLER, C. and SIEGRIST, M., 2015. Ambivalence toward palatable food and emotional eating predict weight fluctuations. Results of a longitudinal study with four waves. Appetite, 85, pp. 138-145.

KELLY, T., YANG, W., CHEN, C., REYNOLDS, K. and HE, J., 2008. Global burden of obesity in 2005 and projections to 2030. International journal of obesity, 32(9), pp. 1431.

KEMPS, E. and TIGGEMANN, M., 2009. Attentional bias for craving-related (chocolate) food cues. Experimental and clinical psychopharmacology, 17(6), pp. 425.

KERÄNEN, A., SAVOLAINEN, M.J., REPONEN, A.H., KUJARI, M., LINDEMAN, S.M., BLOIGU, R.S. and LAITINEN, J.H., 2009. The effect of eating behavior on weight loss and maintenance during a lifestyle intervention. Preventive medicine, 49(1), pp. 32-38.

KESKITALO, K., TUORILA, H., SPECTOR, T.D., CHERKAS, L.F., KNAAPILA, A., KAPRIO, J., SILVENTOINEN, K. and PEROLA, M., 2008. The Three-Factor Eating Questionnaire, body mass index, and responses to sweet and salty fatty foods: a twin study of genetic and environmental associations–. The American Journal of Clinical Nutrition, 88(2), pp. 263-271.

KESKITALO, K., TUORILA, H., SPECTOR, T.D., CHERKAS, L.F., KNAAPILA, A., KAPRIO, J., SILVENTOINEN, K. and PEROLA, M., 2008. The Three-Factor Eating Questionnaire, body mass index, and responses to sweet and salty fatty foods: a twin study of genetic and environmental associations–. The American Journal of Clinical Nutrition, 88(2), pp. 263-271.

KIM, S. and MISRA, A., 2007. SNP genotyping: technologies and biomedical applications. Annu.Rev.Biomed.Eng., 9, pp. 289-320.

KING, N.A., CAUDWELL, P., HOPKINS, M., BYRNE, N.M., COLLEY, R., HILLS, A.P., STUBBS, J.R. and BLUNDELL, J.E., 2007. Metabolic and behavioral compensatory responses to exercise interventions: barriers to weight loss. Obesity, 15(6), pp. 1373-1383.

KING, N.A., HOPKINS, M., CAUDWELL, P., STUBBS, R. and BLUNDELL, J.E., 2008. Individual variability following 12 weeks of supervised exercise: identification and characterization of compensation for exercise-induced weight loss. International journal of obesity, 32(1), pp. 177.

KNÄUPER, B., RABIAU, M., COHEN, O. and PATRICIU, N., 2004. Compensatory health beliefs: scale development and psychometric properties. Psychology & Health, 19(5), pp. 607-624.

KNOWLER, W.C., BARRETT-CONNOR, E., FOWLER, S.E., HAMMAN, R.F., LACHIN, J.M., WALKER, E.A., NATHAN, D.M. and DIABETES PREVENTION PROGRAM RESEARCH GROUP, 2002. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. The New England journal of medicine, 346(6), pp. 393-403.

KOENDERS, P.G. and VAN STRIEN, T., 2011. Emotional eating, rather than lifestyle behavior, drives weight gain in a prospective study in 1562 employees. Journal of occupational and environmental medicine, 53(11), pp. 1287-1293.

KONI, A.C., 2013. Effects of the FTO gene and Environment on Obesity in European Children, .

KUBOTA, N., YANO, W., KUBOTA, T., YAMAUCHI, T., ITOH, S., KUMAGAI, H., KOZONO, H., TAKAMOTO, I., OKAMOTO, S. and SHIUCHI, T., 2007. Adiponectin stimulates AMP-activated protein kinase in the hypothalamus and increases food intake. Cell metabolism, 6(1), pp. 55-68.

LAFAY, L., THOMAS, F., MENNEN, L., CHARLES, M.A., ESCHWEGE, E. and BORYS, J., 2001. Gender differences in the relation between food cravings and mood in an adult community: Results from the Fleurbaix Laventie Ville Sante study. International Journal of Eating Disorders, 29(2), pp. 195-204.

LAKE, A.A., 2018. Neighbourhood food environments: food choice, foodscapes and planning for health. Proceedings of the Nutrition Society, *77*(3), pp.239-246.

LAM, D.D., GARFIELD, A.S., MARSTON, O.J., SHAW, J. and HEISLER, L.K., 2010. Brain serotonin system in the coordination of food intake and body weight. Pharmacology Biochemistry and Behavior, 97(1), pp. 84-91.

LAMBERT, K.G., NEAL, T., NOYES, J., PARKER, C. and WORREL, P., 1991. Food-related stimuli increase desire to eat in hungry and satiated human subjects. Current Psychology, 10(4), pp. 297-303.

LANDRY, J.B. and SOLMON, M.A., 2004. African American women's self-determination across the stages of change for exercise. Journal of Sport and exercise Psychology, 26(3), pp. 457-469.

LAPORTE, D. and STUNKARD, A., 1990. Predicting attrition and adherence to a very low calorie diet: a prospective investigation of the eating inventory. International journal of obesity, 14(3), pp. 197-206.

LARDER, R., CHEUNG, M.M., TUNG, Y.L., YEO, G.S. and COLL, A.P., 2011. Where to go with FTO? Trends in Endocrinology & Metabolism, 22(2), pp. 53-59.

LAROCHE, H.H., WALLACE, R.B., SNETSELAAR, L., HILLIS, S.L. and STEFFEN, L.M., 2012. Changes in diet behavior when adults become parents. Journal of the Academy of Nutrition and Dietetics, 112(6), pp. 832-839.

LARSEN, J.K., BRAND, N., BERMOND, B. and HIJMAN, R., 2003. Cognitive and emotional characteristics of alexithymia: a review of neurobiological studies. Journal of psychosomatic research, 54(6), pp. 533-541.

LARSEN, J.K., VAN STRIEN, T., EISINGA, R. and ENGELS, R.C., 2006. Gender differences in the association between alexithymia and emotional eating in obese individuals. Journal of psychosomatic research, 60(3), pp. 237-243.

LEAHEY, T.M., BOND, D.S., RAYNOR, H., ROYE, D., VITHIANANTHAN, S., RYDER, B.A., SAX, H.C. and WING, R.R., 2012. Effects of bariatric surgery on food cravings: do food cravings and the consumption of craved foods “normalize” after surgery? Surgery for Obesity and Related Diseases, 8(1), pp. 84-91.

LEE, H., KYOUNG KIM, I., KANG, J.H., AHN, Y., HAN, B., LEE, J. and SONG, J., 2010. Effects of common FTO gene variants associated with BMI on dietary intake and physical activity in Koreans. Clinica chimica acta, 411(21-22), pp. 1716-1722.

LEE, M., WU, Y. and FRIED, S.K., 2013. Adipose tissue heterogeneity: implication of depot differences in adipose tissue for obesity complications. Molecular aspects of medicine, 34(1), pp. 1-11.

LEGORRETA, G., BULL, R.H. and KIELY, M.C., 1988. Alexithymia and symbolic function in the obese. Psychotherapy and psychosomatics, 50(2), pp. 88-94.

LEIBOWITZ, S.F. and HOEBEL, B., 2004. Behavioral neuroscience of obesity. The Handbook of Obesity. New York: Marcel Dekker, , pp. 301-371.

LESDÉMA, A., FROMENTIN, G., DAUDIN, J., ARLOTTI, A., VINOY, S., TOME, D. and MARSSET-BAGLIERI, A., 2012. Characterization of the Three-Factor Eating Questionnaire scores of a young French cohort. Appetite, 59(2), pp. 385-390.

LI, H., KILPELÄINEN, T.O., LIU, C., ZHU, J., LIU, Y., HU, C., YANG, Z., ZHANG, W., BAO, W. and CHA, S., 2012. Association of genetic variation in FTO with risk of obesity and type 2 diabetes with data from 96,551 East and South Asians. Diabetologia, 55(4), pp. 981-995. LITTLE, T., HOROWITZ, M. and FEINLE‐BISSET, C., 2005. Role of cholecystokinin in appetite control and body weight regulation. Obesity reviews, 6(4), pp. 297-306.LIU, J., JONES, S.J., SUN, H., PROBST, J.C., MERCHANT, A.T. and CAVICCHIA, P., 2012. Diet, physical activity, and sedentary behaviors as risk factors for childhood obesity: an urban and rural comparison. Childhood Obesity (Formerly Obesity and Weight Management), 8(5), pp. 440-448.

LLEWELLYN, C.H., TRZASKOWSKI, M., VAN JAARSVELD, C.H., PLOMIN, R. and WARDLE, J., 2014. Satiety mechanisms in genetic risk of obesity. JAMA pediatrics, 168(4), pp. 338-344.

LLUCH, A., HERBETH, B., MEJEAN, L. and SIEST, G., 2000. Dietary intakes, eating style and overweight in the Stanislas Family Study. International journal of obesity, 24(11), pp. 1493.

LOAS, G., PARKER, J.D., OTMANI, O., VERRIER, A. and FREMAUX, D., 1997. Confirmatory factor analysis of the French translation of the 20-item Toronto Alexithymia Scale. Perceptual and motor skills, 85(3), pp. 1018-1018.

LOCKE, A.E., KAHALI, B., BERNDT, S.I., JUSTICE, A.E., PERS, T.H., DAY, F.R., POWELL, C., VEDANTAM, S., BUCHKOVICH, M.L., YANG, J. AND CROTEAU-CHONKA, D.C., 2015. Genetic studies of body mass index yield new insights for obesity biology. Nature, 518(7538), p.197.

LÖFFLER, A., LUCK, T., THEN, F.S., LUPPA, M., SIKORSKI, C., KOVACS, P., TÖNJES, A., BÖTTCHER, Y., BREITFELD, J. and HORSTMANN, A., 2015. Age-and gender-specific norms for the German version of the Three-Factor Eating-Questionnaire (TFEQ). Appetite, 91, pp. 241-247.

