Biopsychological examination of changes in food reward during weight loss in women

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The candidate confirms that the work submitted is her own, except where work which has formed part of jointly-authored publications has been included. The contribution of the candidate and the other authors to this work has been explicitly indicated below. The candidate confirms that appropriate credit has been given within the thesis where reference has been made to the work of others.

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The candidate took a primary role in the writing of this systematic review (conceptualisation, search strategy, data extraction, synthesis, writing). Co-authors contributed to this publication in guiding and editing drafts of the manuscripts. The candidate screened twice titles and abstracts and full-text and this was compared with one co-author screening 10% of titles and abstracts, and 2 co-authors screening half of the full-text.

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- **Oustric, P**., Beaulieu, K., Casanova, N., O'Connor, D., Gibbons, C., Hopkins, Blundell, J., Finlayson, G. (2021) Is reward for high-fat sweet a marker of obesity? Appetite. British Feeding and Drinking Group
- **Oustric, P**., Beaulieu, K., Casanova, N., O'Connor, D., Gibbons, C., Hopkins, Blundell, J., Finlayson, G. (2021) Do changes in meal-induced food reward differ between women with or without overweight/obesity? Virtual European/International Congress on Obesity

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Abstract

Background: While taste is a main driver of food choice, food reward is more than just the sensation of taste and interacts with the homeostatic system (e.g. hunger) to create pleasure (liking) and motivation (wanting) for food. Food reward is a driver of food intake and therefore commonly thought to be related to obesity. However, liking/wanting have never been targeted to improve weight management strategies.

Objectives: This thesis aims to explore the role of food reward during 1) weight management, 2) weight loss (WL) and no-contact follow-up, and 3) its association with appetite control and obesity in women.

Methods: Food reward and appetite-related variables (e.g. body composition, energy intake, eating behaviour traits) were investigated during a controlled-feeding WL, 1-year follow-up and a cross-sectional analysis between women with or without overweight/obesity. Liking and implicit wanting were assessed with the Leeds Food Preference Questionnaire.

Results: Contrary to expectations, a systematic review showed that liking and wanting decreased after different weight management interventions. The diet intervention added that liking decreased for all food categories independently from diet modality or improvement in appetite control. After 1-year of no-contact, weight was regained, appetite control weakened and liking returned to baseline levels. Lastly, women with overweight/obesity did not have higher wanting for high-fat sweet but lower wanting for low-fat sweet food compared to women within the normal range of BMI. Importantly, wanting for low-fat food was associated with improved appetite control and less fat mass while it was the contrary for high-fat food.

Conclusions: The role of food reward in weight management distinguishes between liking and wanting and high-fat vs low-fat, as its components dissociated during WL and had opposite impact on appetite control. Food reward does not differ greatly between women with or without overweight/obesity and other appetite-related factors are needed to understand obesity status.

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Abbreviations

AUC – Area under the curve

BES – Binge Eating Scale

BMI – Body mass index

CER – Continuous energy restriction

CoEQ – Control of eating questionnaire

DIVA – Diet-induced variability in appetite

DIVA-1 – Diet-induced WL

DIVA-2 – Cross-sectional analysis between women with overweight/obesity (DIVA-1) and women within the normal range of BMI

DIVA-3 – No-contact follow-up of DIVA-1

fMRI – functional Magnetic Resonance Imaging

HFSA – High-fat-savoury

HFSW – High-fat sweet

IER – Intermittent energy restriction

IES – Intuitive Eating Questionnaire

IQR – Interquartile range

LFPQ – Leeds Food Preference Questionnaire

LFSA – Low-fat savoury

LFSW – Low-fat sweet

MEQ – Mindful Eating Questionnaire

PAL – Physical activity level

PCA – Principal component analysis

PFS – Power of Food Scale

RMR – Resting metabolic rate

SE – Standard error

SD – Standard deviation

SWA – SenseWear Armband

TDEE – Total daily energy expenditure

TFEQ – Three-Factor Eating Questionnaire

VAS – Visual analogue scale

WL – Weight loss

YFAS – Yale Food Addiction Scale

Chapter 1
Theoretical background

Chapter aims:

1. Present and define the main topics of the thesis: obesity, weight management, diet-induced weight loss, continuous and intermittent energy restriction, appetite control and food reward components.
2. Introduce the rationale and aims explored in this thesis.

HIGHLIGHTS

► Obesity is multifactorial, and a multidisciplinary approach is needed to develop successful weight management strategies. However, while food reward is known to be a driver of food intake, targeting one's relationship with food is not usually used as a way to improve weight management strategies.

► Appetite is controlled by a psychobiological system involving an interplay between tonic and episodic signals generating the biological drive to eat. This homeostatic system interacts with the hedonic drive to eat, especially in the obesogenic environment facilitating overconsumption. There is a need to characterise this individual susceptibility to overeat in terms of food reward and eating behaviour traits during energy restriction and obesity.

► Food reward can be separated into liking and wanting, and explicit and implicit levels that are underpinned in the brain and lead eating behaviours. While components of food reward are interrelated with appetite-related variables (e.g. appetite sensations, eating behaviour traits), less is known about these relationships in individuals with overweight/obesity or during weight management interventions.

► Dietary interventions are the most used strategy to lose weight, but they can lead to compensatory responses that attempt to restore a state of neutral energy balance. Furthermore, the asymmetrical responses to energy imbalance (i.e. stronger during negative than positive energy balance), it may be easier to gain than lose weight. However, the role of food reward has never been explored during intermittent and continuous energy restriction nor its relationship with other appetite-related variables, which could lead to improved weight management strategies.

1.1 Obesity, weight loss and weight management

1.1.1 Obesity: the need of a system approach

Obesity is commonly defined by an excessive accumulation of body fat, presenting a risk for health, and measured by a BMI over 30 kg/m^2 (World Health Organization, 2020). It is known that a negative energy balance is required to induce weight loss (WL) over time. However, despite its apparent theoretical simplicity, individual variability in WL and weight management reveal a much more complex picture (Field et al., 2018). The Obesity Systems Map (see Figure 1-1) attests to a broad range of factors influencing obesity, such as individual, societal and environmental influences (Butland et al., 2007). This raised the importance of a systems approach (i.e. integrating a dynamic and interconnected set of parts, forming a complex system (Meadows, 2008)) to inform obesity management treatments. In contrast, the misconception that body weight is exclusively determined by "calories in, and calories out", implies that voluntary decisions to eat less and move more completely control body weight, potentially generating weight stigma (Rubino et al., 2020). This has led to a recent joint international consensus statement for ending obesity stigma to encourage multidisciplinary work, and recognise that obesity is multifactorial (Rubino et al., 2020). Consequently, this thesis will use a bio-psychological approach to obesity, considering individual psychology and behaviour alongside biology.

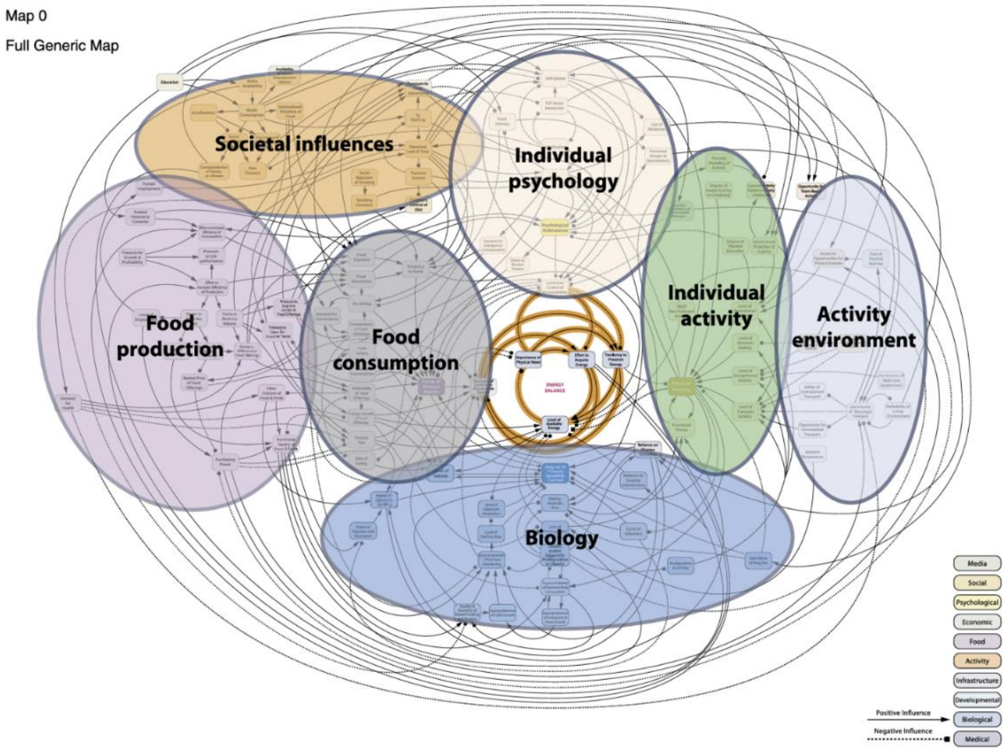

Figure 1-1: Foresight obesity system map with thematic clusters

From Butland et al. (2007). A visual representation of a system mapping approach of obesity describing multifaceted determinants of obesity and their dynamic interactions.

1.1.2 Weight loss and weight management: efficacies and issues

Weight loss and especially long-term WL maintenance is a significant challenge. Only 20% of individuals with overweight succeed in long-term WL maintenance as defined in the National Weight Control Registry as losing at least 10% of initial body weight and maintaining the loss for at least one year (Byrne et al., 2017). Indeed, control over body weight and energy balance is asymmetrical, with stronger physiological and behavioural compensatory responses after energy deficit than energy surfeit (Casanova et al., 2019a). Considering the efficacy of WL programs, a meta-analysis of randomised controlled trials showed that diet-only and diet combined with physical activity led to similar WL in the short to medium term (3 to 6 months), but physical activity alone was less effective (Johns et al., 2014). This highlights that dietary changes are key components for WL. However, it should be kept in mind that behavioural WL interventions have a modest efficacy (<5 kg WL after 2–4 y) compared to pharmacologic therapies (5–10 kg WL after 1–2 y) and surgical therapies (25–75 kg WL after 2–4 y) (Douketis et al., 2005; Stubbs et al., 2021). Nevertheless, pharmacotherapy needs to be used continuously to be effective and bariatric surgery is reserved for severe obesity, so dietary and behavioural WL remain the most common interventions for weight management.

In terms of weight loss maintenance, multidisciplinary approaches, especially lifestyle modification programmes combining dietary, exercise, behavioural and cognitive strategies, are more effective than diet only (Johns et al., 2014; Montesi et al., 2016). Interventions targeting eating behaviour and more particularly the microstructure of meals (such as increasing pauses between bites or reducing eating rate) (Bellisle, 2020) and mathematical modelling of weight regain after WL interventions suggest that changes in eating behaviour and appetite have a large role to play in WL relapse (Polidori et al., 2016). While it is not known whether behavioural and psychological processes involved in successful WL would also be effective for weight loss maintenance, it is likely that some of these processes might be subconscious (e.g. food reward) (Stubbs et al., 2021). However, individuals' hedonic responses to food cues remain under-utilised as a strategy to improve weight management, even though food reward is a common driver of food intake (Finlayson & Dalton, 2012b). Moreover, it remains to be understood whether different type of weight management interventions affect components of food reward differently.

This thesis focuses first on weight management interventions defined in the systematic review (Chapter 2) as all interventions (i.e. WL, weight loss maintenance) aiming to improve weight management outcomes (food intake or weight related) and are therefore not restricted to significant WL in individuals with overweight/obesity. More specifically, weight management refers here to interventions (≥4 weeks) that attempted to measure a change in components of food reward. Therefore, in this thesis, weight management did not extend to include successful restrained eaters managing lean body weight. Secondly, the thesis focuses more specifically on WL achieved through dietary interventions: continuous vs intermittent energy restriction with a no-contact follow-up one year after WL. Finally, the thesis broadens the scope of weight management to focus on obesity, by comparing women with and without overweight/obesity to assess differences in food reward and appetite control.

1.2 Appetite control, episodic and tonic signals

1.2.1 Appetite control: from biological to psychobiological models

The field of appetite control tends to investigate simple questions around eating behaviour: Why do we eat? How much do we eat? What do we eat? Appetite covers the whole field of food intake, selection, motivation and preference (Blundell et al., 2010). However, models explaining the control of appetite have conflicting viewpoints. For some, appetite is regulated, while for others, appetite is not regulated but controlled (Berthoud et al., 2017). The former is based on the regulation of body weight from a set-point perspective, first suggested by Kennedy (1953), and then widely adopted in the 1990s following the discovery of leptin. This "lipostatic model" proposed that fat mass is regulated via a negative-feedback system coordinated in the brain. A discrepancy between the signal from fat mass and the target (set-point) is translated into energy expenditure or energy intake to achieve energy balance (Schwartz et al., 2000).

However, "if such a strong biological feedback system regulating our body fatness exists, then why do most individuals in most western countries gain weight throughout the majority of their lives?" (Speakman et al., 2011, p. 735). This model is generally centred in physiology and does not consider socioeconomic, environmental and psychological factors. Moreover, the timescale of this regulation cannot explain the episodic nature of energy intake, which is discontinuous and extremely variable from meal to meal. More recently, the settling point theory suggested a non-regulated system, mainly explained by the "obesogenic environment" (i.e. increased availability of palatable food and decreased need for physical activity) (Speakman et al., 2011). However, the latter model could not explain the active control over energy intake during WL and starvation (Dulloo et al., 2012). Therefore a dynamic role of fat-free mass has been recently proposed to give some biopsychological insight into the relationships between fat mass, fat-free mass and energy intake (Hopkins et al., 2018). Unfortunately, few studies have integrated physiological, psychological and behavioural factors to model energy balance, so the understanding of a multidisciplinary energy balance framework is limited. To sum up, the complexity of appetite is better considered by a psychobiological system including psychological, behavioural, physiological, metabolic and neurological events (Hopkins et al., 2016a).

1.2.2 Appetite control: an interplay between tonic and episodic signals

This psychobiological system involves interactions between tonic and episodic processes controlling energy intake, as illustrated in Figure 1-2 (Blundell et al., 2020; Hopkins et al., 2016a). Tonic signals are stable and change slowly over time, while episodic signals are variable and occur on a meal to meal basis (Halford & Blundell, 2000). The tonic drive to eat is influenced by fat-free mass via resting metabolic rate (RMR), reflecting the energy needs of vital organs. Whereas, fat mass has been postulated to create a tonic inhibition of energy intake through leptin. These tonic signals are periodically interrupted by episodic gastrointestinal signals generated by food consumption. The latter are often inhibitory and relate to meal initiation, termination and satiety (Hopkins et al., 2016a). Indeed, following food intake, the orexigenic (appetite stimulating) hormone ghrelin is suppressed and other peptides are released from the gut with an anorectic effect (appetite inhibiting) such as cholecystokinin (CCK), glucagon-like peptide 1 (GLP-1) or peptide YY (PYY) mediating meal termination and satiety (see Figure 1-2). Briefly, as described in the satiety cascade proposed by Blundell (1991), the sight and smell of food (sensory and cognitive factors) initiate gastrointestinal signals during the cephalic phase of appetite. Then following food intake and gastric emptying, negative feedback emerges from the stomach and small intestine, leading to satiation (i.e. meal termination) and satiety (i.e. post-meal suppression of hunger). During this postprandial period, the drive to eat arising from RMR is not suppressed and will translate into behaviour after the inhibitory effects from the gastrointestinal activity stops (Blundell et al., 2020). These two sets of signals (tonic and episodic) are interrelated and convey energy need and availability to the central nervous system (Morton et al., 2006) and form the so-called homeostatic system.

The role of behavioural components of food reward in appetite control remains to be investigated in terms of weight management, dietary-induced WL, and obesity status. Therefore, this thesis explores components of food reward with tonic processes (body composition) and episodic processes (appetite sensations, food intake). Appetite control was defined broadly in this thesis to include food intake, appetite sensations, but also eating behaviour traits and body composition to contextualise the changes in food reward. However, the associations between food reward and hormones such as ghrelin and GLP-1, biomarkers or neuronal circuitry are beyond the scope of this thesis, see (Decarie-Spain & Kanoski, 2021; Klockars et al., 2021; Murray et al., 2014).

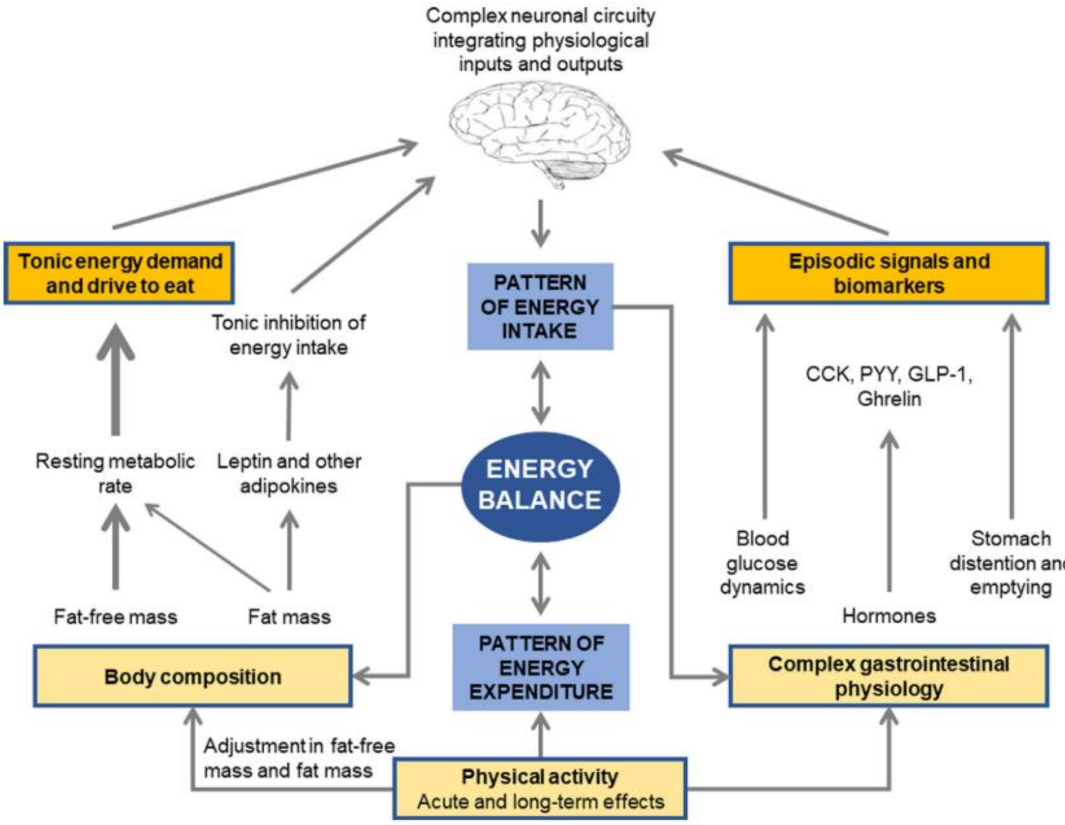

Figure 1-2: Interplay between tonic and episodic signals of appetite control

From Blundell et al. (2020). This model illustrates the interaction between the tonic drive to eat from body composition (drive and inhibition) and the episodic signals from the gastrointestinal physiology (mostly inhibitory) to control appetite. These signals translate into behaviour through their integration in complex neuronal circuitry. Both energy intake and energy expenditure interact to influence tonic and episodic processes.

1.3 Hedonics, susceptibility to overeat and eating behaviour traits

1.3.1 The role of the hedonic drive to eat in the modern environment

Firstly, it is important to distinguish the tonic drive to eat arising from energy requirements with the hedonic drive to eat. The latter encompasses food choices and food reward, which are highly variable among humans and dependent on culture and environment (Blundell et al., 2020). In other words, the biological drive is sufficient to account for how much energy is taken into the body, while the hedonic drive can better account for the quality and timing of food intake in different contexts. We do not eat only in response to hunger; eating is a source of reward, pleasure, satisfaction, which can be difficult to resist considering the high availability of energy-dense food and the permissive social environment (Lowe & Butryn, 2007). From an evolutionary perspective, food reward was needed to motivate food-seeking and guarantee adequate energy intake in a restrictive environment (Zheng et al., 2009). Especially foods rich in fat and sweetness are natural rewards for humans (Volkow et al., 2011). In the modern environment, characterised by abundant palatable food cues, the brain reward system and the lack of adequate inhibition can lead to overconsumption (see Figure 1-3) (DiLeone et al., 2012; Zheng et al., 2009). This is in line with findings from Berthoud et al. (2020) showing that the neural control of food intake has evolved in a restrictive environment. However, while exposure to food cues reliably leads to food intake and weight gain (Boswell & Kober, 2016), not everyone is affected by obesity. Therefore, there is a need to better characterise the individual susceptibility to overeat and explain the difficulty in restricting intake in the omnipresence of food cues (Herman & Polivy, 2008).

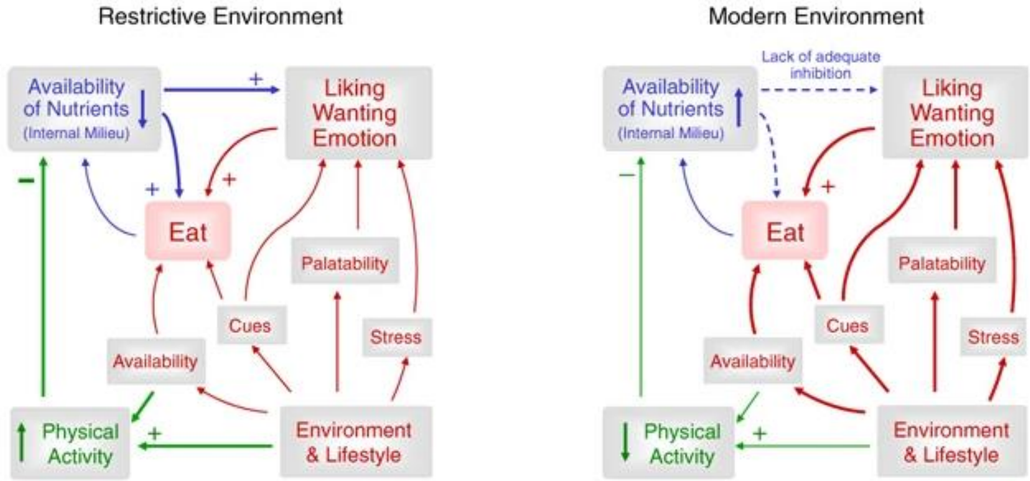

Figure 1-3: Food reward, susceptibility to overeat and the modern environment

From Zheng et al. (2009). This model illustrates major factors influencing food intake in restrictive and modern environments. In a restrictive environment, low availability of nutrients in the internal milieu increases hedonic mechanisms to enable food intake and satisfaction. The susceptibility to overeat emerges from the heightened hedonic and cognitive pressure exerted by the modern environment and the difficulty in suppressing them.

1.3.2 Eating behaviour traits characterising susceptibility to overeat

The susceptibility to overeat when combined with access to palatable food varies among people according to their eating behaviour traits such as disinhibition (Yeomans et al., 2004) or binge eating (Dalton & Finlayson, 2014). Eating behaviour traits characterise individuals' tendencies related to the behavioural act of eating. More specifically, eating behaviour includes selecting and purchasing foods, meal patterns, ingestion, and implies social interactions, cognitive, psychological attitudes, habits and responses to food cues, among many other influences (Bellisle, 2009). Traits represent enduring and resilient features that do not fluctuate within a day (Blundell et al., 2005) and are usually measured through psychometrically validated self-report questionnaires. On the contrary, states such as hunger oscillate episodically with the pattern of eating. While both states and traits influence what we eat through different processes, traits enable us to understand eating tendencies and habits on a long-term basis (Blundell et al., 2005). They are, therefore, essential indicators in the context of weight management and appetite control.

In this thesis, several eating behaviour traits are considered, covering different eating behaviour facets potentially impacting appetite control. See Table 1-1 for the definitions of the different constructs. A primary aim is to investigate the relationship between food reward and Binge Eating (Binge Eating Scale; BES) (Gormally et al., 1982), Disinhibition, Restraint and Susceptibility to Hunger (Three Factor Eating Questionnaire; TFEQ) (Stunkard & Messick, 1985), food cravings and control over craving (Control of Eating Questionnaire; CoEQ) (Dalton et al., 2015; Hill et al., 1991) in the context of diet-induced WL and obesity status. These traits are well studied, related to obesity phenotypes or overconsumption and have previously been associated with food reward measured by the Leeds Food Preference Questionnaire (LFPQ) in different populations and settings (see Chapters 7 and 9) (Carvalho-Ferreira et al., 2019; Dalton et al., 2013b; Finlayson et al., 2012; French et al., 2014). However, less is known about these associations during diet-induced WL.

Recently, other eating behaviour traits have been proposed to understand the psychological impact of the modern food environment (Hedonic Hunger, measured by the Power of Food Scale; PFS) (Lowe et al., 2009); the awareness while eating a food (Mindful Eating, measured by the Mindful Eating Questionnaire; MEQ) (Framson et al., 2009); the connection with internal body cues (intuitive eating, measured by the Intuitive Eating Scale; IES-2) (Tylka & Kroon Van Diest, 2013), and the concept of Food Addiction (measured by the Yale Food Addition Scale; YFAS) (Gearhardt et al., 2009)). While these concepts are still debated, they might bring insights into individual differences in appetite control and obesity (Davis & Fox, 2008; Lowe & Butryn, 2007). For example, Mindful Eating is defined as “recognise but not respond to inappropriate cues for eating such as advertising, boredom, or anxiety" and this awareness of why we eat might be helpful in the response to food cues during WL (Framson et al., 2009, p. 1439). Moreover, Intuitive Eating involves recognising "internal hunger and satiety cues and use these cues to determine when and how much to eat" which could also improve eating habits during WL (Tylka & Kroon Van Diest, 2013, p. 137).

When studying eating behaviour, it is important to analyse both appetitive responses (before ingestion) and consummatory behaviour (determining what and how much is eaten) (Berthoud, 2004; Cornier et al., 2009). The PFS is the only scale focusing on individuals' susceptibility to the food environment, which could help understand susceptibility to overeat rather than obesity status (Cappelleri et al., 2009). It should be noted that the denomination of “hedonic hunger” might not be appropriately termed hunger as it differs from the biological hunger and in PFS refers rather to the responsiveness to the food environment. Lastly, while the concept (i.e. definition, mechanisms) of Food Addiction is still debated (Hebebrand & Gearhardt, 2021) the usefulness of this concept in the context of obesity (i.e. clinical utility) (Gearhardt & Hebebrand, 2021) has been raised to "distinguish between those who simply indulge in unhealthy foods and those who have truly lost control over their eating behaviour" (Gearhardt et al., 2009, p. 435). All these traits (Mindful, Intuitive Eating, Hedonic Hunger and Food Addiction) are associated with either food intake or BMI and relate to the relationship with food (Flint et al., 2014; Framson et al., 2009; Lowe et al., 2009; Tylka & Kroon Van Diest, 2013) but have rarely or never been compared with behavioural measures of food reward. Therefore, these traits are explored as a secondary aim to give an overview of the main eating behaviour traits potentially associated with food reward, in the context of appetite control and obesity.

Table 1-1: Eating behaviour traits related to appetite control and weight management investigated in this thesis

Constructs	Questionnaires	Definition
Binge eating	Binge Eating Scale (BES) (Gormally et al., 1982)	The essential features of binge eating are identified as 1) **Frequency and amount of "Binge"**: ingesting large amounts of food within short periods of time; 2) **Feeling and cognitions:** accompanying fears about not being able to stop eating (Gormally et al., 1982).
Restraint	Three Factor Eating Questionnaire (TFEQ) (Stunkard & Messick, 1985)	"Tendency to **restrict food intake in order to control body weight**" (Stunkard & Messick, 1985, p. 71) "For instance, avoiding fattening foods, eating small portions and stopping eating before reaching satiation" (Bryant et al., 2019, p. 363).
Disinhibition	Three Factor Eating Questionnaire (TFEQ) (Stunkard & Messick, 1985)	Occasional hyperphagia and loss of control, leading to overeating and resulting from breakdown of inhibition or triggered by sensory or emotional factors, for example, in response to negative affect, hunger or due to the palatability of food (Bellisle et al., 2004).
Susceptibility to Hunger	Three Factor Eating Questionnaire (TFEQ) (Stunkard & Messick, 1985)	**Sensibility to the appetite feeling**. For example, intense feelings of hunger resulting in consumption in excess of three meals per day, feeling an absence of satiety, or creating

		unpleasant gastric sensations (Bryant et al., 2019, p. 363).
Craving for sweet or savoury food	Control of Eating Questionnaire (CoEQ) (Dalton et al., 2015)	**Intense desire to eat a specific food** associated with a loss of control over eating. Experiences of craving range from mild to extreme, in normal and disordered eating.
Craving Control	Control of Eating Questionnaire (CoEQ) (Dalton et al., 2015)	**Perceived level of control over resisting a specific craved food.**
Mindful Eating	Mindful Eating Questionnaire (MEQ) (Framson et al., 2009)	"Non-judgmental **awareness of physical and emotional sensations** while **eating** or in a food-related environment "This includes awareness, distraction, disinhibition, emotional and external eating. (Framson et al., 2009, p. 1439)
Intuitive Eating	Intuitive Eating Scale (IES) (Tylka & Kroon Van Diest, 2013)	"An adaptative form of eating characterised by a **strong connection with internal physiological hunger and satiation**" (Tylka & Kroon Van Diest, 2013, p. 137)
Hedonic Hunger	Power of Food Scale (PFS) (Lowe et al., 2009)	"Psychological **impact of living in food-abundant environments**, as reflected in feelings of being controlled by food, independent of food consumption itself. Responsiveness to the food environment involving three levels of food proximity: (1) food available, (2) food present (3) food tasted" (Cappelleri et al., 2009, p. 914)
Food Addiction	Yale Food Addiction Scale (YFAS) (Gearhardt et al., 2009)	Tendency to exhibit symptoms of dependence to certain types of food for example, high in sweet and fat.

1.4 Food reward: the distinction between liking and wanting

This thesis is centred on food reward which is often used as an umbrella term. Indeed, as depicted in Figure 1-4, different terms are used to refer to food reward, and this variability in definitions and methodologies can lead to confusion in the findings which will be further discussed in Chapters 2 and 3. A reward is usually defined as a benefit or value that represents any stimulus generating positive experience, and explaining why people engage in behaviours that are beneficial to them (Zandstra, 2018). Consequently, food products are stimuli that can be rewarding with some taste being inherently rewarding such as sweet taste (Zandstra, 2018). While taste is known to be the main driver of food choice (International Food Information Council Foundation, 2015), food reward is more than the sensation of taste and interacts with the homeostatic system to generate food pleasure and motivation (Berridge, 2018). Understanding what drives eating behaviour is of real concern in the context of overweight and obesity. That's why food reward matters (Zandstra, 2018).

Figure 1-4: Concepts often used to describe food reward in the literature

Word cloud based on the search from the systematic review in Chapter 2 by Oustric et al. (2018a)

1.4.1 Neurological underpinning of liking and wanting

More specifically, food reward is a psychobiological process that contributes to food choice and consumption. It has been previously defined as "the momentary value of a specific food to the individual at the time of ingestion or at a particular moment" (Arumäe et al., 2019; Rogers & Hardman, 2015; p.2). Food reward comprises sub-components (i.e. liking and wanting), of which the concepts and definitions are often debated (Finlayson et al., 2008; Havermans, 2011; Rogers et al., 2021).

The work of Prof. Kent Berridge established the neurobiological underpinning of food reward in the brain and was based on animal models (Berridge, 1996; Berridge & Robinson, 1998). He argued that liking (the hedonic impact of food) and wanting (the incentive salience triggered by food cues) were distinct components and had different brain entities as depicted in Figure 1-5. Liking is mediated by small and fragile hedonic hotspots (and coldspots) and neurochemically induced by opioids. In contrast, wanting is generated by large and robust mesocorticolimbic circuitry via dopamine. Both networks are nested within each other, but wanting can generate appetite and motivation without liking. Indeed, liking and wanting may dissociate under particular conditions such as obesity or eating disorders (Morales & Berridge, 2020).

It is important to distinguish between the cognitive form of wanting (e.g. explicit wanting, goal-oriented) and the incentive salience, which is the mesocorticolimbic form of wanting. Incentive salience increases the attractiveness and attention-grabbing property of food (Berridge, 2018). The incentive sensitisation model postulates that repeated consumption of palatable food will increase incentive salience of these cues (hyper-reactivity) that will then become conditioned to activate reward and lead to overeating (Berridge, 2018). The construct of sensitisation comes from the theory of addiction and means that the stimuli can induce abnormally high activation of the brain in susceptible individuals (Berridge, 2009).

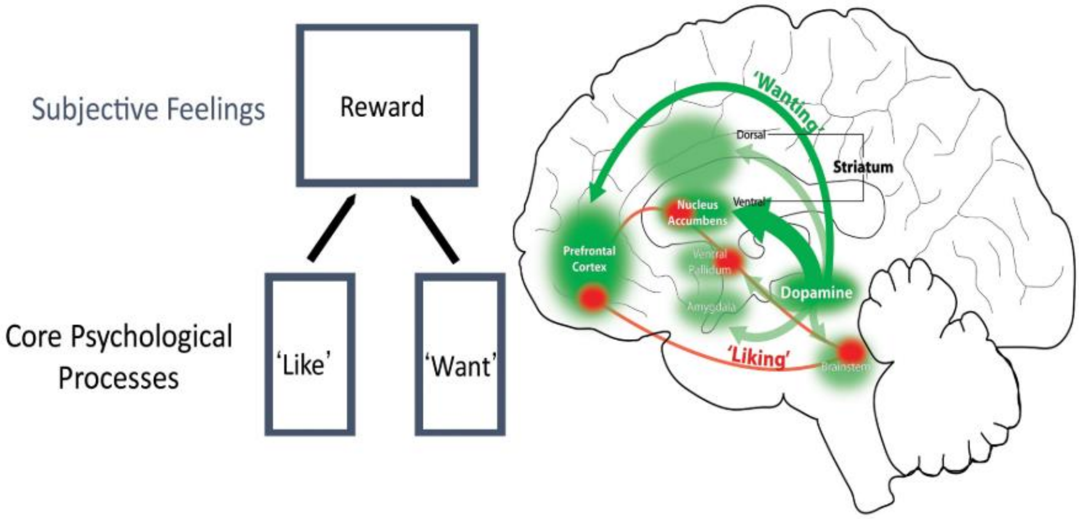

Figure 1-5: Brain systems of implicit wanting and liking

From Berridge (2018). This figure illustrates the large mesocorticolimbic circuitry generating intense wanting (green), which integrates a smaller set of hedonic hotspot inducing liking.

1.4.2 From brain reward to psychological components

Although his work focused on brain reward, Berridge argued that reward could be understood only by parsing it into psychological components. These components include both explicit and implicit levels: "motivation" (including explicit desire to eat and implicit incentive salience), "learning" (cognitive and associative conditioning) and "liking" (explicit liking and implicit affect or objective facial expression) (Berridge & Robinson, 2003). While the learning components of reward are essential to understand the underlying mechanisms linking the pleasantness of the stimulus (liking) with the motivation for this cue (wanting), the work from Berridge seems to have shifted towards the analysis of the endpoints liking and wanting in different contexts (Berridge, 2018; Berridge & Robinson, 2003) and learning components are being explored to understand relations with environmental cues (Ziauddeen et al., 2015) or with cognition (Higgs et al., 2017).

1.4.3 An operationalisation of food reward in human and behavioural science

Later, Finlayson and Blundell used Berridge's work to propose a conceptualisation of liking and wanting as psychological constructs instantiated in human behaviour. To do so, they designed a novel experimental procedure, the LFPQ, to operationalise the separation of liking and wanting and their explicit and implicit levels using a forced-choice paradigm (Finlayson et al., 2007a). This procedure entails two tasks using the same food stimuli varying in fat and taste (see Chapter 3). Liking is conceptualised as "the affective reaction reflecting the acute hedonic impact of a stimulus" in other words, the pleasure of eating a food. Wanting is conceptualised as "the motivational process of the incentive salience", which means the attractive force triggered by the given food cue (Finlayson et al., 2007a, pp. 37,41). Using this approach, they showed that liking and wanting were partially uncoupled across a meal: liking decreased for all food stimuli while implicit wanting increased for food with novel taste properties (sweet food) (Finlayson et al., 2008). Liking is relatively stable (as a learned experience) while wanting, rather than being a constant motivational drive, is triggered by food cues and varies depending on the physiological state or time of day (Dalton & Finlayson, 2014).

1.4.4 Complexity in defining and measuring components of food reward

While Berridge and Finlayson have defined food reward as two separate components: liking and wanting, Rogers defines food reward as the desire to eat a specific food (Rogers & Hardman, 2015). In his model, liking and hunger independently influence food reward and it is reported that wanting cannot be directly measured and, therefore, is conceptualised as desire to eat minus liking. While the concept of wanting is difficult to grasp, Rogers and Hardman’s method might not translate the implicit component of motivation as its measure is based on a subjective rating. A limitation of the latter approach is the lack of an independent measure of wanting (which Berridge has shown is a measurable process in animal).

Importantly, the authors agree that food reward translates the momentary pleasure into a motivation to eat a food that is seen or tasted (Pool et al., 2016). One cannot implicitly get a reward from a food that is not triggered by a cue. Lastly, the complexity of defining and measuring components of food reward rests on their logical status as intervening variables (MacCorquodale & Meehl, 1948). Indeed, liking and wanting cannot be directly observed (e.g. pleasure and motivation cannot easily be reported), but their indirect measurement explains links between other variables such as physiological factors and energy intake. However, it is important to note that both liking and wanting can be operationalised and converted into measurable variables. Therefore, the quantification of wanting can be independent of the measure of liking. In turn these variables can be accessed and replicated by independent groups of researchers and their properties validated. A wide range of methods have been developed to assess components of food reward and will be presented in Chapter 3.

In this thesis, food reward is defined as liking and implicit wanting measured by the LFPQ. This thesis integrates the effect of physiological state (fasted, pre-prandial and post-prandial) here after referred as fasted, hungry and fed state, and implicit and explicit levels on reward processes in order to investigate hedonic drivers of eating behaviour relevant to weight management, diet-induced WL and overweight/obesity status.