LÖFFLER, A., LUCK, T., THEN, F.S., SIKORSKI, C., KOVACS, P., BÖTTCHER, Y., BREITFELD, J., TÖNJES, A., HORSTMANN, A. and LÖFFLER, M., 2015. Eating behaviour in the general population: An analysis of the factor structure of the German version of the three-factor-eating-questionnaire (TFEQ) and its association with the body mass index. PloS one, 10(7), pp. e0133977.

LOOS, R.J., 2018. The genetics of adiposity. Current opinion in genetics & development, 50, pp.86-95.

LOPEZ, R.B., HOFMANN, W., WAGNER, D.D., KELLEY, W.M. and HEATHERTON, T.F., 2014. Neural predictors of giving in to temptation in daily life. Psychological science, 25(7), pp. 1337-1344.

LOWE, M.R. and BUTRYN, M.L., 2007. Hedonic hunger: a new dimension of appetite? Physiology & Behavior, 91(4), pp. 432-439.

LOWE, M.R. and TIMKO, C.A., 2004. What a difference a diet makes: Towards an understanding of differences between restrained dieters and restrained nondieters. Eating Behaviors, 5(3), pp. 199-208.

LU, Y., DAY FR GUSTAFSSON S BUCHKOVICH ML NA J BATAILLE V COUSMINER DL DASTANI Z DRONG AW ESKO T 2016 New loci for body fat percentage reveal link between adiposity and cardiometabolic disease risk. Nature Communications, 7, p.10495.

LUMLEY, M.A., BEYER, J. AND RADCLIFFE, A., 2008. Alexithymia and physical health problems: A critique of potential pathways and a research agenda. In Emotion Regulation (pp. 43-68). Springer, Boston, MA.

LYVERS, M., 2000. " Loss of control" in alcoholism and drug addiction: a neuroscientific interpretation. Experimental and clinical psychopharmacology, 8(2), pp. 225.

MACKINNON, D.P., FAIRCHILD, A.J. and FRITZ, M.S., 2007. Mediation analysis. Annu.Rev.Psychol., 58, pp. 593-614.

MAGNI, P., DOZIO, E., RUSCICA, M., CELOTTI, F., MASINI, M.A., PRATO, P., BROCCOLI, M., MAMBRO, A., MORÈ, M. and STROLLO, F., 2009. Feeding behavior in mammals including humans. Annals of the New York Academy of Sciences, 1163(1), pp. 221-232.

MAHONY, R., BLAKE, C., MATTHEWS, J., DONNOGHUE, G.O. and CUNNINGHAM, C., 2018. Physical activity levels and self-determined motivation among future healthcare professionals: Utility of the Behavioral Regulation in Exercise Questionnaire (BREQ-2). Physiotherapy theory and practice, , pp. 1-7.

MALTBY, J. and DAY, L., 2001. The relationship between exercise motives and psychological weil-being. The Journal of psychology, 135(6), pp. 651-660.

MARKLAND, D. and TOBIN, V., 2004. A modification to the behavioural regulation in exercise questionnaire to include an assessment of amotivation. Journal of Sport and Exercise Psychology, 26(2), pp. 191-196.

MARTEL, P. and FANTINO, M., 1996. Mesolimbic dopaminergic system activity as a function of food reward: a microdialysis study. Pharmacology Biochemistry and Behavior, 53(1), pp. 221-226.

MARTI, A., MORENO-ALIAGA, M., HEBEBRAND, J. and MARTINEZ, J., 2004. Genes, lifestyles and obesity. International journal of obesity, 28(S3), pp. S29.

MARTIN, C.K., MCCLERNON, F.J., CHELLINO, A. and CORREA, J.B., 2011. Food cravings: a central construct in food intake behavior, weight loss, and the neurobiology of appetitive behavior. Handbook of behavior, food and nutrition. Springer, pp. 741-755.

MARTIN, C.K., O'NEIL, P.M., TOLLEFSON, G., GREENWAY, F.L. and WHITE, M.A., 2008. The association between food cravings and consumption of specific foods in a laboratory taste test. Appetite, 51(2), pp. 324-326.

MARTIN, C.K., O'NEIL, P.M. and PAWLOW, L., 2006. Changes in food cravings during low‐calorie and very‐low‐calorie diets. Obesity, 14(1), pp. 115-121.

MARTIN, C.K., ROSENBAUM, D., HAN, H., GEISELMAN, P.J., WYATT, H.R., HILL, J.O., BRILL, C., BAILER, B., MILLER‐III, B.V. and STEIN, R., 2011. Change in food cravings, food preferences, and appetite during a low‐carbohydrate and low‐fat diet. Obesity, 19(10), pp. 1963-1970.

MARTIN, K.S. and FERRIS, A.M., 2007. Food insecurity and gender are risk factors for obesity. Journal of nutrition education and behavior, 39(1), pp. 31-36.

MARTÍNEZ-SÁNCHEZ, F., ATO-GARCÍA, M. and ORTIZ-SORIA, B., 2003. Alexithymia—state or trait? The Spanish journal of psychology, 6(1), pp. 51-59.

MASON, O., TYSON, M., JONES, C. and POTTS, S., 2005. Alexithymia: its prevalence and correlates in a British undergraduate sample. Psychology and Psychotherapy: Theory, Research and Practice, 78(1), pp. 113-125.

MATA, J., RICHTER, D., SCHNEIDER, T. and HERTWIG, R., 2018. How cohabitation, marriage, separation, and divorce influence BMI: A prospective panel study. Health Psychology, 37(10), pp. 948.

MATA, J., SILVA, M.N., VIEIRA, P.N., CARRAÇA, E.V., ANDRADE, A.M., COUTINHO, S.R., SARDINHA, L.B. and TEIXEIRA, P.J., 2009. Motivational "spill-over" during weight control: Increased self-determination and exercise intrinsic motivation predict eating self-regulation. Health Psychology, 28(6), pp. 709.

MCCAFFERY, J.M., PAPANDONATOS, G.D., PETER, I., HUGGINS, G.S., RAYNOR, H.A., DELAHANTY, L.M., CHESKIN, L.J., BALASUBRAMANYAM, A., WAGENKNECHT, L.E. and WING, R.R., 2012. Obesity susceptibility loci and dietary intake in the Look AHEAD Trial–. The American Journal of Clinical Nutrition, 95(6), pp. 1477-1486.

MCKIERNAN, F., HOUCHINS, J.A. and MATTES, R.D., 2008. Relationships between human thirst, hunger, drinking, and feeding. Physiology & Behavior, 94(5), pp. 700-708.

MEGUID, M.M., FETISSOV, S.O., VARMA, M., SATO, T., ZHANG, L., LAVIANO, A. and ROSSI-FANELLI, F., 2000. Hypothalamic dopamine and serotonin in the regulation of food intake. Nutrition, 16(10), pp. 843-857.

MERCER, A.J., HENTGES, S.T., MESHUL, C.K. and LOW, M.J., 2013. Unraveling the central proopiomelanocortin neural circuits. Frontiers in neuroscience, 7, pp. 19.

MERCER, M.E. and D HOLDER, M., 1997. Food cravings, endogenous opioid peptides, and food intake: a review. Appetite, 29(3), pp. 325-352.

MEULE, A. and HORMES, J.M., 2015. Chocolate versions of the Food Cravings Questionnaires. Associations with chocolate exposure-induced salivary flow and ad libitum chocolate consumption. Appetite, 91, pp. 256-265.

MEULE, A., RICHARD, A. and PLATTE, P., 2017. Food cravings prospectively predict decreases in perceived self-regulatory success in dieting. Eating Behaviors, 24, pp. 34-38.

MEULE, A., WESTENHÖFER, J. and KÜBLER, A., 2011. Food cravings mediate the relationship between rigid, but not flexible control of eating behavior and dieting success. Appetite, 57(3), pp. 582-584.

MIQUELON, P., KNÄUPER, B. and VALLERAND, R.J., 2012. Motivation and goal attainment. The role of compensatory beliefs. Appetite, 58(2), pp. 608-615.

MOGG, K., BRADLEY, B.P., O'NEILL, B., BANI, M., MERLO-PICH, E., KOCH, A., BULLMORE, E.T. and NATHAN, P.J., 2012. Effect of dopamine D3 receptor antagonism on approach responses to food cues in overweight and obese individuals. Behavioural pharmacology, 23(5 and 6), pp. 603-608.

MORIGUCHI, Y., MAEDA, M., IGARASHI, T., ISHIKAWA, T., SHOJI, M., KUBO, C. and KOMAKI, G., 2007. Age and gender effect on alexithymia in large, Japanese community and clinical samples: a cross-validation study of the Toronto Alexithymia Scale (TAS-20). BioPsychoSocial medicine, 1(1), pp. 7.

MORREALE, S.J. and SCHWARTZ, N.E., 1995. Helping Americans eat right: developing practical and actionable public nutrition education messages based on the ADA Survey of American Dietary Habits. Journal of the Academy of Nutrition and Dietetics, 95(3), pp. 305-308.

MORRIS, M.J., BEILHARZ, J.E., MANIAM, J., REICHELT, A.C. and WESTBROOK, R.F., 2015. Why is obesity such a problem in the 21st century? The intersection of palatable food, cues and reward pathways, stress, and cognition. Neuroscience & Biobehavioral Reviews, 58, pp. 36-45.

MOSHIER, S.J., LANDAU, A.J., HEARON, B.A., STEIN, A.T., GREATHOUSE, L., SMITS, J.A. and OTTO, M.W., 2016. The development of a novel measure to assess motives for compensatory eating in response to exercise: The CEMQ. Behavioral Medicine, 42(2), pp. 93-104.

MULLAN, E., MARKLAND, D. and INGLEDEW, D.K., 1997. A graded conceptualisation of self-determination in the regulation of exercise behaviour: Development of a measure using confirmatory factor analytic procedures. Personality and Individual Differences, 23(5), pp. 745-752.

MUNT, A., PARTRIDGE, S. and ALLMAN‐FARINELLI, M., 2017. The barriers and enablers of healthy eating among young adults: A missing piece of the obesity puzzle: A scoping review. Obesity Reviews, 18(1), pp. 1-17.

MURAVEN, M. and BAUMEISTER, R.F., 2000. Self-regulation and depletion of limited resources: Does self-control resemble a muscle? Psychological bulletin, 126(2), pp. 247.

MURCIA, J., GIMENO, E.C. and CAMACHO, A.M., 2007. Measuring self-determination motivation in a physical fitness setting: validation of the Behavioural Regulation in

Exercise Questionnaire-2 (BREQ-2) in a Spanish sample. The Journal of Sport Medicine and Physical Fitness, 47, pp. 366-378.

NARUKAWA, M., KAMIYOSHIHARA, A., KAWAE, M., KOHTA, R. and MISAKA, T., 2018. Analysis of aging-dependent changes in taste sensitivities of the senescence-accelerated mouse SAMP1. Experimental gerontology, 113, pp. 64-73.

NEOVIUS, M. and RASMUSSEN, F., 2008. Place of residence and obesity in 1,578,694 young Swedish men between 1969 and 2005. Obesity, 16(3), pp. 671-676.

NG, L. and DAVIS, C., 2013. Cravings and food consumption in binge eating disorder. Eating Behaviors, 14(4), pp. 472-475.

NG, M.C., GRAFF, M., LU, Y., JUSTICE, A.E., MUDGAL, P., LIU, C.T., YOUNG, K., YANEK, L.R., FEITOSA, M.F., WOJCZYNSKI, M.K. AND RAND, K., 2017. Discovery and fine-mapping of adiposity loci using high density imputation of genome-wide association studies in individuals of African ancestry: African Ancestry Anthropometry Genetics Consortium. PLoS genetics, 13(4), p.e1006719.

NICHOLLS, W. and HULBERT-WILLIAMS, L., 2013. British English translation of the Food Craving Inventory (FCI-UK). Appetite, 67, pp. 37-43.

NIEMEIER, H.M., PHELAN, S., FAVA, J.L. and WING, R.R., 2007. Internal disinhibition predicts weight regain following weight loss and weight loss maintenance. Obesity, 15(10), pp. 2485-2494.

NIX, G.A., RYAN, R.M., MANLY, J.B. and DECI, E.L., 1999. Revitalization through self-regulation: The effects of autonomous and controlled motivation on happiness and vitality. Journal of experimental social psychology, 35(3), pp. 266-284.

NOLI, G., CORNICELLI, M., MARINARI, G., CARLINI, F., SCOPINARO, N. and ADAMI, G., 2010. Alexithymia and eating behaviour in severely obese patients. Journal of human nutrition and dietetics, 23(6), pp. 616-619.

NOWAKOWSKI, M.E., MCFARLANE, T. and CASSIN, S., 2013. Alexithymia and eating disorders: a critical review of the literature. Journal of eating disorders, 1(1), pp. 21.

O'CONNOR, D.B., JONES, F., CONNER, M., MCMILLAN, B. and FERGUSON, E., 2008. Effects of daily hassles and eating style on eating behavior. Health Psychology, 27(1S), pp. S20.

ODA-MONTECINOS, C., SALDAÑA, C. and ANDRÉS, A., 2013. Eating behaviors are risk factors for the development of overweight. Nutrition Research, 33(10), pp. 796-802.

O'DRISCOLL, C., LAING, J. and MASON, O., 2014. Cognitive emotion regulation strategies, alexithymia and dissociation in schizophrenia, a review and meta-analysis. Clinical psychology review, 34(6), pp. 482-495.

OKUDA, M., HINODA, Y., OKAYAMA, N., SUEHIRO, Y., SHIRABE, K., SASAKI, S., KUNITSUGU, I., YOSHITAKE, N. and HOBARA, T., 2011. Association between the FTO gene and overweight in Japanese children and adolescents. Pediatric diabetes, 12(5), pp. 494-500.

OLIVER, G., WARDLE, J. and GIBSON, E.L., 2000. Stress and food choice: a laboratory study. Psychosomatic medicine, 62(6), pp. 853-865.

OLIVO, G., WIEMERSLAGE, L., NILSSON, E.K., SOLSTRAND DAHLBERG, L., LARSEN, A.L., OLAYA BÚCARO, M., GUSTAFSSON, V.P., TITOVA, O.E., BANDSTEIN, M. and LARSSON, E., 2016. Resting-state brain and the FTO obesity risk allele: default mode, sensorimotor, and salience network connectivity underlying different somatosensory integration and reward processing between genotypes. Frontiers in human neuroscience, 10, pp. 52.

OLLMANN, M.M., WILSON, B.D., YANG, Y.K., KERNS, J.A., CHEN, Y., GANTZ, I. and BARSH, G.S., 1997. Antagonism of central melanocortin receptors in vitro and in vivo by agouti-related protein. Science (New York, N.Y.), 278(5335), pp. 135-138.

OWEN, K.B., SMITH, J., LUBANS, D.R., NG, J.Y. and LONSDALE, C., 2014. Self-determined motivation and physical activity in children and adolescents: A systematic review and meta-analysis. Preventive medicine, 67, pp. 270-279.

PANDEY, R., MANDAL, M.K., TAYLOR, G.J. and PARKER, J.D., 1996. Cross‐cultural alexithymia: Development and validation of a Hindi translation of the 20‐item Toronto alexithymia scale. Journal of clinical psychology, 52(2), pp. 173-176.

PARK, J.W., PARK, J. and JEE, S.H., 2011. ADIPOQ Gene Variants Associated with Susceptibility to Obesity and Low Serum Adiponectin Levels in Healthy Koreans. Epidemiology and health, 33, pp. e2011003.

PARKER, J.A. and BLOOM, S.R., 2012. Hypothalamic neuropeptides and the regulation of appetite. Neuropharmacology, 63(1), pp. 18-30.

PAUSOVA, Z., SYME, C., ABRAHAMOWICZ, M., XIAO, Y., LEONARD, G.T., PERRON, M., RICHER, L., VEILLETTE, S., SMITH, G.D. and SEDA, O., 2009. A common variant of the FTO gene is associated with not only increased adiposity but also elevated blood pressure in French Canadians. Circulation: Cardiovascular Genetics, 2(3), pp. 260-269.

PELCHAT, M.L., 1997. Food cravings in young and elderly adults. Appetite, 28(2), pp. 103-113.

PELCHAT, M.L., JOHNSON, A., CHAN, R., VALDEZ, J. and RAGLAND, J.D., 2004. Images of desire: food-craving activation during fMRI. NeuroImage, 23(4), pp. 1486-1493.

PELCHAT, M.L. and SCHAEFER, S., 2000. Dietary monotony and food cravings in young and elderly adults. Physiology & Behavior, 68(3), pp. 353-359.

PELLETIER, L.G., 2002. 10: A Motivational Analysis of Self-Determination for Pro-Environmental Behaviors. Handbook of self-determination research, (205),.

PENCHANSKY, R. AND THOMAS, J.W., 1981. The concept of access: definition and relationship to consumer satisfaction. Medical care, pp.127-140.

PÉNEAU, S., MÉNARD, E., MÉJEAN, C., BELLISLE, F. and HERCBERG, S., 2013. Sex and dieting modify the association between emotional eating and weight status–. The American Journal of Clinical Nutrition, 97(6), pp. 1307-1313.

PETERS, K.E., BEILBY, J., CADBY, G., WARRINGTON, N.M., BRUCE, D.G., DAVIS, W.A., DAVIS, T.M., WILTSHIRE, S., KNUIMAN, M. and MCQUILLAN, B.M., 2013. A comprehensive investigation of variants in genes encoding adiponectin (ADIPOQ) and its receptors (ADIPOR1/R2), and their association with serum adiponectin, type 2 diabetes, insulin resistance and the metabolic syndrome. BMC medical genetics, 14(1), pp. 15.

PICARDI, A., FAGNANI, C., GIGANTESCO, A., TOCCACELI, V., LEGA, I. and STAZI, M.A., 2011. Genetic influences on alexithymia and their relationship with depressive symptoms. Journal of psychosomatic research, 71(4), pp. 256-263.

PIKE, C., 2013. The Association between Alexithymia, Impulsivity and Negative Affect in Emotional and External Eating.

PINAQUY, S., CHABROL, H., SIMON, C., LOUVET, J. and BARBE, P., 2003. Emotional eating, alexithymia, and binge‐eating disorder in obese women. Obesity research, 11(2), pp. 195-201.

PINNA, F., LAI, L., PIRARBA, S., ORRU, W., VELLUZZI, F., LOVISELLI, A. and CARPINIELLO, B., 2011. Obesity, alexithymia and psychopathology: a case-control study. Eating and Weight Disorders-Studies on Anorexia, Bulimia and Obesity, 16(3), pp. e164-e170.

POELMAN, M.P., VERMEER, W.M., VYTH, E.L. and STEENHUIS, I.H., 2013. 'I don't have to go to the gym because I ate very healthy today': the development of a scale to assess diet-related compensatory health beliefs. Public health nutrition, 16(2), pp. 267-273.

POPKIN, B.M., ADAIR, L.S. and NG, S.W., 2012. Global nutrition transition and the pandemic of obesity in developing countries. Nutrition reviews, 70(1), pp. 3-21.

POTENZA, M.N. and GRILO, C.M., 2014. How relevant is food craving to obesity and its treatment? Frontiers in psychiatry, 5, pp. 164.

PREACHER, K.J. and HAYES, A.F., 2008. Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. Behavior research methods, 40(3), pp. 879-891.