1.5 Approaches to food reward, appetite control and obesity

1.5.1 Interplay between homeostatic and hedonic systems

One might ask how food reward components specifically relate to appetite control in humans. While Berridge has enabled the underpinning of food reward in the brain, Berthoud has contributed to the understanding of the role of food reward within appetite control and obesity. He has argued that the homeostatic system (nutrients sensing processes coordinated mainly by the hypothalamus) and hedonic system (reward and sensory information processed by cortical and subcortical area) are interrelated in the brain, refuting the previously thought separation between the two systems (Berthoud, 2006; Berthoud et al., 2017). The homeostatic system arises from biological need and internal signals of energy, while the hedonic system considers the sensory and external cues from the environment (Berthoud & Morrison, 2008). More recently, he summarised complex interacting neural pathways between homeostatic and hedonic systems taking into account conscious and subconscious signals from the environment to control energy balance (Berthoud et al., 2020). This includes both bottom-up pathways (e.g. circulating signals of energy availability modulate response to external sensory information and reward) and top-down pathways (e.g. conscious or conditioned behaviours affect food intake).

1.5.2 Interactions between food reward, the environment and cognitive processes

Along the same line, Alonso-Alonso et al. (2015) showed that the interactions between hedonic and homeostatic systems were embedded in specific situations and environment. More specifically, they described four interconnected levels of environmental influences on food reward: individual (e.g. feeding style), family (e.g. food availability), micro-environment (e.g. local community) and macro-environment (e.g. national economy and policies) levels. Similarly, Higgs et al. (2017) outlined the interaction between reward, homeostatic and cognitive processes (i.e. memory, attention learning) in controlling appetite. They detailed cognitive processes influencing eating behaviour and reward during a meal, for example, health goals, expectations and memory of the food or attention can influence food choices. As in Butland et al. (2007), all these models highlight the importance of a systems approach and the interactions between levels to understand food reward and intake.

1.5.3 Interactions between food reward, energy expenditure and physical activity

In terms of the relationship between food reward and energy expenditure (the main component of energy balance with energy intake), Bellisle (1999) previously raised the role of physical activity in determining food choice. Indeed, active individuals reported eating more vegetables and cereal products, but it was not clear whether this resulted from the metabolic effect of exercise or psychological traits of healthy individuals. More recently, a 12-week exercise study was accompanied by improved food reward and overall appetite (e.g. decreased wanting for high-fat food and disinhibition) (Beaulieu et al., 2020c). On the same line, a recent review showed that low levels of physical activity was associated with higher reward for high-energy food (Beaulieu et al., 2020e). Indeed, following the conceptual model of the impact of habitual physical activity on appetite control, it seems that lower physical activity levels are associated with non-regulated appetite control (greater fat mass, weaker satiety but also higher hedonic response). Finally, a cross-sectional analysis on 180 women from 6 studies using identical protocols showed that a large amount of physical activity was associated with preferences for low-fat food while less active individuals preferred high-fat food (Oustric et al., 2018b). All of this suggests that exercise and physical activity can modulate food reward, and as the mechanisms of action are still unknown, it remains to be understood whether different types of weight management interventions affected components of food reward differently.

1.5.4 Interactions between food reward components, physiological state and appetite sensations

Individuals experience sensations of hunger and satiety which reflect the drive and inhibition of eating and are therefore key factors to study in appetite control. A large interindividual variability in these appetite sensations has been reported and might account for the diversity of response to weight management interventions (Gibbons et al., 2019). Food reward components interact with physiological state (e.g. hungry, fed) and their related appetite sensations (Blundell et al., 2005). For example, Kringelbach (2015) has proposed the pleasure cycle (see Figure 1-6) to link food reward with food consumption phases (e.g. appetitive, consumption and satiety phase). Wanting dominates the appetitive phase initiating food procurement. Then liking dominates the consummatory phase followed by satiation, where learning dominates. A recent study developed an effort-based paradigm using hand grip strength to analyse eating motivation dynamics (i.e. wanting) during consumption (Pirc et al., 2019). They showed that wanting was dependent on hunger, declined during food intake and that the first effort exerted to initiate eating determined subsequent food intake. This study replicated previous findings showing that the hungry state is a modulator of reward (Berridge, 2012) and the use of an indirect measure of wanting (effort exertion was used as a proxy) reinforced these findings.

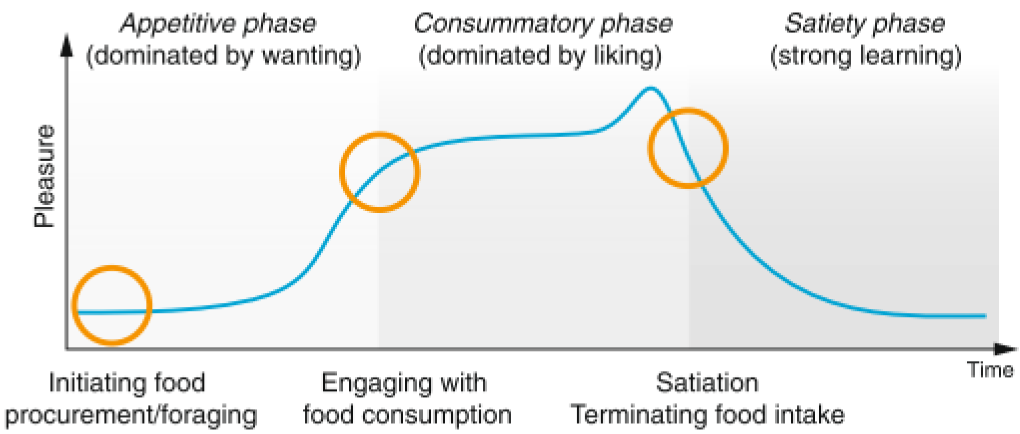

Figure 1-6: The pleasure cycle

From Kringelbach (2015). This model shows the interaction between physiological states, appetite sensations and components of food reward around food consumption.

1.5.5 Relationship between food reward components and energy intake: unresolved association with obesity

With regard to food intake, food reward participates to drive food intake and heightened food reward, especially for high-fat sweet food, has been related to overconsumption

(Dalton et al., 2013a). An earlier review reported the discrepancy between a previous assumption that liking was "the driver of food selection and purchase", and the fact that obesity was related to increased motivation to eat not necessarily with increased pleasure (Mela, 2006, p. 11). Along the same lines, a recent review suggested that the motivation to eat rather than liking drives consumption. Interestingly they showed that the energy content of food was implicitly reinforcing and that gut-brain pathways were involved in food reward and subsequent food intake (de Araujo et al., 2019). Both reviews argued that the distinction between liking and wanting is necessary to better understand food intake and obesity. Indeed, the relationship between food reward and obesity status and more specifically with body composition remains to be investigated as the literature is showing mixed results between individuals with obesity compared to individuals within the normal range of BMI: no differences (Morys et al., 2020; Snoek et al., 2004), higher food reward (Devoto et al. (2018); Stice et al. (2015)), lower food reward (Wang et al. (2001) or inverted U-shape relationship between BMI and sensitivity to reward (Davis & Fox, 2008). Moreover, the literature is often based on brain responses to food, which do not always translate into behavioural liking and wanting (Devoto et al., 2018).

These inconsistencies between studies also raise the idea of heterogeneity in obesity phenotypes (Ziauddeen et al., 2015), which could explain why the hedonic response to food might be elevated in some individuals and not others. There is, therefore, a need to analyse food reward in the context of other appetite-related variables to draw a larger picture of appetite control and hedonic responses. As explained in Figure 1-3, the obesogenic environment (also called modern environment by opposition to the restrictive environment in which brain appetite control evolved) is flagged as one of the causes for heightened response to food cues. More specifically, Berthoud et al. (2020) hypothesised that the obesogenic environment puts pressures on the interactions between hedonic and homeostatic system and stimulates consumption even in the absence of metabolic deficit. However, this consumption can be 'passive' via the unrecognised energy density or portion size of foods (Blundell & Macdiarmid, 1997; Viskaal-van Dongen et al., 2009). This raises implications in terms of obesity prevention and treatment: as the obesogenic environment (physical and socio-cultural) is not easy to reverse, one approach would be "to change people's relationship with the obesogenic environment" (Berthoud et al., 2020, p. 7). This would not be easy but it is a reason why this thesis questions whether food reward could be targeted to improve weight management strategies. Therefore, this thesis aims to explore the role of food reward during energy restriction (ubiquitous dieting) and to give insight into the relationship between food reward components and obesity status in the context of additional appetite-related variables.

This thesis investigates the role of food reward with appetite sensations, energy intake, eating behaviour traits and body composition during diet-induced WL and among BMI status (women with overweight/obesity vs women within the normal range of BMI) to understand characteristics explaining susceptibility to overeat.

1.6 Diet, continuous and intermittent energy restriction

1.6.1 Continuous energy restriction: usual dietary approach leading to compensatory responses

Diets (low-calorie diets) are the traditional and most used approach to lose weight. They are usually defined as "a balanced ratio of protein, carbohydrate, and fat in reduced quantities to provide an energy intake of 800 to 1500 kcal per day" (Finer, 2001, p. 290). However, their efficiency is often reduced by compensatory responses that may contribute to weight regain (Melby et al., 2017). These compensatory responses appear to be asymmetrical (i.e. stronger during periods of negative energy balance), partially explaining why it is usually easier to gain weight than to lose weight. Figure 1-7 illustrates physiological and behavioural responses during chronic energy deficit and energy surfeit (Casanova et al., 2019a). However, psychobehavioural compensatory responses involving eating behaviour traits and food reward were not mentioned in this figure and are explored in this thesis.

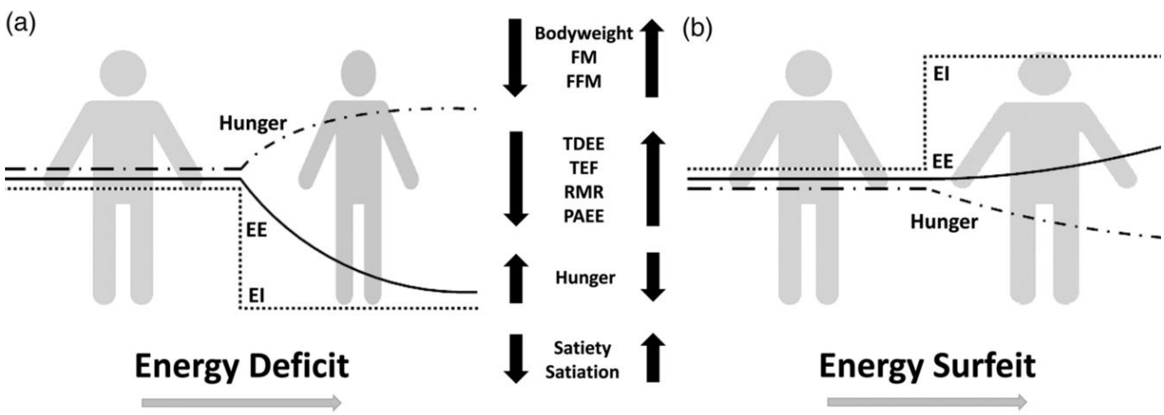

Figure 1-7: Compensatory responses between chronic energy deficit or surfeit

From Casanova et al. (2019a); EI, energy intake; EE, energy expenditure; TDEE, total daily energy expenditure; PAEE, physical activity energy expenditure; TEF, thermic effect of food; FFM, fat-free mass; FM, fat mass; RMR, resting metabolic rate. This figure illustrates compensatory responses during energy deficit and surfeit showing a greater force resisting weight loss than weight gain.

Physiological compensatory responses include decreased energy expenditure (i.e. RMR, the energy cost of physical activity and thermic effect of food). RMR usually decreases after energy restriction, even with minimal WL (e.g. 1-2kg) (Nymo et al., 2018), but a short-term 4-day energy restriction showed no changes (Doucet et al., 2004). A decrease in physical activity energy expenditure (Nymo et al., 2018) and the thermic effect of food

(Westerterp, 2004) have also been shown following energy restriction but these will not be explored in this thesis. Polidori et al. (2016) have shown that a covert WL (induced by pharmacotherapy so that patients were not aware of the energy deficit) led to increased energy intake post-WL. This raised the role of appetite adaptations (both conscious and subconscious) related to WL and leading to increases in energy intake. However, this pharmacological study was a placebo-controlled trial and food intake behaviour was not measured but estimated. Moreover, it did not assess underlying appetite mechanisms such as eating behaviour traits and reward, therefore the effect of diet-induced WL on energy intake adaptations remains to be fully explored.

In terms of psychological compensatory responses, reviews have reported an increase in the appetite sensation of hunger suggested to resist WL (Hintze et al., 2017; Melby et al., 2017; Sumithran et al., 2011). On the contrary, other diet-induced WL showed decreased appetite sensations (Andriessen et al., 2018; Sayer et al., 2018) or no change (Coutinho et al., 2018). The discrepancy in the results could be explained by the different methodology used to assess appetite sensations (e.g. fasted, in response to a test meal or recalled at the end of each day). Also, even using the same validated procedure, the individual profiles of appetite sensations (e.g. hunger) are highly variable (Gibbons et al., 2019). The question of whether or not WL leads to an increase or decrease in hunger is a critical issue that should be resolved. It is interesting to note that the theory depicting fat-free mass as a driver of appetite (Hopkins et al., 2016b) would predict a lowering of the drive to eat (hunger) following weight (fat-free mass) loss. However, some data has suggested that losses of fat-free mass may lead to compensatory increases in energy intake, inducing an hyperphagic response resulting in weight regain (Dulloo et al., 1997; Turicchi et al., 2020).

Secondly, improvement in eating behaviour traits, such as increased restraint and decreased disinhibition, has been shown after diet-induced WL (Chaput et al., 2005; Sanchez et al., 2017; Urbanek et al., 2015) but less is known on the other eating behaviour traits such as Mindful, Hedonic or Intuitive Eating which would help to evaluate the effect of WL on other facets of the relationship with food. Finally, it is often suggested that poor response to diet-induced WL is due to increased motivation to eat and food reward (Hintze et al., 2017). However, the role of food reward components and appetite-related variables during diet-induced WL remains to be fully understood as a large range of methodologies are used to measure reward and do not always distinguish the components of liking and wanting or explicit from implicit level.

1.6.2 Intermittent energy restriction: an alternative dietary approach supposed to reduce compensatory responses

An alternative dietary approach named intermittent energy restriction (IER) has been proposed to attenuate some compensatory responses previously described in continuous energy restriction (CER) (Varady, 2011). This approach involves repeated patterns of short-term severe energy restriction ("fast day", at least 75% energy restriction) with normal feeding ("feed day", *ad libitum* days) (Varady et al., 2009). IER has been proposed as an alternative to CER, and was designed to be easier to follow in terms of adherence, as the restriction is not required daily and influence the frequency of eating rather than what is eaten (Alhamdan et al., 2016; Varady, 2011). Different types of IER have been reported depending on the frequency of the restriction: every other day or 5:2 (5 'feed' days followed by 2 ‘fast' days) and on the presence of a fasting component (alternate day fasting) (Davis et al., 2016). To sum up, the core concept of IER is the alternance between days with and without energy restriction.

In terms of compensatory responses, IER has been shown to produce a lower reduction in RMR when adjusted for changes in fat mass and fat-free mass compared to CER in a 16-week RCT (Byrne et al., 2018). However, this study is difficult to compare with others as they used a 2:2 blocks system with 2 weeks of energy restriction interspersed with 2 weeks of energy balance which is different from the usual alternate day fasting pattern. In terms of body composition, two recent RCTs of 12 and 24 weeks have failed to report differences between IER and CER (Coutinho et al., 2018; Trepanowski et al., 2017) as reported in a review from Varady (2011), showing that IER might be more effective for the retention of fat-free mass. The discrepancy between results might be due to the use of different methods to measure body composition between CER and IER, and the fact that a systematic review of longer-term interventions (>6 months) showed no differences between the two dietary approaches is in line with similar changes in body composition between diets (Headland et al., 2016).

Similarly, IER is often proposed to reduce the increase in appetite sensations following energy restriction; however, the evidence is scarce. For example, hunger at the end of fast day has been shown to decrease during IER intervention (after 2 weeks) and remain low during the follow-up phase of self-selected feeding (Klempel et al., 2010). Using a similar design and methods (4-week controlled feeding and 8-week self-selected feeding, alternating fast day (25% energy needs) with feed day (*ad libitum* feeding)), Bhutani et al. (2013) showed that hunger decreased and fullness increased at the end of fast day during a 12-week intervention. However, both studies had no CER comparator arm. Moreover, some IER studies showed no change in fasting and postprandial hunger, including IER of 3 non-consecutive partials restriction days (Coutinho et al., 2018) and an 8-week alternate day fasting (fast day: 25% of energy need) (Hoddy et al., 2016). On the contrary, an IER study using a 5:2 approach reported increased hunger in IER than CER. However, none of these studies measured appetite sensations following a standardised protocol with a fixed breakfast and an *ad libitum* test meal to assess more accurately hunger and satiety (Bhutani et al., 2013; Coutinho et al., 2018; Hoddy et al., 2016; Klempel et al., 2010). Therefore, appetite responses during controlled IER and CER remain to be investigated.

The differential effects of IER and CER on eating behaviour traits have rarely been explored. Bhutani et al. (2013) showed an increase in restraint (measured with TFEQ) after 12 weeks of IER, while a 12-month alternate day fasting intervention showed no change in restraint and no difference with CER (Kroeger et al., 2018). These discrepancies might be due to the fact that dietary counselling was weekly in Bhutani et al. (2013) while in Kroeger et al. (2018) it was only in the WL phase (months 3 to 6). Interestingly, IER vs CER's effect on binge eating, food cravings, or intuitive or mindful eating has never been explored and would give insight into changes in the relationship with food during these diets. Along similar lines, changes in food reward components between CER and IER have never been compared. This could add to the understanding of behavioural compensatory responses during WL and whether hedonic responses could explain potential weight regain.

To conclude, there is a need to investigate the effect of CER and IER on appetite-related variables, including physiological, psychological and behavioural factors, to have a full picture of appetite control. It is also important to highlight that some studies did not have a comparative CER arm to IER (Bhutani et al., 2013; Klempel et al., 2010), and the studies that did compare IER and CER were not matched for WL as they compared the efficiency of the diets on WL (Coutinho et al., 2018; Kroeger et al., 2018; Trepanowski et al., 2017). Interestingly, the degree of WL can impact changes in appetite sensations (Nymo et al., 2017) and possibly other appetite-related variables. Therefore, comparing the effect of matched-WL through CER or IER on appetite control is needed to understand WL and weight regain mechanisms. This thesis consequently compares matched WL via CER and IER to assess their impact on food reward in the context of appetite control.

1.7 Overall thesis aims

Food reward components are known to be involved in overeating. However, liking and wanting have not been widely considered as targets for improving weight management. This could be achieved through the attenuation of the attraction of high-energy food, for example. This thesis aims to explore the role of food reward during weight management, matched diet-induced WL to ≥5% and no-contact follow-up and its association with appetite control and overweight/obesity status in adult women (Figure 1-8).

As obesity is a complex and dynamic system (Finegood, 2011) there is a need to zoom out and integrate different levels to investigate weight management. This thesis uses a psychobiological system approach - set in the experimental platform of the Human Appetite Research Unit (HARU) (Caudwell et al., 2011) - to analyse food reward within appetite control using biological, behavioural and psychological aspects of energy balance.

AIM 1: **Systematically examine changes in food reward components during weight management.**

- Evaluate whether components of food reward are amenable to change after weight management. (Ch.2)
- Determine which interventions are effective in changing components of food reward. (Ch.2)
- Explore the association between changes in food reward and weight management outcomes. (Ch.2)

AIM 2: Explore changes in liking and implicit wanting during a controlled diet-induced WL to ≥5% and follow-up in women with overweight/obesity.

- Determine the effect of diet-induced WL to ≥5% and duration of energy restriction on food reward. (Ch. 5)
- Determine the effect of IER vs CER on food reward. (Ch. 5)
- Summarise and visualise individual changes in food reward during diet-induced WL. (Ch. 6)
- Explore the relevance of changes in food reward by investigating their relationships with changes in appetite-related variables. (Ch. 7)
- Explore the changes in food reward after 1-year no-contact follow-up. (Ch. 8)

AIM 3: Explore food reward in relation to appetite control and overweight/obesity status in women.

- Compare food reward and appetite control in women with overweight/obesity or within the normal range of BMI. (Ch. 9)
- Determine the relationship between food reward and appetite control. (Ch. 9)

Cross-cutting aim: improve the methodology to measure and analyse food reward

- Improve the methodology to measure and analyse food reward with the LFPQ. (Post Script)
- Develop methods to describe changes in food reward at the individual level taking into account multiple variables of reward and food categories. (Ch. 6)

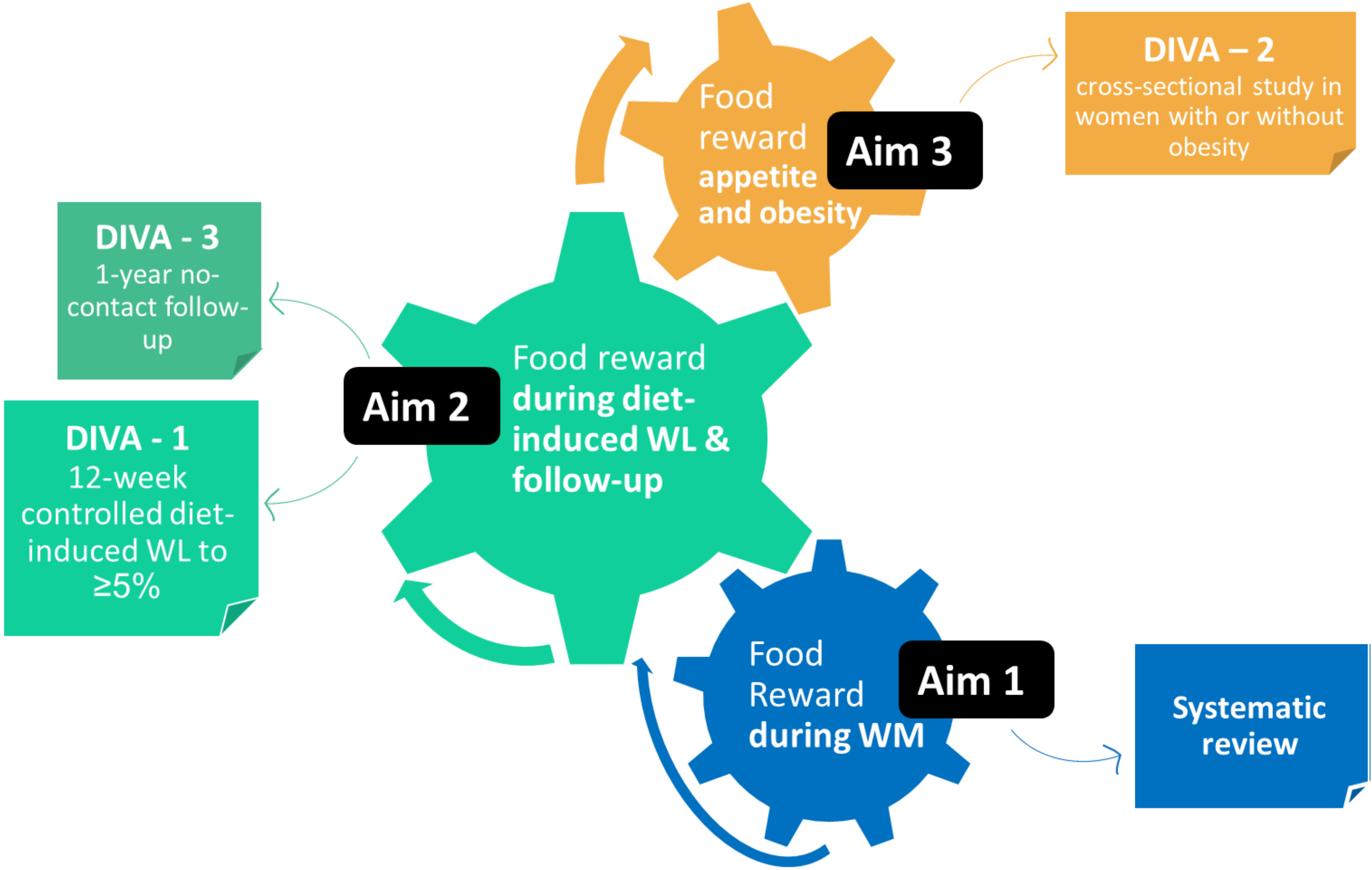

Figure 1-8: Overview of the Thesis aims and studies

WL: weight loss, WM: weight management, DIVA-1,2,3: experimental studies

Chapter 2

Changes in food reward during weight management interventions – a systematic review

Chapter aims:

1. Evaluate whether components of food reward are subject to change after different types of weight management interventions.

2. Explore whether observed changes in food reward are related to weight management outcomes.

HIGHLIGHTS

- ► Liking and wanting for high-energy food mostly decreased during weight management interventions. Dietary interventions reduced liking for both low- and high-energy food.
- ► Different types of interventions - dietary, behavioural, cognitive and pharmacological - seemed to be effective in decreasing liking and/or wanting for high-energy food.
- ► The relationship between changes in food reward and changes in weight management outcomes was less clear.
- ► Food reward should be measured in a consistent manner in future weight management interventions to allow systematic reviews to quantify its effect on outcomes.

2.1 Introduction

Increasing obesity rates have necessitated a multidimensional approach to the investigation of weight management (Higgs et al., 2017; Hopkins et al., 2018). Currently, weight management interventions are based on comprehensive multidisciplinary lifestyle modification, including dietary programmes, exercise, cognitive and behavioural components. However, in the current obesogenic environment hedonic influences tend to determine food choices, leading to excessive energy intake (Berthoud et al., 2011; Lowe & Butryn, 2007). Surprisingly, food reward seems not to have been systematically examined as a target for improving weight management outcomes (Finlayson & Dalton, 2012b). Therefore, a systematic review of the literature is warranted to investigate the role of food reward in the context of weight management interventions.

Food reward comprises sub-components (e.g. liking and wanting) which are likely to play specific roles in weight management (Finlayson et al., 2007b). Indeed, these psychological processes have a major influence on food intake and seem to function differently (Finlayson & Dalton, 2012b; Hopkins et al., 2016a). Preferences for energy-dense and highly palatable foods are related to excess energy intake in free-living settings (De Castro et al., 2000; French et al., 2014). However, liking accounts only for a small proportion of the variance in intake, and liking alone may not explain the whole picture of reward-induced food intake (Cox et al., 1999; De Castro et al., 2000). The processes of wanting may increase the reactivity to palatable food (compared to non-eating activities) in women with obesity (Saelens & Epstein, 1996). In daily life, wanting triggered by environmental cues (such as food advertising) may be more important than liking to motivate food intake (Mela, 2006).

Few studies have investigated the relationship between food reward and physiological factors. Some showed a positive association between preferences for high-fat foods and fat mass (Mela & Sacchetti, 1991), independent of genetic background (Rissanen et al., 2002). However, the relationship between food reward and body mass index (BMI) may not be linear. The sensitivity to reward in people ranging in body weight status has been suggested to follow an 'inverted-U' relationship (Davis & Fox, 2008). Given that behaviour accounts for 100% of energy intake (Blundell & Finlayson, 2004), identifying interventions that modulate the hedonic aspects of food intake (Batterham et al., 2007) may provide a novel approach to tackle obesity and improve weight management.

2.2 Objectives

The primary research question was: Do components of food reward change after weight loss? Secondary questions were: Which interventions are effective in changing components of food reward and what is the associated effect on weight management outcomes? The population targeted was healthy adults with overweight or obesity. Weight management interventions (≥4 weeks) that attempted to target or measure a change in components of food reward were assessed. Weight management included all interventions (e.g. weight loss, weight maintenance) that aimed to improve weight management outcomes.

The primary outcome was food reward (i.e. liking, wanting or overall palatability see section 1.4.3.1 for definitions) measured directly or indirectly, and secondary outcomes included food intake and weight outcomes (e.g. body weight, fat mass, waist circumference). All methods to measure food intake (e.g. diary, 24-h recall) and weight outcomes (e.g. calibrated scales) were included. All primary and secondary outcomes had to be measured pre and post weight management intervention. All interventional study designs were included.

2.3 Method

2.3.1 Literature search strategy

Four electronic bibliographic databases were searched: MEDLINE (Ovid), EMBASE (Ovid), PsycINFO (EBSCOHost) and Cochrane Library. The search strategy was organised in two key blocks of terms: interventions (aiming at improving weight management outcomes) and food reward (all terms related to liking and wanting for food). The specific keywords used are listed in Table A1 in Appendix A. Previous reviews were screened to identify adequate keywords. The search terms were a combination of medical subject headings (MESH terms) and text-words (title and abstract) and were adapted for use in each database. Searches were supplemented by reading the reference lists of eligible studies and systematic reviews. Limits were set to include all papers published in English or French after 1990, in healthy human adults. The last search was run in April 2018.

2.3.2 Inclusion and exclusion criteria

Articles were included if they involved longitudinal measures (≥4 weeks (Beaulieu et al., 2016)) taken pre and post weight management intervention in healthy adults with overweight or obesity. All types and design of intervention were included, and all comparator treatments were considered. Articles were excluded if they involved animals, children, adolescents or elderly, and participants with pregnancy, disease, an eating disorder or who smoked. Interventions were excluded if they only measured food reward through neuroimaging techniques such as functional magnetic resonance imaging (fMRI) without a supplementary psychometric assessment of food reward. Indeed, all psychometric measures of food reward either direct (e.g. ratings of pleasantness or desire to eat) or indirect (e.g. measure of the willingness to work to obtain a food or reaction time) were included. Trait measurements of food reward were not included (e.g. sensitivity to reward).

2.3.3 Data extraction and synthesis

Search results from each database were exported to Endnote and duplicates were removed. Study selection was undertaken using Covidence ("Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia,"). Titles and abstracts were screened twice by the main reviewer, and 10% were screened independently by a second reviewer. Full-texts of retained studies were accessed and further screened according to the eligibility criteria by 3 reviewers (one reviewer screened all and the other two screened half). Any disagreements over the eligibility of particular studies were resolved through discussion with a third reviewer. One author extracted the following information into an Excel spreadsheet: study information (e.g. authors, years, and title), baseline characteristics of participants (sample size, age, sex, BMI, weight), details of the intervention (intervention type, control conditions, study methodology, study completion rates, design), outcome measures and methods (food reward, food intake and physiological measures), information for assessment of the risk of bias.

2.3.4 Outcome measures

Risk of bias was assessed by two reviewers using the Cochrane Collaboration's tool (Higgins & Green, 2011). Disagreements were discussed with a third reviewer. Seven criteria were assessed: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcomes data, incomplete outcome data, selective reporting and other bias.

Only significant changes in food reward, food intake or weight outcomes were reported as an increase or decrease, otherwise no change over time was stated. Psychological outcomes were reported if they contributed in explaining the change in outcomes. Differences between arms of interventions (i.e. intervention effect) were also reported. The results are presented with a qualitative synthesis as the methods to report food reward components were not consistent across studies. The magnitude of the change over time was reported in % pre to post-intervention to compare studies, except when data were not available.

2.4 Results

2.4.1 Study selection

Out of 239 full-texts assessed in 2017, 14 originally met the inclusion criteria (see Figure 2-1 for the flow diagram). The last update of the search in 2018 led to a total of 17 longitudinal studies. Eighty studies among the 135 excluded for being acute interventions will be reported in another review to assess the role of food reward in acute weight management outcomes.

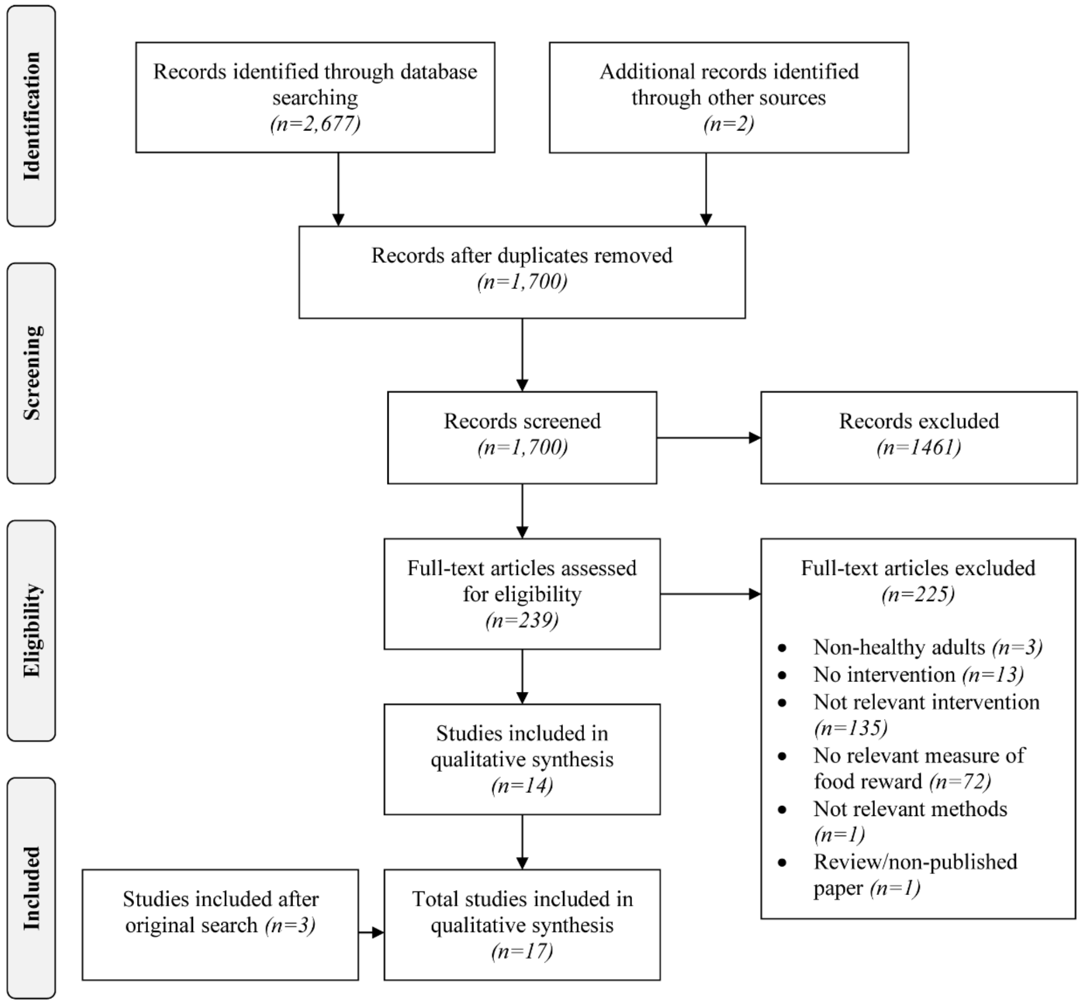

Figure 2-1: Systematic review flow diagram

2.4.2 Risk of bias

The selection bias (i.e. sequence generation and allocation concealment) was judged to be low risk in 59% (N = 10) and 18% (N = 3) of the studies, respectively. The performance bias (i.e. blinding participants and personnel) was judged high risk in 53% (N = 9) of the studies and 71% (N = 12) of the studies were judged high risk as they did not blind assessors about outcomes. Attrition bias (i.e. incomplete data) was unclear in 65% (N =

11) of the studies and reporting bias (i.e. selective outcome) was unclear in 88% (N = 15) of the studies. Other biases were judged low risk in 59% (N = 10) of the studies. See Table 2-1 for the details of each study.

Table 2-1: Risk of bias for the 7 criteria within each study

	Sequence generation	Allocation concealment	Blinding participants and	Blinding outcome assessors	Incomplete outcome data	Selective outcome	Other bias
Aberg 2008	low	unclear	high	unclear	unclear	unclear	low
Alkahtani 2014	high	high	high	unclear	unclear	unclear	high
Andriessen 2018	high	high	high	high	low	low	high
Astell 2013	low	low	low	high	low	unclear	low
Blundell 2017	low	unclear	low	unclear	low	low	low
Cameron 2008	high	high	high	high	unclear	unclear	high
Demos 2017	unclear	unclear	unclear	unclear	unclear	unclear	high
Grieve 2003	high	high	high	high	unclear	unclear	high
Hopkins 2014	high	high	high	high	unclear	unclear	high
Johnstone 2008	low	high	high	unclear	unclear	unclear	low
Martin 2011	low	unclear	unclear	high	unclear	unclear	low
Martins 2017	low	unclear	unclear	high	unclear	unclear	low
McVay 2016	unclear	unclear	unclear	high	unclear	unclear	high
Newman 2016	low	unclear	unclear	high	low	unclear	low
Raynor 2006	low	unclear	high	high	unclear	unclear	low
Raynor 2012	low	low	high	High	low	unclear	low
Stice 2017	low	low	unclear	High	low	unclear	low

2.4.3 Food reward definition and measurements

In this review psychometric assessments of food reward were considered as they have been shown to have an impact on eating behaviour. The first finding was the diversity of the measurements of food reward assessed in the studies. Therefore, measures were grouped in categories - liking, wanting and overall palatability - to enable comparisons between studies.

2.4.3.1 Defining liking, overall palatability and wanting

"Liking" was the most reported (16 out of 17 studies) and covered two different notions "overall palatability" (Aberg et al., 2008; Astell et al., 2013; Blundell et al., 2017; Cameron et al., 2008; Johnstone et al., 2008) and "liking for a specific food at this moment" (Alkahtani et al., 2014; Andriessen et al., 2018; Blundell et al., 2017; Cameron et al., 2008; Demos et al., 2017; Hopkins et al., 2014; Martin et al., 2011; Martins et al., 2017; McVay et al., 2016; Newman et al., 2016; Raynor et al., 2006; Raynor et al., 2012; Stice et al., 2017). For the latter notion, "liking" measures were labelled as such in 6 studies (Alkahtani et al., 2014; Blundell et al., 2017; Cameron et al., 2008; Hopkins et al., 2014; Martins et al., 2017; Newman et al., 2016) but also included different terms such as "tastiness" (Demos et al., 2017), "food preferences" (Andriessen et al., 2018; Martin et al., 2011; McVay et al., 2016), "pleasantness" (Raynor et al., 2006; Raynor et al., 2012) and "palatability" (Stice et al., 2017). Given that they all referred to the hedonic value of the taste of a specific food at a given time (ingestion or viewing), these terms were reported as liking in this review.

In contrast, overall palatability refers to evaluation of the taste of the diet as a whole and does not refer specifically to a particular food or food type. This category will therefore be reported separately from liking. Wanting, the motivational drive to eat, was measured in 7 out of 17 studies and included implicit wanting (Alkahtani et al., 2014; Blundell et al., 2017; Cameron et al., 2008; Hopkins et al., 2014; Martins et al., 2017) and explicit wanting, also termed "desire to eat" (Grieve & Vander Weg, 2003; Stice et al., 2017).