Public Health England (2017) Health matters: obesity and the food environment.

QI, Y., TAKAHASHI, N., HILEMAN, S.M., PATEL, H.R., BERG, A.H., PAJVANI, U.B., SCHERER, P.E. and AHIMA, R.S., 2004. Adiponectin acts in the brain to decrease body weight. Nature medicine, 10(5), pp. 524.

QUINDRY, J.C., YOUNT, D., O'BRYANT, H. and RUDISILL, M.E., 2011. Exercise engagement is differentially motivated by age-dependent factors. American Journal of Health Behavior, 35(3), pp. 334-345.

RABIA, M., KNÄUPER, B. and MIQUELON, P., 2006. The eternal quest for optimal balance between maximizing pleasure and minimizing harm: The compensatory health beliefs model. British journal of health psychology, 11(1), pp. 139-153.

RAMACHANDRAN, A. and SNEHALATHA, C., 2010. Rising burden of obesity in Asia. Journal of obesity, 2010, pp. 10.1155/2010/868573. Epub 2010 Aug 30.

RAMACHANDRAPPA, S. and FAROOQI, I.S., 2011. Genetic approaches to understanding human obesity. The Journal of clinical investigation, 121(6), pp. 2080-2086.

RAMANATHAN, S. and MENON, G., 2006. Time-varying effects of chronic hedonic goals on impulsive behavior. Journal of Marketing Research, 43(4), pp. 628-641.

RAMZI, N.H., YIORKAS, A.M., SEBERT, S., KEINÄNEN-KIUKAANNIEMI, S., ALA-MURSULA, L., SVENTO, R., JOKELAINEN, J., VEIJOLA, J., AUVINEN, J. and MIETTUNEN, J., 2018. Relationship between BMI and emotion-handling capacity in an adult Finnish population: The Northern Finland Birth Cohort 1966. PloS one, 13(9), pp. e0203660.

RANKINEN, T. and BOUCHARD, C., 2006. Genetics of food intake and eating behavior phenotypes in humans. Annu.Rev.Nutr., 26, pp. 413-434.

RAYNOR, H.A. and EPSTEIN, L.H., 2003. The relative-reinforcing value of food under differing levels of food deprivation and restriction. Appetite, 40(1), pp. 15-24.

RAZQUIN, C., MARTI, A. and MARTINEZ, J.A., 2011. Evidences on three relevant obesogenes: MC4R, FTO and PPARγ. Approaches for personalized nutrition. Molecular nutrition & food research, 55(1), pp. 136-149.

REITZ, C., TOSTO, G., MAYEUX, R. and LUCHSINGER, J.A., 2012. Genetic variants in the Fat and Obesity Associated (FTO) gene and risk of Alzheimer's disease. PloS one, 7(12), pp. e50354.

RENNER, B., SPROESSER, G., STROHBACH, S. and SCHUPP, H.T., 2012. Why we eat what we eat. The Eating Motivation Survey (TEMS). Appetite, 59(1), pp. 117-128.

RHIND, C., BONFIOLI, E., HIBBS, R., GODDARD, E., MACDONALD, P., GOWERS, S., SCHMIDT, U., TCHANTURIA, K., MICALI, N. and TREASURE, J., 2014. An examination of autism spectrum traits in adolescents with anorexia nervosa and their parents. Molecular autism, 5(1), pp. 56.

RIDOUT, N., THOM, C. and WALLIS, D.J., 2010. Emotion recognition and alexithymia in females with non-clinical disordered eating. Eating Behaviors, 11(1), pp. 1-5.

RIVAS, A.M.O., SANTOS, J.L., VALLADARES, M.A., CAMERON, J. and GOLDFIELD, G., 2018. Association of the FTO fat mass and obesity–associated gene rs9939609 polymorphism with rewarding value of food and eating behavior in Chilean children. Nutrition, 54, pp. 105-110.

RODRIGUEZ, S., FERNANDEZ, M.C., CEPEDA-BENITO, A. and VILA, J., 2005. Subjective and physiological reactivity to chocolate images in high and low chocolate cravers. Biological psychology, 70(1), pp. 9-18.

RODRIGUEZ, S., MATA, J.L., MORENO, S., FERNANDEZ, M.C. and VILA, J., 2007. Psychophysiological mechanisms involved in the affective regulation and food restriction of women at risk of suffering from bulimia nervosa. Psicothema, 19(1), pp. 30-36.

ROH, D., KIM, W. and KIM, C., 2011. Alexithymia in obsessive-compulsive disorder: clinical correlates and symptom dimensions. The Journal of nervous and mental disease, 199(9), pp. 690-695.

ROHRER, J.E., VICKERS-DOUGLAS, K.S. and STROEBEL, R.J., 2009. Uncontrolled eating and obesity in adult primary care patients. Obesity research & clinical practice, 3(2), pp. 115-121.

ROSENHECK, R., 2008. Fast food consumption and increased caloric intake: a systematic review of a trajectory towards weight gain and obesity risk. Obesity reviews, 9(6), pp.535-547.

ROZIN, P., LEVINE, E. and STOESS, C., 1991. Chocolate craving and liking. Appetite, 17(3), pp. 199-212.

RUTTERS, F., NIEUWENHUIZEN, A.G., LEMMENS, S.G., BORN, J.M. and WESTERTERP‐PLANTENGA, M.S., 2009. Acute stress‐related changes in eating in the absence of hunger. Obesity, 17(1), pp. 72-77.

RYAN, R.M. and DECI, E.L., 2000. Self-determination theory and the facilitation of intrinsic motivation, social development, and well-being. American psychologist, 55(1), pp. 68.

RYAN, R.M., PATRICK, H., DECI, E.L. and WILLIAMS, G.C., 2008. Facilitating health behaviour change and its maintenance: Interventions based on self-determination theory. European Health Psychologist, 10(1), pp. 2-5.

SANDHOLT, C., HANSEN, T. and PEDERSEN, O., 2012. Beyond the fourth wave of genome-wide obesity association studies. Nutrition & diabetes, 2(7), pp. e37.

SCHMIDT, U., JIWANY, A. and TREASURE, J., 1993. A controlled study of alexithymia in eating disorders. Comprehensive psychiatry, 34(1), pp. 54-58.

SCHUBERT, M.M., DESBROW, B., SABAPATHY, S. and LEVERITT, M., 2013. Acute exercise and subsequent energy intake. A meta-analysis. Appetite, 63, pp. 92-104.

SCUTERI, A., SANNA, S., CHEN, W., UDA, M., ALBAI, G., STRAIT, J., NAJJAR, S., NAGARAJA, R., ORRÚ, M. and USALA, G., 2007. Genome-wide association scan shows genetic variants in the FTO gene are associated with obesity-related traits. PLoS genetics, 3(7), pp. e115.

SERGI, G., BANO, G., PIZZATO, S., VERONESE, N. and MANZATO, E., 2017. Taste loss in the elderly: Possible implications for dietary habits. Critical reviews in food science and nutrition, 57(17), pp. 3684-3689.

SEVGI, M., RIGOUX, L., KUHN, A.B., MAUER, J., SCHILBACH, L., HESS, M.E., GRUENDLER, T.O., ULLSPERGER, M., STEPHAN, K.E., BRUNING, J.C. and TITTGEMEYER, M., 2015. An Obesity-Predisposing Variant of the FTO Gene Regulates D2R-Dependent Reward Learning. The Journal of neuroscience : the official journal of the Society for Neuroscience, 35(36), pp. 12584-12592.

SHELDON, K.M. and ELLIOT, A.J., 1998. Not all personal goals are personal: Comparing autonomous and controlled reasons for goals as predictors of effort and attainment. Personality and Social Psychology Bulletin, 24(5), pp. 546-557.

SHIFFMAN, S., 2000. Comments on craving. Addiction, 95(8s2), pp. 171-175.

SHUNGIN, D., WINKLER, T.W., CROTEAU-CHONKA, D.C., FERREIRA, T., LOCKE, A.E., MÄGI, R., STRAWBRIDGE, R.J., PERS, T.H., FISCHER, K., JUSTICE, A.E. AND WORKALEMAHU, T., 2015. New genetic loci link adipose and insulin biology to body fat distribution. Nature, 518(7538), p.187.

SIFNEOS, P.E., 1996. Alexithymia: past and present. The American Journal of Psychiatry, 153(7), pp. 137.

SIFNEOS, P.E., 1973. The prevalence of 'alexithymic' characteristics in psychosomatic patients. Psychotherapy and psychosomatics, 22(2), pp. 255-262.

SILVA, I., 2015. Importance of emotional regulation in obesity and weight loss treatment. Fractal: Revista de Psicologia, 27(3), pp. 286-290.

SMEMO, S., TENA, J.J., KIM, K., GAMAZON, E.R., SAKABE, N.J., GÓMEZ-MARÍN, C., ANEAS, I., CREDIDIO, F.L., SOBREIRA, D.R. and WASSERMAN, N.F., 2014. Obesity-associated variants within FTO form long-range functional connections with IRX3. Nature, 507(7492), pp. 371.

SONESTEDT, E., ROOS, C., GULLBERG, B., ERICSON, U., WIRFÄLT, E. and ORHO-MELANDER, M., 2009. Fat and carbohydrate intake modify the association between

genetic variation in the FTO genotype and obesity–. The American Journal of Clinical Nutrition, 90(5), pp. 1418-1425.

SPEAKMAN, J.R., 2008. Thrifty genes for obesity, an attractive but flawed idea, and an alternative perspective: the 'drifty gene'hypothesis. International journal of obesity, 32(11), pp. 1611.

SPEAKMAN, J.R., RANCE, K.A. and JOHNSTONE, A.M., 2008. Polymorphisms of the FTO gene are associated with variation in energy intake, but not energy expenditure. Obesity, 16(8), pp. 1961-1965.