"Specific food" referred to different food labelling such as low/high-fat (Andriessen et al., 2018; Grieve & Vander Weg, 2003; McVay et al., 2016; Newman et al., 2016), low/high fat and sweet/savoury (Alkahtani et al., 2014; Blundell et al., 2017; Hopkins et al., 2014; Martins et al., 2017; Raynor et al., 2006), healthy/unhealthy (Demos et al., 2017), low/high-carbohydrate (Andriessen et al., 2018; Martin et al., 2011; McVay et al., 2016), energy-dense (Cameron et al., 2008; Raynor et al., 2006; Raynor et al., 2012), and low/high-calorie food (Stice et al., 2017). These different labels were grouped in this review as low-energy food or high-energy food.

2.4.3.2 Measurements of liking and wanting

Two different methods were used to measure liking: visual analogue scales (VAS) (Cameron et al., 2008; Raynor et al., 2006; Raynor et al., 2012) such as the Leeds Food Preference Questionnaire (Dalton & Finlayson, 2014) (LFPQ) (Alkahtani et al., 2014; Blundell et al., 2017; Hopkins et al., 2014; Martins et al., 2017), and Likert scales (Demos et al., 2017; Newman et al., 2016; Stice et al., 2017) such as the food preferences questionnaire from Geiselman et al. (1998) (FPQ) (Martin et al., 2011; McVay et al., 2016). Overall palatability was also measured using VAS (Aberg et al., 2008). Two VAS were 100 mm (Raynor et al., 2006; Raynor et al., 2012) and one was 150 mm (Cameron et al., 2008) and performed under a similar design that consisted in rating liking just after tasting a snack food. One difference was the hunger state before the VAS. In Raynor et al. (2012), a preload was given before tasting the snack to account for homeostatic drive whereas in Cameron et al. (2008) and Raynor et al. (2006) participants were in a hungry state. LFPQ measured liking by VAS in response to viewing food images of high or low-fat content and sweet or savoury taste. The Likert scales used were 5-, 9- or 10-point scales and the ratings were based either on low- or high-fat food tasting (Newman et al.,

2016) or viewing of food pictures (Demos et al., 2017; Martin et al., 2011; McVay et al., 2016; Stice et al., 2017).

Implicit wanting was measured indirectly by a forced-choice reaction time paradigm (i.e. LFPQ) (Alkahtani et al., 2014; Blundell et al., 2017; Hopkins et al., 2014; Martins et al., 2017), and via a progressive ratio computer task (Cameron et al., 2008). Explicit wanting was assessed through a 5-point scale assessing the desire to eat low, medium or high-fat food over the last 7 days (Grieve & Vander Weg, 2003) and by the willingness to pay for a food (Stice et al., 2017)

2.4.4 Study characteristics

2.4.4.1 Intervention types

Five types of intervention emerged from this systematic review: 1) dietary (Aberg et al., 2008; Andriessen et al., 2018; Cameron et al., 2008; Johnstone et al., 2008; Martin et al., 2011; McVay et al., 2016; Newman et al., 2016), 2) exercise (Alkahtani et al., 2014; Hopkins et al., 2014; Martins et al., 2017), 3) pharmacological (Astell et al., 2013; Blundell et al., 2017), 4) cognitive (Stice et al., 2017) and 5) behavioural/multidisciplinary (Demos et al., 2017; Grieve & Vander Weg, 2003; Raynor et al., 2006; Raynor et al., 2012).

Dietary interventions included nutritional manipulations such as the macronutrient content of the diet (low or high-fat, high-protein, low or medium-carbohydrate) or energy restriction. Behavioural interventions incorporated a combination of dietary, exercise, behavioural therapy or food variety interventions and not a single intervention. Exercise studies included moderate-intensity interval training (MIIT), moderate-intensity continuous training (MICT), high-intensity interval training (HIIT), or aerobic exercise. The pharmacological studies included nutraceutical (*C. fimbriata* extract) (Astell et al., 2013) or pharmaceutical (semaglutide) (Blundell et al., 2017) compounds, and followed a pharmacological approach to deliver the treatment (e.g. refined and encapsulated or injected). The cognitive study consisted of a food response and attention training intervention.

2.4.4.2 Study design

Concerning the study design, 10 studies were randomised controlled trials (RCT) (Aberg et al., 2008; Astell et al., 2013; Blundell et al., 2017; Johnstone et al., 2008; Martin et al., 2011; Martins et al., 2017; Newman et al., 2016; Raynor et al., 2006; Raynor et al., 2012; Stice et al., 2017), and 5 had no control group (Andriessen et al., 2018; Cameron et al., 2008; Demos et al., 2017; Grieve & Vander Weg, 2003; Hopkins et al., 2014) and were embedded in either RCT or in a pre-post design. The weight management intervention duration ranged from 4 weeks to 2 years with a median of 12 weeks and full study duration (including for example detraining wash-out) ranged from 6 weeks to 2 years.

2.4.4.3 Secondary outcomes and methods

The main outcomes assessed were changes in food reward and the methods are reported above. The secondary outcomes assessed were changes in food intake-related measures (12 out of 17 studies) which are eating behaviour assessments such as food intake (qualitative assessment of eating behaviour) (Grieve & Vander Weg, 2003), energy intake (in kcal) (Aberg et al., 2008; Alkahtani et al., 2014; Astell et al., 2013; Blundell et al., 2017; Hopkins et al., 2014; Johnstone et al., 2008; Martins et al., 2017; Newman et al., 2016; Raynor et al., 2012) and energy intake from fat (in kcal) (Alkahtani et al., 2014; Astell et al., 2013), and/or weight/anthropometric outcomes (15 out of 17 studies) such as waist circumference (Astell et al., 2013), fat mass (Alkahtani et al., 2014; Blundell et al., 2017; Hopkins et al., 2014; Stice et al., 2017) and body weight (Aberg et al., 2008; Andriessen et al., 2018; Astell et al., 2013; Blundell et al., 2017; Cameron et al., 2008; Demos et al., 2017; Hopkins et al., 2014; Johnstone et al., 2008; Martin et al., 2011; Martins et al., 2017; McVay et al., 2016; Newman et al., 2016; Raynor et al., 2006; Raynor et al., 2012).

However, the methods used to measure each outcome varied markedly across studies. Food intake-related measures were assessed by food diaries (Aberg et al., 2008; Astell et al., 2013; Johnstone et al., 2008; Martins et al., 2017; Newman et al., 2016; Raynor et al., 2006), *ad libitum* test meal (Alkahtani et al., 2014; Blundell et al., 2017; Hopkins et al., 2014), food frequency questionnaires (Newman et al., 2016; Raynor et al., 2012), 24-h recall (Raynor et al., 2012), or a 48-item questionnaire (Grieve & Vander Weg, 2003). Body weight was measured by weighing scale (Aberg et al., 2008; Astell et al., 2013; Cameron et al., 2008; Johnstone et al., 2008; Newman et al., 2016; Raynor et al., 2006; Raynor et al., 2012), fat mass by bio impedance spectroscopy (BIS) (Alkahtani et al., 2014), air displacement plethysmography (ADP) (Blundell et al., 2017; Hopkins et al., 2014; Stice et al., 2017) or dual-energy X-ray absorptiometry (DXA) (Cameron et al., 2008), and waist circumference by a measuring tape above the umbilicus (Astell et al., 2013).

2.4.5 Participant characteristics

All studies (N = 17) included individuals with obesity and some also included people who had either overweight or obesity (Alkahtani et al., 2014; Andriessen et al., 2018; Astell et al., 2013; Hopkins et al., 2014; Stice et al., 2017). Participants' median (range) BMI and age were 33.7 kg/m^2 (30.5-38.5) and 44.6 years (29.0-56.5), respectively. Two studies were only in men (Alkahtani et al., 2014; Johnstone et al., 2008). The median percentage of women was 68%. The number of participants in the intervention ranged from 10 to 136 with a median of 27 and the total number of participants across all studies was 1312.

2.4.6 Study results

All results from the weight management interventions (N = 17) are summarised in Table 2-2.

Table 2-2: Data extraction of the 17 weight management interventions

STUDY	PARTICIPANTS (N, sex, BMI, age)	INTERVENTION (duration, characteristics, control, design)	MEASUREMENTS (outcomes, methods)	RESULTS (change over time ↑ and magnitude pre to post WL in %, difference between groups/conditions and => correlations)	CONCLUSION
Aberg, 2008	100 women and men with obesity Low-fat diet BMI: 36.6 ± 4.5 kg/m^2 Age: 37.9 ± 6.2 y High-fat diet BMI: 36.5 ± 4.6 kg/m^2 Age: 38.2 ± 8.3 y	10-week dietary intervention study with two hypocaloric diets: low-fat (LF: 20-25%) or high-fat (HF: 40-45%) in free-living setting RCT	**Food reward:** Overall palatability of the diet *(VAS end-of-day)* **Food intake:** Total daily energy intake *(weighed food diaries)* **Physiological:** Body weight *(calibrated scale)*	↑ by 11% (LF) and by 7% (HF) over time, but no difference between diets ↓ by 26% (LF) and by 24 % (HF) over time ↓ with a median weight loss of 7%, no difference between diets	A free-living diet intervention increased the overall palatability of the diet but manipulating fat content did not influence palatability.
Alkahtani, 2014	10 men with overweight and obesity BMI: 30.7 ± 3.4 kg/m^2 Age: 29 ± 3.7 y	Two 4-week training interventions of 12 cycling sessions in each intervention (MIIT or HIIT) separated by a 6-week detraining wash-out Crossover design	**Food reward:** Liking and wanting *(LFPQ)* **Food intake:** *(ad libitum test meal)* - Energy intake of the meal - Energy intake from fat **Physiological:** Fat mass *(BIS)*	Exercise-induced-liking for HFNS food trend for ↓ after HIIT (–10 mm), and ↑ after MIIT (+5 mm) → over time, no difference between conditions ↑ by 38% after MIIT, ↓ by 16% after HIIT, difference approaching significance → over time, no difference between conditions	HIIT seemed to decrease liking for energy-dense food and fat intake after 4-week training compared to MIIT.

Andriessen, 2018	123 women and men with overweight and obesity BMI: N/A Age: 41.2±5.2 y	8-week low calorie dietary intervention Sub-group of the DiOGenes study that was randomised intervention study, no control group	**Food reward:** Food preferences *(Food Preference Checklist)*		Low calorie diet induced weight loss decreased preference for high-fat-, high-carbohydrate, and low-energy foods.
			- Low-energy foods	↓ by 1.9% (fasted) and by 13.5% (fed) over time	
			- High-carbohydrate foods	↓ by 11.4% (fasted) and by 17.4% (fed) over time	
			- High-fat foods	↓ by 16.2% (fasted) and by 22.7% (fed) over time	
			- High-protein foods	→ over time	
			- Food choice (*Forced Choice Photographic Questionnaire)*	→ over time	
			Physiological: Body Weight *(N/A)*	↓ by 11.1% over time	
Astell, 2013	33 women and men with overweight and obesity Experimental group: BMI: 32.5 ± 6.4 kg/m^2 Age: 46.7 ± 9.7 y Placebo group: BMI: 31.8 ± 4.1 kg/m^2 Age: 46.4 ± 10.4 y	12-week supplement (*C. fimbriata* extract) vs placebo intervention with dietary intake and exercise monitored RCT double blind placebo	**Food reward:** Overall palatability of the test breakfast meal *(VAS)*	↓ by 5% (experimental group) vs no change (placebo)	Supplementation with *C. fimbriata* extract was associated with a decrease in overall palatability and a reduction in central adiposity.
			Food intake: *(food diaries)*		
			- Total daily energy intake	→ over time, no difference between groups	
			- Energy intake from fat	↓ by 46% (experimental group) and by 38% (placebo), but no difference between groups	
			Physiological:		
			- Body weight *(digital scales)*	↓ by 2% (experimental group) and by 3% (placebo) over time, but no difference between groups	
			- Waist circumference *(above the umbilicus)*	↓ by 6% (experimental group) vs only 3% (placebo)	

Blundell, 2017	30 women and men with obesity BMI: 33.8 ± N/A kg/m^2 Age: 42 ± N/A y	12-week treatment with once-weekly subcutaneous Semaglutide (S), dose-escalated to 1.0 mg Randomised, double-blind, placebo-controlled, two-period crossover trial	**Food reward:**		Semaglutide-induced weight loss reduced energy intake and was associated with lower relative preference for fatty, energy-dense foods.
			- Palatability of the *ad libitum* meal *(VAS)*	N/A over time, no difference between conditions	
			- Liking for HFNS *(LFPQ)*	↓ more in S, with (-13.9 mm) difference	
			- Wanting for HFNS *(LFPQ)*	↓ more in S, with (-15.8 no unit) difference	
			- Wanting for LFS *(LFPQ)*	↑ more in S, with (+13.9 no unit) difference in S vs placebo	
			Food intake:		
			- Total daily energy intake *(ad libitum test meals lunch, dinner and snack)*	↓ more in semaglutide, with 24% difference in semaglutide vs placebo	
			- Energy intake from HFNS *(ad libitum evening snacks)*	↓ more in semaglutide, with 35% difference in semaglutide vs placebo	
			Physiological:		
			- Body weight (*N/A*)	↓ by 5% (semaglutide) vs ↑ by 1% (placebo)	
			- Fat mass *(ADP)*	↓ by 3.5kg (semaglutide) vs ↑ by 0.3kg (placebo) (% pre to post N/A)	
Cameron, 2008	15 women and men with obesity BMI: 35.7 ± 4.3 kg/m^2 Age: 33.6 ± 7.4 y	8-week of caloric deprivation (-700 kcal/day) Secondary analysis from a RCT, no control group	**Food reward:**		Prolonged caloric deprivation increased liking of the food reinforcers but not the RRV of palatable foods, except for subjects with high disinhibition
			- Liking for a standard lunch test meal *(VAS)*	→ over time	
			- Liking for the snack food reinforcer *(VAS)*	↑ by 9% over time	
			- Relative-reinforcing value (RRV) of snack foods versus fruits/vegetables *(progressive ratio computer task prior to*	→ over time	

			lunch and food reinforcers)		scores who tended to have an increase in the RRV of snack food.
			Psychological: Dietary disinhibition *(TFEQ)*	⇨ Correlation between high disinhibition scores and increase in the RRV post-weight-loss	
			Physiological:	⇨ No significant correlations between pre- or post-fat mass, fat-free mass and liking.	
			- Body weight *(digital scale)*	↓ by 5.2 ± 2.7%	
			- Body composition *(DXA)*	↓ by 8.2 ± 6.7% for fat mass and by 4.5 ± 3.3% for fat free mass	
Demos, 2017	37 women with obesity BMI: 33.5 ± 3.9 kg/m^2 Age 47.0 ± 7.9 y Baseline control: normal weight BMI: 22.7 ± 1.8 kg/m^2 Age: 44.0 ± 8.9 y	12 to 16-week behavioural weight loss (BWL) interventions incorporating diet, exercise, and behavioural therapy delivered by face-to-face group meetings (N = 31) or via the internet (N = 6) Non randomised trial, no control group completed the intervention	**Food reward:** Tastiness of snack food pictures *(5-point scale (-2 to 2))*		Tastiness and especially tastiness of unhealthy food decreased following BWL.
			- Mean taste	↓ by 31% pre to post intervention - no difference with the control mean taste	
			- Healthy food	↑ by 5% pre to post intervention	
			- Neutral food	↓ by 22% pre to post intervention	
			- Unhealthy food	↓ by 71% pre to post intervention	
			Food choice: Food choice task (*4-point scale)*	↑ in healthier, less tasty food choices post-treatment but less than in the control ⇨ BWL enhanced the valuation of health and diminished the valuation of taste in food choice	
			Physiological: Body weight (*N/A*)	↓ by 6.62%, no differences between the face-to-face program, the internet-delivered program, the 12-week or 16-week interventions	

Grieve, 2003	118 women with obesity Responders: BMI: 33.7 ± 6.1 kg/m^2 Age: 45.2 ± 11.4 y Non-Responders: BMI: 35.6 ± 7.3 kg/m^2 Age: 40.4 ± 12.4 y	12-week behavioural intervention including a reduction in energy and dietary fat intake as well as an increase in physical activity Secondary analysis of a single group intervention, no control group	**Food reward:** Desire to eat in the past 7 days *(48-item questionnaire)* - Low-fat foods - High-fat foods - Medium-fat foods and drinks **Food intake:***(48-item questionnaire)* - Low-fat foods - High-fat foods - Medium-fat foods and drinks	↑ by 9 % over time ↓ by 12% over time → over time ⇨ Strong positive association between change in desire to eat and change in consumption of these foods. ↑ over time ↓ over time → over time	Changes in consumption were associated with changes in desire to eat low-fat and high-fat foods.
Hopkins, 2014	46 women and men with obesity Women: BMI: 30.8 ± 3.5 kg/m^2 Age: N/A Men: BMI: 30.5 ± 4.7 kg/m^2. Age: N/A	12-week supervised aerobic exercise program designed to expend 2500 kcal/week Single group intervention no control group	**Food reward:** Liking and wanting before a fixed-energy meal (*LFPQ*) **Food intake:** Total daily energy intake (*test meals*) **Physiological**: - Body weight (*N/A*) - Fat mass *(ADP)*	→ between baseline and post-intervention ⇨ Fat mass and fat-free mass were associated with explicit liking for high fat foods ⇨ Implicit wanting was only associated with fat mass → between baseline and post-intervention ↓ by 2% pre to post intervention ↓ by 6% pre to post intervention	12 weeks of exercise did not significantly change food reward nor food intake but decreased body weight and fat mass.
Johnstone, 2008	17 men with obesity	Two 4-week dietary interventions comparing high protein diets either	**Food reward:** Overall pleasantness of each meal *(computerised VAS, post meal)*	→ over time, no difference between diets	No influence of carbohydrate content on overall

	BMI: 35.1 ± 3.8 kg/m^2 Age: 38 ± 10 y	low-carbohydrate (LC: 4%) or medium-carbohydrate (MC: 35%) RCT, crossover design	**Food intake:** Total daily energy intake *(food diaries)* **Physiological:** Body weight *(scale)*	↓ with an average difference of 294 kcal/d in LC vs MC diet ⇨ No correlation between pleasantness and energy intake of the 2 diets ↓ by 5.8% (LC) vs 4.0% (MC)	pleasantness of meals.
Martin, 2011	270 women and men with obesity BMI: 36 ± 3,3 kg/m^2 Age: 45.2 ± 9.8 y	2-year dietary intervention comparing a low-carbohydrate diet (LCD) with a low-fat diet (LFD) RCT	**Food reward:** Food preferences *(FPQ (Geiselman et al., 1998))* - High-carbohydrate - High-sugar food - Low-carbohydrate/high-protein foods **Physiological:** Body weight (*N/A*)	 ↓ more in the LCD vs LFD ↓ more in the LCD vs LFD ↓ more in the LFD vs LCD at 18 months ↓ by 7.2% at 24 months for the whole sample, no difference between diets ⇨ No correlation between FPQ scores and weight loss at any time-point	LCD and LFD decreased preferences for high-carbohydrate, high-sugar and low carbohydrate foods.
Martins, 2017	46 women and men with obesity BMI: 33.3 ± 2.9 kg/m^2 Age: 34.4 ± 8.8 y	12-week supervised exercise program with three training groups: MICT, HIIT, or short-duration HIIT RCT	**Food reward:** Food reward *(LFPQ)* **Food intake:** Total daily energy intake *(food diaries)* **Physiological:** Body weight (*N/A*)	→ over time, no difference between groups → over time, no difference between groups ↓ over time with an overall reduction of (-1.2 ± 2.5 kg), difference between groups N/A	Chronic HIIT had no independent effect on food reward compared with an isocaloric program of MICT in individuals with obesity.
McVay, 2016	105 women and men with obesity BMI: 36 ± 6 kg/m^2	48-week dietary intervention comparing 2 arms: low-fat diet (LFD) or	**Food reward:** Food preferences *(FPQ (Geiselman et al., 1998))* - High-fat/high-sugar	*Difference between groups: N/A ↓ by 13% (LCD), by 8% (LFD)*	LFD and LCD decreased food preferences for

	Age: 55 ± 11 y	low-carbohydrate diet (LCD) A secondary analysis of data from a randomised clinical trial	- High-fat/high-complex carbohydrate - Low-fat food absolute congruency - Low-carbohydrate absolute congruency **Physiological:** Body weight (*N/A*)	↓ by 17% (LCD), by 14% (LFD)* ↓ by 10% (LCD), by 5% (LFD)* → (LCD), ↓ by 6% (LFD)* ⇨ In the LCD, increase in preference for diet-congruent foods during the first 12 weeks of the intervention was associated with greater weight loss between 12 and 24 weeks	high and low-energy foods.
Newman, 2016	53 women and men with obesity BMI: 32.3 ± 5.1 kg/m^2 Age: 56.5 ± 13.8 y	6-week low-fat (LF) or portion control (PC) diet matched for weight loss RCT	**Food reward:** Liking of regular-fat and LF foods *(9-point hedonic scale)* **Food intake:** Total daily energy intake *(food diaries, FFQ)* **Physiological:** Body weight *(scale)*	↑ for LF food cream cheese only and not across all foods over time, no difference between diets ↓ by 14% (LF) and by 22% (PC) over time but no difference between diets ↓ by 3% over time, no difference between diets	Low-fat or portion control diets did not change liking for most of the low fat and regular food.
Raynor, 2006	30 women and men with obesity Reduced variety BMI: 32.2 ± 2.8 kg/m^2 Age: 50.9 ± 8.4 y Control BMI: 32.3 ± 3.8 kg/m^2 Age: 48.2 ± 11.4 y	8-week behavioural intervention, which reduced variety of snack foods in the diet (reduced variety) or limit snack food intake to <1 serving/day (control) RCT	**Food reward:** Pleasantness of tasting chosen sweet or savoury high-energy dense snack *(VAS)* **Food intake:** Energy intake from snacks per week *(food diaries)* **Physiological:** Body weight *(calibrated scale)*	↓ by 21% for the chosen snack food over time vs ↓ by 5% for other snack foods in the reduced variety group, no change in the control. ↓ by 63% (reduced variety) and by 51% (control) but no difference between groups ↓ by 3.33 ± 2.61 kg post intervention, no difference between groups	Limiting snack variety decreased liking of eaten snack food over time and more than other snack foods not consistently consumed.

Raynor, 2012	202 women and men with obesity BMI: 34.9 ± 4.3 kg/m^2 Age: 51.3 ± 9.5 y	18-month behavioural intervention comparing 2 arms: Lifestyle + limited variety of non-nutrient-dense, energy-dense foods (NND-EDFs) with a control (Lifestyle) RCT	**Food reward:** Pleasantness of tasting 2 chosen NND-EDFs *(VAS)* **Food intake:** *(24-h dietary recalls + 28-day FFQ)* - Energy intake from NND-EDFs - Total daily energy intake **Physiological:** Body weight *(calibrated digital scale)*	↓ for only one of the chosen NND-EDF and more in the intervention (-7.4 ± 13.4 mm) than in the control (-1.4 ± 12.3 mm) ↓ by 56% (intervention) vs 40% (control) ⇨ No correlation between pleasantness and energy intake from NND-EDFs ↓ by 27% (intervention) and by 20% (control) over time, but no difference between groups ↓ by 9.9 ± 7.6% (intervention), by 9.6 ± 9.2% (control), no difference between groups	Limiting the variety of NND-EDF decrease the pleasantness of one of the chosen food with no relationship with the decrease of energy intake from this food.
Stice 2017	47 women and men with obesity Intervention BMI: 38.5 ± 9.8 kg/m^2 Age: 32.8 ± 8.3 y Control BMI: 35.0 ± 7.7 kg/m^2 Age: 32.4 ± 8.4 y	Four weekly training sessions comparing food response and attention training with a parallel generic response training (and 6-month follow-up) Pilot RCT	**Food reward:** - Palatability of high-calorie foods *(200 food pictures rated on a 10-point scale)* - Palatability of low-calorie foods - Willingness to pay for high calorie foods *(<$1 to $10+ for a serving of each of the foods)* - Willingness to pay for low calorie foods **Physiological**: Body fat *(ADP)*	↓ over time, twice as more after a food response and attention training intervention than control → over time, no difference between groups ↓ (food response), → (generic response) → over time, no difference between groups ↓ (food response), → (generic response) No change after 6-month follow-up. ⇨ A marginal correlation between fat mass and palatability ratings for high-calorie foods	Food response training intervention reduced palatability ratings and monetary valuation of high-calorie foods, but not low-calorie foods, and resulted in greater body fat loss over a 4-week period, though this effect was not significant by 6-month follow-up.

	Other: Brain reward area activation *(fMRI food image exposure paradigm)*	↓ in reward (putamen, mid insula) regions in response to high-calorie vs low-calorie food images ⇨ Correlation between decrease in palatability and willingness to pay for high calories foods and decrease in brain activation in reward regions.

BMI: Body Mass Index, LF: Low-fat, HF: High-fat, RCT: Randomised-control-trial, VAS: Visual Analogue Scale, WL: Weight loss, MIIT: Moderate Intensity Interval Training, HIIT: High Intensity Interval Training, LFPQ: Leeds Food Preferences Questionnaire, HFNS: High fat non-sweet foods, BIS: bio impedance spectroscopy, HFNS: High fat-non-sweet foods, LFS: Low fat sweet foods, N/A: Not available, S: Semaglutide condition, ADP: Air displacement plethysmography, RRV: Relative-reinforcing value of a food, TFEQ: Three Factor Eating Questionnaire, DXA: dual-energy X-ray absorptiometry, BWL: Behavioural weight loss, LC: low-carbohydrate diet, MC: medium-carbohydrate diet, LCD: low-carbohydrate diet, LFD: low-fat diet, FPQ: Food Preferences questionnaires, MICT: moderate-intensity continuous training, PC: portion control, FFQ: Food Frequency Questionnaire, NND-EDF: non-nutrient-dense-energy-dense foods

2.4.6.1 Changes in food reward

Twelve studies reported a significant change in a component of food reward (liking, implicit or explicit wanting, or overall palatability) over time. Liking changed in 9 out of 13 studies (Andriessen et al., 2018; Blundell et al., 2017; Cameron et al., 2008; Demos et al., 2017; Martin et al., 2011; McVay et al., 2016; Raynor et al., 2006; Raynor et al., 2012; Stice et al., 2017). Overall palatability changed in 2 out of 5 studies (Aberg et al., 2008; Astell et al., 2013). Wanting changed in 3 out of 7 studies (Blundell et al., 2017; Grieve & Vander Weg, 2003; Stice et al., 2017).

Concerning the direction and magnitude of the change: liking for high-energy food (high-fat, high-carbohydrate, high-calorie, high-energy-dense, and unhealthy food) decreased significantly in 8 studies (Andriessen et al., 2018; Blundell et al., 2017; Demos et al., 2017; Martin et al., 2011; McVay et al., 2016; Raynor et al., 2006; Raynor et al., 2012; Stice et al., 2017). The same trend was reported in Alkahtani et al. (2014) but was not significant. However, one study reported an increase in liking for a favourite high-energy food snack (Cameron et al., 2008). When data were available, percentages of change pre to post weight loss were calculated. The median decrease in liking for high-energy food was 16% (Andriessen et al., 2018; Demos et al., 2017; McVay et al., 2016; Raynor et al., 2006) and the increase was 9% (Cameron et al., 2008). Liking for low-energy food was reported in 10 studies. It decreased in 3 studies (Andriessen et al., 2018; Martin et al., 2011; McVay et al., 2016) with a median of 5.9% and increased in one study (Demos et al., 2017) by 5%. Wanting for high-energy food decreased in 3 out of 7 studies (Blundell et al., 2017; Grieve & Vander Weg, 2003; Stice et al., 2017) and 2 out of 6 studies (Blundell et al., 2017; Grieve & Vander Weg, 2003) reported an increase in wanting for low-energy food. The magnitude of the decrease in wanting pre to post intervention in percentage was not calculated due to data not being available.

A further question is whether there was an effect of intervention type on the change in food reward. Five out of 12 interventions reported a decrease in liking for high-energy food with a difference between experimental groups/conditions (Blundell et al., 2017; Martin et al., 2011; Raynor et al., 2006; Raynor et al., 2012; Stice et al., 2017) showing that different types of interventions (i.e. pharmacological, dietary, behavioural, cognitive) can all be effective in reducing liking for high-energy food. Of the 3 studies (Andriessen et al., 2018; Martin et al., 2011; McVay et al., 2016) that decreased both liking for low and high-energy food, only one intervention (Martin et al., 2011) reported a group effect (i.e. a difference between intervention arms with a greater decrease in preferences for high-carbohydrate food in the low-carbohydrate diet a larger decrease in preferences for high-fat food in the low-fat diet). For overall palatability, only one study out of the 5 showed a difference between experimental groups with an effect of the nutraceutical on the decrease of overall palatability (Astell et al., 2013). Two out of

7 interventions showed reduction in wanting for high-energy food compared to control (Blundell et al., 2017; Stice et al., 2017) and one of the pharmacological interventions (Blundell et al., 2017) found reduced wanting for high-energy food and increased wanting for low-energy food. Two out of 6 interventions (Blundell et al., 2017; Stice et al., 2017) found a decrease in both liking and implicit wanting for high-energy food.

2.4.6.2 Association between changes in food reward and food intake

One study measured the intake of low and high-fat food (Grieve & Vander Weg, 2003) and reported a significant decrease in intake of high-fat food and an increase in intake of low-fat food after a behavioural intervention. There was a strong positive association between change in desire to eat and change in consumption of these foods. Two studies measured energy intake from fat (Alkahtani et al., 2014; Astell et al., 2013), one of which reported a significant decrease in energy intake from fat (46%) in the nutraceutical condition compared to the control (Astell et al., 2013). The correlation between change in overall palatability and change in energy intake from fat was not assessed.

Eight studies measured total daily energy intake (Aberg et al., 2008; Astell et al., 2013; Blundell et al., 2017; Hopkins et al., 2014; Johnstone et al., 2008; Martins et al., 2017; Newman et al., 2016; Raynor et al., 2012) and 3 studies (Aberg et al., 2008; Blundell et al., 2017; Johnstone et al., 2008) reported an effect of the intervention on decreasing energy intake. Only Johnstone et al. (Johnstone et al., 2008) assessed the correlation between change in overall palatability and change in total daily energy intake but they were not associated.

Three studies measured energy intake for high-energy food specifically (Blundell et al., 2017; Raynor et al., 2006; Raynor et al., 2012); 2 studies (Blundell et al., 2017; Raynor et al., 2012) reported a significant decrease in the intervention arm. Only Raynor et al. (2012) analysed the association between change in liking and energy intake from this food but found no correlation. To conclude, few studies reported a significant effect of the intervention on food intake. Even fewer studies analysed the relationship between change in food reward and change in food intake-related measures.

2.4.6.3 Association between changes in food reward and weight outcomes

The 14 studies that measured body weight all reported a decrease ranging from 2% to 10% with a median weight loss of 5% (Andriessen et al., 2018; Astell et al., 2013; Blundell et al., 2017; Cameron et al., 2008; Demos et al., 2017; Hopkins et al., 2014; Johnstone et al., 2008; Martin et al., 2011; Newman et al., 2016; Raynor et al., 2012). Three studies (Blundell et al., 2017; Johnstone et al., 2008; McVay et al., 2016) showed a difference between intervention arms. Only McVay et al. (McVay et al., 2016) assessed the association between changes in body weight with changes in food reward and showed that an increase in liking for low-energy (diet-congruent) foods was associated with greater weight loss. However, this was only significant for 1 out of 4 time points where liking was measured.

Four studies measured fat mass (Alkahtani et al., 2014; Blundell et al., 2017; Hopkins et al., 2014; Stice et al., 2017), and 2 studies (Blundell et al., 2017; Stice et al., 2017) reported a decrease in fat mass in the intervention arm compared to the control. Only Stice et al. (Stice et al., 2017) assessed the relationship between food reward and fat mass, and reported a marginal positive correlation between pre to post fat mass and decrease in palatability ratings for high-energy foods. This association between liking and fat mass was also reported in Hopkins et al. (2014).

To conclude, 5 studies (Aberg et al., 2008; Cameron et al., 2008; Martin et al., 2011; McVay et al., 2016; Stice et al., 2017) assessed the relationship between changes in food reward and changes in weight outcomes: 2 studies (McVay et al., 2016; Stice et al., 2017) showed an association between decreased liking for high-energy food and reductions in fat mass or body weight; one study (Cameron et al., 2008) found an increase in liking was not correlated with changes in fat or fat-free mass; one study (Martin et al., 2011) found no correlation between a decrease in liking with weight loss; and in one study (Aberg et al., 2008) there was no relationship between change in overall palatability and weight loss.

2.4.6.4 Association between changes in food reward and psychological measures

One study (Cameron et al., 2008) reported a moderating effect of trait disinhibition (measured by the Three Factor Eating Questionnaire (TFEQ)) on wanting pre to post weight loss. Individuals with obesity who scored high in disinhibition tended to work harder to earn snacks post weight loss.

2.5 Discussion

The aim of this systematic review was to assess whether components of food reward change during weight management interventions and whether any changes were related to weight management outcomes. Both liking and wanting for high-energy food tended to decrease post-intervention. Wanting for low-energy food increased and liking for low-energy food increased in one behavioural intervention and decreased in dietary interventions. A range of intervention types - dietary, behavioural, cognitive and pharmacological - seemed to be effective in decreasing liking and/or wanting for high-energy food. However, the relationship between changes in food reward and change in weight management outcomes was less clear. Only a few studies assessed this relationship and showed that a decrease in liking for high-energy food was associated with a decrease in body weight or fat mass. Changes in wanting appeared to be more related to changes in food intake. However, these associations need to be confirmed.

2.5.1 Methodological considerations

The definition and measurement of food reward can be confusing, as shown in this and previous reviews (Pool et al., 2016). The complexity of defining and measuring components of food reward in theory rests on their logical status as intervening variables (i.e. liking and wanting cannot be directly observed) (MacCorquodale & Meehl, 1948). However, in modern psychological science, liking and wanting are regarded as psychological states that can be measured through procedures such as rating scales or forced-choice. Trait measures of reward such as sensitivity to reward, or general food craving were not considered as food reward in this review as they don't measure the pleasure or motivation to eat a specific food at the time of viewing or ingestion (Meule et al., 2014). Definitions of liking across studies were consistent but some studies explicitly defined liking as the "pleasantness of the taste of the food", whereas others only used the word "liking" or "palatability" without giving more information, which may add some flaws in the comparison of studies. Other potential bias across studies could be the time of day of the measurement and the state of hunger. The hedonic value of food may differ between morning, noon and evening, or when fasted compared to fed (Finlayson et al., 2008). Food reward may also change across the lifespan and differ in children or the elderly and for this reason the focus was on adults only. Furthermore, smokers were excluded as they may not have the same sensibility to palatable food due to changes in sensory perception or reward function (Tang et al., 2012).

A variety of methods were reported to measure liking and wanting, raising the question of whether measures can be compared. For liking measurements, the main differences were whether participants rated liking after having seen pictures of food or eaten food, and whether they were rating a small or large set of food items covering different aspects of the diet (fat, carbohydrate, low or high-energy content). Firstly, seeing a food picture instead of tasting/consuming reflects more the expected pleasantness than the hedonic experience of liking (Pool et al., 2016). Secondly examining changes in liking on a limited set of foods may not accurately represent changes in high-energy or low-energy foods and could explain some of the discrepancies in the results. VAS ratings are seen as accurate to report changes in subjective sensations of appetite (Flint et al., 2000), but use of Likert scales compared to VAS may not have the same sensitivity to detect an impact on the change of liking. In this review, one measure of explicit wanting was quite remote as it measured the desire to eat a specific food but over the past 7 days and not at the moment of ingestion (or viewing).

Measurements of food reward should ideally target a specific food at a given time, taking into account the time of day and physiological state. Consistent methodology would yield more accurate and comparable measures (e.g. broad set of foods, same wording and definition of liking and wanting). To be more discriminating, measures of food reward should allow the distinction between liking and wanting. Also, indirect measures of implicit wanting (e.g. willingness to exert an effort to obtain a food or reaction time of responses to a food) should be used more often as they are more representative of implicit motivational process.

2.5.2 Role of food reward in weight management

It is frequently assumed by researchers that weight loss will lead to compensatory increases in homeostatic responses that drive up food intake to protect energy stores. This has led some to hypothesise that food reward will also increase after weight loss (Cameron et al., 2008; Hintze et al., 2017). Indeed, studies have shown that acute food deprivation increases food reward (Berthoud, 2011; Cameron et al., 2014). Furthermore, a recent review showed that extended energy restriction, brain regions related to liking were minimally affected while food-cue reactivity in wanting regions were suppressed (Kahathuduwa et al., 2016). However, the present systematic review suggested that different types of interventions report a decrease in liking and wanting in the context of weight management. How can these contradictory views be resolved?

Methodological differences might explain some of the discrepancy in findings. Firstly, there are contradictory findings in fMRI studies with studies reporting increased and decreased brain responses to food (Versteeg, 2017). Furthermore, studies reporting an increase in BOLD signal may not translate into cognitive or behavioural hedonic responses. More studies are needed to validate the brain responses to food cues in relation to food reward measured by psychometric methodologies. Another explanation could be due to the extent of the induced energy deficit between studies, where a larger deficit could lead to greater reductions in food reward compared to a smaller deficit. However, the data from this review do not allow this question to be quantitatively examined.

Finally, the duration of energy restriction should be taken into account. It has been shown that short-term (a day or less) nutrient depletion increases liking and wanting for specific foods (Griffioen-Roose et al., 2012; Masic & Yeomans, 2017) and that acute (3-day) fasting increases liking and wanting for high-energy foods (Cameron et al., 2014). It could be hypothesised that short-term food deprivation may enhance food reward whereas longer-term deprivation will attenuate it. Is there a minimum time needed to observe a decline in food reward? The shift in reward for low and high-energy foods may occur as weight loss goals become internalised and more automatic, representing an alignment between cognitions and eating behaviour. For instance, dietary interventions (Andriessen et al., 2018; Martin et al., 2011; McVay et al., 2016) from this review that showed reduced intake of high-energy food during weight loss also reported a decrease in liking for high-energy food.

In this review, only one study (Cameron et al., 2008) found an increase in liking for palatable food after weight loss. This result needs to be considered carefully as the study had a high risk of bias. Inconsistencies in the design of this study and especially in the assessment of food reward may account for this contrary finding. Firstly, this study was a secondary analysis with no control group and consequently difficult to attribute changes in liking to the weight loss intervention per se. Secondly, in other studies (Andriessen et al., 2018; Martin et al., 2011; McVay et al., 2016) liking was assessed for different types of food categorised as low or high-energy whereas in this study (Cameron et al., 2008) liking was measured only for one specific high-energy food (i.e. the participant's preferred palatable snack). It is not clear whether this very specific intervention can be generalised to different types of interventions or high-energy foods that were not specifically preferred.

Another question concerns the discrepancies found in changes in liking for low-fat food. Three dietary interventions (Andriessen et al., 2018; Martin et al., 2011; McVay et al., 2016) reported a decrease and one behavioural intervention found an increase (Demos et al., 2017). What differed between these studies was the assessment of liking. The discrepant study (Demos et al., 2017) measured the tastiness for perceived unhealthy or healthy snacks and this latter categorisation of food may not correspond exactly to high/low-energy foods which may weaken the comparison. With regards to wanting measures, all the interventions from this review that reported a change in wanting showed a decrease for high-energy food and/or an increase for low-energy food. All together these results suggest that reductions in wanting and liking for food are generally achieved following weight management interventions.

2.5.3 Implications for weight management

All the studies reported here were not acute studies (i.e. ≥4 weeks) giving more clinical relevance to the food reward changes. However, only a few studies assessed the relationship between food reward changes and weight management outcomes, and one was at high risk of bias (Grieve & Vander Weg, 2003) therefore implications for weight management need to be confirmed. Interventions included individuals with overweight and/or obesity but data were not available to analyse the role of food reward by subgroups of BMI classification.

Can conclusions be drawn on which type of intervention is most effective to change food reward? Dietary interventions seem effective as 4 out of 5 studies reported a change in liking for high or low-energy food. Newman et al. (Newman et al., 2016) reported no change in liking for low or regular-fat products, only liking for low-fat cream cheese increased over time. The measure of liking appeared quite strong as they assessed liking just after tasting each food item. However, they only assessed liking for a limited set of food that did seem to have been screened for acceptability, palatability and macronutrient content. A broader and more controlled set of foods would throw light on this question.

Surprisingly, none of the exercise studies reported changes in food reward. These studies used the same methodology to measure liking and wanting (i.e. LFPQ) which is a robust method for detecting changes in food reward in different settings (Dalton & Finlayson, 2014). Furthermore, acute exercise has been shown to have different effects on food reward (measured by LFPQ) depending on the population (Cameron et al., 2016) or the dose of exercise (cNeil et al., 2015; Martins et al., 2015). Several hypotheses can be proposed to explain the null findings in the longitudinal exercise studies from this review. The main reason might be that measures of food reward were not consistent across studies. Indeed they all used LFPQ, but food reward was measured before and after the acute exercise (Alkahtani et al., 2014), or in a fasted state before lunch (Hopkins et al., 2014) or pre and post breakfast (Martins et al., 2017). Besides, one study (Hopkins et al., 2014) had no control group and the others (Alkahtani et al., 2014; Martins et al., 2017) were based on a limited sample (i.e. $n < 14$) questioning whether the lack of changes could really be attributed to the intervention and not to lack of power. In sum, more consistency in the design, duration, and energy deficit is required to determine which type of intervention is the most effective to reduce food reward while improving weight management outcomes.

2.5.4 Limitations and strengths

The main limitation encountered by this review was the complexity in the definition and measurement of food reward, which may lead to confusion when grouping and synthesising outcomes. Changes in food reward were reported qualitatively due to lack of available data. In future, given more studies, a meta-analysis of the changes in liking and wanting would provide a more powerful analysis. Also, only a few studies measured implicit or explicit wanting which weakens the ability to compare changes in liking versus wanting in response to weight management, which would be theoretically and clinically relevant (Finlayson & Dalton, 2012b). The studies were mainly on women (median of 68%), limiting the generalisation of results to men. Five papers had a high risk of bias but these were not impacting the main results. Only 17 interventions were included, but this review used high methodological standards that assured quality. It is important to consider drop-out rates in weight management interventions, and in this review the median attrition rate was 19% which is not unusual. However, no studies adjusted for this in their analyses (e.g. intent-to-treat analyses). Finally, only peer-reviewed studies were considered for inclusion in this review and future updates could include grey literature.

2.6 Conclusion

This review used a systematic approach to examine changes in food reward during weight management interventions. It revealed that liking and wanting for high-energy food mostly decreased during weight management, and different types of interventions were effective to reduce food reward. The associations between food reward and weight management outcomes need to be confirmed. The synthesised findings may help to elucidate some of the previous uncertainty on whether components of food reward increase as a compensatory response to weight loss. Some of the confusion may arise due to the difficulty in defining the components of food reward and the discrepancies between measures of food reward. Food reward should be measured in a consistent manner in future weight management interventions to allow systematic reviews to quantify its effect on outcomes. Weight loss interventions that facilitate reductions in the reward for high-energy food (or increased liking and wanting for low-energy food) may be beneficial for weight loss maintenance, and it remains to be examined whether hedonic rather than homeostatic mechanisms could be responsible for weight regain after weight loss (Berthoud et al., 2017; Dulloo et al., 2012).

Chapter 3
Assessment of Food Reward

Chapter aims:

1. Summarise the methods used to measure components of food reward.

2. Justify the use of the Leeds Food Preference Questionnaire to assess liking and implicit wanting in the context of weight management.

HIGHLIGHTS

- ► A wide variety of methods are used to measure components of food reward, and definitions of these components might vary.
- ► The Leeds Food Preference Questionnaire (LFPQ) allows the assessment of the dissociation between liking and implicit wanting for food (e.g. pre to post a meal) and reflects sensory-specific satiety.
- ► The LFPQ enables the assessment of reward components for a range of common foods varying in taste (sweet or savoury) and fat (low-fat or high-fat) which is meaningful in the context of weight management.

3.1 Introduction

Food reward is not directly observable nor an absolute measure of what we eat. However, it contributes to food choices and is important for understanding eating behaviour and appetite control. The previous chapter and systematic review by Oustric et al. (2018a) and Pool et al. (2016) raised the methodological limitations of the literature, with the key issue being the variability in the definitions and measurements of food reward. Indeed, food reward is not a homogenous construct. It comprises components often described in terms of liking vs wanting and explicit vs implicit. These components can dissociate under specific conditions and have a specific role in appetite control (Morales & Berridge, 2020). Therefore, for measures of food reward to be meaningful and plausible, they need to reflect the distinction between these components (Gibbons et al., 2019). Most of the work on the dissociation of liking and wanting comes from animal neuroscience, and developing robust quantitative tools measuring these components at both implicit and explicit levels in humans remains a challenge (Ziauddeen et al., 2014).

This short methodological chapter aims to put into perspective the Leeds Food Preference Questionnaire (LFPQ) among the different methods assessing food reward. Firstly, a brief overview of the main methods used to measure components of reward is drawn from behavioural assessments of liking and wanting to functional neuroimaging and brain responses to food. Then the specificity of the LFPQ, to assess separate liking and wanting for different categories of food and the task procedures is presented. Finally, its validity and potential usefulness in the context of weight management is discussed.

3.2 Overview of methods assessing components of food reward[1]

The most common measures of food reward comprise explicit liking (i.e. the hedonic experience) (Pool et al., 2016), implicit wanting (i.e. the indirect motivation to eat a specific food) (Berridge, 2009) and explicit wanting (i.e. the cognitive desire) (Berridge, 2009). Explicit components are usually measured through self-report psychometric techniques, which have the advantage of being quick and easy for participants, whereas implicit components are assessed indirectly. Table 3-1 gives an overview of different techniques assessing flavour and food liking and wanting at the explicit and implicit levels, specifying the reward component's denominations, methods, and stimuli. It shows that the constructs being measured vary among the studies for each component (e.g. food preferences, fat preferences, or palatability for "liking"). The stimuli used to assess food

[1] The methods reported in this Chapter are sampled from the systematic search leading to the Oustric et al. (2018a) review and the updates from this search (see Appendix A for the search strategy).

reward also differ between studies; from food pictures (Geiselman et al., 1998) that vary in categories, to real food tasted (Flint et al., 2000). Beyond liking for food, liking methodology has been used for odours, and applied to olfactory stimuli (Brondel et al., 2011; Cereghetti et al., 2020).

3.2.1 Behavioural measures of Liking

Because liking is the experienced pleasure of a food, it is mostly measured explicitly through self-reported assessment. The techniques used are often questionnaires, with numerical scales (Geiselman et al., 1998), lists (Blundell & Rogers, 1980), or visual analogue scales (VAS (Dohle et al., 2014; Finlayson et al., 2007a; Flint et al., 2000)) asking, for example, 'How pleasant would it be to taste some of this food now?' (Finlayson et al., 2008). Some techniques use forced-choice (Lemmens et al., 2009) or ranking tests (de Bruijn et al., 2017) to measure food choice or the relative preference for a food category compared to another.

The methodology used can lead to some difference in the construct being measured under the umbrella of "liking". For example palatability is a complex notion that has many definitions (Bellisle, 1989) but often refers to the sensory pleasure of eating a meal and not a specific food (Flint et al., 2000). For example, Cameron et al. (2008) measured hedonic rating as a global evaluation of multiple food items but named it interchangeably with liking. Moreover, liking assessment usually refers to the pleasantness from the taste in the mouth (Ledikwe et al., 2007) but some studies have used "desire to eat" (de Bruijn et al., 2017) instead, which can lead to confusion with the explicit motivational component of reward (e.g. wanting).

Another difference explaining the heterogeneity between methods is the variety of stimuli used to elicit food reward. These are mostly food pictures, or real food consumption and the numbers of food and types of the categories vary (e.g. high-fat, low-energy). Some studies have used one food (snack) (Cameron et al., 2008) or a few stimuli to assess a type of food (Ouwehand & de Ridder, 2008) while others have used a variety of food for each food category (Ledikwe et al., 2007).

With self-reported techniques, reporting bias (e.g. social desirability) or methodological issues such as end avoidance can occur. However, VAS are sensitive to the physiological state (fasted, fed) and predict food intake (Flint et al., 2000). Indeed, measures of liking have been related to food intake, with increased liking for a self-prepared milkshake increasing its consumption, and preference for fat associated with dietary fat intake (Geiselman et al., 1998; Ledikwe et al., 2007). It should be noted that the sample size was small and restricted to men in Geiselman et al. (1998).

While being reported less frequently, techniques have been developed to assess the implicit component of liking via orofacial reactions to tastes (Steiner et al., 2001) or via implicit associations between food and valanced words (Greenwald et al., 1998). Moreover, objective hedonic reactions have been validated in rodents (Berridge, 2000), primates (Steiner et al., 2001) and human infants (Hetherington et al., 2016) but are more difficult to assess in adults humans (Ziauddeen et al., 2014). For example, Hetherington et al. (2016) have developed a direct measure of liking (with facial expression in response to food) and wanting (feeding behaviour and rate of acceptance) in early life and the two-factor structure of the tool suggests the separation between liking and wanting.

3.2.2 Behavioural measures of Wanting

While it seems straightforward to report liking, it is more difficult to determine one's implicit wanting for food. As implicit wanting encompasses the motivational drive to eat, measures of wanting should be as spontaneous as possible to reduce contamination with subjective processes. There are two main indirect measures of the motivational aspect of food reward (i.e. implicit wanting): the willingness to exert an effort to obtain a food and the reaction time of responses to a food. Both techniques require a physical response in relation to stimuli which can either be real food or food cues.

Briefly, the first category of techniques entails the relative reinforcing value of food which can be defined as the willingness to work for points to obtain the preferred stimuli compared to an alternative (e.g. healthy snack food, money, non-food activity) (Epstein et al., 2007). The relative reinforcing value of food has been related to energy intake and BMI (Epstein et al., 2011). Moreover, using a choice paradigm has been shown to be ecologically valid as in the real-world food consumption usually happens in a context where several food options are possible. The grip force also measures the amount of physical effort individuals will expend to receive a reward (e.g. measure of food-related motivation) (Ziauddeen et al., 2014). The second category of techniques measures the response speed of a behavioural choice. For example, in the LFPQ, the individual's reaction time to food images is interpreted as a relative motivational value of the food (Finlayson et al., 2008). While the reinforcing value of food and the grip force are usually based on a restricted type of food reward such as a single preferred food or snack, the LPFQ uses an array of common foods that represent distinct categories varying in fat and taste. Another food categorisation has been proposed by Lemmens et al. (2009): bread, filling, drinks, dessert, and sweets compared to stationery. Their wanting measure is based on a memory game assuming that success in the memory game using a food category will be related to the wanting for this food category which might not correspond to real-life food seeking and is not based on the incentive salience theory.

Other techniques include attentional bias, which can be defined as the tendency to favour salient information in the environment over more neutral information (Mathews & MacLeod, 2005). Attentional bias has been shown to predict snack intake in individuals within the normal range of BMI and to be sensitive to physiological state and BMI (Nijs et al., 2010). This construct related to "wanting" also uses reaction times towards a stimulus. For example, the visual probe task created by MacLeod et al. (1986) was adapted to measure the attentional bias for healthy food compared to unhealthy food. Participants are first presented with a fixation cross, then with a pair of food pictures and finally with a probe stimulus, and they have to indicate as quickly as possible whether the probe replaced the picture on the left or on the right. An attentional bias for salient information, here healthy food, is apparent when reaction times are faster when the probe replaces the healthy food compared to the control image (here unhealthy food) (Kakoschke et al., 2014). Another technique used to assess the attentional bias is the modified Stroop task using food-related words (i.e. participants have to name the ink colour of each word presented, as quickly and accurately as possible (Nathan et al., 2012)). Lastly, measures of approach bias with the approach avoidance task also use the reaction time of approaching or avoiding stimuli (Phaf et al., 2014). Recently it has been adapted to food using touchscreen technology where participants move their hand either towards or away from an image of a high-calorie food, a low-calorie food, or a neutral object (Kahveci et al., 2021). This measure is associated with preferences and calorie content but its association with food intake has not been measured. To conclude, these techniques of attentional or approach bias represent implicit measures but might differ from the wanting measured by the LFPQ. Indeed, their operationalisation reflects rather the attention grabbing properties of types of food which is different from the internal motivation behind non-verbal food choices in the LFPQ and their translation to food intake (Dalton, 2013).

Another indirect way to assess "wanting" is the willingness to pay used as a measure of goal value. The objectivity of this measure depends on the technique used via computerised auction procedure (Ziauddeen et al., 2014) to a food utility rating (Brunstrom & Rogers, 2009). Finally, explicit wanting is measured directly through questionnaires asking "how much did you want to eat what you just saw?" and often reported as desire to eat to reflect the motivational aspect of eating (Sanmiguel et al., 2017).

3.2.3 Functional neuroimaging and brain responses to food

In the field of appetite, the study of the brain activity has been made possible with functional neuroimaging techniques such as electro-encephalography (EEG), positron emission tomography (PET) and more recently, functional magnetic resonance imaging (fMRI) (Behary & Miras, 2014; Neary & Batterham, 2010). The latter translates structural and functional information on brain activation in response to food images (Rosenbaum et al., 2008). Blood-oxygen-level-dependent (BOLD) signals indicate changes in local blood flow to transcribe increased or decreased neural processing (Smeets et al., 2012). While fMRI is now the most used method for its high spatial resolution, it has a lower temporal resolution, is costly and is an indirect measure of neuronal activity. The simplest method is the EEG, consisting of electrodes attached to the scalp to directly detect electric signals generated by neuronal activity. This method has a high temporal resolution, is portable and cheap, but its sensitivity to detect is limited. Lastly, PET uses a radioisotope injected in the peripheral circulation, of which concentrations can be visualised in brain regions to show differences in metabolic rate or blood flow (Neary & Batterham, 2010). It reports markers of neural activation but more specifically can inform about neurotransmission and neuroreceptor availability (Behary & Miras, 2014). However, this method has a lower spatial resolution than fMRI and is both costly and invasive.

While neuroimaging techniques enable the study of the brain in vivo and potential substrates for food reward formation, they don't always translate into behavioural responses (Devoto et al., 2018). A review by Ziauddeen et al. (2012a) has summarised the findings of fMRI studies exploring responses to food (both anticipation and consumption) in individuals with obesity or binge eating compared to controls, and showed poor replicability of the findings. More recently, Yokum et al. (2021) reported a poor test-retest reliability of temporal fMRI. The large discrepancies and variability of neuroimaging findings attest to the heterogeneity of the methods (Morys et al., 2020). This heterogeneity can be explained by the low statistical power associated with large individual variability and the need for standardisation of the study designs (e.g. fMRI tasks, anticipatory or consummatory reward, standardised food stimuli). To improve the quality of neuroimaging studies and meta-analyses, Morys et al. (2020) recommended using large sample sizes, appropriate statistical thresholding and ideally preregistered analyses, but also to consider confounding factors such as age, self-control, food craving, impulsivity, hunger or dietary restraint. In conclusion, to be meaningful, neuroimaging techniques should be combined with direct assessments of eating behaviour to better understand the underlying processes of behaviour.

Table 3-1: Overview of techniques measuring liking and wanting

	Food reward components	Methods	Stimuli
Exp. Liking	Food pref	**Food preferences checklist** (Blundell & Rogers, 1980)	30 basic food pictures high in protein or carbohydrate
	Macronutrient pref	**Food preferences questionnaire** (forced-choice preference test) (Hill, 1986)	Pictures of foods high in carbohydrate, protein or low-calorie foods
	Macronutrient pref	**Food Preference Questionnaire** (Likert scale (Geiselman et al., 1998)	72 foods pictures: (High Fat, Low Fat)×(Carbohydrates (CHO): High Simple Sugar, High Complex CHO, and Low CHO/High Protein)
	Palatability/ liking	**VAS** (Flint et al., 2000)	Originally palatability of the test meal but can be used for food tasted (Dohle et al., 2014) or food pictures (Finlayson et al., 2007a)
	Fat pref	**Fat Preference Questionnaire** (select the food which tastes better and is eaten more frequently (Ledikwe et al., 2007)	19 sets of foods from a variety of food groups, with sets containing two or three similar foods that vary in fat content
	Sweet pref	**Sweet tasting** (Likert scale) (Ouwehand & de Ridder, 2008)	Three sucrose-in-water solutions: 0% sugar, 20% sugar, and 40% sugar solution.
	Macronutrient pref	**Macronutrient and Taste Preference Ranking Task** (ranking how much they desire to eat the products) (de Bruijn et al., 2017)	Food pictures of high-carbohydrate, high-fat, high-protein and low-energy foods
Imp. Likin	Obj. affective expression	**Orofacial expressions** (grouped into positive, neutral, and aversive categories) (Steiner et al., 2001).	Tastes of sucrose, quinine, water, etc.
	Implicit affect	**Implicit associations test** (Greenwald et al., 1998)	Food-related (healthy/unhealthy) vs valenced words (positive/negative)
Exp. Wanting	Desire to eat	**VAS** (Flint et al., 2000)	Desire to eat something fatty, salty, sweet or savoury
		VAS (Sanmiguel et al., 2017)	Foods (high-calorie: sweets and savoury; and low calorie: fruits and salads)
	Wanting	**LFPQ** (VAS) (Finlayson et al., 2007a)	16 food pictures varying in fat (high/low) and taste (savoury/sweet)
Imp. Wanting	Motivation to eat	**Grip force** (Ziauddeen et al., 2012b)	Effort to win two food rewards: pizzas (savoury) and cake (sweet).
		Grab-to-Eat Task (Pirc et al., 2019)	Eating motivation dynamics throughout consumption of chocolate milk
	Wanting	**Relative reinforcing value task** (Goldfield et al., 2005)	Work to obtain snacks vs alternative reinforcer
		LFPQ (forced-choice) (Finlayson et al., 2007a)	16 food pictures varying in fat (high/low) and taste (savoury/sweet)
		Memory game (Lemmens et al., 2009)	Motivation to eat bread, filling, drinks, dessert, sweets, and stationery

Exp: explicit, Imp: implicit, pref: preferences, obj: objective

3.3 The specificity of the Leeds Food Preference Questionnaire

3.3.1 A tool assessing liking and wanting separately for the same food

The chosen method to measure food reward in this thesis is the LFPQ as it is designed to measure, with a single instrument, the constructs of liking and wanting according to key dimensions of food (HFSA: high-fat savoury, LFSA: low-fat savoury, HFSW: high-fat sweet and LFSW: low-fat sweet). This computer-based platform comprises two sub-tasks: 1) a direct measure of "explicit liking and wanting" using VAS, and 2) an indirect measure of "implicit wanting" using the reaction time of decisions between foods pairs. The tasks are either randomised or counterbalanced and the total procedure lasts approximately 6–8 min. The stimuli used in the LFPQ are an array of 16 food pictures pre-validated such that the macronutrient content of the foods define their categories (high-fat:>40% energy from fat, low-fat:<20% energy from fat, while matching protein content as possible). Importantly, the perceived attributes of the pictures need to be tested such that the food pictures are well-recognised, frequently eaten, adequately liked, correctly identified as sweet/savoury, low- or high-fat, and suitable for the intended time of day (e.g. breakfast see Figure 3-1or lunch see Table 3-2). A detailed protocol of the task and procedures has been developed by Oustric et al. (2020).

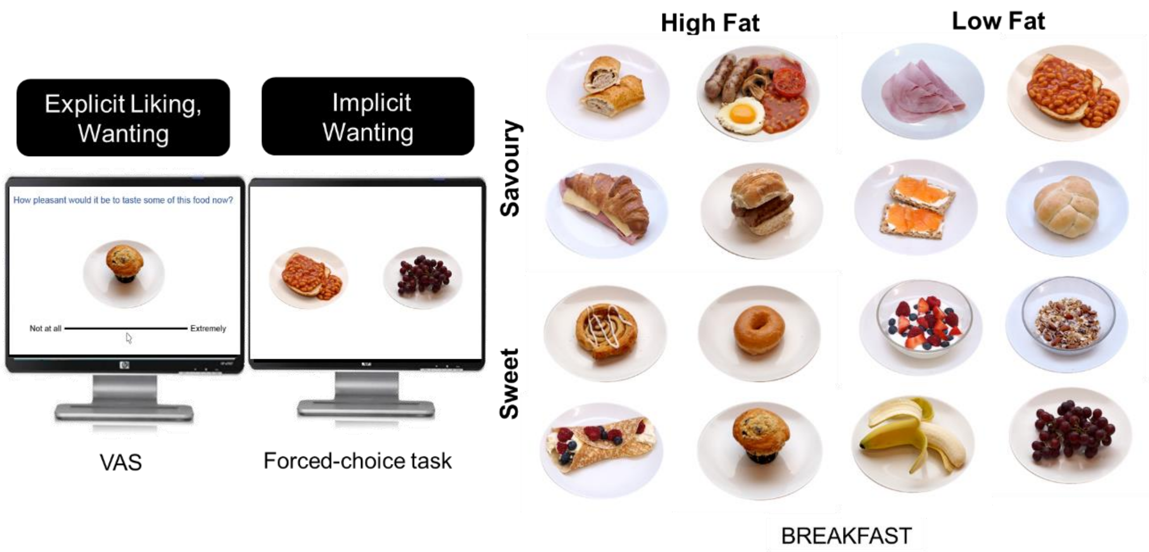

Figure 3-1: Summary of the LFPQ procedure

The LFPQ includes two tasks 1) explicit liking/wanting via 100-unit VAS and 2) implicit wanting via a forced-choice task, using the same stimuli: 16 food pictures varying in fat and taste and culturally adapted to the time of day (e.g. breakfast/fasted state). Portion sizes usually represent common portions and participants are told to think about the food in itself and imagine they can have as much or as little as they want. While the core pictures are validated through a questionnaire (Oustric et al., 2020), a screening of the pictures is also made by each participant prior to each study to adapt for individual preferences and change foods individuals would never/rarely eat or don't know/recognise.

Table 3-2: List of food used in the LFPQ at lunch time

Food Categories	High-fat	Low-fat
Savoury	Cheese Peanuts Crisps Fries	Boiled potatoes Pasta in sauce Rice Bread loaf
Sweet	Jam bun Milk chocolate Blueberry muffins Donuts	Jelly beans Popcorn Marshmallow Fruit salad

3.3.1.1 Understanding the measurement of explicit liking and wanting

For the explicit measures, individuals rate "How pleasant would it be to taste some of this food now?" (explicit liking) and "How much do you want some of this food now?" (explicit wanting) on VAS of single food images randomly presented to them. The two questions (explicit liking vs wanting) are counterbalanced and are presented with different font colours to better discriminate the constructs. Explicit liking is computed by food category (e.g. HFSW), ranges from 0 to 100 mm and is simple to interpret. A higher score indicates a greater explicit liking for the specific food.

As this thesis focuses on the impact of weight management and overweight/obesity on the separate components of liking and implicit wanting, only one measure of wanting is reported for conciseness (i.e. implicit wanting). While it can be noted that explicit measures of liking and wanting are often associated, it has been shown that giving the opportunity to rate both explicit liking and wanting minimises the confounding between these two directly reported cognitive processes of pleasure and motivation (Finlayson et al., 2007b). However, using a separate methodology (i.e. the forced-choice task to evaluate implicit wanting while using VAS for liking) prevents from cross-contamination and therefore liking is most likely to dissociate from the implicit component of wanting. Moreover, the implicit wanting task is non-verbal and therefore words cannot be used to mediate the response. The reaction time measure is also used to prevent mediation by slow deliberate cognitive processing.

3.3.1.2 Understanding the measurement of implicit wanting

In the forced-choice task, the participant is required to choose between food pairs as quickly as possible: "Which food do you most want to eat now?". Every food picture from one food category is compared to every other food from the alternative categories over 96 trials. For each food category, the frequency of choice and non-choice, and the reaction time of each trial is recorded. The measure of implicit wanting is calculated by frequency-weighted algorithm (FWA) that accounts for both the speed and frequency of choosing or avoiding a food in each category (see equation in Figure 3-2).

Figure 3-2: Measurement and calculation of implicit wanting with the LFPQ

This figure illustrates the measurement (forced choice task) and calculation (equation) of implicit wanting trough the example of HFSW. The algorithm includes the reaction time from choosing HFSW food (here the muffin) against another category (here LFSW) and the reaction time when avoiding HFSW food. Formula legend: I_A = Implicit wanting for category A; N_{choice} = number of times category A was selected; $N_{non\text{-}choice}$ = number of times category A was not selected; $\bar{t}$ = mean of all reaction times.

Consequently, implicit wanting is a relative measure of motivation for one food category compared to the alternative categories. Therefore, a positive score indicates a more rapid motivation for one category over the other and a negative score indicates the opposite. A zero score indicates that the category is equally preferred to the other categories. Due to reaction times values, there is no fixed min–max value for implicit wanting but a score usually ranges between -100 to 100, and is reported with no unit.

3.3.2 A validated tool in the context of appetite control

A method is meaningful if the constructs measured translate into interpretable behaviour. In terms of eating behaviour traits, the LFPQ has been shown to be sensitive to individual differences in TFEQ Disinhibition (Finlayson et al., 2012), TFEQ Susceptibility to Hunger (French et al., 2014) and Binge Eating (Dalton et al., 2013a). Greater implicit wanting for HFSW has been interpreted as a feature for susceptibility to overeat in women and should be further studied to improve appetite control (Dalton & Finlayson, 2014). Regarding food intake, the LFPQ has been validated against actual food selection and consumption (Griffioen-Roose et al., 2010; Griffioen-Roose et al., 2011) and is associated with food choice and intake in both laboratory and free-living settings (Dalton & Finlayson, 2014; French et al., 2014). Moreover, the LFPQ is also sensitive to macronutrient imbalance (Griffioen-Roose et al., 2011). Griffioen-Roose et al. (2011) showed that after a 14-day diet-induced protein deficit, implicit wanting and intake (but not explicit liking) for savoury high-protein food increased, potentially as a compensatory mechanism to restore protein status. Interestingly, the authors suggest that during macronutrient balance, explicit and implicit reward are similar but during macronutrient imbalance, the implicit processes appear to have a stronger influence on what to eat.

One key feature of the LFPQ is the dissociation of liking and wanting and its sensitivity to hunger manipulation (i.e. fasted vs fed states) which is true of real world liking and wanting. This sensitivity is consistent with sensory-specific satiety (i.e. decrease in the pleasantness of an eaten food more than a non-eaten food (Griffioen-Roose et al., 2010)) and alliesthesia (Cameron et al., 2014). The latter is defined as the influence of the internal physiological state on taste pleasantness (Cabanac & Duclaux, 1973). It has previously been shown that pre to post meal, liking decreases for all the food categories whereas implicit wanting decreases for savoury while increasing for sweet categories (Alkahtani et al., 2016; Carvalho-Ferreira et al., 2019; Finlayson et al., 2008). This thesis replicated this dissociation between liking (Figure 3-3) and wanting (Figure 3-4) across the course of a meal using a sample of 92 women varying in BMI status. Figure 3-3 and Figure 3-4 further illustrate the sensitivity of the LFPQ to the dissociation of liking and wanting relative to the physiological state and also the food category (sweet vs savoury, low-fat vs high-fat).

The LFPQ is a simple and versatile tool that has the advantages of being quick and easy to use in different appetite-related contexts and especially in weight management (e.g. dietary intervention (Buckland et al., 2018), exercise intervention (Beaulieu et al., 2020c), pharmacological intervention (Blundell et al., 2017), bariatric surgery (Redpath et al., 2018). Contrary to most measures of wanting restricted to a single palatable food (e.g. snack (Cameron et al., 2008)), the LFPQ enables the assessment of a variety of foods including low-fat food which is meaningful in terms of weight management. Indeed, increasing low-energy food consumption has been shown to reduce reward and intake for high-energy food and to a lesser extent reward for low-energy food in the satiated state (i.e. fed state) (Buckland et al., 2018). The LFPQ also enables the separation between reward for sweet and savoury. While it is known that sweet taste is an innate reward and can increase the palatability and stimulate food intake (Bellisle, 2015), the relationship between preference for sweet food and obesity is still controversial (Armitage et al., 2021; Lampuré et al., 2016). The role of reward for savoury food in weight management remains to be investigated.

It is important to note that foods used to elicit reward in the LFPQ are not tasted or ingested but only seen, which might not translate direct sensory pleasure but expected pleasure which involves learning. However, both real encounters with the food cue and food photographs have been associated with the elicitation of wanting (Pool et al., 2016).

This is why the selection and validation of an appropriate array of food pictures plays an important role and has raised the need for a standardised protocol to provide meaningful measures comparable between studies. These best practice recommendations to improve data quality and comparison between studies have now been developed by Oustric et al. (2020) and will be discussed in Post Script. Table 3-3 proposes a summary of strengths and limitations of the LFPQ.

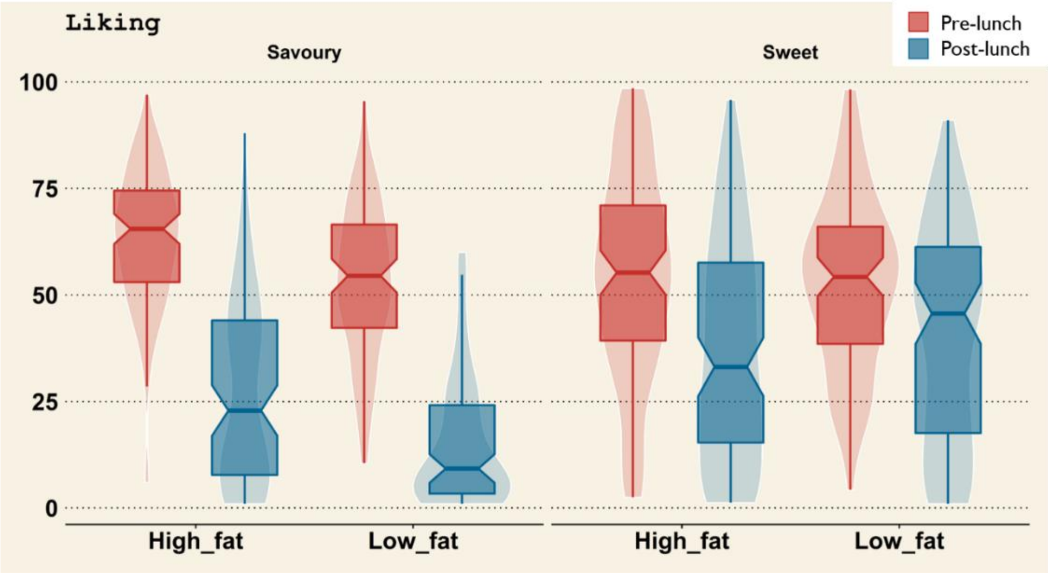

Figure 3-3: Liking for 4 food categories at hungry and fed states

Liking for the 4 categories decreased pre- (red) to post-lunch (blue) in 92 women varying in weight status, see Chapter 9. (Linear mixed models showed an effect of the physiological state on liking $p < .001$)

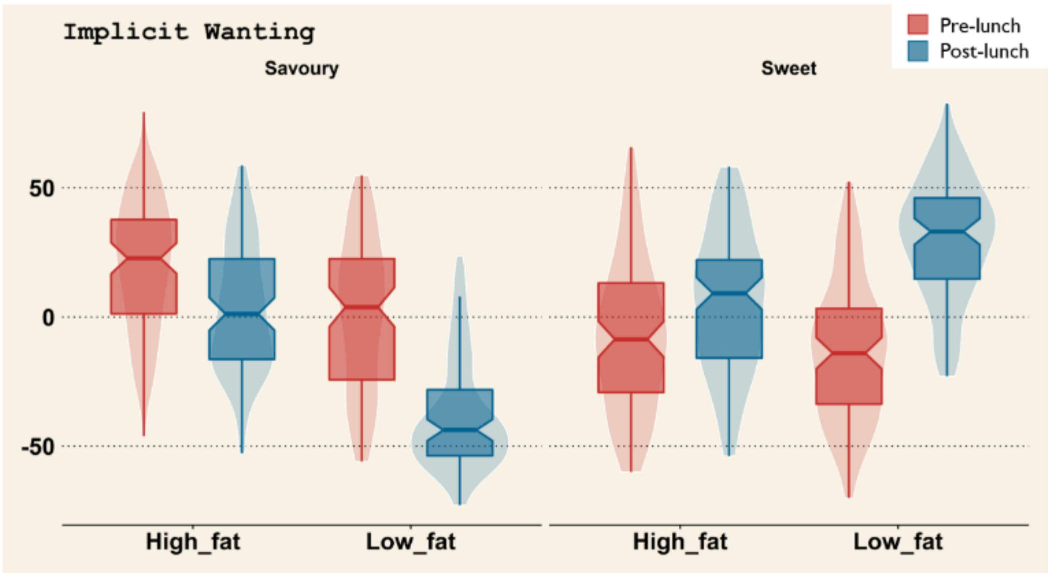

Figure 3-4: Wanting for 4 food categories at hungry and fed states

Wanting for savoury decreased while wanting for sweet increased post-lunch (N = 92). (Paired comparison using Wilcoxon test at hungry and fed state for the 4 food categories. HFSA decreased by a median of -16.62, CI = (-22.81, -10.64), $p < .001$ and LFSW increased by 43.41, CI = (37.16, 49.62), $p < .001$)

Table 3-3 Summary of the strengths and limitations of the LFPQ

	Strengths	Limitations
Tool	- Distinct methods to assess liking (VAS) and implicit wanting (non-linguistic task) to reduce the contamination (Finlayson et al., 2007b) - Measure of implicit wanting using reaction time and frequency of choice and non-choice (Oustric et al., 2020) - Ecological validity of the forced-choice task, as wanting occurs mostly in the presence of choices (Finlayson et al., 2007b) - Simple tool, relatively quick (Oustric et al., 2020) - Versatile, used in different contexts due to the flexibility of the forced-choice task (Oustric et al., 2020) - The FWA takes into account every trial where a food category is present accounting for participants avoiding a food category	- This tool is an operationalisation of a specific framework developed by Berridge (e.g. (Berridge, 2009)); other behavioural methods might be needed to cover different facets underpinning wanting - This tool is currently designed for an adult population and will need to be adapted to children
Food	- Array of foods varying in fat and taste enabling the assessment of low-fat and high-fat, sweet and savoury food - Use of specific food to enable the measure of the direction of liking and wanting as opposed to a non-specific drive to eat (Finlayson et al., 2007b)	- Use of pictures and not real food, which might result in expected pleasure (Pool et al., 2016) - A strong validation of the pictures is a prerequisite to be sensitive to the culture, specific population, and time of day (Oustric et al., 2020)
Validation	- Predictor of food intake, sensitive to physiological state and associated with eating behaviour traits (Dalton et al., 2013c; Finlayson et al., 2012; French et al., 2014; Griffioen-Roose et al., 2010) - Bland-Altman plots showed no pattern in the data, a mean difference between weekly measures approaching zero attesting of the test-retest reliability of the LFPQ (Oustric et al., 2020) - Validated against other tools such as the reinforcing value of food (French et al., 2014), the grip force (Arumäe et al., 2019) and biometric measures (Pedersen et al., 2021) - Translated linguistically in more than 16 languages including Chinese (Zhou et al., 2019) and Arabic (Alkahtani et al., 2016) - Following the protocol by Oustric et al. (2020), adaptable to different times of day (Beaulieu et al., 2020d) and cultures	- Mostly used in the laboratory due to its computerised nature - The clinical threshold of changes in liking and wanting are not known - While the LFPQ has been used with fMRI (Charbonnier et al., 2015; Griffioen-Roose et al., 2014), direct comparisons remain to be performed to establish associations and causality between brain and behavioural reward

3.4 Conclusion

Understanding and measuring food reward has a central role in human appetite research. Liking and wanting components of food reward are key drivers of food choice at a given time in a given context. However, various methods are used to measure components of food reward and often reflect diversity in the definitions of those constructs. Explicit components are the simplest to assess but reporting bias can occur and to fully understand eating behaviour they need to be associated with implicit motivational processes. Techniques have also been developed to assess implicit levels of wanting (and to a lesser extent liking), but cues to elicit the reward vary and are often restricted to a limited range of high-energy foods. In the context of weight management, it is important to distinguish between liking and wanting at implicit and explicit levels but also between different categories of food varying in taste and fat. Moreover, the LFPQ is a versatile tool, sensitive to eating behaviour traits and associated with objectively measured food intake. For all these reasons, the LFPQ has been chosen in this thesis to assess components of food reward. This thesis will provide information about the usefulness of the LFPQ to analyse individual changes during diet-induced WL.