SPELIOTES, E.K., WILLER, C.J., BERNDT, S.I., MONDA, K.L., THORLEIFSSON, G., JACKSON, A.U., ALLEN, H.L., LINDGREN, C.M., LUAN, J. and MÄGI, R., 2010. Association analyses of 249,796 individuals reveal 18 new loci associated with body mass index. Nature genetics, 42(11), pp. 937.

SPITZER, R.L., DEVLIN, M., WALSH, B.T., HASIN, D., WING, R., MARCUS, M., STUNKARD, A., WADDEN, T., YANOVSKI, S. and AGRAS, S., 1992. Binge eating disorder: A multisite field trial of the diagnostic criteria. International Journal of Eating Disorders, 11(3), pp. 191-203.

ST-ONGE, M., 2005. Relationship between body composition changes and changes in physical function and metabolic risk factors in aging. Current Opinion in Clinical Nutrition & Metabolic Care, 8(5), pp. 523-528.

STORY, M., KAPHINGST, K.M., ROBINSON-O'BRIEN, R. AND GLANZ, K., 2008. Creating healthy food and eating environments: policy and environmental approaches. Annu. Rev. Public Health, 29, pp.253-272.

STOTLAND, S. and LAROCQUE, M., 2005. Early treatment response as a predictor of ongoing weight loss in obesity treatment. British journal of health psychology, 10(4), pp. 601-614.

STRACK, F. and DEUTSCH, R., 2004. Reflective and impulsive determinants of social behavior. Personality and social psychology review, 8(3), pp. 220-247.

STRATIGOPOULOS, G., PADILLA, S.L., LEDUC, C.A., WATSON, E., HATTERSLEY, A.T., MCCARTHY, M.I., ZELTSER, L.M., CHUNG, W.K. and LEIBEL, R.L., 2008. Regulation of Fto/Ftm gene expression in mice and humans. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology, 294(4), pp. R1185-R1196.

STUNKARD, A.J. and MESSICK, S., 1985. The three-factor eating questionnaire to measure dietary restraint, disinhibition and hunger. Journal of psychosomatic research, 29(1), pp. 71-83.

SUN, X., LUQUET, S. and SMALL, D.M., 2017. DRD2: Bridging the genome and ingestive behavior. Trends in cognitive sciences, 21(5), pp. 372-384.

SWINBURN, B. AND EGGER, G., 2002. Preventive strategies against weight gain and obesity. Obesity reviews, *3*(4), pp.289-301.

SWINBURN, B., KRAAK, V., RUTTER, H., VANDEVIJVERE, S., LOBSTEIN, T., SACKS, G., GOMES, F., MARSH, T. AND MAGNUSSON, R., 2015. Strengthening of accountability systems to create healthy food environments and reduce global obesity. The Lancet, *385*(9986), pp.2534-2545.

SWINBURN, B.A., SACKS, G., HALL, K.D., MCPHERSON, K., FINEGOOD, D.T., MOODIE, M.L. and GORTMAKER, S.L., 2011. The global obesity pandemic: shaped by global drivers and local environments. The Lancet, 378(9793), pp. 804-814.

SYVÄNEN, A., 2001. Accessing genetic variation: genotyping single nucleotide polymorphisms. Nature Reviews Genetics, 2(12), pp. 930.

TAN, J.T., DORAJOO, R., SEIELSTAD, M., SIM, X.L., ONG, R.T., CHIA, K.S., WONG, T.Y., SAW, S.M., CHEW, S.K., AUNG, T. and TAI, E.S., 2008. FTO variants are associated with obesity in the Chinese and Malay populations in Singapore. Diabetes, 57(10), pp. 2851-2857.

TANOFSKY-KRAFF, M., HAN, J.C., ANANDALINGAM, K., SHOMAKER, L.B., COLUMBO, K.M., WOLKOFF, L.E., KOZLOSKY, M., ELLIOTT, C., RANZENHOFER, L.M. and ROZA, C.A., 2009. The FTO gene rs9939609 obesity-risk allele and loss of control over eating. The American Journal of Clinical Nutrition, 90(6), pp. 1483-1488.

TARRAGON, E., STEIN, J. and MEYER, J., 2017. Psychometric properties of the German translated version and adaptation of the Food Craving Inventory. Frontiers in psychology, 8, pp. 736.

TAYLOR, G., BAGBy, rM, & PArker, JdA (1997). Disorders of affect regulation: Alex ithymia in medical and psychiatric Illness, .

TAYLOR, G.J., BAGBY, R.M. and PARKER, J.D., 2016. What's in the name 'alexithymia'? A commentary on "Affective agnosia: Expansion of the alexithymia construct and a new opportunity to integrate and extend Freud's legacy.". Neuroscience & Biobehavioral Reviews, 68, pp. 1006-1020.

TAYLOR, G.J., BAGBY, R.M. and PARKER, J.D., 2003. The 20-Item Toronto Alexithymia Scale: IV. Reliability and factorial validity in different languages and cultures. Journal of psychosomatic research, 55(3), pp. 277-283.

TAYLOR, G.J., BAGBY, R.M. and PARKER, J.D., 1999. Disorders of affect regulation: Alexithymia in medical and psychiatric illness. Cambridge University Press.

TAYLOR, G.J. and BAGBY, R.M., 2004. New trends in alexithymia research. Psychotherapy and psychosomatics, 73(2), pp. 68-77.

TCHERNOF, A. and DESPRÉS, J., 2013. Pathophysiology of human visceral obesity: an update. Physiological Reviews, 93(1), pp. 359-404.

TEIXEIRA, P.J., GOING, S.B., HOUTKOOPER, L.B., CUSSLER, E.C., METCALFE, L.L., BLEW, R.M., SARDINHA, L.B. and LOHMAN, T.G., 2006. Exercise motivation, eating, and body image variables as predictors of weight control. Medicine & Science in Sports & Exercise, 38(1), pp. 179-188.

TETLEY, A., BRUNSTROM, J. and GRIFFITHS, P., 2009. Individual differences in food-cue reactivity. The role of BMI and everyday portion-size selections. Appetite, 52(3), pp. 614-620.

THAMOTHARAN, S., LANGE, K., ZALE, E.L., HUFFHINES, L. and FIELDS, S., 2013. The role of impulsivity in pediatric obesity and weight status: a meta-analytic review. Clinical psychology review, 33(2), pp. 253-262.

THOMAS, T., 2016. An investigation of the association of BMI and body fat percentage to eating behaviors as measured by the three factor eating questionnaire-R18 in University students.

TIGGEMANN, M. and KEMPS, E., 2005. The phenomenology of food cravings: the role of mental imagery. Appetite, 45(3), pp. 305-313.

TIMKO, C.A. and PERONE, J., 2005. Rigid and flexible control of eating behavior in a college population. Eating Behaviors, 6(2), pp. 119-125.

TIMPSON, N.J., EMMETT, P.M., FRAYLING, T.M., ROGERS, I., HATTERSLEY, A.T., MCCARTHY, M.I. and DAVEY SMITH, G., 2008. The fat mass–and obesity-associated locus and dietary intake in children–. The American Journal of Clinical Nutrition, 88(4), pp. 971-978.

TOWNSHEND, T. AND LAKE, A.A., 2009. Obesogenic urban form: theory, policy and practice. Health & place, 15(4), pp.909-916.

TOWNSHEND, T.G., 2017. Toxic high streets. Journal of Urban Design, *22*(2), pp.167-186.

TOWNSHEND, T. AND LAKE, A., 2017. Obesogenic environments: current evidence of the built and food environments. perspectives in public health, 137(1), pp.38-44.

TREASURE, J. and SCHMIDT, U., 2013. The cognitive-interpersonal maintenance model of anorexia nervosa revisited: a summary of the evidence for cognitive, socio-emotional and interpersonal predisposing and perpetuating factors. Journal of eating disorders, 1(1), pp. 13.

TUOMISTO, T., HETHERINGTON, M.M., MORRIS, M., TUOMISTO, M.T., TURJANMAA, V. and LAPPALAINEN, R., 1999. Psychological and physiological characteristics of sweet food “addiction”. International Journal of Eating Disorders, 25(2), pp. 169-175.

VAN STRIEN, T., ENGELS, R.C., VAN LEEUWE, J. and SNOEK, H.M., 2005. The Stice model of overeating: tests in clinical and non-clinical samples. Appetite, 45(3), pp. 205-213.

VAN STRIEN, T., HERMAN, C.P. and VERHEIJDEN, M.W., 2012. Eating style, overeating and weight gain. A prospective 2-year follow-up study in a representative Dutch sample. Appetite, 59(3), pp. 782-789.

VAN STRIEN, T., HERMAN, C.P. and VERHEIJDEN, M.W., 2009. Eating style, overeating, and overweight in a representative Dutch sample. Does external eating play a role? Appetite, 52(2), pp. 380-387.

VAN STRIEN, T., KONTTINEN, H., HOMBERG, J.R., ENGELS, R.C. and WINKENS, L.H., 2016. Emotional eating as a mediator between depression and weight gain. Appetite, 100, pp. 216-224.

VASAN, S.K., FALL, T., NEVILLE, M.J., ANTONISAMY, B., FALL, C.H., GEETHANJALI, F.S., GU, H.F., RAGHUPATHY, P., SAMUEL, P. and THOMAS, N., 2012. Associations of variants in FTO and near MC4R with obesity traits in South Asian Indians. Obesity, 20(11), pp. 2268-2277.

VERZIJL, C.L., AHLICH, E., SCHLAUCH, R.C. and RANCOURT, D., 2018. The role of craving in emotional and uncontrolled eating. Appetite, 123, pp. 146-151.

VOLKOW, N.D., WANG, G.J., FOWLER, J.S. and TELANG, F., 2008. Overlapping neuronal circuits in addiction and obesity: evidence of systems pathology. Philosophical transactions of the Royal Society of London.Series B, Biological sciences, 363(1507), pp. 3191-3200.