Chapter 4
General Methods

4.1 Ethical considerations

This thesis is based on one main study (Diet-Induced Variability in Appetite; DIVA) involving adult participants for which ethical approval was obtained by the School of Psychology Research Ethics Committee, University of Leeds: for Chapters 5, 6 and 7 (DIVA-1: weight loss, from February 2018 to September 2018): ref PSC-238,10/01/2018; for Chapter 8: amendment to include 1-year follow-up (DIVA-3: follow-up, from May 2019 to 12 December 2019): ref PSC-669,11/04/2019; for Chapter 9 (DIVA-2: control within the normal range of BMI, from February 2019 to October 2019): ref PSC-551 12/12/2018. The general objectives and procedures were explained to all participants before obtaining written consent. Primarily to avoid influencing eating behaviours during the investigation, specific objectives were not fully disclosed until study was completed. At the end of the study, participants were then fully debriefed about the investigation's objectives and given the opportunity to ask questions.

4.2 Recruitment strategy

Recruitment took place in the University of Leeds (Leeds, UK) and surrounding area via poster advertisements and mailing lists. Interested participants were provided with a participant information sheet, including all the study details. They were then invited to complete an online screening questionnaire assessing their eligibility, with questions concerning medical history, anthropometrics, diet and physical activity history, food allergies and intolerances, and food preferences. Specific inclusion and exclusion criteria are detailed below and in the experimental chapters. Inclusion and exclusion criteria common to all experimental studies are the following:

Inclusion Criteria:

- Female participants aged between 18 and 55 years at the time of signing the informed consent.

Exclusion Criteria

- Significant health problems which might jeopardise participant's safety or compliance with the protocol;
- History of eating disorders;
- Medication or supplements known to affect appetite or weight within the past month;
- Pregnant, planning to become pregnant or breastfeeding;
- Food allergies or food intolerances (including a history of anaphylaxis to food);
- Current Smoker or had recently ceased smoking (<6 months);
- Significant changes in body weight in the previous 6 months (±4 kg);
- Exercising >3 days per week or significant changes in physical activity patterns in the past 6 months or intending to change them during the study;
- Working in appetite or feeding-related area or shift workers;
- Low liking or acceptance of the study foods.

4.3 DIVA Study design

DIVA-1 (Chapters 5 to 7) is a randomised controlled trial (RCT) investigating changes in appetite-related variables during controlled weight loss (WL) to ≥5% via intermittent (IER) or continuous (CER) energy restriction in women with overweight/obesity. This thesis focuses on food reward outcomes which was a secondary outcome of DIVA. DIVA-2 (Chapter 9) is a baseline control arm of DIVA-1, with no-WL intervention. Women within the normal range of BMI were invited to complete the same baseline measurements in order to compare food reward and appetite control between women with and without overweight/obesity. DIVA-3 (Chapter 8) is the 1-year no-contact follow-up of DIVA-1 to investigate food reward and appetite control 1-year after the WL intervention.

4.3.1 DIVA-1: Diet-induced WL

The trial is registered at clinicaltrials.gov as NCT03447600 and follows the CONSORT guidelines see Beaulieu et al. (2020b).

4.3.1.1 Participants

Women with overweight or obesity were recruited for a study examining 'The effects of a personalised weight loss meal plan on body composition and metabolism'. Additional inclusion and exclusion criteria to the ones mentioned in section 1.2 included a BMI between 25.0-34.9 kg/m^2 and not currently enrolled in a weight loss programme or following a specific diet plan. Volunteers were remunerated £100 for participating, received free food for all the study and received detailed information about their health after the study.

4.3.1.2 Screening

After an online pre-screening questionnaire assessing general eligibility criteria (including liking for the study foods), participants were invited to the Human Appetite Research Unit (HARU) at the School of Psychology, University of Leeds, UK for a full screening session where anthropometrics were measured, eligibility determined and consent forms signed. Participants were told not to change their physical activity habits during the full study and that the details of their “personalised meal plan” would be known after the baseline measurements.

4.3.1.3 Randomisation & Blinding

DIVA-1 is a parallel-group controlled-feeding randomised controlled trial. Participants were blinded to the existence of 2 arms (advertised as "personalised meal plan") and, upon consent to take part, were randomised (randomization.com) to IER or CER using a 1:1 ratio in blocks of 6 stratified by age (18-36 / 37-55 years) and BMI (25-29.9 / 30-34.9 kg/m^2). Both participants and investigators were blinded to the treatment allocation until the end of the baseline measurements. At this point, the research dietitian informed each participant of their meal plan (i.e. IER or CER), retrieved on a case-by-case basis from an independent co-investigator. To minimise attrition bias, the diet allocation of those withdrawing from the study were re-allocated to new participants (8 pre-diet allocation, 6 after allocation). To reduce ascertainment bias, outcome assessors (i.e. completing data collection) were blinded to the diet allocation until the end of the intervention. At the end of the intervention, participants were informed about the 2 arms of the trial.

4.3.1.4 Procedure

DIVA-1 comprises three days of assessment referred to as “measures days” (in the lab) and three weeks of assessment called “measures weeks” (under free-living conditions) at baseline, week 2 and post-WL (in the final week of the intervention) as shown in Figure 4-1. Measures weeks included daily assessment of body weight with a provided scale (Salter scale model 9206, UK), an online food diary (myfood24), a physical activity monitor (SenseWear Armband) to assess minutes of physical activity and estimate the PAL which was used to personalise meal plans. This thesis does not focus on these measures, and more details can be found in Beaulieu et al. (2020b). Upon completing these free-living measures, participants attended the laboratory for a measures day (for IER this was completed after a fast day in week 2 and in the final week of the diet to ensure that participants were assessed on an *ad libitum* eating day).

All measures days (see Figure 4-1) took place after a 10-12-h overnight fast, and participants were told to refrain from drinking coffee or alcohol and refrain from exercising for 24h before measurements. Fasting appetite sensations and food reward, body composition, and resting metabolic rate (RMR) were assessed. This was followed by a fixed breakfast (25% of RMR measured with indirect calorimetry) and an *ad libitum* lunch 3 hours later to determine appetite sensations (assessed pre- and post-breakfast, every 30 minutes between meals and post-lunch) and food reward (pre- and post-lunch). At the end of the session, participants were provided with paper versions of eating behaviour questionnaires (see section 1.5) to complete at home that evening and bring back at their next meeting with the dietitian.

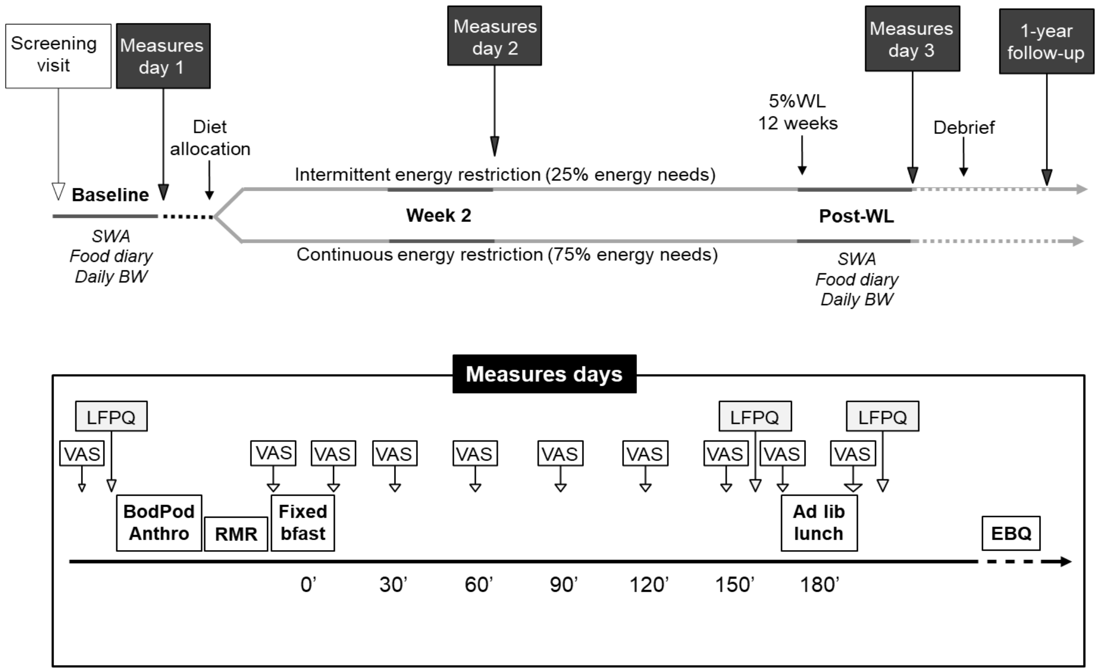

Figure 4-1: Design of DIVA trial

Ad lib lunch: *Ad libitum* lunch Anthro: anthropometrics; Bfast: breakfast; BodPod: air displacement plethysmography measuring body composition; BW: body weight; EBQ: eating behaviour questionnaires; LFPQ: Leeds Food Preference Questionnaire; RMR: resting metabolic rate; SWA, SenseWear Armband; VAS: visual analogue scales for appetite ratings; WL: weight loss.

4.3.1.5 Measurements

This thesis focuses on components of food reward: liking and implicit wanting for food categories (high-fat savoury, low-fat savoury, high-fat sweet and low-fat sweet). Other appetite-related outcomes are reported to contextualise food reward results from a system perspective: anthropometrics (BMI, weight), body composition, RMR, appetite sensations, food intake and eating behaviour traits (see section 1.3.3).

4.3.1.6 Diet Intervention

Following baseline measurements, participants met with the research dietitian to be allocated to a diet and received an explanation of the specifics of their meal plan (IER or CER). After consenting to the terms of their meal plan, a weekly appointment with the dietitian was scheduled for food collection and diet monitoring. Each meal plan was calculated based on energy requirements (measured RMR × physical activity level[2]), personalised based on food preferences, and modified weekly according to participants' feedback. All foods were provided to the participants (only fast days in IER) and were pre-portioned (except for the milk where a measuring cup was also provided) with minimal preparation required and accompanied by daily food checklists. Participants were permitted to consume black coffee/tea or with the milk provided by the researchers and other energy-free beverages, sugar-free gum, and were encouraged to drink plenty of water. Participants were instructed to note on their food checklists whether all foods were consumed, specify how much was left, or whether extra food or drinks were eaten, and the time eaten. Two 'days off' the meal plan per month were allowed.

In CER, participants consumed 75% of their daily energy needs each day (mean energy provided 1515.76 ± 216.38 kcal) from provided commercially available products, estimated to induce a similar WL based on current clinical nutrition practices (British Dietetics Association, 2017). The diet's macronutrient composition was 50-55% carbohydrate, 30-35% fat and 15-20% protein, based on national guidelines (British Nutrition Foundation, 2017). Three main meals and snacks were provided to be consumed without time restrictions or specific number of eating episodes. During the weekly meetings with the dietitian, prescribed food intake was adjusted if WL was not achieved or if it plateaued while being compliant to the diet.

In IER, food was only provided for fast days, and volunteers consumed 25% of their daily energy requirements (mean energy provided 544.69 ± 89.68 kcal) from total diet replacement products (LighterLife Ltd, UK, food supplier). On feed days, volunteers ate *ad libitum* from their own foods. Each product provided a similar energy content (~150 kcal) and macronutrient composition (~36% carbohydrate, ~27% fat and ~37% protein), and ensured a daily protein intake of 49.2 ± 8.2 g. This is in line with the recommended 50 g to 100g of protein by the European guidelines on total diet replacement products for weight management (EFSA NDA Panel, 2015). Similarly, to

[2] Physical activity level: total daily energy expenditure divided by RMR; obtained from the SenseWear Armband

CER, there were no time restrictions to consume the food packs (ranging from 3 to 5 full packs plus an additional bar portion to make up the difference if needed). When requested, participants were also provided milk portions for coffee/tea (and deducted from the daily allocated calories) but were required not to consume any other energetic beverages. During the weekly meetings with the dietitian, food intake on feed days was discussed and general guidance was offered if WL was not achieved while adhering to the diet.

As WL was monitored each week, the dietitian adjusted energy intake if needed. When reaching ~5% WL at a weekly weigh-in, participants underwent a final measures week while continuing the dietary intervention and emailed their fasted body weight (Salter scale model 9206, UK) each day to the research dietitian. Participants were included in the per-protocol analysis (≥5% WL) if self-reported body weight was ≥5% WL on at least 4/7 days leading to the last measures day and objectively confirmed during the final measures day. Those who did not achieve the ≥5% WL criterion were still tested after 12 weeks but were considered completers and not included in the per-protocol analyses.

Figure 4-2: Pre-portioned food given during the diet intervention

On the left, examples of fresh foods given for the CER diet (pre-portioned and minimal cooking preparation). On the right, a weekly serving for the IER diet (diet replacement products (LighterLife Ltd, UK)).

4.3.1.7 Adherence to the intervention

Participants were considered adherent to the meal plans when reported energy intake from the weekly meal plan booklets did not exceed the prescribed energy intake by >75 kcal (Hoddy et al., 2014). If this occurred, that day was considered non-adherent. Weekly adherence (%) was calculated by dividing the number of adherent days by the number of prescribed meal plan days × 100.

4.3.2 DIVA-2: Control within the normal range of BMI for DIVA-1

Women within the normal range of BMI (N = 46, BMI = 18.5-24.9 kg/m^2) were recruited to compare baseline measures of food reward and appetite control with the data collected from women with overweight or obesity in DIVA-1. These women were recruited to be matched in age to the women with overweight/obesity. See Chapter 9 for details.

4.3.3 DIVA-3: 1-year no-contact follow-up of DIVA-1

Participants from DIVA-1, having completed the final measures day and consented to be contacted about future studies (N = 37) were individually invited four weeks prior to the 1-year date to return for a 1-year follow-up (measures day and week). Participants were not aware of the follow-up measures upon initiation of the WL intervention and no contact was made until invitation to participate in the follow-up study visits, therefore participants did not receive recommendations to pursue their diets after the end of the intervention. Participants were re-screened to confirm eligibility. See Chapter 8 for details. The rationale of DIVA-3 was to explore whether the controlled diet intervention will have a sustained effect on appetite variables and food reward, however as there was no contact during the 1-year follow-up, weight regain might be expected.

4.4 Measuring food reward

Food reward is the core outcome of this thesis and Chapter 3 is dedicated to present the details on the methods and measures. In brief, the Leeds Food Preference Questionnaire (LFPQ) (Finlayson et al., 2008) was used in DIVA-1,2 and 3 during each measures day before breakfast and pre- and post-lunch consumption to assess explicit liking and implicit wanting for an array of food images chosen to vary in fat (low, high) and taste (sweet, savoury). To measure explicit liking, the food images were presented individually, in a randomised order and participants were required to rate "*How pleasant* *would it be to taste some of this food now?*" on 100-mm visual analogue scales (VAS). To measure implicit wanting, participants were presented with 96 food pairs and asked to respond as quickly as possible according to "*Which food do you most want to eat now?*" Reaction times for all responses are recorded and used to compute mean response times for each food type after adjusting for frequency of selection and overall mean response time.

4.5 Measuring eating behaviour traits

All eating behaviour traits were assessed at the end of the day (measures day) on pen and paper in the participant's home environment. As explained in Chapter 1, eating behaviour traits are included to give some context to food reward measures during WL (Chapters 6,7,8) and related to BMI status (Chapter 9). The primary analysis focuses on Restraint, Disinhibition and Susceptibility to Hunger (TFEQ), Binge Eating (BES), and Food Cravings (CoEQ), whereas the secondary analysis focuses on Mindful Eating (MEQ), Intuitive Eating (IES), Hedonic Hunger (PFS) and Food Addiction (YFAS).

4.5.1 Three Factor Eating Questionnaire (TFEQ)

The TFEQ developed by Stunkard and Messick (1985) is a widely used and validated 51-item scale assessing three dimensions of eating behaviour: Dietary Restraint (21 items), Disinhibition (16 items) and Susceptibility to Hunger (14 items), see definitions in Chapter 1. In part 1 of the questionnaire (questions 1-36), participants respond true or false to statements. In part 2 (questions 37-51), they choose on a 4-point scale assessing frequency or agreement to an eating behaviour statement. Higher scores indicate greater disturbances in eating behaviour. The TFEQ has demonstrated to have good internal consistency, with Cronbach's alpha ranging from 0.79 to 0.92 in a sample mainly composed of women varying in BMI status (Allison et al., 1992; Stunkard & Messick, 1985).

4.5.2 Binge Eating Scale (BES)

The BES developed by Gormally et al. (1982) is a validated 16-item scale now regarded as measuring the severity of binge eating. More particularly, 8 items describe behavioural manifestations of binge eating and the other 8 relate to the feelings and cognitions associated with binge eating. For each item, participants are required to choose among 3-4 descriptive statements increasing in severity. Scores range from 0 to 46 with higher scores indicated greater binge eating. The BES has been shown to have good internal validity in women, with a Cronbach's alpha of 0.89 (Freitas et al., 2006).

4.5.3 Control of Eating questionnaire (CoEQ)

The CoEQ developed by Hill et al. (1991) and validated by Dalton et al. (2015) is a 21-item scale measuring the severity and types of food cravings over the past 7 days: Craving Control, Craving for Sweet, Craving for Savoury and Positive Mood. Each item is rated on a 100-mm VAS from "not at all" to "extremely", and higher scores mean greater (better) craving control and positive mood and higher cravings for savoury and sweet foods. Concerning internal consistency, the Cronbach's alpha values were 0.88 for Craving Control, 0.74 for Positive Mood, 0.66 for Craving for Savoury and 0.67 for Craving for Sweet in women varying in BMI status (Dalton et al., 2015).

4.5.4 Mindful Eating questionnaire (MEQ)

The MEQ developed by Framson et al. (2009) is a 28-item scale measuring mindful eating based on 5 factors: Awareness (7 items), Distraction (3 items), Disinhibition (8 items), Emotional responses (4 items), External cues (6 items). Each item is rated on a 4-point frequency scale from "rarely/never" to "usually/always". This thesis presents the total (or summary) score of the MEQ computed from the mean of all factors. The internal reliability of the MEQ subscales have been shown to range from 0.64 to 0.83 and was of 0.64 for the summary score in women varying in BMI status (Framson et al., 2009).

4.5.5 Intuitive Eating Scale-2 (IES-2)

The IES developed by Tylka and Kroon Van Diest (2013) is a 23-item scale measuring intuitive eating based on 4 factors: Eating for Physical Rather Than Emotional Reasons, Unconditional Permission to Eat (i.e. individuals' willingness to eat whenever hungry), Reliance on Hunger and Satiety Cues, Body-Food Choice Congruence (i.e. extent to which individuals match their food choices with their bodies' needs). Each item is rated on a 5-point Likert scale from "strongly disagree" to "strongly agree". Similarly to MEQ, this thesis presents the total score based on the average of the items. The internal reliability of the total score has been shown to range from 0.85 to 0.89 in different samples of undergraduate men and women varying in BMI status (Tylka & Kroon Van Diest, 2013).

4.5.6 Power of Food Scale (PFS)

The PFS was developed by Cappelleri et al. (2009) is a 15-item scale measuring hedonic hunger based on 3 factors: Food available, Food present, Food tasted. Each item is rated on a 5-point Likert scale from "I don't agree" to "I strongly agree". The total score calculated from the average of the items is reported in this thesis. The internal reliability of the total score (or aggregate score) has been shown to range from 0.88 to 0.90 in a sample of men and women varying in BMI status (Cappelleri et al., 2009).

4.5.7 Yale Food Addiction Scale (YFAS)

The YFAS, developed by Gearhardt et al. (2009), is a 25-item scale measuring Food Addiction. Items include dichotomous categories (Yes/No) and a 5-point frequency scale from "never" to "four or more times per week or daily". This thesis reports the continuous scale "symptoms count" (0 to 7), which is computed by adding the scores. The internal reliability was 0.75 in a large sample of undergraduate composed of men and women and varying in BMI status with a lesser proportion of individuals with obesity (Gearhardt et al., 2009).

4.6 Measuring appetite sensations (VAS)

Appetite ratings (i.e. hunger, fullness, desire to eat, prospective consumption) were assessed throughout the morning of the measures day (before and after meals, and every 30 min in between meals) via VAS. VAS have been shown to be valid and reproducible in measuring appetite sensations (Flint et al., 2000). More specifically, this thesis uses a validated electronic portable device called Electronic Appetite Rating System (EARS-II) see Figure 4-3 (Gibbons et al., 2011). Each of the following questions were answered on a horizontal line anchored at each end by the words "Not at all" and "Extremely" with ratings ranging from 0-100:

- **How HUNGRY do you feel now?**
- **How FULL do you feel now?**
- How THIRSTY do you feel now?
- **How strong is your DESIRE TO EAT?**
- **How MUCH food could you eat now?**
- How NAUSEOUS do you feel now?
- How IRRITABLE do you feel now?
- How CONTENT do you feel now?
- How TIRED do you feel now?
- How ALERT do you feel now?
- How BLOATED do you feel now?

Only questions on hunger, fullness, desire to eat, and prospective consumption were analysed and the others were used to hide the direct purpose of the study to the participants. Appetite sensations are reported as the area under the curve (AUC) using the trapezoid method (Matthews et al., 1990).

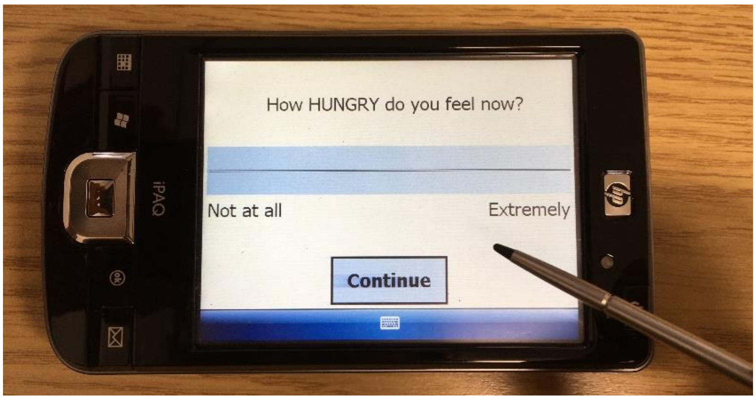

Figure 4-3: Electronic Appetite Rating System assessing appetite sensations

4.7 Measuring food intake

In this thesis, energy intake is assessed using laboratory-based test meals. All test meals were served in separate feeding cubicles free from distractions (participants were alone and not allowed to use their phone or read) within the HARU. All meals were weighed before and after consumption to the nearest 0.1 g, and macronutrient intake was calculated from the manufacturers' food labels. Energy intake was calculated using energy equivalents for protein, fat, and carbohydrate of 4, 9, and 3.75 kcal/g, respectively. Before taking part in the study, liking of the study foods was assessed within the screening questionnaires and participants who strongly dislike any of the study foods were considered not eligible to participate in the study since it could influence their eating behaviours.

4.7.1 Fixed energy test meals

A fixed breakfast was served in each measures day to provide an energy intake corresponding to 25% of measured RMR. Participants were instructed to consume all the food and drink provided within 15 min. This meal was individually calibrated based on RMR as it has been shown to be a strong determinant of daily energy intake (Blundell et al., 2015). The breakfast ingredients consisted of muesli (Holland & Barret), raisins and sultanas (Holland & Barret), honey (Sainsbury's) and whole milk natural yogurt (Yeo Valley). As for the beverage, participant could choose at the beginning of the study between 300 grams of coffee (Nescafe Gold), tea (Yorkshire Tea) or water see Figure 4-4. To take into account individual milk habits in the beverage, 40 grams of semi-skimmed milk (Sainsbury's) could be added either to the drink or to the muesli. The participants were allowed to leave the laboratory in between breakfast and lunch but were not allowed to eat any food or to drink anything except water from the bottle provided.

Figure 4-4: Fixed energy breakfast tailored to 25% of participants' RMR

4.7.2 *Ad libitum* test meals

Three hours after breakfast, participants consumed an *ad libitum* lunch carefully designed to offer two components (sweet and savoury) with the same energy density (~1.5 kcal/g) and water, served in excess of expected consumption. The participants were instructed to eat as much or as little as they wished until comfortably full and were told that more food was available if wanted. The lunch was composed of risotto (Uncle Ben's Tomato & Herb; 1.51 kcal/g), yoghurt (Yeo Valley Strawberry and MyProtein Maltodextrin; 1.48 kcal/g) and 300 g of water (see Figure 4-5 for a photograph of the lunch and Table 4-1 for the composition of the test meal).

Figure 4-5: ***Ad libitum*** **test lunch: tomato & herb risotto and strawberry yoghurt**

Table 4-1 Ingredients and macronutrients composition of the test meal

	g	kcal	CHO	%CHO	PRO	%PRO	FAT	%FAT	ED
Risotto	900	1511.2	282.6		33.5		35.3		
Hot Water	100	0.0	0.0		0.0		0.0		
Total Risotto	**1000**	**1511.2**	**282.6**	**70.1**	**33.5**	**8.9**	**35.3**	**21.0**	**1.51**
Yoghurt	425	403.2	46.3		19.1		17.0		
Maltodextrin	100	375.0	100.0		0.0		0.0		
Total Yoghurt	**525**	**778.2**	**146.3**	**70.5**	**19.1**	**9.8**	**17.0**	**19.7**	**1.48**

CHO: carbohydrate, PRO: protein, ED: energy density

4.8 Measuring physiological outcomes

4.8.1 Anthropometric and body composition

Anthropometric variables and body composition were assessed with participants wearing tight-fitting clothes (swimwear, lycra/compression shorts, sports bra) and a swim cap without shoes, between 7 and 9 am following an overnight fast. Standing height was measured to the nearest 0.1 cm using a stadiometer (Leicester height measure, SECA; UK). Body weight was measured using an electronic balance and recorded to the nearest 0.1 kg. Body mass index (BMI) was determined with the following equation:

$$BMI\ (kg/m^2) = \ body\ mass\ (kg)/height^2\ (m^2)$$

Fat mass, fat-free mass and percentage body fat (%Fat) were estimated to the nearest 0.01 kg using air displacement plethysmography (BodPod, Life Measurement, Inc., Concord, USA;). The BodPod (see Figure 4-6) determines body volume (via measurement of air displacement within a dual chamber) and calculates body density. Measures were performed following the manufacturer's instructions and using the Siri equation (Siri, 1961) adapted for the general population:

$$Body\ density\ (kg/m^3) = \ body\ mass\ (kg)/\ body\ volume\ (m^3)$$

$$Body\ fat\ (\%)\ =\ (4.95\ /\ body\ density - \ 4.5)\ x\ 100$$

The BodPod is an accurate method to measure body composition in both normal weight and individuals with overweight/obesity and is less burdensome than the dual-energy x-ray absorptiometry (DXA) (Lowry & Tomiyama, 2015).

Figure 4-6: Air displacement plethysmography (BodPod)

4.8.2 Resting metabolic rate (RMR)

RMR was measured in the morning following an overnight fast (10-12 hours) with an indirect calorimeter fitted with a ventilated hood see Figure 4-7 (GEM; Nutren Technology Ltd) following the guidelines of The American Dietetic Association (Compher et al., 2006). Participants were required to remain awake while lying down without any movements for 45 minutes. The indirect calorimeter (i.e. gas collection system) used a dilution technique to measure inspired and expired air with a constant airflow in the ventilated hood (see Figure 4-7). An individual calibration, including adjustments in the airflow, was performed before each measurement and room temperature was kept constant (22ºC). VO_2 and VCO_2 were calculated from O_2 and CO_2 concentrations in inspired and expired air diluted in a constant airflow of ~40 L/min (individually adjusted) and averaged over 30-second intervals. The average of the last 30 minutes of collection was used to determine RMR and extreme values (above and below 10% of the mean) were removed.

Figure 4-7: Indirect calorimeter fitted with a ventilated hood

4.8.3 Physical activity level and total energy expenditure

During the free-living measures week, at baseline, participants (individuals with or without overweight/obesity) wore a physical activity monitor (SenseWear Armband; BodyMedia, Inc., Pittsburgh, USA); to measure 7-day physical activity, total energy expenditure and physical activity level. The physical activity level was used in the DIVA-1 study to calculate individualised energy intake for their meal plan. Chapter 9 explored differences in energy expenditure and physical activity between women with or without overweight/obesity to give some context to the food reward measures.

Participants were instructed to wear the SenseWear Armband on their non-dominant arm for at least 23 hours per day (awake and asleep, except for the time around showering, bathing or swimming as the device is not waterproof). The SenseWear Armband estimates energy expenditure and activity using motion (tri-axial accelerometer), galvanic skin response, skin temperature and heat flux. The SenseWear Armband has been shown to accurately estimate energy expenditure at rest and during free-living light and moderate-intensity physical activity (Berntsen et al., 2010; Malavolti et al., 2007), however the algorithm is not accessible.

4.9 Statistical analyses

Statistical analyses are performed using R (R Core Team, 2018), and specific packages are reported in each Chapter. Throughout this thesis, exploratory data visualisation is carefully used as a preliminary step to understand the data better, outline individual variability, inspect for normality and outliers (using densities, boxplot, and individual data points). Data are reported as mean ± standard deviation, with figures reporting mean ± standard error of the mean. If the data are not normally distributed (visual inspection and using the Shapiro-Wilk test), they are reported as the median and interquartile range (IQR). The primary outcomes of this thesis are components of food reward (i.e. implicit wanting and liking for 4 food categories). Moreover, this core outcome is investigated within the context of appetite control (i.e. appetite-related variables) and obesity (group comparisons). Statistical methods (e.g. ANOVA, linear mixed model) are specified in each Chapter depending on the scientific questions and the characteristics of the data and design (e.g. repeated measures with missing data). Statistical significance is established at $p < .05$ unless specified. Power calculation of DIVA-1 was based on changes in energy intake during the test-meal as it was the main outcome registered in https://clinicaltrials.gov/ct2/show/NCT03447600. Therefore, the actual power for changes in food reward components and the cross-sectional analysis was reported and discussed.

Chapter 5

DIVA-1: Changes in pre-lunch food reward during a controlled diet-induced weight loss

Chapter aims:

1. Investigate the effect of diet-induced weight loss (WL) to ≥5% and duration of energy restriction on food reward components.

2. Analyse the effects of modalities of diet-induced WL through continuous or intermittent energy restriction on food reward components.

HIGHLIGHTS

- ► There was no short-term increase (2 weeks of diet) on food reward components.
- ► Liking but not implicit wanting decreased after diet-induced WL (at pre-lunch state).
- ► There was no effect of diet modalities (CER vs IER) on food reward components.
- ► Changes in food reward might occur based on the exposure to the diet (i.e. participation to the dietary intervention) rather than being associated to the %WL per se.

5.1 Introduction

Reward components - liking and wanting - for high-energy foods have been shown to decrease rather than increase in response to WL through dietary, pharmacological, behavioural, and cognitive interventions (Oustric et al., 2018a). This finding opposes the common belief that energy restriction leads to compensatory increases in hedonic responses, an assumption that was often based on results from short-term energy restriction interventions. Indeed, fMRI studies, which are not always comparable to behavioural measures of hedonics, showed that "long-term" caloric restriction, only minimally decreased neural responses to food-cues related to liking but suppressed other brain regions involved in food reward (Kahathuduwa et al., 2016).

Interestingly, in the systematic review conducted by Oustric et al. (2018a), dietary interventions decreased both liking for high- and low-energy foods. However, none of these studies measured implicit wanting. It remains to be elucidated whether dietary interventions may have a different impact on liking and implicit wanting. Indeed, liking and wanting are separate entities that may have independent roles in characterising susceptibility to weight gain (Finlayson et al., 2007b). The inconsistencies in operationalising the separation between liking and wanting might also contribute to the observed discrepancies between studies (Pool et al., 2016). Therefore, measures of food reward should allow the distinction between liking and implicit wanting (Dalton & Finlayson, 2014). For example, a 12-week supervised exercise training study (Beaulieu et al., 2020c) and a single session of high-intensity interval exercise (Miguet et al., 2018) led to a reduction in implicit wanting scores for high-fat food but not liking in adults and adolescents with obesity. However, the effect of dietary interventions on components of food reward remains to be explored.

Further, it is unknown whether different diet modalities (intermittent energy restriction: IER or continuous energy restriction: CER) might differently affect food reward. A compensatory increase in hunger sensations following WL, which may lead to weight regain, has been observed following CER interventions (Melby et al., 2017). It has been postulated that IER may reduce these adaptative responses to energy restriction and possibly attenuate this compensatory increase in the drive to eat (Seimon et al., 2015). However, the effect on food reward remains unknown. Duration of exposure has been hypothesised to have a differential impact on food reward with long-term WL interventions decreasing reward while short-term interventions may increase it (Kahathuduwa et al., 2016; Meule, 2020; Oustric et al., 2018a). A heightened hedonic response to food (liking, wanting) has been associated with overconsumption, binge eating and vulnerability to weight gain (Finlayson & Dalton, 2012b; Finlayson et al., 2007b). Consequently, it could be hypothesised that IER, acting as a repeated short-term severe energy restriction interspersed with unrestricted energy intake, would increase food reward during fast days and lead to overconsumption on feed days, potentially resisting WL, as reported with short-term energy restriction. Indeed, liking, hedonic ratings of food and food intake were shown to increase after a 24-hour total fast (Cameron et al., 2014). As the effect of IER on food reward is unknown an intervention comparing CER and IER would allow to revise the main hypothesis that food reward decreases during WL.

Therefore, the DIVA (Diet-Induced Variability in Appetite) study aimed to address these questions by exploring the effect of 2 types of diet-induced WL (IER and CER) and by making assessments at 2 time-points: "short-term" (after 2 weeks) and "long-term" (after ≥5% WL or 12 weeks, whichever came first), on food reward in women with overweight or obesity. The main aim of this study was to compare responses after a matched WL to ≥5% via an individually prescribed and controlled diet (IER and CER). Consequently, the variability in the degree of WL was minimised by a design that did not intend to compare the interventions' efficacy in terms of WL. An exploratory analysis was performed to examine whether changes in food reward during WL resulted from WL per se or the consequence of the exposure to the diets.

In this study, liking and implicit wanting were studied in a pre-lunch, hungry state. Other nutritional states (fasted overnight, post-lunch) may have different effects on food reward (Cameron et al., 2014). Pre-lunch rewards allowed control over the morning period so that all participants are in the same state. Moreover, pre-lunch rewards have been shown to reflect the motivation and pleasure to eat and, therefore, affect both the quality and the quantity of food eaten (French et al., 2014; Griffioen-Roose et al., 2012; Griffioen-Roose et al., 2011). Therefore, pre-lunch liking and implicit wanting were studied to investigate the potential effect of reward on food intake during diet-induced WL.

Based on the systematic review findings (chapter 2), it was hypothesised that:

1) achieving WL (assessed at ≥5% WL) over 12 weeks would decrease food reward;

2) liking would be more affected than implicit wanting by the diet intervention;

3) food reward would decrease in the long-term but increase in the short-term; and

4) CER would have a greater beneficial effect on food reward compared to IER.

5.2 Method

5.2.1 Diet intervention: DIVA-1

This series of analyses is based on the DIVA-1 study, a controlled diet-induced WL intervention (see Chapter 4 for the detailed study design). Forty-six women with overweight or obesity were allocated to either CER (25% energy restriction each day with all foods provided) or IER (*ad libitum* day alternating with 75% energy restriction day with LighterLife total diet replacement products provided) until ≥5% WL within 12 weeks. All food was prepared, portioned and provided for the CER group and the fast day in IER. Before an *ad libitum* meal (pre-lunch), at baseline, after two weeks and after ≥5% WL, the LFPQ was used to assess explicit liking and implicit wanting components of food reward according to 4 categories of food (high-fat savoury; HFSA, low-fat savoury; LFSA, high-fat sweet; HFSW and low-fat sweet; LFSW).

5.2.2 Statistical analysis

Per-protocol analyses were conducted on the 30 individuals that achieved ≥5% WL (confirmatory analyses were also performed on the 37 completers). The statistical analyses were performed step by step in 3 models to examine each hypothesis (i.e. effect of WL (2 time points), effect of time (3 time points) and effect of diet (2 diets)).

To assess the effect of ≥5% WL on food reward, within-subject ANOVA pre- and post-WL were performed on the 30 individuals. The effect of duration of exposure was assessed by within-subject ANOVA at baseline, after two weeks and after WL. Pairwise comparisons were performed using the Bonferroni correction. The effect of the type of diet (CER vs IER) was analysed with a mixed ANOVA pre- to post-WL. To explore whether changes were due to exposure to diet or %WL, the analysis was also computed on the 37 completers, and descriptive statistics were performed on the seven individuals that did not reach ≥5% WL. Consequently, a repeated measure ANCOVA was performed on the 37 completers using linear mixed models to control for %WL. Time and %WL were entered as fixed effect and participants as a random effect.

When possible, changes in food reward were reported alongside their confidence intervals (CI) and several measures of effect size to help interpret compatibility of findings with the data. Indeed, partial eta squared generalised (η^2_G) are more appropriate for repeated measures than partial eta squared and it is recommended to indicate the possible inflation of the effect (bias representation of the population) by reporting omega (ω) (Fritz et al., 2012; Wasserstein et al., 2019). As there is no specific threshold for food reward, Bakeman (2005) suggests to use Cohen's threshold of .02 as small, one of .13 as medium, and one of .26 as large for interpreting cautiously η^2_G. All the analyses were performed on R (R Core Team, 2018). Linear mixed models were performed with the function lmer from package lme4 (Bates et al., 2015), effect size using DescTools (Signorell, 2019), ANOVAs using function aov and ez package (Lawrence, 2016).

5.3 Results

5.3.1 Main results of the DIVA-1 intervention

Figure 5-1 presents the participant flow chart during the intervention and Table 5-1 gives the baseline characteristics of the 30 women with overweight and obesity who reached ≥5% WL.

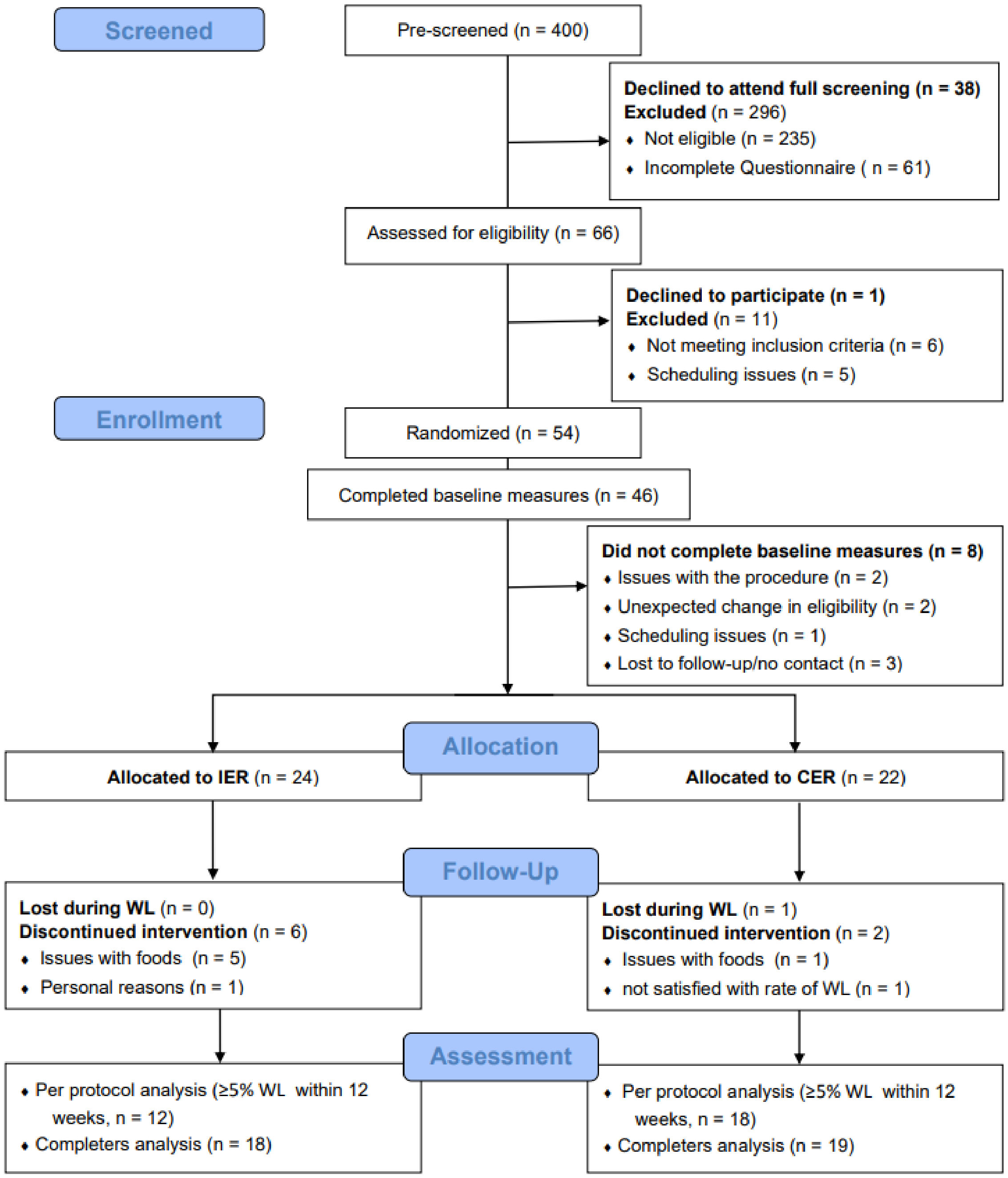

Figure 5-1: Consort flow diagram

CER: continuous energy restriction; IER: intermittent energy restriction; WL: weight loss.

Table 5-1: Baseline characteristics of the 30 women achieving ≥5% WL

	CER	IER	p-value
Per protocol (≥5% WL)	**N = 18**	**N = 12**	
Age (years)	35 ± 9	34 ± 10	0.80
Body mass (kg)	79.2 ± 10.4	81.1 ± 12.2	0.64
Height (cm)	165 ± 7.8	167 ± 9.2	0.58
BMI (kg/m2)	29.1 ± 2.4	29.1 ± 2.5	0.95
Fat mass (kg)	32.5 ± 8.3	34.0 ± 7.2	0.60
Fat-free mass (kg)	46.7 ± 5.5	47.1 ± 6.6	0.85
Body fat (%)	40.6 ± 6.2	41.7 ± 4.1	0.60
RMR (kcal/day)	1456 ± 214	1441 ± 201	0.85

Means ± SD; BMI: body mass index; CER: continuous energy restriction; IER: intermittent energy restriction; RMR: resting metabolic rate; WL: weight loss. P-values are results of independent sample t-test

The attrition rate did not differ between groups (CER: 14% N = 19, compared with IER: 25% N = 18, p = .33), but more completers in CER achieved ≥5% WL within 12 weeks compared with IER (respectively 95%, N = 18 and 67%, N = 12, p = .03).

In terms of WL results and duration of the interventions: 37 women completed the study but did not necessarily achieve ≥5% WL within 12 weeks. Mean WL for the completers was -5.9 ± 1.6% and a range from -8.3% to +0.7%. Thirty participants lost an average of -6.4 ± 0.9% weight, with no difference between diets (CER: 6.3 ± 0.8% in 57 ± 16 days, IER: 6.6 ± 1.1% in 67 ± 13 days) in terms of %WL (p = .43) or days to reach ≥5% WL (p = .10). While there were no significant differences between WL duration, the average final measures day was at day 61 (9 weeks) ranging from day 35 to 93[3] (5 to 12 weeks).

The adherence measured by the weekly meal plan booklets did not differ between groups (CER: 89.0 ± 9.7%, IER: 81.4 ± 14.6%; p = .13). Mean calculated daily energy requirements (RMR * PAL) were 2155 ± 399 kcal for CER and 2196 ± 358 kcal for IER (p = .78). Mean energy prescription was 71.0 ± 4.7% energy requirements for CER (with dietitian adjustments for WL plateauing) and 24.8 ± 0.3% energy requirements for IER on fast days.

Body composition, eating behaviour traits, appetite sensations and food intake results are reported in Chapter 7. Briefly, there was a main effect of time on body composition variables but no difference between diets. Restraint increased, Disinhibition and Susceptibility to Hunger decreased at post-WL. There was an effect of diet only on disinhibition with CER group having a greater decrease than IER. Hunger, desire to eat (measured as the area under the curve in response to the fixed breakfast) decreased at post-WL but no effect on fullness and no change in test meal food intake.

[3] One participant achieved the ≥5% WL at the end of 12 weeks but had a glass of wine before her final measures days which had to be consequently delayed for a week.

5.3.2 Effect of diet-induced WL to ≥5% on food reward

Food reward changes pre- to post-WL at pre-lunch are reported in Table 5-2 along with their effect size. Liking for all food categories decreased pre- to post-WL with small effect size and a large range of individual changes from -56.5mm (LFSW) to +29mm (LFSA) (see mean changes in Table 5-2). Decreases in liking for LFSW were not significant ($F[1,29] = 3.824$, $p = .060$) and the effect size was also small. Using common language effect size (Fritz et al., 2012), the decrease in liking for high-fat food can be interpreted as 60% of the women before WL had a higher liking compared to post-WL.

Implicit wanting changes (no unit) showed high individual variability from -80.4 (HFSA) to +61.7 (LFSA), and the decrease was minimal, with no apparent significant effect of WL. Figure 5-2 illustrates that during a controlled diet-induced WL liking but not implicit wanting decreased and the individual variability was large.

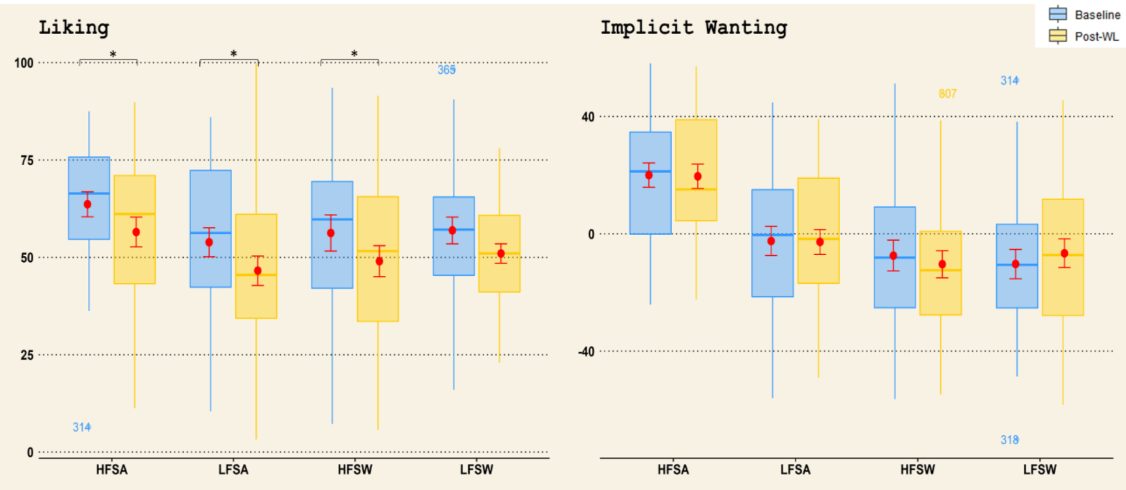

Figure 5-2: Changes in liking and implicit wanting pre- to post-WL (N = 30)

Boxplots represent the variability of changes in liking (mm) and implicit wanting (no unit) during WL at pre-lunch. Means are represented by red points with error bar (SE). *significant changes during WL (*p < .05).

Table 5-2: Food reward pre and post ≥ 5% WL

	N = 30	Baseline	Post-WL	Change	P-value	CI of the difference	η^2_G	ω
Liking	HFSA	63.6 ± 17.6	56.5 ± 21.0	-7.1 ± 15.1	0.015	-1.47 to -12.76	0.034	0.029
	LFSA	53.9 ± 20.4	46.6 ± 20.7	-7.3 ± 14.9	0.012	-1.74 to -12.87	0.032	0.027
	HFSW	56.3 ± 25.4	49.0 ± 21.8	-7.3 ± 17.3	0.029	-0.79 to -13.73	0.024	0.019
	LFSW	56.9 ± 18.7	51.0 ± 13.6	-5.9 ± 16.5	0.06	-0.27 to 12.1	0.032	0.024
Implicit Wanting	HFSA	20.0 ± 22.6	19.6 ± 22.7	-0.4 ± 20.2	0.914	-7.16 to 7.96	8.13e-05	-0.007
	LFSA	-2.4 ± 27.1	-2.7 ± 23.3	-0.3 ± 21.2	0.933	-7.59 to 8.24	4.32e-05	-0.006
	HFSW	-7.4 ± 28.6	-10.3 ± 25.4	-2.9 ± 19.8	0.423	-4.46 to 10.35	0.003	-0.002
	LFSW	-10.3 ± 27.4	-6.6 ± 26.8	3.7 ± 18.2	0.279	-3.13 to 10.48	0.005	0.001

Data are mean ± SD, pre-lunch food reward

5.3.3 Effect of duration of exposure to the diet on food reward

The effect of energy restriction in the short-term (i.e. after 2 weeks/week 3 in the intervention) and longer-term (i.e. post-WL, ≥5% WL to up to 12 weeks) are reported in Table 5-3. There was a main effect of duration of WL for HFSA ($F[2,58] = 3.724$, $p = 0.030$) and LFSA ($F[2,58] = 3.716$, $p = .030$). Pairwise comparisons revealed a decrease from pre- to post-WL for HFSA and LFSA. There was also an increase in implicit wanting for LFSW from week 3 to post-WL ($p = .028$), and the role of wanting for LFSW will be further discussed in Chapters 9 and 10.

Table 5-3: Food reward pre-, during and post-WL

	N = 30	Baseline (1)	Week 3 (2)	Post-WL (3)	P-value	Pairwise comparison
Liking	HFSA	63.6 ± 17.6	63.4 ± 19.7	56.5 ± 21.0	0.030	1-3 (*) p=0.049
	LFSA	53.8 ± 20.4	51.2 ± 22.4	46.6 ± 20.7	0.030	1-3 (*) p=0.021
	HFSW	56.3 ± 25.4	54.7 ± 21.4	49.0 ± 21.7	0.057	
	LFSW	56.9 ± 18.7	54.0 ± 15.5	51.0 ± 13.6	0.129	
Implicit Wanting	HFSA	20.0 ± 22.6	22.9 ± 21.3	19.6 ± 22.7	0.512	
	LFSA	-2.4 ± 27.0	-1.5 ± 22.6	-2.7 ± 23.3	0.928	
	HFSW	-7.3 ± 28.6	-7.6 ± 27.7	-10.3 ± 25.4	0.529	
	LFSW	-10.2 ± 27.4	-13.8 ± 24.1	-6.59 ± 26.8	0.041	2-3 (*) p=0.028

Figure 5-3 showed no short-term increase in food reward from baseline to week 3, and that significant changes in liking seemed to rather occur pre- to post-WL than week 3 to post-WL.

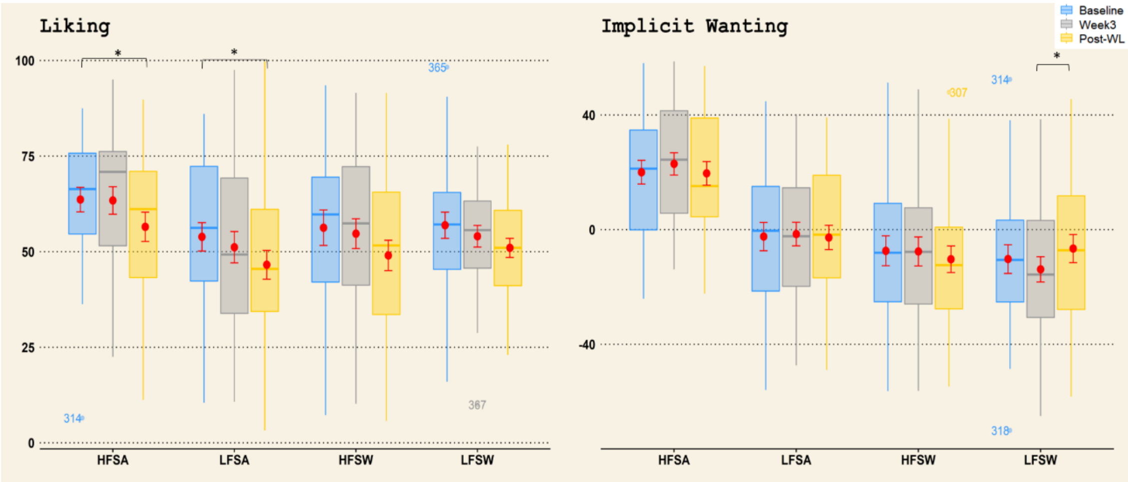

Figure 5-3: Changes in liking and wanting at short- and long-term WL (N = 30)

Boxplots represent the variability of changes in liking and implicit wanting during the short-term (after 2 weeks) and longer-term WL (≥5% WL or 12 weeks) at pre-lunch. Means are represented by red points with error bar (SE). *significant changes during WL (*$p < .05$).

5.3.4 Effect of the type of diet on food reward

For liking, mixed ANOVA between diet and duration of exposure showed an effect of time ($p < .05$, $\eta^2_G > .02$) but no effect of diet ($p > .24$, $\eta^2_G < .04$) and no interaction between diet and time ($p > .39$, $\eta^2_G < .004$). Surprisingly, one post hoc pairwise comparison for LFSA showed a greater decrease in IER than CER ($p = .025$). For implicit wanting, there was no effect of time, diet or interaction between diet and time. See Table 5-4 for liking and implicit wanting values for each food category pre- to post-WL in CER and IER. T-test showed no differences in baseline values between diets.

Table 5-4: Liking and wanting per diet pre- to post-WL

	N = 30	CER Baseline	CER Post-WL	IER Baseline	IER Post-WL
Liking	HFSA	60.0 ± 18.3	53.8 ± 24.5	68.9 ± 15.6	60.6 ± 14.3
	LFSA	51.3 ± 20.8	45.9 ± 24.2	57.7 ± 20.0	47.5 ± 15.2
	HFSW	54.2 ± 21.8	47.7 ± 20.7	59.4 ± 30.7	50.9 ± 24.1
	LFSW	55.0 ± 17.7	50.8 ± 12.5	59.7 ± 20.7	51.3 ± 15.8
Implicit Wanting	HFSA	21.2 ± 24.2	19.8 ± 23.4	18.3 ± 20.8	19.5 ± 22.6
	LFSA	-1.6 ± 27.5	-0.0 ± 25.4	-3.7 ± 27.5	-6.8 ± 19.9
	HFSW	-9.7 ± 27.0	-10.0 ± 23.5	-3.9 ± 31.8	-10.8 ± 29
	LFSW	-9.9 ± 31.5	-9.7 ± 28.9	-10.8 ± 20.9	-1.9 ± 23.7

Figure 5-4 illustrates the effect of CER vs IER on changes in liking HFSW and showed that there seemed to be no specific effect of diet on food reward components.

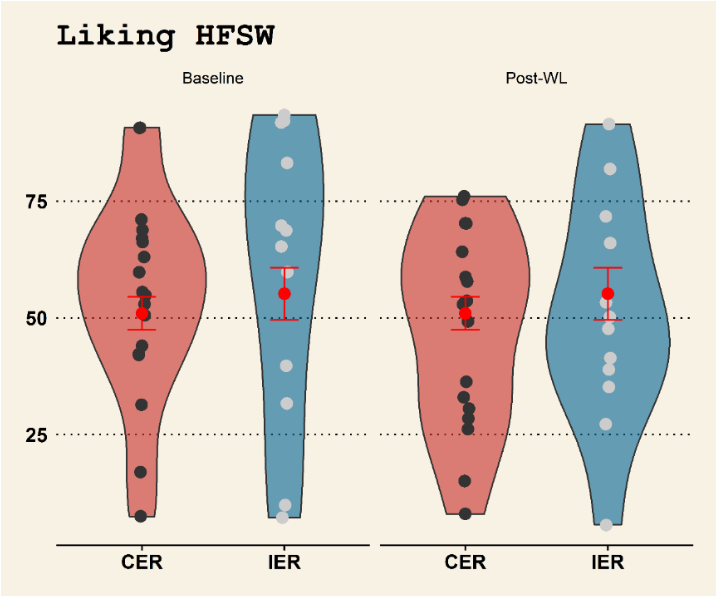

Figure 5-4: Comparison of CER and IER on changes in liking HFSW (N = 30)

Violin plots represent the variability among liking values during WL and show the normality of the data. Points represent the individuals' data (CER and IER). Means are represented by red points with error bar (SE)

5.3.5 Disentangling the effect of WL from exposure to the diet

The following analysis was exploratory and needs to be taken with caution as WL's degree was clamped during the DIVA study. The variability in the results was, therefore, limited due to the design. Consequently, this analysis was preliminary to explore whether changes in food reward during WL resulted from the WL per se or the consequence of exposure to the diets.

Completers analysis (N = 37)

ANOVA pre- to post-WL were performed on the 37 completers. It revealed that liking still decreased but only significantly for HFSA ($p = .011$, $\omega^2 = .033$, $\eta^2_G = .04$) and LFSA ($p = .003$, $\omega^2 = .030$, $\eta^2_G = .03$) food categories. No main effect on implicit wanting was demonstrated ($p > .141$ $\omega^2 < .005$, $\eta^2_G < .008$). The following analysis explored the effect of %WL in HFSA and LFSA changes.

Effect of %WL

Mixed models on the 37 women completing the intervention, using %WL and time as fixed effects, explored food reward changes when controlling for the percentage of WL. Results showed no main effect of the percentage of WL on changes in liking for HFSA (p = .885), but approaching significance for LFSA (p = .052) and the main effect of time remained significant for HFSA and LFSA (p = .011 and p = .003, respectively).

Figure 5-5 illustrates the absence of a significant relationship between %WL and changes in liking HFSA or LFSA. It also confirmed that the range of WL percentage was limited and future research on a wider range of %WL is needed to provide better conclusions.

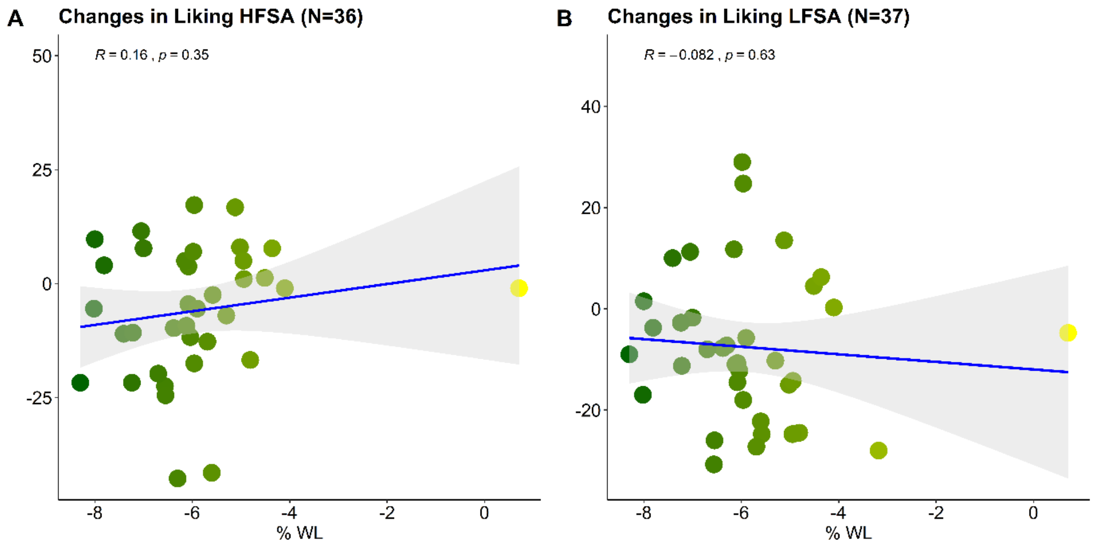

Figure 5-5: Correlations between changes in liking and %WL

The scatter plots represent changes in liking HFSA (A) and LFSA (B) alongside %WL. Individuals were represented by points which colour gradient illustrate %WL. The yellow point represents the individual that increased weight during WL by 0.71%.

Descriptive analysis of the 7 completers who did not reach ≥5% WL

Changes pre- to post-WL for the 7 women that did not reach ≥5% WL are reported in Table 5-5. Increases in liking are highlighted, however, patterns of increase or decrease in liking were not easy to identify. Indeed, one participant might increase liking for one food category but not all. Therefore, it cannot be concluded that on the whole, liking increased more in the 7 women who lost less weight. As there were only 7 participants that did not reach ≥5% WL, they cannot be statistically compared to the 30 that did reach ≥5% WL. In the whole sample, liking decreased for all the food categories, but in the 7 women who lost less weight, the increase in liking for sweet appeared more pronounced.

Table 5-5: Changes in liking during WL for the 7 completers

PPID	Diet	%WL	HFSA	LFSA	HFSW	LFSW
321	CER	-5.0%	8	-15	5.2	1.5
305	IER	-4.8%	-16.7	-24.5	4.5	-1
317	IER	-4.5%	1.2	4.5	-3.2	-4
330	IER	-4.4%	7.7	6.2	38.7	6.5
361	IER	-4.1%	-1	0.2	-1.2	3.5
371	IER	-3.2%	-64.5	-28	-36.5	-33.2
328	IER	0.7%	-1	-4.7	33.75	30.7
mean (N = 7)		-3.6%	-9.5	-8.7	5.9	0.6
mean (N = 30)		-6.4%	-7.1 ± 15.1	-7.3 ± 14.9	-7.3 ± 17.3	-5.9 ± 16.5

Increases in liking are highlighted

5.4 Discussion

This chapter aimed to investigate the effect of diet-induced WL, energy restriction duration, and the type of dietary restriction (CER vs IER) on components of food reward at pre-lunch. This study showed that: 1) as hypothesised, achieving WL (assessed at ≥5% WL) decreased liking but not implicit wanting; 2) a decrease in liking after WL was achieved, but contrary to expectations, there was no increase in the short-term (after two weeks); 3) there was no effect of diet modalities on food reward. Exploratory analysis of the completers seemed to suggest that changes in food reward during WL might not result from the WL per se.

5.4.1 Effect of diet-induced WL on food reward components

This current diet-induced WL study replicated the findings from the systematic review conducted by Oustric et al. (2018a) and reported a decrease in liking for high- and low-energy food following long-term dietary interventions as previously shown (Andriessen et al., 2018; Martin et al., 2011; McVay et al., 2016). This result was in line with other WL studies reporting a decrease in hedonic hunger (measured by Power of Food Scale; PFS), a construct similar to reward, after a 12-week commercial WL program (O'Neil et al., 2012) and a 15-week partial meal replacement intervention (Theim et al., 2013). Both studies showed that the decrease in hedonic hunger was associated with WL and was inversely associated with weight control behaviours. This could suggest that individuals with poorer WL and increased hedonic hunger could benefit from stimulus control (i.e. to help with the high susceptibility to the food environment by removing cues/occasions that can elicit cravings) (O'Neil et al., 2012). Along the same line, recent reviews reported decreased food craving after long-term energy restriction, supporting a deconditioning model (i.e. uncoupling the association between the craved food and the stimuli) (Kahathuduwa et al., 2017; Meule, 2020). Few fMRI studies have investigated the effect of chronic energy restriction on brain activation (Kahathuduwa et al., 2016), but their findings align with the current study. In Jakobsdottir et al. (2016), activation of fasted brain regions associated with reward systems disappeared after 4 weeks of energy restriction and were more in concordance with findings in individuals within the normal range of BMI. In Kahathuduwa et al. (2018), a decrease in food craving was associated with negative modulation of food reward regions and increased executive function after 3 weeks of total meal replacement.

A contradictory review from Hintze et al. (2017) suggested an increase in liking and wanting following WL. However, in terms of liking they report only one longitudinal WL study (8 weeks of caloric deprivation) by Cameron et al. (2008) in which the measure of liking differed from the other studies described in Oustric et al. (2018a). Indeed, in Cameron et al. (2008) liking was measured by the participants' preferred high-energy food. It could be suggested that frequent exposure to these items had already produced a preference for that food (Cameron et al., 2008). Moreover, hunger and desire to eat decreased after the WL, which seemed contradictory to the increase in liking, so interpretations need to be taken with caution. It should be noted that this review (Hintze et al., 2017) reported craving as a measure of wanting, and while both constructs are similar, the implicit drive to eat does not always translate to a food craving. When looking at the studies included in this review, Gilhooly et al. (2007) reported no significant changes in cravings and a decrease in giving in to cravings, and in Jakubowicz et al. (2012) craving increased only in the low-carbohydrate breakfast diet and decreased in the high-carbohydrate breakfast diet. To conclude, there seemed to be less evidence for an increase in reward for high-energy food following WL.

Why did liking decrease and what does it mean? The current analysis did not explore the mechanisms for the decrease in liking during WL, which will be addressed in Chapter 7. Indeed, changes in liking need to be explored in the context of other appetite-related variables to understand the clinical significance of a modest decrease in liking on eating behaviour. One might ask whether the percentage of WL or rate of WL could have affected the changes in food reward. In this study, the percentage of WL was clamped to ≥5%, and there was no difference between diets nor between durations to achieve this WL. A preliminary analysis of the 37 completers suggested that WL's percentage was not associated with changes in liking. Moreover, there were no correlations between rate of WL (defined as % WL/duration of WL in days) and changes in liking during WL (data not reported here). While the mechanisms of changes in food reward during WL remain to be fully explored in a larger sample, it seems that changes in liking are more related to the consequences of the dietary intervention on individuals eating behaviour (i.e. the participation to the diet intervention,) rather than the WL per se. Indeed low-energy and pre-portion food was provided during the whole intervention and could have affected both the effect of the food environment and eating habits on liking.

Several studies support this hypothesis. The Kahathuduwa et al. (2017) meta-analysis reported no associations between reductions of food cravings and WL per se during extended energy restriction interventions. Similarly, Ross et al. (2020) reported a decrease in 3 measures of sensitivity and impulsivity to reward during a 3-month WL which were not associated with weight changes. None of these studies had a control group to assess whether repeated measures or time could be responsible for the changes in food reward. However, they suggest that taking part in diet-induced WL study might lead to changes in reward-related measures via self-monitoring and changes in the food environment. Indeed recent reviews suggested that dietary interventions could change the eating habits through dissociations between stimuli and food consumption and therefore reduce cravings or reward (Kahathuduwa et al., 2017; Meule, 2020).

Finally, food reward is integrated into biopsychological and social mechanisms and cannot be explained by a single model. Neurological, cognitive and physiological models remain to be explored. Neuroimaging studies have shown enhancement of executive inhibitory control during extended energy restriction (Kahathuduwa et al., 2016; Rosenbaum et al., 2008), and behavioural studies have linked the inhibitory system and effortful control to food reward (Higgs et al., 2017; Mackey et al., 2019; Yang et al., 2019b). Consequently, the role of the inhibitory system on food reward during energy restriction remains to be explored.

5.4.2 Effect of short-term energy restriction and diet modalities

As reported in Oustric et al. (2018a), it was hypothesised that short-term energy restriction would increase food reward. Indeed, Kahathuduwa et al. (2017) noted that as the duration of energy restriction increased, cravings decreased and that short-term interventions were associated with increases in craving. Similarly, food deprivation studies ranging from 1 day to 14 days found an increase in cravings for the avoided food (Meule, 2020). However, the current study failed to show an effect of 2 weeks of dietary intervention on liking or implicit wanting. One might ask what is the minimum duration to drive a change in food reward? While 12 weeks is often the standard duration for dietary interventions, 4 weeks has often been used as a cut-off between short-term interventions and those that allow sufficient time to reveal physiological adaptations to the interventions (Beaulieu et al., 2016). Guidelines for clinical practice use 1-year interventions as a minimum to examine "long-term" WL (Jensen et al., 2014). In Oustric et al. (2018a) dietary interventions ranging from 8 weeks to 2 years reported decreased liking, while 4-week interventions (diet or exercise) did not affect food reward. It can be proposed that changes in food reward are not linear with the duration of energy restriction, with the first few days potentially increasing reward, 8 to 12 weeks decreasing reward, while at 3 to 4 weeks no changes may be observed. This could be explained by the fact that the mechanisms of change in food liking such as changes in eating habits take time to occur. Also, there might be a high inter-individual variability (Gibbons et al., 2019) with the time to elicit changes in reward differing between individuals.

Similarly, it was hypothesised that IER would act as a repeated short-term energy restriction and increase food reward as seen after a 24-h fast in Cameron et al. (2014) and in Thivel et al. (2018). Both studies measured food reward with LFPQ before lunch on the day after the fast day, which corresponds to the feed day of the current study. However, no difference between diet modalities was observed for liking or implicit wanting. While this is the first study analysing the effect of CER and IER on food reward, this finding was in line with other studies reporting no differences in appetite sensations after CER or IER and no compensatory mechanisms after IER (Alhamdan et al., 2016; Coutinho et al., 2018). IER has been shown to have better cardiometabolic effects than CER (Antoni et al., 2017) and might prevent fat-free mass loss (Varady, 2011). However, another study failed to show a differential impact of CER and IER on body composition or metabolic profile (Arguin et al., 2012). To conclude, the effect of the type of energy restriction on liking and implicit wanting remains to be clarified and should be investigated using a larger sample size.

5.4.3 Dissociation of liking and implicit wanting

The most important finding from this study was the decrease in liking (albeit modest) but not in implicit wanting after WL to ≥5%. This was consistent with Berridge's theory showing that liking and wanting are underpinned by different neural networks (Berridge & Robinson, 2016). Liking and wanting have been shown to dissociate in some individuals under particular brain conditions (Morales & Berridge, 2020). Interestingly, the incentive sensitisation related to over-eating is characterised by excessive wanting without increased in liking. In the current study, the opposite happened as liking decreased but not wanting, which could be explained by the context of energy restriction. It should also be noted that the individual variability in wanting responses to food was large, and therefore larger sample sizes are required to detect changes (see Chapter 10).

One might also ask the clinical implication of a decrease in liking and not implicit wanting in terms of weight management. Both liking and implicit wanting for high-energy food were associated with excess energy intake both in free-living and laboratory settings

(Dalton & Finlayson, 2014; French et al., 2014). However, implicit wanting has been shown to play a larger role than liking in driving overeating (de Araujo et al., 2019; Mela, 2006) and this can be seen in this study as food intake did not change during WL while liking decreased (cf Chapter 7). The different roles of liking and wanting in weight management could rely on their mode of operation. Liking operates rather during the consummatory phase, whereas wanting is the anticipatory reward or desire to eat that exerts an influence before the initiation of the consumption (Pool et al., 2016).

A recent study (Gong et al., 2020) analysing the neurological underpinning of seeking and consummatory behaviour reported that palatability during consumption could inhibit neurons that will prolong ingestion duration and contribute to hedonic overeating. However, these findings were animal-based, and the link with brain and behavioural liking and implicit wanting remains to be explored in humans. Moreover, liking for high-fat food has been associated with eating behaviour traits associated with loss of control of appetite such as disinhibition (Finlayson et al., 2012; French et al., 2014). A 10-year longitudinal study reported that preferences for sweet food were a predictor of weight gain among Japanese adult women (Matsushita et al., 2009) and preferences for fat have also been associated with fat mass or weight gain in population with obesity (Drewnowski et al., 1985; Mela, 2006; Rissanen et al., 2002; Salbe et al., 2004). A recent cognitive behavioural therapy-induced WL reported normalisation of hedonic but not sensory components of sweet taste in women with obesity compared to lean but did not measure the changes during WL (Nishihara et al., 2019). To conclude, liking also seemed to play a role in weight management and should be explored alongside wanting using behavioural and neurological methods.

5.4.4 Limitations and future perspectives

This study had some limitations that need to be acknowledged. In terms of design, while the CER group was given pre-portioned food for all days, the IER group were provided with food packs for the fast days only. The fact that the nature of the food was different in terms of familiarity, type, energy density (LighterLife ready meal foods vs typical food from the supermarket) and that IER groups had access to their own food on 'feed days' (self-reported intake with myfood24), could have impacted food reward. However, the CER group was provided with the same number of food packs per week to mitigate any exposure effects to these products. The diets were individually monitored weekly in both groups to take into account preferences, and no difference in food reward was detected between CER and IER. Also, measures days were after a fast day, so it was impossible to compare food reward on fast and feed days. Interestingly, daily craving reported on both fast and feed days (Beaulieu et al., 2020a) did not differ between days, so more studies are needed to investigate the effect of fasting on food reward.

Moreover, the design was clamped to 5% WL, reducing the variability in physiological variables and limiting the capacity of the analysis to decipher whether the changes observed were due to the WL per se or the dietary interventions. It should also be acknowledged that the sample size was small. Considering the high apparent variability in food reward changes (especially implicit wanting), larger randomised controlled trials are warranted to confirm the dissociation in liking and wanting and the role of food reward during energy restriction. Also, in this study food reward was investigated at 3-time points during WL it would have been interesting to increase the number of measures days to determine at which points liking begins to decrease, to replicate the short-term increase in food reward. Finally, this study focused on pre-lunch food reward to determine whether food reward relates to immediately following food intake (see Chapter 7). The analysis of changes in food reward in a fasted state before breakfast and post-lunch are reported in Appendix B showing that changes in liking were only significant at pre-lunch.

5.5 Conclusion

This is the first randomised controlled trial analysing the role of liking and implicit wanting during CER and IER to ≥5% WL in women with overweight or obesity. This study was consistent with Oustric et al. (2018)'s findings, showing a decrease in food reward during diet-induced WL and highlighted a new finding, the dissociation between liking and wanting after both dietary interventions. However, the decrease in liking was of small effect size and its clinical significance remains to be further investigated. There was no effect of the type of energy restriction on liking or implicit wanting and no increase in reward after two weeks of diet. Exploratory analyses in the whole sample of completers suggested that the decrease in liking could result from the consequences of dietary intervention rather than the WL per se, as reported in other reviews. It could be suggested that the decrease in liking needs sufficient time to occur due to changes in eating habits and deconditioning associated with diet intervention. The mechanisms of the decrease in liking, such as the role of inhibitory control, remain to be explored. Studies comparing neurological and behavioural measures of food reward are needed to investigate the role of liking and implicit wanting during dietary interventions.

Chapter 6

DIVA-1: Statistical exploration and visualisation of individual changes in pre-lunch food reward during a controlled diet-induced weight loss.

Chapter aims:

1. Develop methods to describe changes in food reward at the individual level taking into account multiple variables of reward and food categories.

2. Summarise and visualise individual changes in food reward during diet-induced WL.

HIGHLIGHTS

► Multivariate analyses and visualisation can give a better understanding of individual variability during WL.

► Changes in implicit wanting were distinguishable from liking, as were responses to sweet versus savoury, but high-fat versus low-fat food categories were not distinguishable.

► Changes in implicit wanting and liking for HFSW accounted for the most variance in a sample of 30 women with overweight or obesity achieving ≥5% WL.

► Three main patterns of dietary-WL-induced changes in food reward were identified: 1) increase in liking; 2) decrease/increase in sweet and opposing change in savoury categories; 3) decrease in liking and implicit wanting.

6.1 Introduction

"There probably isn't one magic bullet for obesity -- if there is a magic bullet, it's going to be different for different groups of people" (Brown University, 2018). Recognising obesity as a complex psychobiological phenomenon means taking into account multiple variables concomitantly but also acknowledging interindividual variability when developing WL strategies. Recently, multidisciplinary platforms (behavioural, cognitive and biological measures) and multi-omics biomarkers have attempted to characterise this individual variability and identified obesity phenotypes that predict WL and may help tailor better weight management strategies in the future (Acosta et al., 2018; Field et al., 2018). For example, phenotyping individuals may result in the development of a blood-based biomarker for tailored pharmaceutical WL or predict for who bariatric surgery may be the most beneficial.

Interindividual variability has also been studied in the field of hedonics and appetite in behavioural WL (e.g. lifestyle WL interventions). Acute exercise studies have shown large interindividual variability in response to exercise. Some individuals characterised as compensators or non-responders, increased their wanting for high-fat sweet (HFSW) which was related to either overconsumption (Finlayson et al., 2009) or less body fat loss (Finlayson et al., 2011). A more recent study (Beaulieu et al., 2020c) showed a decrease in wanting for fat but not liking after exercise-induced-WL with a large interindividual variability in both WL and food reward changes.

However, changes in food reward after diet-induced WL have not been explored statistically at the individual level (i.e. analysis of individual responses instead of taking the sample's average). In Chapter 5 it was shown that liking (e.g. mean change in HFSW = -7.3 mm, $p = .029$) but not implicit wanting decreased after a WL of 6.40%. There was large variability around the mean changes in food reward. However, it remains to be demonstrated whether this variability could be explored at the individual level, simultaneously taking into account the multiple endpoints of the LFPQ. Indeed, to get the full picture of the impact of WL on food reward, it is essential to explore the changes concomitantly instead of choosing one separately from the others.

One way this can be done is by performing a multivariate analysis named Principal Component Analysis (PCA) which aims to summarise and visualise the most important information (i.e. variability) from a dataset. The PCA allows the user to: 1) determine the linear relationship between the LFPQ endpoints and examine coherence with the theoretical structure of the tool; 2) detect the principal dimensions of variability (i.e. select reward variables that characterise most of the variability of the sample); and 3) examine similarities between individuals taking into account all the variables and identify distinct profiles (i.e. patterns of changes in reward) (Cornillon et al., 2012; Husson et al., 2017).