VANDEVIJVERE, S., CHOW, C.C., HALL, K.D., UMALI, E. AND SWINBURN, B.A., 2015. Increased food energy supply as a major driver of the obesity epidemic: a global analysis. Bulletin of the World Health Organization, *93*, pp.446-456.

WADDEN, T.A., BROWNELL, K.D. and FOSTER, G.D., 2002. Obesity: responding to the global epidemic. Journal of consulting and clinical psychology, 70(3), pp. 510.

WALTER, N.T., MONTAG, C., MARKETT, S.A. and REUTER, M., 2011. Interaction effect of functional variants of the BDNF and DRD2/ANKK1 gene is associated with alexithymia in healthy human subjects. Psychosomatic medicine, 73(1), pp. 23-28.

WANG, Y.C., MCPHERSON, K., MARSH, T., GORTMAKER, S.L. and BROWN, M., 2011. Health and economic burden of the projected obesity trends in the USA and the UK. The Lancet, 378(9793), pp. 815-825.

WARDLAW, S.L., 2011. Hypothalamic proopiomelanocortin processing and the regulation of energy balance. European journal of pharmacology, 660(1), pp. 213-219.

WARDLE, J., LLEWELLYN, C., SANDERSON, S. and PLOMIN, R., 2009. The FTO gene and measuredfood intake in children. International journal of obesity, 33(1), pp. 42.

WARDLE, J., CARNELL, S., HAWORTH, C.M., FAROOQI, I.S., O'RAHILLY, S. and PLOMIN, R., 2008. Obesity associated genetic variation in FTO is associated with diminished satiety. The Journal of Clinical Endocrinology & Metabolism, 93(9), pp. 3640-3643.

WARDLE, J., WALLER, J. and RAPOPORT, L., 2001. Body dissatisfaction and binge eating in obese women: the role of restraint and depression. Obesity research, 9(12), pp. 778-787.

WEINGARTEN, H.P. and ELSTON, D., 1991. Food cravings in a college population. Appetite, 17(3), pp. 167-175.

WEINGARTEN, H.P. and ELSTON, D., 1990. The phenomenology of food cravings. Appetite, 15(3), pp. 231-246.

WERLE, C.O., WANSINK, B. and PAYNE, C.R., 2015. Is it fun or exercise? The framing of physical activity biases subsequent snacking. Marketing Letters, 26(4), pp. 691-702.

WERLE, C.O., WANSINK, B. and PAYNE, C.R., 2011. Just thinking about exercise makes me serve more food. Physical activity and calorie compensation. Appetite, 56(2), pp. 332-335.

WEST, N.R., DORLING, J., THACKRAY, A.E., HANSON, N.C., DECOMBEL, S.E., STENSEL, D.J. and GRICE, S.J., 2018. Effect of obesity-linked FTO rs9939609 variant on physical activity and dietary patterns in physically active men and women. Journal of obesity, 2018.

WESTENHOEFER, J., STUNKARD, A.J. and PUDEL, V., 1999. Validation of the flexible and rigid control dimensions of dietary restraint. International Journal of Eating Disorders, 26(1), pp. 53-64.

WESTENHÖFER, J., 1992. Gezügeltes Essen und Störbarkeit des Essverhaltens. Verlag für Psychologie, Hogrefe.

WHITE, M.A. and GRILO, C.M., 2005. Psychometric properties of the Food Craving Inventory among obese patients with binge eating disorder. Eating Behaviors, 6(3), pp. 239-245.

WHITE, M.A., WHISENHUNT, B.L., WILLIAMSON, D.A., GREENWAY, F.L. and NETEMEYER, R.G., 2002. Development and validation of the food‐craving inventory. Obesity research, 10(2), pp. 107-114.

WHO EXPERT CONSULTATION 2004. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet, 363, 157-63.

WILKS, R., ROTIMI, C., BENNETT, F., MCFARLANE‐ANDERSON, N., KAUFMAN, J., ANDERSON, S., COOPER, R., CRUICKSHANK, J. and FORRESTER, T., 1999. Diabetes in the Caribbean: results of a population survey from Spanish Town, Jamaica. Diabetic Medicine, 16(10), pp. 875-883.

WILLETT, W.C., DIETZ, W.H. and COLDITZ, G.A., 1999. Guidelines for healthy weight. New England journal of medicine, 341(6), pp. 427-434.

WISE, T.N., SIMPSON, N. and SHERIDAN, M.J., 2000. Comparison of 26-item and 20-item versions of the Toronto Alexithymia Scale for psychiatric outpatients. Psychological reports, 87(1), pp. 127-132.

WORLD HEALTH ORGANIZATION, 2016. Obesity and overweight [Internet]. Fact sheet, 311.

WORLD HEALTH ORGANIZATION, 2000. Obesity: preventing and managing the global epidemic. World Health Organization.

WU, J., XU, J., ZHANG, Z., REN, J., LI, Y., WANG, J., CAO, Y., RONG, F., ZHAO, R. and HUANG, X., 2014. Association of FTO polymorphisms with obesity and metabolic parameters in Han Chinese adolescents. PloS one, 9(6), pp. e98984.

XU, B., GOULDING, E.H., ZANG, K., CEPOI, D., CONE, R.D., JONES, K.R., TECOTT, L.H. and REICHARDT, L.F., 2003. Brain-derived neurotrophic factor regulates energy balance downstream of melanocortin-4 receptor. Nature neuroscience, 6(7), pp. 736.

XU, Y., JONES, J.E., KOHNO, D., WILLIAMS, K.W., LEE, C.E., CHOI, M.J., ANDERSON, J.G., HEISLER, L.K., ZIGMAN, J.M. and LOWELL, B.B., 2008. 5-HT 2C Rs expressed by pro-opiomelanocortin neurons regulate energy homeostasis. Neuron, 60(4), pp. 582-589.

YANG, J., LOOS, R.J., POWELL, J.E., MEDLAND, S.E., SPELIOTES, E.K., CHASMAN, D.I., ROSE, L.M., THORLEIFSSON, G., STEINTHORSDOTTIR, V. and MÄGI, R., 2012. FTO genotype is associated with phenotypic variability of body mass index. Nature, 490(7419), pp. 267.

YEO, G.S. and HEISLER, L.K., 2012. Unraveling the brain regulation of appetite: lessons from genetics. Nature neuroscience, 15(10), pp. 1343.

ZAVATTARI, P., LOCHE, A., PILIA, S., IBBA, A., MOI, L., GUZZETTI, C., CASINI, M.R. and LOCHE, S., 2011. rs9939609 in the FTO gene is associated with obesity but not with several biochemical parameters in Sardinian obese children. Annals of Human Genetics, 75(6), pp. 648-654.

ZELLNER, D., GARRIGA-TRILLO, A., ROHM, E., CENTENO, S. and PARKER, S., 1999. Food liking and craving: A cross-cultural approach. Appetite, 33(1), pp. 61-70. ZHAO, X., YANG, Y., SUN, B., ZHAO, Y. and YANG, Y., 2014. FTO and obesity: mechanisms of association. Current diabetes reports, 14(5), pp. 486.

8 APPENDICES

8.1 Appendix 1: Three factor eating questionnaire

Three Factor Eating Questionnaire (TFEQ)

Name…… Date……

Please answer the following questions by circling the response.

1. I deliberately take small helpings as a means of controlling my weight.

definitely true mostly true mostly false definitely false

2. I consciously hold back at meals in order not to gain weight.

definitely true mostly true mostly false definitely false

3. I do not eat some foods because they make me fat.

definitely true mostly true mostly false definitely false

4. How frequently do you avoid 'stocking up' on tempting foods?

almost never seldom usually almost always

5. How likely are you to consciously eat less than you want?

unlikely slightly likely moderately likely very likely

6. On a scale of 1 to 8, where 1 means no restraint in eating (eating whatever you want, whenever you want it) and 8 means total restraint (constantly limiting food intake and never 'giving in'), what number would you give yourself?

Eat whatever I want, whenever I want it

1

2

3

4

5

6

7

8

Constantly limiting food intake, never 'giving in'

7. When I smell a sizzling steak or a juicy piece of meat, I find it very difficult to keep from eating, even if I have just finished a meal.

definitely true mostly true mostly false definitely false

8. Sometimes when I start eating, I just can't seem to stop.

definitely true mostly true mostly false definitely false

9. Being with someone who is eating often makes me hungry enough to eat also.

definitely true mostly true mostly false definitely false

10. When I see a real delicacy, I often get so hungry that I have to eat right away.

definitely true mostly true mostly false definitely false

11. I get so hungry that my stomach often seems like a bottomless pit.

definitely true mostly true mostly false definitely false

12. I am always hungry, so it is hard for me to stop eating before I finish the food on my plate.

definitely true mostly true mostly false definitely false

13. I am always hungry enough to eat at any time.

definitely true mostly true mostly false definitely false

14. How often do you feel hungry?

only at mealtimes sometimes between meals

often between meals almost always

15. Do you go on eating binges though you are not hungry?

never rarely sometimes at least once a week

16. When I feel anxious, I find myself eating.

definitely true mostly true mostly false definitely false

17. When I feel blue, I often overeat.

definitely true mostly true mostly false definitely false

18. When I feel lonely, I console myself by eating.

definitely true mostly true mostly false definitely false

8.2 Appendix 2: Food Craving Inventory

FOOD CRAVING INVENTORY (FCI)

Name: _____ Date: _____

Food craving is defined as an intense desire to consume a particular food (or food type) that is difficult to resist.

For each of the foods listed below (Items 1-28), please circle the appropriate letter using the following scale.

Over the past month, how often have you experienced a craving for the food?