This chapter proposes a novel statistical approach to analyse individual variability in multivariate outcomes of food reward using the LFPQ. As the dataset is limited, the results are intended to illustrate the approach rather than to explain and generalise how people will respond to a controlled diet-induced WL. Therefore, the ability to better summarise individual variability in changes in food reward during WL from a wider dataset may lead to better, more tailored weight management strategies.

6.2 Method

6.2.1 Diet intervention: DIVA-1

This series of analyses is based on the DIVA-1 study, a controlled diet-induced WL intervention (see Chapter 4 for the detailed design). Forty-six women with overweight or obesity were allocated to either a continuous (25% energy restriction each day) or intermittent energy restriction (*ad libitum* day alternating with 75% energy restriction day) until ≥5% WL within 12 weeks. All food was prepared, portioned and provided for the CER group and for the fast day in IER. Before an ad-libitum meal (pre-lunch), at baseline, week 3 and after WL had been achieved, the LFPQ was used to assess explicit liking and implicit wanting components of food reward according to 4 categories of food (high-fat savoury; HFSA, low-fat savoury; LFSA, high-fat sweet; HFSW and low-fat sweet; LFSW).

6.2.2 Statistical analysis

The analyses were conducted on the 30 individuals that achieved ≥5% WL (confirmatory analyses were also performed on the 37 completers). To explore the individual changes in food reward, a PCA and cluster analysis were performed on the changes in 8 variables of food reward from the LFPQ (liking and implicit wanting for the four food categories HFSA, LFSA, HFSW, LFSW) at pre-lunch. Data were standardised to give them equal influence. The hierarchical clustering was performed on the PCA results (HCPC: hierarchical clustering on the principal components). The HCPC used Euclidean distances and Ward's method of partitioning. The multivariate analyses were performed on R (R Core Team, 2018) using the FactoMineR (Lê et al., 2008) and factoextra (Kassambara & Mundt, 2017) packages.

6.3 Results

6.3.1 Defining the need to describe and summarise changes in food reward at the individual level

To explore the effect of diet-induced WL on food reward, the first step was to analyse the changes at the group level. This analysis was performed in the previous chapter and revealed a decrease in liking but not in implicit wanting following ≥5% WL. Figure 6-1 illustrates the interindividual variability in the changes and shows that it is highly dependent on the individual and on the variable considered. For example, the decrease in liking HFSW post-WL can be interpreted as 60% of the women had a lower liking for HFSW after WL. Figure 6-1 depicts that most individuals are decreasing in liking HFSW, but that some individuals are also increasing (individual lines). Therefore, there is a need to investigate changes at the individual level.

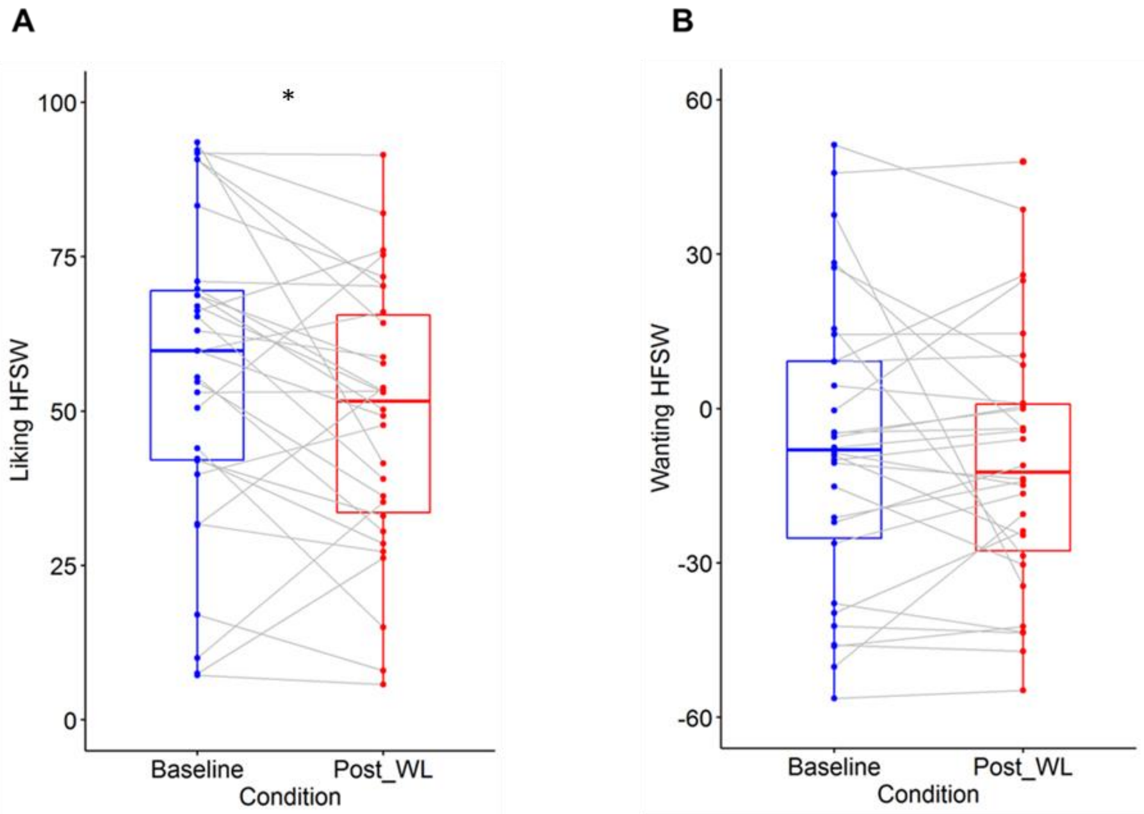

Figure 6-1: Interindividual variability in changes in liking and wanting for HFSW

This figure illustrates the changes in liking (mm) (A) and implicit wanting (no unit) (B) for HFSW at pre-lunch pre- to post-WL. Individual values of food reward are represented by the points, the absolute changes pre to post are pictured by the grey lines and the descriptive statistics by boxplot with median. The figure expresses both the effect of WL on food reward (difference between the boxplot) and the interindividual variability in the changes. Repeated measures ANOVA showed that liking HFSW decreased pre to post WL ($p = .029$, $\eta^2G = .024$) whereas wanting HFSW did not ($p = .423$, $\eta^2G = .003$).

Moreover, changes may depend on the food reward variable. Food reward can be described in terms of liking and implicit wanting but also in terms of taste (sweet vs savoury) and fat (high vs low-fat). The same individual may be decreasing in some variables and increasing in others. For example (see Table 6-1), individual 301 decreased in the four liking variables but increased in two implicit wanting variables. Is this variability meaningful in terms of the structure of the task and in terms of the pattern of response? For these changes to be interpretable, there is a need to statistically summarise the changes in food reward by taking into account all the variables simultaneously.

Consequently, to reduce the complexity of analysing changes of the 8 variables of reward, it is necessary to:

1) understand the relationships between the variables of reward;

2) determine which variable(s) participants varied in the most in order to select the variables that best summarise the sample; and

3) identify potential patterns of response among sub-groups of individuals. This exploratory multivariate approach will develop a method to map the changes in reward across all the endpoints of the LFPQ.

Table 6-1: Individual changes in food reward for the 30 women achieving ≥5% WL

	Pre-lunch							
	Change in liking (mm)				Change in implicit wanting (no unit)			
	HFSA	LFSA	HFSW	LFSW	HFSA	LFSA	HFSW	LFSW
301	-41.50	-22.25	-29.00	-7.75	-7.49	4.28	9.63	-6.42
304	3.75	-14.50	-25.00	-1.50	-3.30	-19.62	3.81	19.11
307	-22.50	-30.75	-0.25	-6.00	-19.04	-0.86	2.15	17.75
308	-2.50	-24.75	-9.00	1.75	17.85	-15.61	4.86	-7.09
312	-11.00	10.00	-52.00	-30.25	11.60	24.11	-3.40	-32.32
314	11.50	11.25	18.75	10.75	4.28	-3.88	15.89	-16.29
315	-17.50	-18.00	-11.50	-15.25	-14.23	21.64	5.98	-13.39
316	-42.75	-7.25	-10.50	0.00	-28.27	-8.24	16.74	19.76
318	-10.75	-11.25	-11.00	-9.75	1.24	-13.79	0.75	11.80
322	-24.50	-26.00	-18.50	-22.00	-1.60	-14.01	7.11	8.51
324	-11.75	-12.25	24.75	11.25	-14.54	-34.00	25.23	23.31
326	-9.75	-7.75	0.25	7.00	-5.11	-5.98	0.16	10.93
327	5.00	11.75	9.75	8.25	-0.33	15.30	-3.12	-11.85
332	-9.25	-11.00	-4.50	-16.25	4.60	-25.03	1.57	18.85
333	-7.00	-10.25	-0.75	0.25	2.47	22.31	-15.19	-9.59
334	7.00	29.00	-26.50	-29.50	40.29	61.68	-72.13	-29.84
335	4.00	-3.75	6.25	10.50	-10.60	4.24	-18.90	25.26
336	7.75	-1.75	-14.00	3.00	11.51	-16.55	-15.55	20.59
338	-21.75	-9.00	-26.25	-28.50	17.36	-27.38	1.25	8.76
339	-12.75	-27.25	-13.75	-7.75	17.54	8.92	-6.31	-20.15
340	17.25	24.75	-9.00	10.00	-1.19	6.66	-1.31	-4.16
362	-5.50	-17.00	-16.50	6.00	6.65	-27.58	-5.51	26.44
363	16.75	13.50	25.25	-4.25	15.31	38.78	-44.05	-10.05
364	-19.75	-8.00	22.25	-2.50	-80.41	21.35	29.57	29.49
365	-21.75	-2.75	-18.50	-56.50	0.99	4.31	3.20	-8.50
366	9.75	1.50	-4.25	15.50	0.89	-5.64	11.02	-6.27
367	1.00	-14.25	-1.50	7.00	11.62	-22.46	-1.21	12.05
368	-4.50	-10.75	8.00	9.75	-6.23	-5.97	4.09	8.10
372	5.00	-24.75	-20.50	-28.00	17.95	6.02	-12.60	-11.37
374	-5.50	-5.75	-10.25	-12.50	-1.90	-2.78	-32.10	36.79
Mean ± SD	-7.12 ± 15.12	-7.31 ± 14.91	-7.26 ± 17.33	-5.91 ± 16.55	-0.4 ± 20.25	-0.33 ± 21.2	-2.95 ± 19.84	3.67 ± 18.23

6.3.2 Determining the relationships between the variables of reward

The first aim of the PCA was to assess the relationship between the endpoints of the LFPQ. The PCA was performed on the changes in food reward pre to post WL presented in Table 6-1 (30 women with overweight and obesity and 8 variables of changes in food reward pre to post WL). Positive changes represent an increase in reward while negative changes represent a decrease. The first step of the PCA consisted of choosing the number of dimensions (i.e. principal components) to examine. This was done by comparing the variability associated with a component using a reference table of the same dimension on the basis of a normal distribution (Husson et al., 2017). The first two dimensions expressed 64.06% of the total dataset inertia (>46.19% = reference). In other words, more than 60% of the total variability is represented by keeping only the first two dimensions, which is enough to understand the structure of the data (Husson et al., 2017). The third dimension represented 14.26% of the total variability and the analysis of the scree plot (percentage of explained variance by dimensions) confirmed that further analyses can be limited to the 2 first dimensions.

The representation of the variables along these 2 principal components (see Figure 6-2) gives a rapid visualisation of the relationship between the variables. Savoury variables were negatively correlated with sweet variables and 4 groups can be distinguished: implicit wanting for sweet, liking for sweet, liking for savoury and implicit wanting for savoury. There was a clear distinction between the taste variables but not between the fat variables (i.e. high-fat was not distinguished from low-fat). More importantly, implicit wanting variables were correlated with each other (dimension 1) but separated from the liking variables (dimension 2).

In other words, the PCA revealed that changes in implicit wanting were distinct from liking as were responses to sweet versus savoury but not high-fat versus low-fat food categories.

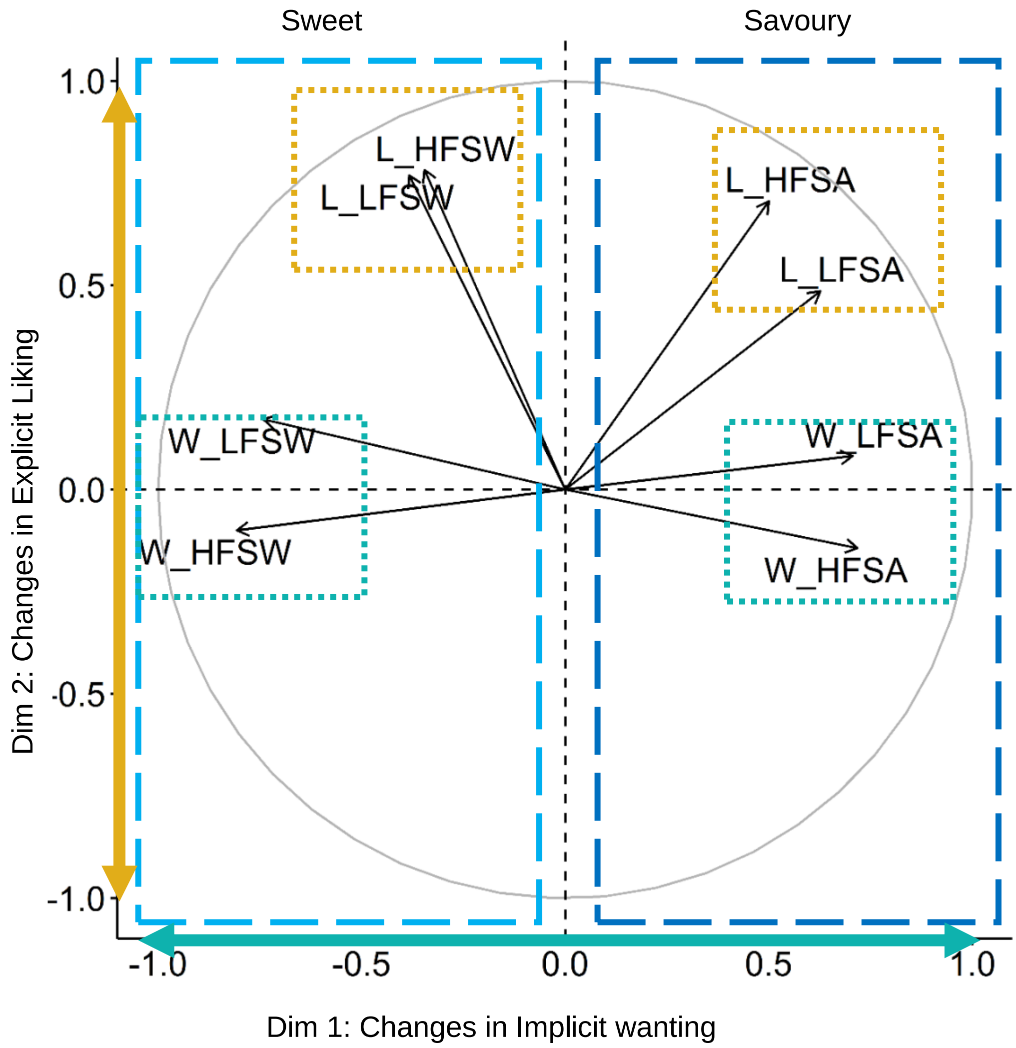

Figure 6-2: Graph of the variables of the PCA

L: Changes in liking, W: changes in implicit wanting, HFSA: high-fat savoury, LFSA: low-fat savoury, HFSW: high-fat sweet, LFSW: low-fat sweet at pre-lunch. This figure represents the cloud of variables from the PCA. The 8 variables of change in reward have been projected in the plan constructed by the 2 first principal components (i.e. best representation of the variability of the changes in food reward pre to post WL). The circle is a correlation circle and allows the visualisation of the linear relationship between the variables. The closer the variables, the stronger the correlation. Dimension 1 is separating savoury from sweet taste and 4 groups of closely related variables can be visualised: wanting for savoury and liking for savoury and both of them are negatively correlated with liking for sweet and wanting for sweet.

6.3.3 Summarising the changes in food reward by detecting the principal dimensions of the variability

The second aim of the PCA was to select the changes in food reward that best characterise the sample. Indeed, the 8 endpoints could be examined separately to understand the effect of WL on food reward (and this has been done in Chapter 5). However, in order to build a model to explain the changes in food reward (see Chapter 7), performing 8 models is meaningful only if the variables are independent from each other. Therefore, the PCA provides the possibility of summarising among the 8 changes in reward those that are statistically relevant to explore. The variability of the 8 endpoints of the LFPQ is summarised by using the first 2 principal components which express 64.06% of the total variability. The first principal component summarises 39.03% of the total variability and the second 25.04%. In other words, from these 2 synthetic variables, it is possible to summarise the most important information provided by the 8 variables.

Figure 6-3 illustrates the correlation between the variables and the principal components to facilitate their interpretation. Principal component 1 concerns changes in savoury and sweet variables. This can be seen in Figure 6-3 with sweet and savoury variables being negatively correlated with each other. Implicit wanting variables are strongly correlated (r > .7) with principal component 1, therefore this dimension can be summarised and labelled as "change in implicit wanting". Principal component 2 is mainly correlated with all the variables of liking (r > .7) with the exception of LFSA (r = .5) and can be labelled as "change in liking".

All the variables correlated with dimension 1 show intercorrelations (e.g. wanting for HFSA and LFSA), and the same applies for variables correlated with dimension 2. The two dimensions were independent from each other. To summarise the changes in food reward, it is relevant to select the single variables that were the most correlated with dimension 1 and 2 as exemplars of the most important sources of variability in the data. Therefore, changes in implicit wanting and liking for HFSW were best able to summarise the sample.

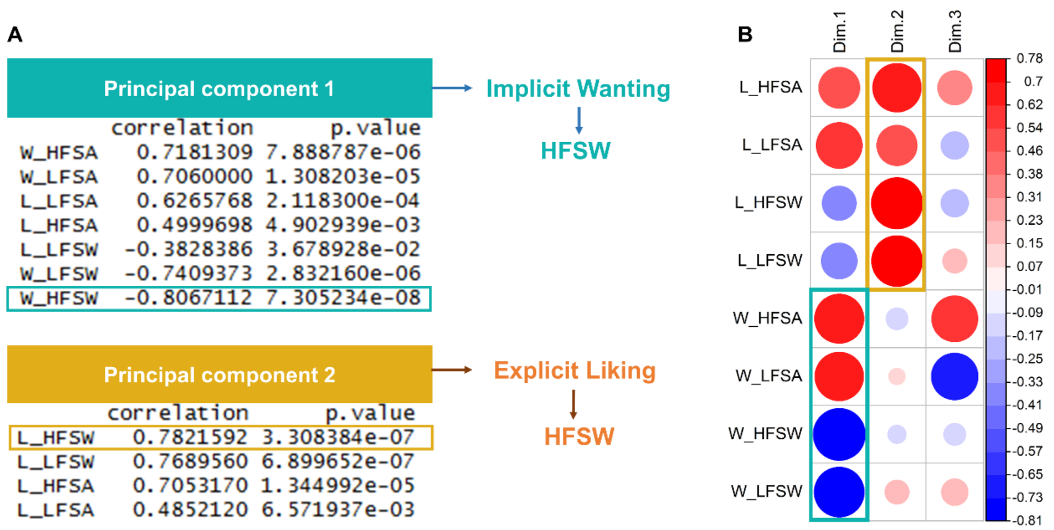

Figure 6-3: Correlation between variables and principal components

This figure illustrates the linear relationship between the principal components and the 8 reward variables at pre-lunch. (A) gives the correlations (Pearson's r and p-value) between principal components and variables and (B) summarises the same results visually to better understand the contrast between the variables. The bigger the circle, the stronger the correlation. Red scale representing positive correlations and blue scale negatives one.

Finally, it is important to check whether the chosen variables have a good quality of representation on the principal components. Indeed, only variables that are well represented in the PCA plan can be statistically interpreted. The cos2 (squared cosine) is used as a measure of the quality of representation as shown in Figure 6-4. To conclude, changes in liking variables are well represented, followed by changes in implicit wanting variables. The least representative of the variability is change in implicit wanting for LFSA. Both changes in liking and implicit wanting for HFSW have sufficient quality to represent the PCA dimensions and therefore, can be used for scientific interpretation. These 2 variables will be used in models in Chapter 7 to try to understand the changes in food reward following a controlled diet-induced WL.

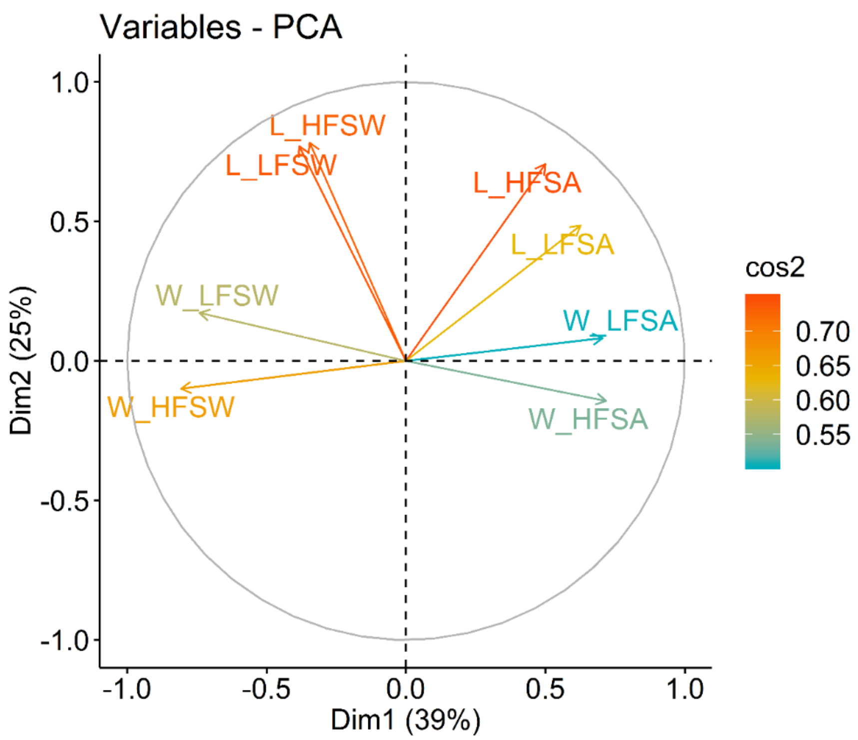

Figure 6-4: Quality of representation of the variables on the principal components

This figure illustrates the quality of representation of each variable on the dimensions of the PCA. The higher the cos2, the better the quality of representation of the variables. This can be seen also with the length of the arrow, the closer to the circle of correlations, the better the representation of the variable and the more important it is to interpret the variable.

6.3.4 Identifying distinct patterns of change in food reward in the sample

Finally, the PCA allows the identification of similarities between individuals and to characterise them according to all the variables. Indeed, the last challenge is to summarise the effect of diet-induced WL on all the food reward endpoints concomitantly. After having shown the individual responses for specific food reward, this analysis aims to summarise and map, for each individual their global response to WL while taking into account all the food categories. Figure 6-5 illustrates the relationship between the 30 women with overweight or obesity and the 8 endpoints on the LFPQ. The colour of the individual data points indicates the quality of their representation on the PCA plan.

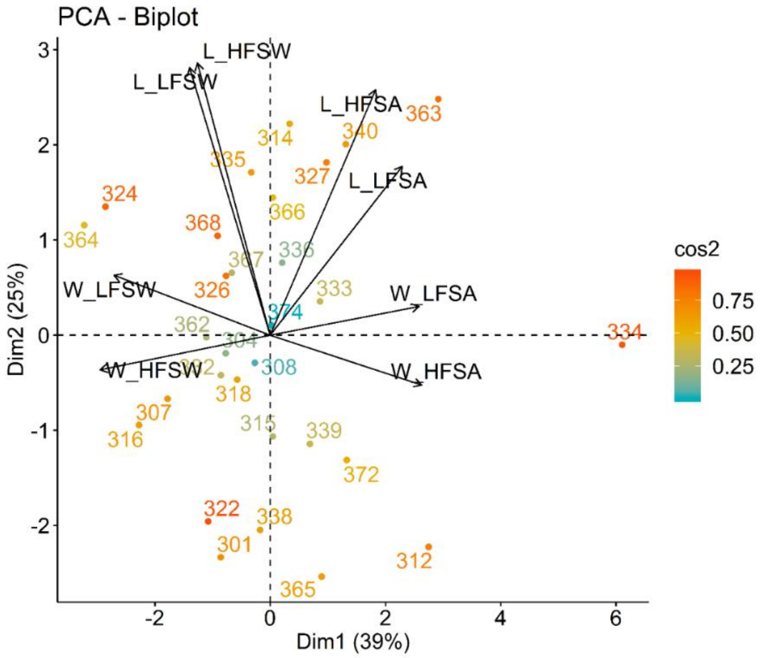

Figure 6-5: PCA Biplot representing both individuals and variables

This biplot illustrates the relationship between the individuals and the 8 changes in reward at pre-lunch. Individuals are represented on the same side as their corresponding variables with high values, and opposite their corresponding variables with low values. Individuals with high cos2 are well represented in the plan which means they are useful for the interpretation. As an example, participants 364, 324 and 316 can be characterised by an increase in reward for sweet and a decrease in reward for savoury and this is in contrast to participant 334.

Depending on their position on the plot, individuals were mostly characterised by an increase and/or decrease in savoury vs sweet. This analysis allows individuals to be classified according to their most typical changes in reward while taking into account all the other variables. This also shows the interindividual variability of this controlled diet-induced-WL on reward.

To identify whether individuals can be characterised by specific patterns of changes in reward, such as a main decrease in all the reward variables, a hierarchical clustering was performed on the PCA results (i.e. HCPC). The HCPC determines groups of individuals which are interpretable alongside the variables and could help summarise changes in reward. The shape of the dendrogram and the analysis of the inertia gain suggested partitioning the tree in 5 clusters. The description of each cluster is specified in Table 6-2 and allows the interpretation of the clusters in terms of patterns of change in reward.

Cluster 1 is mainly characterised by a decrease in reward for savoury with a mean decrease of implicit wanting HFSA of -35.56 compared to a decrease of -0.40 in the overall sample. Overall, Cluster 1 characterises individuals decreasing their reward (i.e. both liking and implicit wanting) for savoury while increasing reward for sweet. Cluster 2 presents the same characteristics; decrease for savoury and increase for sweet but only for reward for low-fat food. Cluster 5 has the opposite pattern and is described by a decrease in sweet reward and an increase in savoury but mainly driven by a mean decrease in implicit wanting for HFSW of -72.13 compared to -2.94 in the overall sample. Cluster 4 is characterised by an increase in all the liking variables driven by a mean increase in liking for HFSA of 8.18mm compared to an overall decrease of -7.12mm. On the contrary, cluster 3 is characterised by a decrease in both liking and wanting variables and driven by a mean decrease in liking for sweet greater than -23.75mm compared to decrease from -5.90mm in the overall sample.

To sum up, 3 main patterns of WL-induced changes in food reward can be identified from the 5 clusters: 1) increase in liking; 2) decrease in sweet and increase in savoury categories and vice versa; and 3) decrease in liking and implicit wanting.

It is also interesting to look at the overall mean results and report that all the liking variables are decreasing as reported in the ANOVA and variables of wanting are also decreasing except for wanting for LFSW which is increasing. The role of wanting for LFSW in appetite control will be further explored in Chapter 9 and 10.

Figure 6-6 offers a visual summary of the cluster interpretation by juxtaposing the clusters of individuals with the corresponding variables needed to explain them.

Table 6-2: Description of each cluster by the food reward variables

	Variables	V.test	Mean in category	Overall mean	SD in category	Overall SD	P-value
Cluster 1	W_HFSW	2.31	18.42	-2.95	10.47	19.51	0.02
	W_LFSW	2.23	22.58	3.67	4.46	17.92	0.03
	L_HFSW	2.02	9.06	-7.26	14.91	17.04	0.04
	L_HFSA	-2.43	-24.19	-7.12	11.42	14.86	0.02
	W_HFSA	-3.73	-35.56	-0.40	26.36	19.91	0.00
Cluster 2	W_LFSW	2.57	15.76	3.67	11.11	17.92	0.01
	W_LFSA	-2.78	-15.54	-0.33	8.06	20.85	0.01
Cluster 3	W_LFSW	-2.36	-9.36	3.67	12.85	17.92	0.02
	L_HFSA	-2.43	-18.22	-7.12	12.39	14.86	0.02
	L_HFSW	-3.14	-23.75	-7.26	11.98	17.04	0.00
	L_LFSW	-3.71	-24.50	-5.91	14.74	16.27	0.00
Cluster 4	L_HFSA	3.06	8.18	-7.12	7.81	14.86	0.00
	L_LFSA	2.89	6.96	-7.31	10.96	14.66	0.00
	L_HFSW	2.41	6.57	-7.26	11.47	17.04	0.02
	L_LFSW	2.41	7.29	-5.91	6.33	16.27	0.02
Cluster 5	W_LFSA	2.97	61.68	-0.33	0.00	20.85	0.00
	L_LFSA	2.48	29.00	-7.31	0.00	14.66	0.01
	W_HFSA	2.04	40.29	-0.40	0.00	19.91	0.04
	W_HFSW	-3.55	-72.13	-2.95	0.00	19.51	0.00

W_HFSW Increase in reward W_HFSW Decrease in reward

Table 6-2 shows the food reward pattern from each cluster at pre-lunch. The v.test allows a description of the cluster according to the variables by comparing the mean in the category with the overall mean. If the test is positive, the variable has a greater mean in this category compared to the overall mean (and vice versa if the test is negative). For example, cluster 4 is characterised mainly by an increase in liking for HFSA.

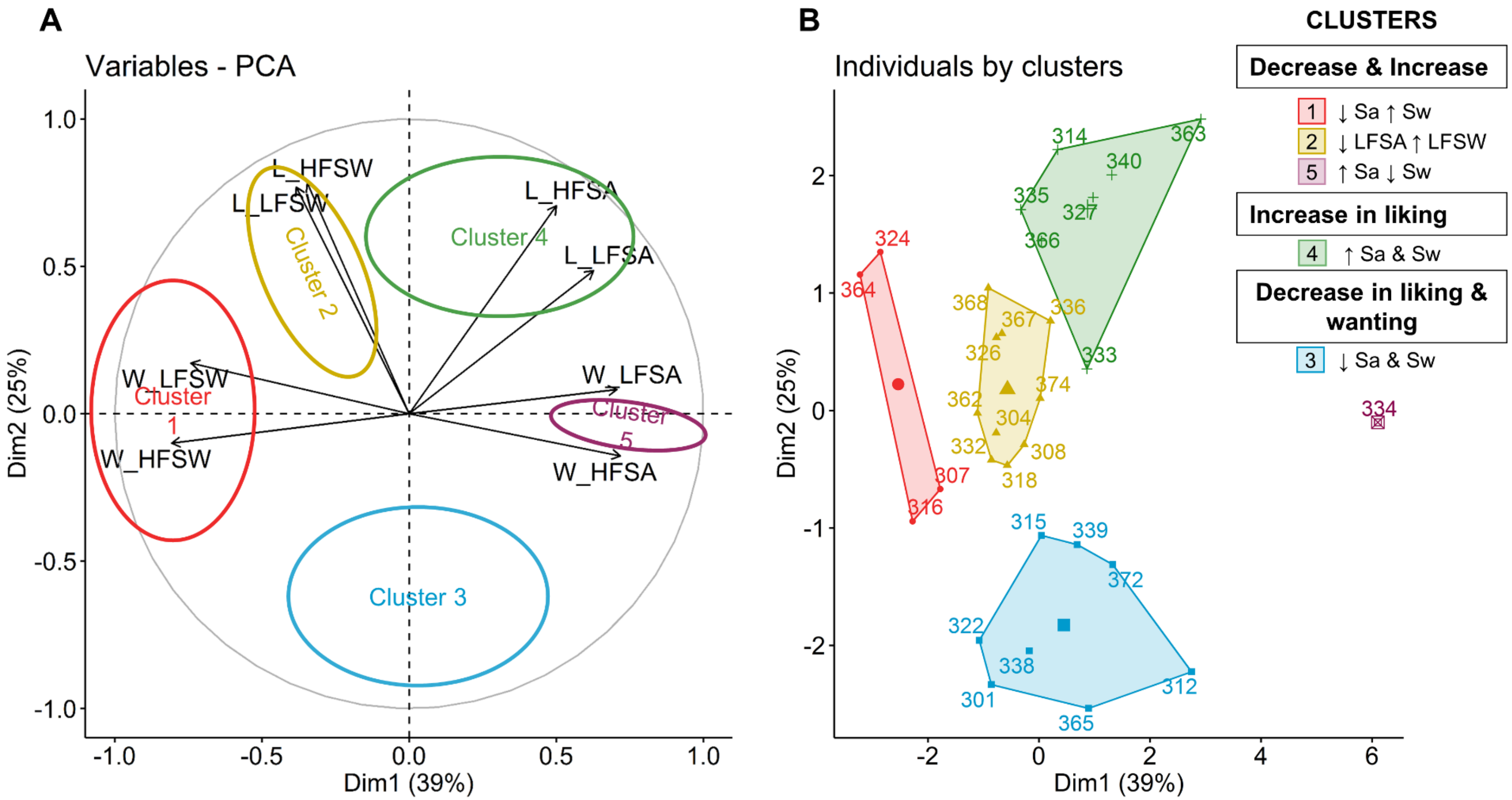

Figure 6-6: Summary of patterns of changes in food reward: (A) variables characterising the cluster, (B) individuals by clusters

This figure proposes a visual interpretation of the clusters of individuals according to the main changes in food reward at pre-lunch. Each cluster on the graph (B) is characterised by its corresponding variables on the graph (A). For a quicker interpretation, clusters (B) have been superimposed on the graph of variables (A). For example, cluster 3 is the only cluster with no corresponding variables, this means that this cluster is driven by a decrease in all the endpoints of the LFPQ.

6.3.5 Can we explain the patterns of changes in food reward?

Among the 5 clusters, 3 main patterns of changes in food reward were identified to interpret the effect of diet-induced WL on food reward categories. As the sample size was limited, it is not appropriate to interpret the clusters as "phenotypes" nor to generalise the findings. However, they illustrate a method to identify potential patterns of changes in food reward for this and other samples. It remains to be understood why some groups of individuals increase their food reward while others decrease. Especially one of these patterns (cluster 3) was characterised by a decrease in all food reward variables, which may have positive implications for weight maintenance after WL. Therefore, it is worth trying to predict which baseline characteristics may differentiate this cluster from the others. The following analysis illustrates how PCA/clustering analysis approach can be implemented in future trials to interpret patterns of changes and explain variability.

To interpret these clusters, potential baseline variables (anthropometric, psychological and physiological) were plotted as supplementary variables on the PCA to analyse the relationship between the changes in reward and baseline characteristics. This complementary analysis is displayed in Figure 6-7. For any correlation to be interpreted, the supplementary variables need to be well represented (i.e. by a long arrow close to the correlation circle) (Husson et al., 2017). Baseline characteristics such as craving, eating behaviour traits or physiological factors were not well represented enough in the PCA plan for the correlations to be interpreted. Therefore, the clusters cannot be explained by these baseline characteristics. However, baseline liking for sweet (represented in Figure 6-7) was quite well represented in the plan and juxtaposed with cluster 3. These findings could carefully suggest that people with higher preference for sweet are those that decrease their reward the most after a controlled dietary intervention resulting in 5% WL.

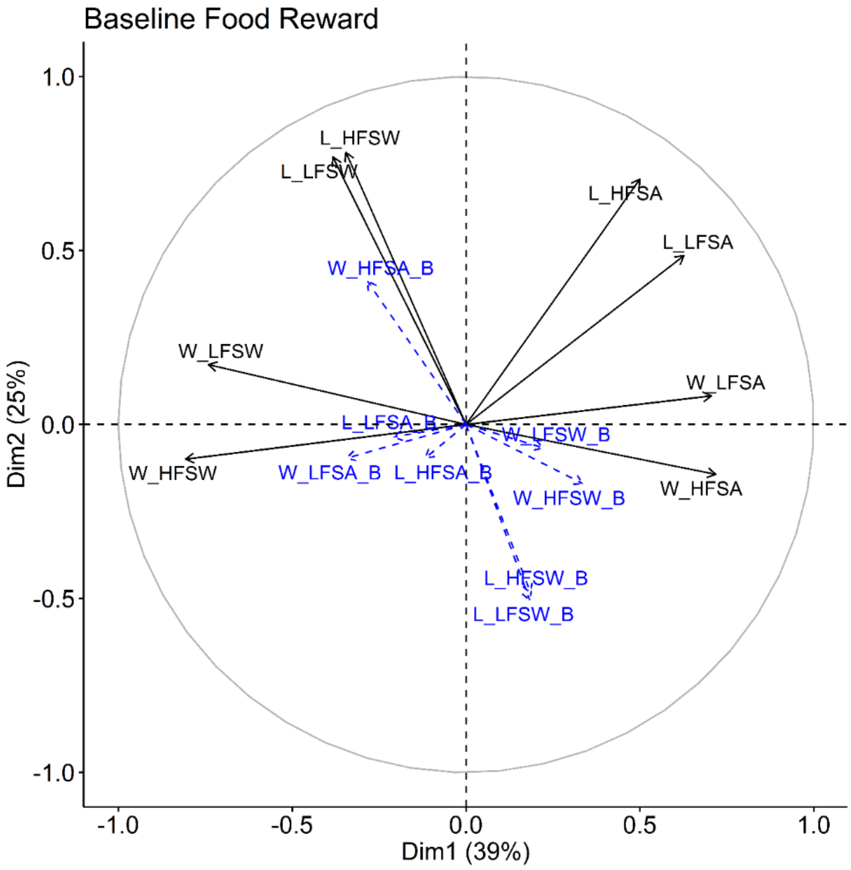

Figure 6-7: Correlation between baseline food reward with changes in food reward

PCA with baseline food reward at pre-lunch as supplementary quantitative variables (in blue). Only supplementary variables that are well represented in the plan can be interpreted. A well represented variable is characterised by a longer arrow towards the circle, which means that they can be explained by the principal components. In this graph, only baseline liking for HFSW and LFSW are quite well represented (approaching r = .5) and pointing in the same direction as cluster 3 (decrease in all reward). This can be interpreted as individuals with higher liking for sweet decreased the most their reward during this diet-induced WL.