A = Never

B = Rarely (once or twice)

C = Sometimes

D = Often

E = Always/almost every day

List of foods	Never	Rarely	Sometimes	Often	Almost everyday
Cakes	A	B	C	D	E
Pizza	A	B	C	D	E
Fried Chicken	A	B	C	D	E
Sausages	A	B	C	D	E
French Fries/Chips	A	B	C	D	E
Rice	A	B	C	D	E
Sausage Rolls	A	B	C	D	E
Gravy	A	B	C	D	E
Hamburger/Beefburger	A	B	C	D	E
Biscuits	A	B	C	D	E
Ice Cream	A	B	C	D	E

List of foods	Never	Rarely	Sometimes	Often	Almost Everyday
Pasta	A	B	C	D	E
Fried Fish	A	B	C	D	E
Cookies	A	B	C	D	E
Chocolate	A	B	C	D	E
Pancakes/Waffles	A	B	C	D	E
Bread Rolls/Bagels/Baps	A	B	C	D	E
Doughnuts	A	B	C	D	E
Sweets	A	B	C	D	E
Brownies/Muffins	A	B	C	D	E
Bacon	A	B	C	D	E
Steak	A	B	C	D	E
Danish pastry	A	B	C	D	E
Baked Potatoes	A	B	C	D	E
Sponge Cake	A	B	C	D	E
Cereals	A	B	C	D	E
Sandwich Bread	A	B	C	D	E
Crisps	A	B	C	D	E

8.3 Appendix 3 : Behaviour Regulations Exercise questionnaire BREQ2

EXERCISE REGULATIONS QUESTIONNAIRE (BREQ-2)

Age: _____ years Sex: male female (please circle)

WHY DO YOU ENGAGE IN EXERCISE?

We are interested in the reasons underlying peoples' decisions to engage, or not engage in physical exercise. Using the scale below, please indicate to what extent each of the following items is true for you. Please note that there are no right or wrong answers and no trick questions. We simply want to know how you personally feel about exercise. Please CIRCLE your response.

		Not true for me		Sometimes true for me		Very true for me
1	I exercise because other people say I should	0	1	2	3	4
2	I feel guilty when I don't exercise	0	1	2	3	4
3	I value the benefits of exercise	0	1	2	3	4
4	I exercise because it's fun	0	1	2	3	4
5	I don't see why I should have to exercise	0	1	2	3	4
6	I take part in exercise because my friends/family/partner say I should	0	1	2	3	4
7	I feel ashamed when I miss an exercise session	0	1	2	3	4
8	It's important to me to exercise regularly	0	1	2	3	4
9	I can't see why I should bother exercising	0	1	2	3	4
10	I enjoy my exercise sessions	0	1	2	3	4
11	I exercise because others will not be pleased with me if I don't	0	1	2	3	4
12	I don't see the point in exercising	0	1	2	3	4
13	I feel like a failure when I haven't exercised in a while	0	1	2	3	4
14	I think it is important to make the effort to exercise regularly	0	1	2	3	4
15	I find exercise a pleasurable activity	0	1	2	3	4
16	I feel under pressure from my friends/family to exercise	0	1	2	3	4
17	I get restless if I don't exercise regularly	0	1	2	3	4
18	I get pleasure and satisfaction from participating in exercise	0	1	2	3	4
19	I think exercising is a waste of time	0	1	2	3	4
20	I don't exercise because of the pain	0	1	2	3	4

8.4 Appendix 4: Toronto Alexithymia Scale TAS 20

TAS 20 Toronto Alexithymia Scale

Please indicate to what extent each of the following statements is true for you. Please note there are no right or wrong answers or trick questions. We simply want to know how hard or easy it is for you to identify your feelings. Please CIRCLE your response.

1. I am often confused about what emotion I am feeling.
Strongly Disagree……Moderately Disagree……Neither Disagree or Agree……Moderately Agree……Strongly Agree

2. It is difficult for me to find the right words for my feelings.
Strongly Disagree……Moderately Disagree……Neither Disagree or Agree……Moderately Agree……Strongly Agree

3. I have physical sensations that even doctors don't understand.
Strongly Disagree……Moderately Disagree……Neither Disagree or Agree……Moderately Agree……Strongly Agree

4. I am able to describe my feelings easily.
Strongly Disagree……Moderately Disagree……Neither Disagree or Agree……Moderately Agree……Strongly Agree

5. I prefer to analyse problems rather than just describe them.
Strongly Disagree……Moderately Disagree……Neither Disagree or Agree……Moderately Agree……Strongly Agree

6. When I am upset, I don't know if I am sad, frightened or angry.
Strongly Disagree……Moderately Disagree……Neither Disagree or Agree……Moderately Agree……Strongly Agree

7. I am often puzzled by sensations in my body.
Strongly Disagree……Moderately Disagree……Neither Disagree or Agree……Moderately Agree……Strongly Agree

8. I prefer to just let things happen rather than to understand why they turned out that way.
Strongly Disagree……Moderately Disagree……Neither Disagree or Agree……Moderately Agree……Strongly Agree

9. I have feelings that I can't quite identify.
Strongly Disagree……Moderately Disagree……Neither Disagree or Agree……Moderately Agree……Strongly Agree

10. Being in touch with emotions is essential.
Strongly Disagree……Moderately Disagree……Neither Disagree or Agree……Moderately Agree……Strongly Agree

11. I find it hard to describe how I feel about people.
Strongly Disagree……Moderately Disagree……Neither Disagree or Agree……Moderately Agree ……Strongly Agree

12. People tell me to describe my feelings more.
Strongly Disagree……Moderately Disagree……Neither Disagree or Agree……Moderately Agree……Strongly Agree

13. I don't know what is going on inside me.
Strongly Disagree……Moderately Disagree……Neither Disagree or Agree……Moderately Agree……Strongly Agree

14. I often don't know why I am angry.
Strongly Disagree……Moderately Disagree……Neither Disagree or Agree……Moderately Agree……Strongly Agree

15. I prefer talking to people about their daily activities rather than their feelings.
Strongly Disagree……Moderately Disagree……Neither Disagree or Agree……Moderately Agree……Strongly Agree

16. I prefer to watch 'light' entertainment shows, rather than psychological dramas.
Strongly Disagree……Moderately Disagree……Neither Disagree or Agree……Moderately Agree……Strongly Agree

17. It is difficult for me to reveal my innermost feelings, even to close friends.
Strongly Disagree……Moderately Disagree……Neither Disagree or Agree……Moderately Agree……Strongly Agree

18. I can feel close to someone, even in moments of silence.
Strongly Disagree……Moderately Disagree……Neither Disagree or Agree……Moderately Agree……Strongly Agree

19. I find examination of my feelings useful in solving personal problems.
Strongly Disagree……Moderately Disagree……Neither Disagree or Agree……Moderately Agree……Strongly Agree

20. Looking for hidden meanings in movies or plays distracts from their enjoyment.
Strongly Disagree……Moderately Disagree……Neither Disagree or Agree……Moderately Agree……Strongly Agree

8.5 Appendix 5: Consent form 1

Sheffield Hallam University

Faculty of Health and Wellbeing Research Ethics Committee

Biomedical Research Centre Ethics Review Group

INFORMED CONSENT FORM	
TITLE OF PROJECT: Relationship between eating behaviours and food cravings; influence of FTO genotype	
Please read the questions below and circle your answer. If you do not understand any of the questions, please ask the researcher.	
Have you read and understood the Participant Information Sheet?	YES/NO
Have you had an opportunity to ask questions and discuss this study?	YES/NO
Have you received satisfactory answers to all of your questions?	YES/NO
Have you received enough information about the study?	YES/NO
To whom have you spoken? ..... Do you understand that you are free to withdraw from the study? ☐ at any time ☐ without having to give a reason for withdrawing	YES/NO
Do you agree to the secure storage of your anonymised data?	YES/NO
Do you agree to provide blood samples and a DNA sample; these will also be stored securely?	YES/NO
Do you agree to take part in this study?	YES/NO
Signed..... Date ..... (NAME IN BLOCK LETTERS)	

8.6 Appendix 6: Participant information sheet 1

Faculty of Health and Wellbeing Research Ethics Committee

Biomedical Research Centre Review Group

Participant Information Sheet

Project Title	Relationship between eating behaviours and food cravings; influence of FTO genotype

Supervisor/Director of Studies	Dr. Caroline Dalton

Principal Investigator	Hanan Abdella, Hameida Elfaressi.

Principal Investigator **telephone/mobile number**	0114 225 3695

Purpose of Study and Brief Description of Procedures

You are being invited to take part in a research study. Before you decide if you wish to take part it is important for you to understand why the research is being undertaken and what it will involve for you. Please take time to read the following information carefully. The investigators will go through this information sheet with you and answer any questions you have. Please ask if there is anything that is not clear or if you would like more information. Take your time to decide if you would like to take part.

Procedures

- **Read participant information sheet**
- **Consider study, ask questions**
- **Complete and sign consent form**
- **Height and weight measurements**
- **Completion of eating behaviours and food cravings questionnaires**
- **Collection of a cheek cell sample. The process to take the cheek cell sample is entirely painless; it is very similar to gently brushing the inside of your cheek with a toothbrush. You would carry out this process yourself with help from our researcher (if required).**
-

21. Benefits of the study

The study will provide important information regarding eating behaviours and food cravings and the influence of genetics on these effects. The study is anonymised, so we will not be able to give you any individual feedback on your results, but we will be happy to discuss the overall findings of the study with you.

What will happen to the results at the end of the study?

The results will be published as academic reports in scientific journals. There will be no identifying information published. We will also write a summary report of anything we discover which we will send to any of the people who participated in the study who want to see it. This will not contain any identifying information.

Will my taking part in this study be kept confidential?

Yes, no one will know you have taken part in the study except the members of the research team. Your consent form will be placed by you in a sealed envelope separate from the questionnaires and the DNA sample. You will be allocated a participant number, and this will not be linked to your consent form therefore the data we collect from you will be completely anonymous and cannot be traced back to you.

What will happen to my DNA sample?

Your DNA sample will be stored in our laboratories which have restricted access. The samples will be coded with a participant number which cannot be traced back to you. We will only use the sample to study genes involved in the topics covered by this ethics application and we will not allow access to your dna sample by any third party.

Has this study got ethical approval?

Yes, this study was approved by the local Ethics Committee. This means that experts who are not involved in the study have carefully considered the aims and methods of the study and agreed that they meet their guidelines. You can find out more about their work on their website

www.sth-research.group.shef.ac.uk/research/index.html

Right to Withdraw

Remember that you always have the right to withdraw from the study at any time.

It has been made clear to me that, should I feel that these Regulations are being infringed or that my interests are otherwise being ignored, neglected or denied, I should inform Dr Nikki Jordan-Mahy, Chair of the Faculty of Health and Wellbeing Research Ethics Committee (Tel: 0114 225 3120) who will undertake to investigate my complaint.

8.7 Appendix 7: Consent form 2

	
INFORMED CONSENT FORM	
TITLE OF PROJECT: Study to investigate the factors influencing body weight plan IRAS number: 208879	
Please read the questions below and circle your answer. If you do not understand any of the questions, please ask the researcher.	
Have you read and understood the Participant Information Sheet? (version 3 January 2017)	YES/NO
Have you had an opportunity to ask questions and discuss this study?	YES/NO
Have you received satisfactory answers to all of your questions?	YES/NO
Have you received enough information about the study?	YES/NO
To whom have you spoken? ..... Do you understand that you are free to withdraw from the study? □ at any time □ without having to give a reason for withdrawing	YES/NO
Do you agree to the secure storage of your anonymised data?	YES/NO
Do you agree to provide blood samples and a DNA sample; these will also be stored securely?	YES/NO
Do you agree that your samples and data can be used in future studies?	YES/NO
Do you agree that medical notes and data collected during the study can be looked at by individuals from regulatory authorities or sponsors, where it is relevant to you taking part in the research?	YES/NO

Do you agree to take part in this study?	YES/NO

Signed..... Date .....

(NAME IN BLOCK LETTERS) .....

Original to be filed in the Investigator site file, 1 copy for patient, 1 copy to be kept in the patient's medical records at RIO.

8.8 Appendix 8: Participant information sheet 2

Participant information Sheet **version 3 Jan 2017**

Project Title	**Study to investigate factors influencing the body a weight IRAS number: 208879**
Principal Investigator	Dr Caroline Dalton Biomolecular Sciences Research Centre Sheffield Hallam University
Principal Investigator **telephone/email**	0114 225 3695/c.f.dalton@shu.ac.uk

Purpose of Study and Brief Description of Procedures

You are being invited to take part in a research study. Before you decide if you wish to take part it is important for you to understand why the research is being undertaken and what it will involve for you. Please take time to read the following information carefully. One of our team is available to go through this information sheet with you and answer any questions you have. Please ask if there is anything that is not clear or if you would like more information. Take your time to decide if you would like to take part.

The project aims to establish whether it is possible to identify the biological and psychological factors that are associated with success on a weight management plan.

We think that there are differences in how people respond when they try to manage their weight. These individual differences may be due to genetic or hormonal variability, or they may be due to psychological differences. If we can identify factors that are associated with increase in body .we may be able to design better programmes to also help those people who find weight management more difficult.

If you choose to participate in this study, you will be asked to fill in some questionnaires about your attitudes to food and exercise and your feelings.

We also want to test your hormones and analyse your DNA, to do this we will need to take a DNA swab from your mouth.

Procedures:

Meeting 1 (after your 1st appointment at RIO, 30 minutes)

- Read participant information sheet
- Consider study, ask questions
- Complete and sign consent form
- Fill in questionnaires
- Give a DNA sample by swabbing your mouth (this is painless and similar to using a toothbrush)

Meeting 2: **(2 hours, at RIO, a few days after meeting 1, or during the following week)**

- Collection of blood sample. For the blood prick sample, you need to carry out a 12 hour overnight fast. A blood prick sample will be collected in the morning when you first arrive using a finger prick device

(similar to that used by diabetics to test their insulin levels), this will be analysed for hormones.

- Test breakfast and questionnaires. Once you have given the blood sample you will be asked to fill in a questionnaire about how hungry you feel, then you will be given a breakfast of cornflakes, milk and orange juice. If you are allergic to any of these items, we can offer an alternative e.g. rice krispies/soya milk. You will be asked to record how hungry you feel at time points during the next 1 hour and 45 minutes. During this time, you need to stay at RIO but are free to read or use your phone. At the end of this time the test will finish, and you can leave.
- You will be given £5 at the end of this session to cover your transport costs.

Possible risks and discomforts:
The blood prick sample procedure is mildly uncomfortable, no other risks or discomforts are anticipated.

Benefits of the study:
The study will provide important information regarding whether It is possible to identify what factors predict success for people on a weight management programme. However, you will not be told your individual results.

What will happen to my DNA and blood sample?

Your DNA and blood samples will be stored in our laboratories which have restricted access. The samples will be coded with a participant number which cannot be traced back to you. We will not allow access to your samples by any third party.

What will happen to my samples and data at the end of the study?

We would like to store your samples and data so at the end of the study so that we can use them in similar research projects. If you would prefer that we did not do this, you can indicate this on the consent form and we will destroy your samples and remove your data from the database at the end of the study.

What will happen to the results at the end of the study?

The results will be published as academic reports in scientific journals. There will be no identifying information published. We will also write a summary report of anything we discover which we will send to any of the people who participated in the study who want to see it. This will not contain any identifying information. The report will be available in mid-2018. If you would like to have a copy of the report, please contact RIO nearer the time on 01709 720193.

Will my taking part in this study be kept confidential?

Yes, no one will know you have taken part in the study except the members of the research team. Your consent form will be placed by you in a sealed envelope separate from the questionnaires, the blood samples and the DNA sample. You will be allocated a participant number, and this will not be linked to your consent form therefore the data we collect from you will be completely anonymous and cannot be traced back to you.

Has this study got ethical approval?

Yes, this study was approved by the local Ethics Committee. This means that experts who are not involved in the study have carefully considered the aims and methods of the study and agreed that they meet their guidelines.

Right to Withdraw:

Remember that you always have the right to withdraw from the study at any time.

If you feel that these Regulations are being infringed or that your interests are otherwise being ignored, neglected or denied, you should inform Dr Nikki Jordan-Mahy, Chair of the Faculty of Health and Wellbeing Research Ethics Committee art Sheffield Hallam University (Tel: 0114 225 3120 email n.jordan-mahy@shu.ac.uk) who will undertake to investigate your complaint.

8.9 Appendix 9

Table8-1 outputs from the mediation analysis model between BMI, cognitive restraint and sweet craving for ≤25 Years

Antecedent		Consequent						
		M(COGNITIVE RESTRAINT)			Y(SWEET CRAVING)			
		Coeff.	*SE*	*P*		*Coeff.*	*SE*	*P*
X(BMI)	*a*	.1521	.0588	.0102	*c'*	-.0361	.1511	.8112
M(FCOGNITIVE RESTRAINT)					*b*	-.7010	.1608	.0000
C2(SEX)	*f1*	-.3662	.4549	.4217	*g1*	-2.5390	1.1560	.0290
C3(FTO GENOTYPE)	*f2*	.3438	.4828	.4771	*g2*	.9289	1.2264	.4495
Constant	*i1*	9.8993	1.4919	.0000	*i2*	31.4370	4.1072	.0000
		R^2=.0301 F(2.57)=12.812 P=.0545			R^2=.0894 F(6.087)=82.507,P<.001			

```
Run MATRIX procedure:

*************** PROCESS Procedure for SPSS Version 3.1
*****************

          Written by Andrew F. Hayes, Ph.D.       www.afhayes.com
    Documentation available in Hayes (2018). www.guilford.com/p/hayes3

**************************************************************************
****
Model  : 4
    Y  : sweet
    X  : bmi
    M  : cr

Covariates:
 sex      fto

Sample
Size:  253

**************************************************************************
****
OUTCOME VARIABLE:
 cr

Model Summary
          R       R-sq        MSE          F        df1        df2
p
      .1734      .0301    12.8116     2.5744     3.0000
249.0000      .0545

Model
             coeff         se          t          p       LLCI
ULCI
constant     9.8993     1.4919     6.6352      .0000     6.9609
12.8377
bmi           .1521      .0588
2.5885      .0102      .0364      .2678
sex          -.3662      .4549     -.8049      .4217    -
1.2622      .5299
fto           .3438      .4828      .7121      .4771     -.6070
1.2946

**************************************************************************
****
OUTCOME VARIABLE:
 sweet

Model Summary
          R       R-sq        MSE          F        df1        df2
p
      .2990      .0894    82.5070     6.0873     4.0000
248.0000      .0001

Model
             coeff         se          t          p       LLCI
ULCI
constant    31.4370     4.1072     7.6541      .0000    23.3475
39.5265
bmi          -.0361      .1511     -.2391      .8112     -
.3337      .2615
```

```
cr           -.7010      .1608    -4.3587      .0000    -1.0177     -
.3842
sex         -2.5390     1.1560    -2.1964      .0290    -4.8158     -
.2622
fto           .9289     1.2264      .7575      .4495    -1.4865
3.3444

****************** DIRECT AND INDIRECT EFFECTS OF X ON Y
*****************

Direct effect of X on Y
     Effect         se          t          p       LLCI       ULCI
     -.0361      .1511     -.2391      .8112     -.3337      .2615

Indirect effect(s) of X on Y:
       Effect     BootSE   BootLLCI   BootULCI
cr     -.1066      .0536     -.2297     -.0226

*********************** ANALYSIS NOTES AND ERRORS
************************

Level of confidence for all confidence intervals in output:
  95.0000

Number of bootstrap samples for percentile bootstrap confidence
intervals:
  10000

------ END MATRIX -----
```