6.3.6 Can we explain changes in food reward in individuals who did not reach 5% WL?

Lastly, to reflect on the research question from Chapter 5 on the effect of WL per se on food reward changes, it is interesting to analyse the pattern of changes in food reward of the 7 individuals who did not reach 5% WL. Indeed, in Chapter 5, the analysis of the changes in reward for the separate variables (see Table 5-5) did not succeed in detecting any pattern as each individual was increasing in some variables but not in others. A PCA could solve this problem by summarising the main changes in reward for each individual.

This led to an examination of whether the PCA analysis remains similar when adding the 7 individuals that did not reach 5% WL. Figure 6-8 answers this question and showed that the pattern of changes in food reward stayed similar when adding those 7 individuals.

This reinforced the stability of the findings from the PCA and confirmed the findings from Chapter 5 that percentage of WL per se may not drive the change in food reward.

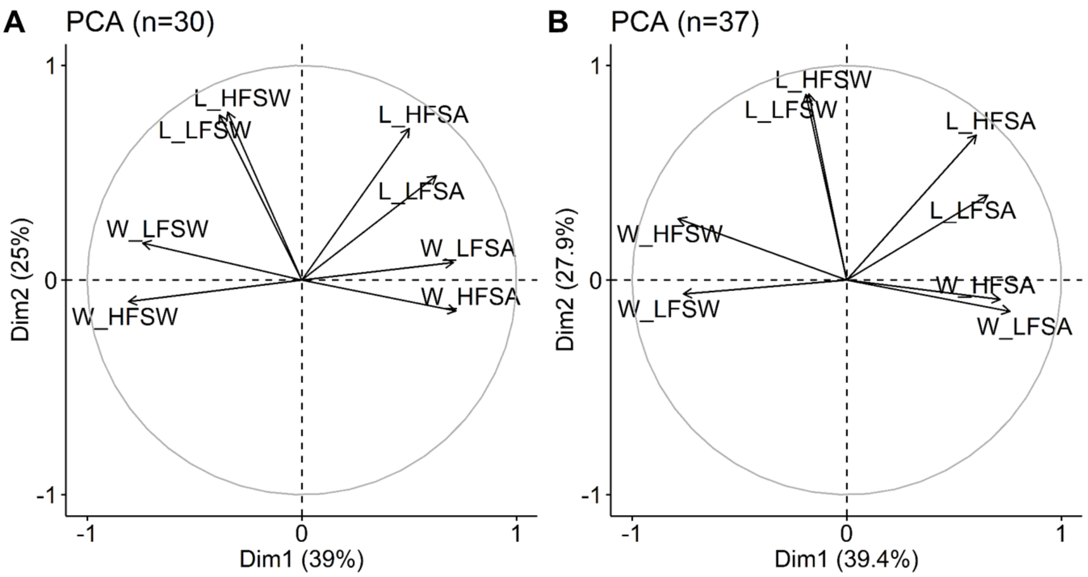

Figure 6-8: Comparison between the PCA on the 30 individuals achieving 5% WL (A) and the 37 completers (B)

This figure compares the PCA with the 30 individuals that reached 5% WL (A) and the PCA with the 37 completers (B). The relationship between the variables at pre-lunch is similar and not affected by the addition of the 7 individuals that did not reach the 5% WL.

A further question was to summarise the main changes in reward for these 7 individuals to establish whether they are mainly increasing or decreasing in reward. This is pictured in Figure 6-9. It seems that the 7 individuals are mainly increasing reward (located in the upper part of the graph) either in sweet or savoury with the exception of one individual that is mostly decreasing. However, these 7 individuals do not seem to separate clearly from the 30 individuals that reached ≥5% WL. A larger sample size would be needed to draw a conclusion on the food reward pattern of the individuals that did not reach 5% WL.

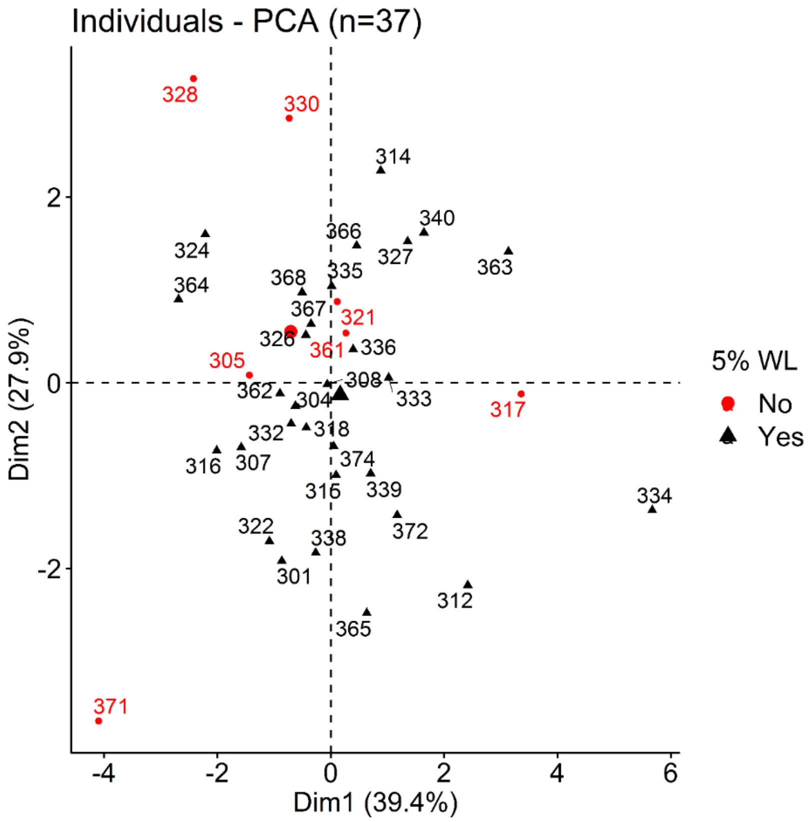

Figure 6-9: PCA with the addition of the 7 individuals that did not reach 5% WL

This graph represents the individuals that reached ≥5% WL (black) and those who did not (red) in the PCA plan. As the principal components are really similar to the PCA with the 30 ≥5% WL individuals, the same interpretation applies. The individuals in red seem not to separate clearly from the others, 371 has mainly a decrease in all reward, while 328 and 330 are increasing in reward for sweet and 317 increasing in reward for savoury. The PCA does not allow conclusions about specific food reward patterns to be made for these 7 individuals.

6.4 Discussion

This novel, exploratory, multivariate approach provides a visual mapping of the changes in pre-lunch food reward during a controlled diet-induced WL intervention at the individual level. Through studying individual variability in food reward during this study, it was revealed that: 1) individual responses were distinguished according to liking and implicit wanting subcomponents of food reward and sweet or savoury categories of food, but not low-fat versus high-fat; 2) among the 8 variables of reward, changes in implicit wanting and liking for HFSW were the best for summarising the changes in food reward; and 3) three distinct patterns of dietary-WL-induced changes in food reward were identified among the individual changes, increase in liking, opposing changes in sweet and savoury, and decrease in liking and implicit wanting.

This chapter developed a novel approach to analysing complex LFPQ datasets at the individual level. However, the results discussed serve to illustrate the methods for future research rather than to propose an explanation valid for the population. The exploratory nature of the analyses and the limited sample size do not allow an extrapolation of the results beyond the current dataset.

6.4.1 Relationship between food reward variable and validity of the LFPQ task

The analysis of the relationship between the 8 variables of reward is the first proof of the statistical validity of the constructs of the LFPQ. Indeed, the LFPQ is based on the theoretical distinction between liking and implicit wanting that is grounded in neurobiological work (Berridge et al., 2009; Berthoud et al., 2017). Liking and implicit wanting have indeed different neurochemical substrates in the brain and one can be expressed without the other (Berridge, 2009). To study the behavioural expression of these constructs, the LFPQ task has been created (Dalton & Finlayson, 2014; Finlayson et al., 2007a). In the LFPQ, the distinction between liking and implicit wanting is based upon the methodology that conceptualises these constructs. Liking is a measure of the pleasure to eat a specific food based on a VAS, while implicit wanting is a measure of the relative motivation to eat based on a forced-choice task (Dalton & Finlayson, 2014).

While the distinction between liking and wanting has been debated (Finlayson & Dalton, 2012a; Havermans, 2011; Havermans, 2012), the LFPQ has shown distinct responses in liking and implicit wanting depending on the motivational state (i.e. hungry or fed) (see Chapter 3). All of these findings support the theory of the distinction between liking and implicit wanting measured by the LFPQ. However, this distinction has never been statistically tested. The PCA offered the opportunity to test the relationship between liking and implicit wanting in the context of a controlled diet-induced WL intervention. The principal components clearly separate the changes in liking from the changes in implicit wanting, attesting to the distinction between liking and implicit wanting. Studies using the LFPQ have also shown this distinction: implicit wanting but not liking decreased after an exercise intervention (Beaulieu et al., 2020c) while liking but not implicit wanting decreased after a controlled diet intervention (see DIVA study Chapter 5). Increased implicit wanting for HFSW when fed, but not liking, was found in individuals with obesity and binge eating compared to non-binge eaters (Dalton et al., 2013a).

Another feature of the LFPQ is based on the distinction between sweet and savoury food. This distinction has been shown to characterise phenotypes of obesity, with higher reward for HFSW being a characteristic of individuals with obesity and binge eating (Dalton et al., 2013b). In the current analysis, the 2 dimensions of the PCA visually separated sweet and savoury variables, which shows that participants were able to distinguish between sweet and savoury, and that sweet and savoury foods have different rewarding properties. One limitation of the LPFQ is that the participants are seeing but not tasting the foods pictured. It is therefore difficult to determine whether the distinction between sweet and savoury is made on the real taste of the food or on an imaginary perception. The PCA shows a statistical distinction between sweet and savoury reward but this will be meaningful only if this is grounded in physiology. It has recently been shown that the taste of food translates onto the macronutrient content of the food and that individuals can distinguish between sweet and savoury based on the disaccharide, sodium or protein content of the food (Martin & Issanchou, 2019). The association between sweet taste and fat content may lead to overconsumption and is of particular importance for appetite control (Dalton et al., 2013b; Finlayson et al., 2012). Sweet food preferences are often innate and modulated by early life exposure (Drewnowski, 1989), but less is known about savoury food preference. Future research could investigate whether there is implication for weight management to have greater reward for savoury than sweet independently from fat content.

Lastly, the LFPQ task separates food according to their fat content (i.e. high-fat and low-fat). Fatty foods have been associated with overconsumption and obesity; it is also suggested that in general high-fat foods are the most palatable food. However, it is not clear whether this overconsumption is due to a higher reward or lower sensitivity to fat in individuals with obesity compared to individuals within the normal range of BMI (Bartoshuk et al., 2006; Drewnowski & Almiron-Roig, 2010). Preference for fat has been related to fat mass (Mela & Sacchetti, 1991), and has been shown to be either acquired independently from genetic background (Rissanen et al., 2002) or associated with genetic mechanisms (Van der Klaauw et al., 2016). It is still debated whether liking or wanting for fat is associated with BMI and will be discussed in Chapter 9. However, reward for high-fat has been shown to decrease after different types of interventions (Oustric et al., 2018a) and even more recently after an exercise intervention (Riou et al., 2019) and snack manipulation (Hollingworth et al., 2019). Therefore, it is meaningful to distinguish between high and low-fat food in the LFPQ.

The current PCA analysis however revealed no clear distinction between low and high-fat variables. This could be explained by the fact that the participants did not succeed in distinguishing between low and high-fat food pictures during the task. One hypothesis could be that the food pictures presented during the task were validated in 2004 (Finlayson, 2006) and may need some updates to continue to reflect the actual distinction between low and high-fat pictures. The PCA analysis was replicated on another set of pictures used for the LFPQ (Beaulieu et al., 2017) and the distinction between high-fat and low-fat was apparent. This distinction is also visible on the breakfast pictures of DIVA. Besides, the PCA on the same DIVA lunch dataset at post-lunch showed similar relationship between variables compared to the one at pre-lunch, ruling out a possible effect of the physiological state. All of these suggest that this is rather driven by the food pictures rather than a particularity of the population. This analysis highlights a limitation of the set of pictures used in the DIVA analysis. However, another explanation could be due to the fact that the PCA was run on “changes“ and that changes in reward during WL might not distinguish between high and low-fat. Analysis of baseline data (Chapter 9) showed that correlations between food reward and appetite control differed between low and high-fat, suggesting that reward for low- and high-fat had an opposite impact on appetite control. Therefore, the LFPQ with this set of pictures does translate into meaningful behaviour based on the distinction between fat and taste, but further study should use an updated version of the task as developed recently by Oustric et al. (2020).

This methodology could be employed in a broader perspective to assess the distinction between liking and implicit wanting in different populations or in different contexts (e.g. WL, eating behaviour traits). However, for the results to be interpretable beyond the sample, larger datasets are needed. Therefore, it is planned to repeat the PCA analysis with a larger sample to confirm or challenge these exploratory findings.

6.4.2 Changes in food reward that best describe the present sample

The second question aimed to select among the 8 variables of reward, the changes that best describe the sample. The LFPQ provided 8 different endpoints from 4 categories of food and 2 theoretically distinct processes. Usually, researchers select according to the theory the variable of interest to describe food reward. For example, preference for high-fat against low-fat food (corresponding to the fat appeal bias from the LFPQ) is usually used as the preferred food reward in weight management studies. This choice is made upon the hypothesis that decreasing reward for high-fat food might decrease overconsumption of these foods. Indeed, Fat Appeal bias scores have been previously used in different studies such as exercise interventions (Martins et al., 2017; Riou et al., 2019), sleep restriction (McNeil et al., 2017) or following high-fat or high-carbohydrate meals (Hopkins et al., 2016c). Reward for HFSW has also been chosen as a variable of interest in studies on snacking (Fay et al., 2015) and on cognition (Mackey et al., 2019).

However, another approach is to study the multiple endpoints of the LFPQ concomitantly. Indeed, the DIVA analysis aimed to explore the effect of WL on food reward; therefore, it is necessary to study these 8 endpoints together to get the full picture as diet-induced WL may affect food reward variables differently. Selecting statistically independent variables that best summarised the variability in the dataset had not been performed before. Among the 8 food reward, the PCA distinguished 2 principal components (i.e. synthetic variables) interpreted as "changes in implicit wanting" and "changes in liking". The variables that were the most related to these components were change in implicit wanting and liking for HFSW. These variables of reward explained the most variability and could therefore be used in models to better understand the effect of a controlled diet-induced WL on food reward by looking at correlation with changes in other psychobiological factors (see Chapter 7). Given the context of WL, it is coherent that changes in implicit wanting and liking for HFSW were the most representative variables. It is in line with results from other studies that have used reward for HFSW as a variable of interest to analyse changes during WL (Dalton et al., 2013c).

6.4.3 Identifying patterns of changes in food reward

Another way to visualise the effect of this controlled diet-induced WL on food reward is to look at the similarities between individuals when taking into account their changes for all the variables. Therefore, the third question aimed to explore the similarities between individual patterns of changes in food reward during WL. Given that changes in reward were dependent upon its sub-components, the dimensions of the foods and the individuals, it was necessary to investigate the presence of distinct patterns of changes to interpret the individual changes. Among the 5 clusters, 3 distinct patterns of WL-induced changes were identified: increase in liking, decrease in sweet and increase in savoury and vice versa, and decrease in liking and implicit wanting. This suggests that a controlled diet-induced WL affects individual reward differently but that overall main patterns can be identified. This is consistent with the theory that no one strategy will fit all individuals.

In the present sample, all clusters of individuals were decreasing in at least one aspect of food reward except for cluster 4 that increased across all dimensions. This latter response type could be more at risk of weight regain compared to individuals who decreased in food reward (Finlayson & Dalton, 2012b). Interestingly, for the 3 clusters that increased and decreased in reward, the shift was based on the separation between sweet and savoury reward with some people decreasing in sweet and others in savoury reward. There is no known hypothesis explaining this difference apart from personal food preferences. The PCA has also been run by diets (i.e. IER and CER), but as shown in Chapter 5 there were no effect of a specific diet on the changes in food reward. Also, as the reward for high and low-fat were not distinguished it is not possible to disentangle whether these patterns are in favour of weight management.

The only pattern to stand out with potential benefits for weight management was cluster 3 with a decrease in both liking and implicit wanting. It remains to be understood what makes this group of individuals respond differently to this study compared to others and whether they will really achieve better WL maintenance outcomes. Individual baseline characteristics have been sought to explain this pattern. Low disinhibition and high restraint are potential baseline characteristics related with successful WL (Finlayson et al., 2012; Yeomans et al., 2004). However, no eating behaviour traits from baseline appeared to be correlated with the changes describing cluster 3. The only baseline characteristic that was correlated with cluster 3 was liking for sweet, suggesting that individuals with high liking for sweet at baseline will decrease their reward the most after diet-induced WL. This finding could be a result of the regression to the mean tendency with higher scores at baseline decreasing the most, but the tendency that high baseline craving was also associated with decrease in food reward (i.e. cluster 3) may suggest otherwise. To conclude there is very little explanation available in this sample for the patterns in change in reward. Similarly, it is not possible to conclude on the pattern in change in food reward for those who did not reach ≥5% WL as there are only 7 individuals, a larger sample is needed to conclude on this point.

6.5 Conclusion

Multivariate analyses offer new insight to visualise and summarise the interindividual variability of multiple measures of pre-lunch food reward during diet-induced WL. Liking and implicit wanting in the LFPQ appeared to be distinct variables as conceptualised by the neurobiological theory they are inspired from Berridge and Robinson (1998). Changes in implicit wanting and liking for HFSW captured the most unique variability in changes occurring during controlled dietary intervention. In this limited sample, three main patterns of change in food reward were identified: increase in liking, decrease/increase in sweet reward and opposing change in savoury reward categories, and decrease in liking and implicit wanting. This is the first statistical approach to characterise the individual variability in food reward changes after a controlled dietary intervention to ≥5% WL. While the results need to be cautiously interpreted, it provides an illustration for mapping complex changes in reward. It remains to be investigated whether any psychological or physiological factors could explain these patterns. Potential application of this approach in future research could help tailor weight management strategies depending on individual characteristics.

Chapter 7
DIVA-1: Exploring the mechanisms and relevance of the changes in pre-lunch food reward during controlled diet-induced weight loss in terms of appetite control

Chapter aims:

1- Analyse changes in appetite-related variables (body-composition, eating behaviour traits, appetite sensations and food intake) pre to post weight loss (WL) in order to contextualise changes in food reward

2- Explore the mechanisms and relevance of changes in pre-lunch food reward by investigating their relationships with changes in appetite-related variables

HIGHLIGHTS

► Dietary induced-WL led to improvements in body composition, better eating behaviour traits and appetite sensations but no changes in test-meal food intake.

► The decrease in liking for high-fat sweet (HFSW) was not associated with any changes in biopsychological variables and was not associated with subsequent changes in appetite sensations or food intake.

► Changes in food reward, appetite sensations, and eating behaviour traits were highly variable in response to clamped WL

7.1 Introduction

Food reward is often thought to be responsible for overeating and weight regain after WL. However, several WL interventions have reported a decrease in components of food reward (Beaulieu et al., 2020c; Kahathuduwa et al., 2016; Oustric et al., 2018a) raising the question of the potential mechanisms underlying these changes. More interestingly, as presented in Chapter 5, diet-induced WL seemed to decrease liking more than implicit wanting (Andriessen et al., 2018), which invites further investigation into the relevance and implications of those changes for weight management. Chapter 6 illustrated the extent of the interindividual variability, with some individuals showing a decrease while others increased their food reward depending on the food category. Consequently, PCA and cluster analyses were performed and showed that changes in food reward during the WL intervention could be most parsimoniously summarised by liking and implicit wanting for high-fat sweet (HFSW). However, correlations with baseline characteristics could not explain the patterns of changes observed. Therefore, the underpinning of these changes remains to be explained as well as their implication in terms of appetite control (e.g. whether it leads to reduce food intake).

Changes in food reward during diet-induced WL need to be investigated within the context of other variables involved in appetite control. Indeed, food reward is not a sole or independent system in the control of appetite but is characterised by complex interactions of biological, psychological and environmental processes leading to food intake (Berthoud et al., 2020; Casanova et al., 2019b). Therefore, analysing the contextual changes of food reward such as changes in body composition, eating behaviour traits, appetite sensations, and food intake are key in understanding the role of food reward during WL.

Tonic signals (day-to-day) from fat-free mass rather than fat mass have been shown to create a functional drive to eat which is moderated by RMR (Hopkins et al., 2018). Moreover, during energy restriction, it has been suggested that fat-free mass loss may generate an orexigenic signal promoting energy intake (Casanova et al., 2019b). Therefore, changes in body composition during WL are key in understanding tonic signals of appetite. Episodic signals (meal-to-meal) such as food reward have been suggested to override tonic or episodic homeostatic signals (Berthoud, 2006); however, the relationship between food reward and body composition is not clear. One study by Hopkins et al. (2014) found cross-sectional associations between fat mass and liking and wanting for high-fat food. However, those associations were not found during the 12-week exercise intervention leading to fat-mass loss. The relationship between changes in food reward during diet-induced WL and changes in body composition remains to be elucidated.

Similarly, cross-sectional analyses have reported psychological correlates of food reward. Liking and implicit wanting have been moderately associated with Disinhibition (Finlayson et al., 2012) and Susceptibility to Hunger (French et al., 2014). Higher Binge Eating (Binge Eating Scale) has been associated with a greater liking for food overall and enhanced desire and cravings for high-fat sweet foods (Dalton et al., 2013c). However, beyond these moderate correlations, less is known about these relationships during dietary WL. Other eating behaviour traits such as Mindful or Intuitive Eating and Hedonic Hunger (PFS) have been proposed to describe one's relationship towards food in terms of awareness to external and body cues (Espel-Huynh et al., 2018; Framson et al., 2009; Tylka & Kroon Van Diest, 2013). Even fewer studies have investigated the relationships between the latter eating behaviour traits with food reward (Hong et al., 2011) while they could contribute in explaining hedonic processes. An increase in Restraint has been associated with WL (Morin et al., 2018). However, the association between changes in food reward and changes in Binge Eating, Restraint, Disinhibition, Cravings and other traits during dietary restriction needs to be further explored.

Therefore, this Chapter aimed to explore: 1) Changes in appetite-related variables described as body composition, eating behaviour traits, appetite and food intake to contextualise changes in food reward during diet-induced WL. 2) The underlying mechanisms and relevance of the changes in liking by exploring the relationship between these changes and changes in other appetite-related variables.

To do so, the analysis explored the effect of a matched WL to ≥5% through individually prescribed and controlled continuous or intermittent energy restriction (CER or IER) on the aforementioned appetite-related variables. Given the aim was to assess the effect of a clinically significant WL, the analyses were performed on the 30 women that achieved to ≥5% within 12 weeks. It should be noted that the variability in the degree of WL was intentionally minimised. Consequently, changes in physiological variables were more controlled, less variable and unlikely to explain variability in the changes in food reward. Changes in fat mass and fat-free mass were not clamped (only body weight was), so their relationship with changes in food reward was analysed with caution. It was hypothesised that fat mass would be a physiological correlate and might predict changes in food reward (Hopkins et al., 2014). In terms of psychological correlates, it was hypothesised that a decrease in Disinhibition and an increase in Restraint and Craving Control would be associated with a decrease in liking for HFSW.

7.2 Method

7.2.1 Diet intervention: DIVA-1

This series of secondary analyses were conducted after the DIVA-1 study, a controlled diet-induced WL intervention (see Chapter 4 for the detailed design). Forty-six women with overweight or obesity were allocated to either a continuous (25% energy restriction each day) or intermittent energy restriction diet (ad-libitum day alternating with 75% energy restriction day) until ≥5% WL within 12 weeks. All food was prepared, portioned and provided for the CER group and the fast day in IER, and WL monitored weekly. Measures days were conducted at baseline and post-WL and included several appetite-related outcomes.

This Chapter investigates potential physiological correlates of food reward: body composition (fat mass, FM; fat-free mass, FFM), resting metabolic rate (RMR) but also psychological correlates: eating behaviour traits (primary: TFEQ, BES, CoEQ, secondary: MEQ, IES, PFS, see Chapter 1), behavioural outcomes such as test meal energy intake, and appetite sensations (reported as AUC and standardised hungry state – pre-lunch rating, 3 hours after a standardised breakfast calibrated to 25% RMR). The LFPQ was used to assess explicit liking and implicit wanting components of food reward before an ad-libitum test meal. Following Chapter 6, food reward variables were represented in this Chapter by pre-lunch <u>liking and implicit wanting for HFSW</u> to investigate mechanisms and the relevance of changes for appetite control.

7.2.2 Statistical analysis

Per-protocol analyses were conducted on the 30 individuals that achieved ≥5% WL out of the 37 completers consistent with previous chapters, as the main question was to investigate the effect of clinically significant WL. Repeated measures mixed ANOVAs were performed to analyse the effect of time and diet on the appetite-related variables. As there were almost no differences between CER and IER in all the outcomes of interest (e.g. physiological, psychological and behavioural), the analyses report the main effect of time on the 30 women. The main effect of diet or interactions were further specified if significant.

All variables were plotted, and the normality of their distribution was further checked by the Shapiro test. For parametric data, mean and SD were reported. As the design was unbalanced (CER = 18, IER = 12) type 3 ANOVAs were performed using the package afex (Singmann et al., 2019) and the repeated ANOVA function aov_ez. For variables not normally distributed, the median and interquartile range was specified. The effect of time and diet was assessed by robust ANOVA-type statistics appropriate for nonparametric factorial longitudinal data with the package nparLD (Noguchi et al., 2012).

Each outcome of interest was plotted to visualise both the mean changes and the apparent individual variability graphically. Each graph displays individual measures by diet group, the density, the mean and standard error of the mean, and individual changes pre to post WL. In the previous Chapter, the PCA showed that changes in pre-lunch food reward after diet-induced WL could be most parsimoniously represented by liking and implicit wanting for HFSW. Pearson's correlations were performed between these variables of reward and changes in other appetite-related variables. All the analyses were performed on R (R Core Team, 2018). P-values are reported as much as possible as equality with 3 decimals unless too small and then reported as < .0001.

7.3 Results

7.3.1 Physiological correlates of changes in food reward

7.3.1.1 Changes in physiological variables pre to post WL

All physiological factors reported in Table 7-1 decreased pre to post WL except for RMR. There was no difference between diets.

Table 7-1: Physiological variables pre to post WL (N = 30).

Factors	Baseline	Post-WL	Changes	P-value
Body mass (kg)	79.9 ± 11.0	74.8 ± 10.3	-5.1 ± 1.0	<.0001
FM (kg)	33.1 ± 7.7	29.3 ± 7.3	-3.82 ± 1.3	<.0001
FFM (kg)	46.8 ± 5.8	45.5 ± 5.7	-1.3 ± 0.8	<.0001
Percentage Fat	41.0 ± 5.4	38.8 ± 5.7	-2.3 ± 1.2	<.0001
BMI ($kg.m^{-2}$)	29.1 ± 2.4	27.2 ± 2.3	-1.9 ± 0.3	<.0001
RMR (kcal)	1450.18 ± 205.79	1448.39 ± 191.21	-1.79 ± 120.37	.86

Data are mean ± SD, FM: fat mass, FFM: fat-free mass

Figure 7-1 displays both mean changes and the apparent individual variability in the changes following the intervention. The latter seemed small, especially for body weight and BMI. This can be explained by the study's design, which voluntarily monitored and controlled the WL percentage. As the variability was less controlled for fat mass, %fat, fat-free mass and RMR, their correlation with changes in food reward can be interpreted with caution.

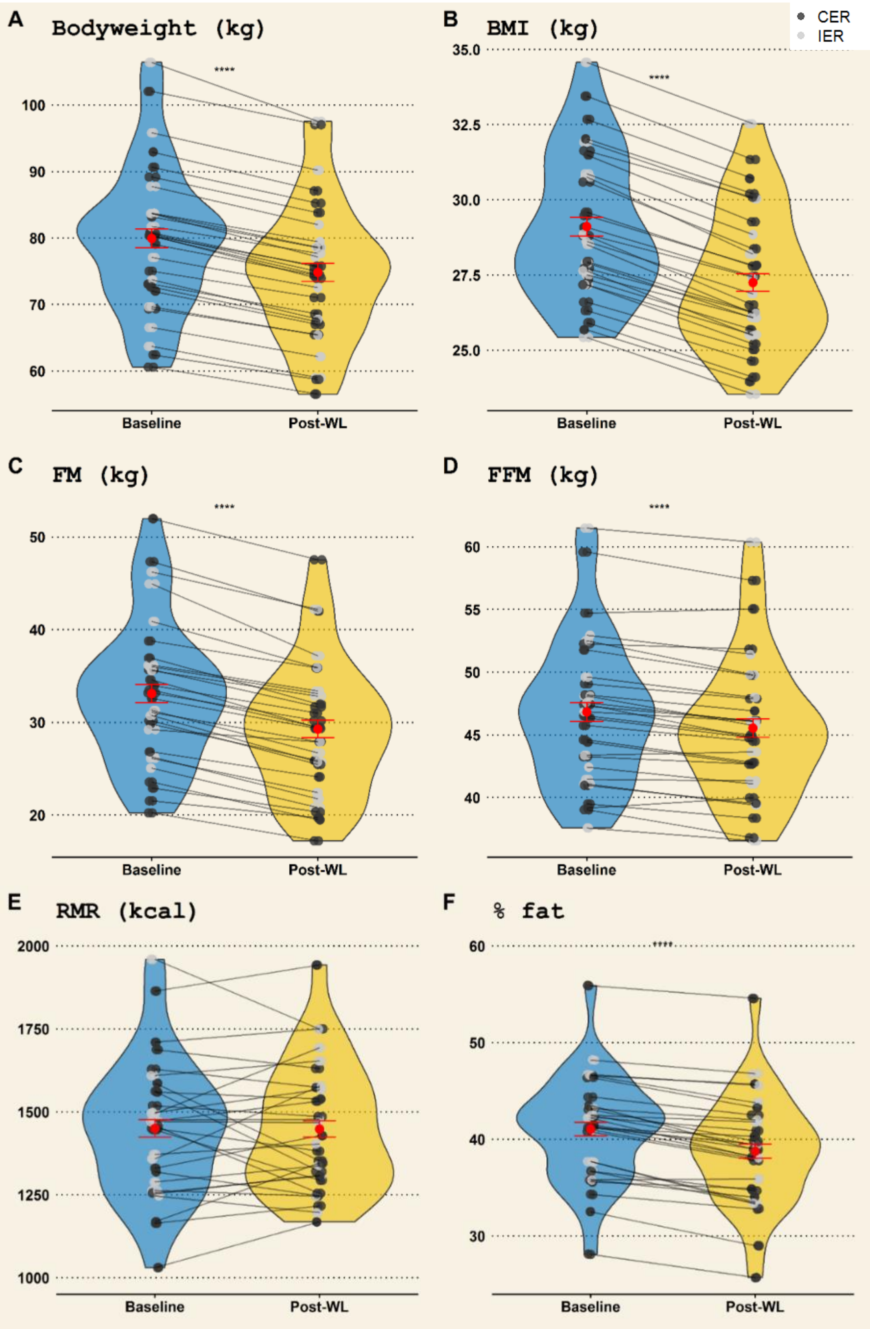

Figure 7-1: Changes in physiological variables (N = 30)

The individual data are represented by points (light grey for CER and dark grey for IER) and showed no difference between diets. Means are represented by red points with error bar (SE). Violin plots represent the variability of the data and the distribution. *significant changes between baseline, post-WL (**p < .01, ***p < .001, ****p < .0001), CER: continuous energy restriction IER: intermittent energy restriction. FM: fat mass, FFM: fat-free mass

7.3.1.2 Relationship with changes in food reward

There was no association between changes in food reward and changes in body composition. See Figure C1 in Appendix C for the correlation matrix with significant associations in colours. It can be noticed that the correlation coefficient between change in liking and change in fat mass or %fat was moderate ($r = .3$). However, the p-value was high ($p = .124$ and $p = .580$, respectively), indicating a lack of power in this analysis.

7.3.2 Psychological correlates of changes in food reward

7.3.2.1 Changes in eating behaviour traits variables pre to post WL

Table 7-2 reports changes pre to post WL for eating behaviour trait variables. There was a main effect of time but no effect of diet except for Disinhibition, PFS and Craving Savoury. Restraint (TFEQ), Craving Control (CoEQ), MEQ and IES increased while Susceptibility to Hunger (TFEQ), Disinhibition (TFEQ), PFS, Craving for Sweet and Savoury (CoEQ) decreased pre to post WL. There was a main effect of diet on Disinhibition (p = .022) and an interaction between diet and time (p = .051) with CER showing a greater decrease in Disinhibition. There was a main effect of diet on PFS (p = .023) and Craving Savoury (p = .008) with IER having higher PFS and Craving Savoury scores than CER. It should be noticed that for those variables, IER had a greater value at baseline.

Table 7-2: Changes in eating behaviour traits (N = 30)

	Baseline	Post-WL	Changes	P
Craving Sweet	41.5 (23.6; 62.6)	23 (9.7; 40.7)	-16.7 (-28.5; -1.5)	<.0001
Craving Savoury	50.7 (22; 66)	20 (14.3; 42.7)	-16 (-31.2; 0.9)	<.0001
Craving-control	46.4 ± 19.2	68.9 ± 19.4	22.5 ± 18.3	<.0001
BES	14 (9;19)	10.5 (5.2; 14)	-4 (-8.7; -2)	<.0001
Disinhibition	9.5 (7; 11.7)	7 (5; 9)	-1 (-5; 0.7)	<.0001
Restraint	8.3 ± 4.2	12.6 ± 4.6	4.3 ± 3.8	<.0001
Susceptibility Hunger	6.5 ± 3.1	3.8 ± 2.4	-2.7 ± 3.0	<.0001
PFS	3.1 (2.0; 3.6)	2 (2; 3)	-0.6 (-1.1; 0.1)	<.0001
MEQ	2.6 ± 0.3	2.8 ± 0.32	0.18 ± 0.32	. 008
IES	3.15 ± 0.49	3.40 ± 0.50	0.26 ± 0.32	.0003

Data are mean ± SD for parametric data and median (IQR) for non-parametric

Finally, these results can be summed up into categories, eating behaviour traits that increased during the dietary intervention (Figure 7-2) and those that decreased (Figure 7-3). Those changes favour improved appetite control by decreasing traits that lead to overconsumption and increasing traits that reinforce appetite control.

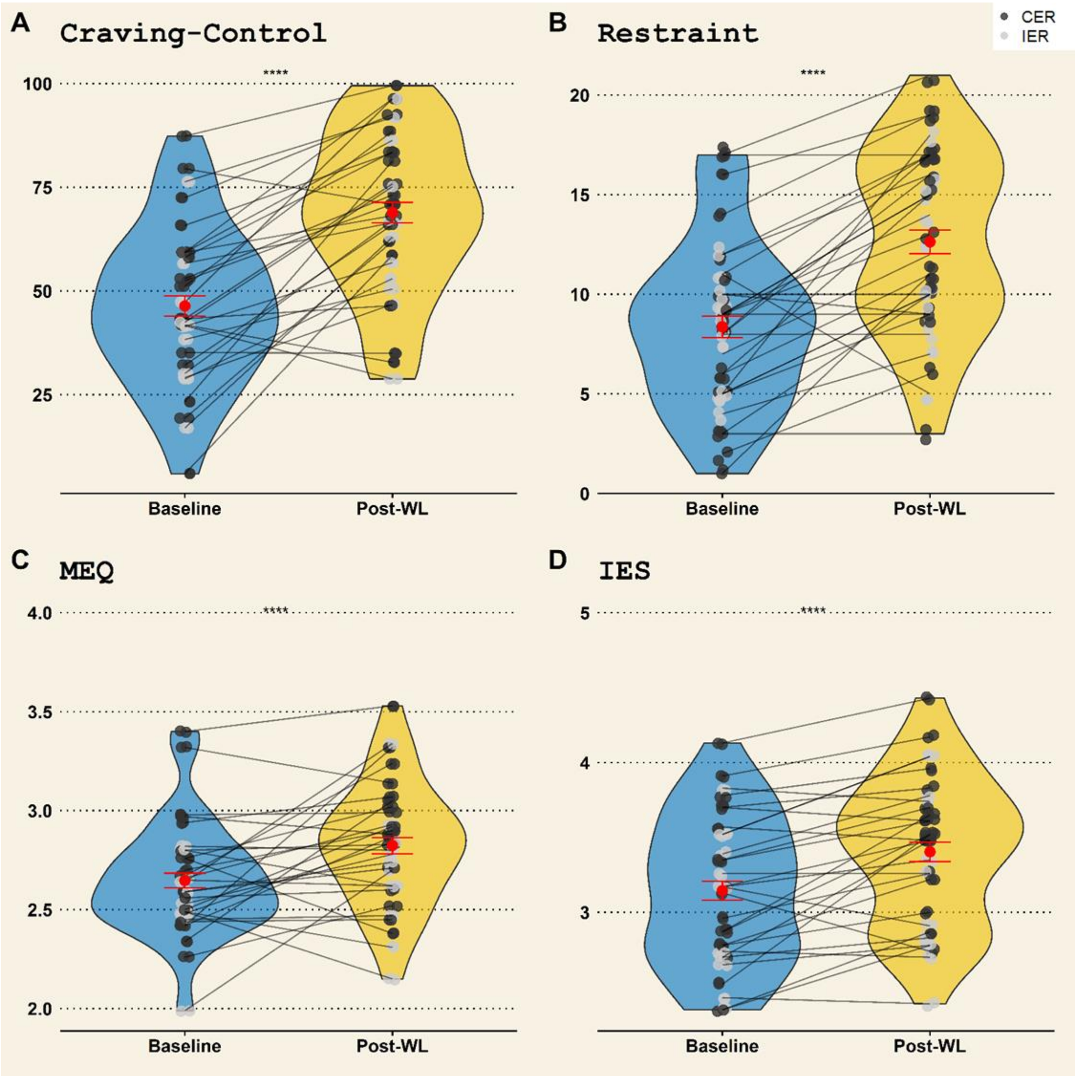

Figure 7-2: Increase in eating behaviour traits improving appetite control (N = 30)

The individual data are represented by points (light grey for CER and dark grey for IER) and showed no difference between diets. Means are represented by red points with error bar (SE). Violin plots represent the variability of the data and the distribution. *significant changes between baseline, post-WL (**p < .01, ***p < .001, ****p < .0001), CER: continuous energy restriction IER: intermittent energy restriction, MEQ: mindful eating questionnaire, IES: intuitive eating questionnaire

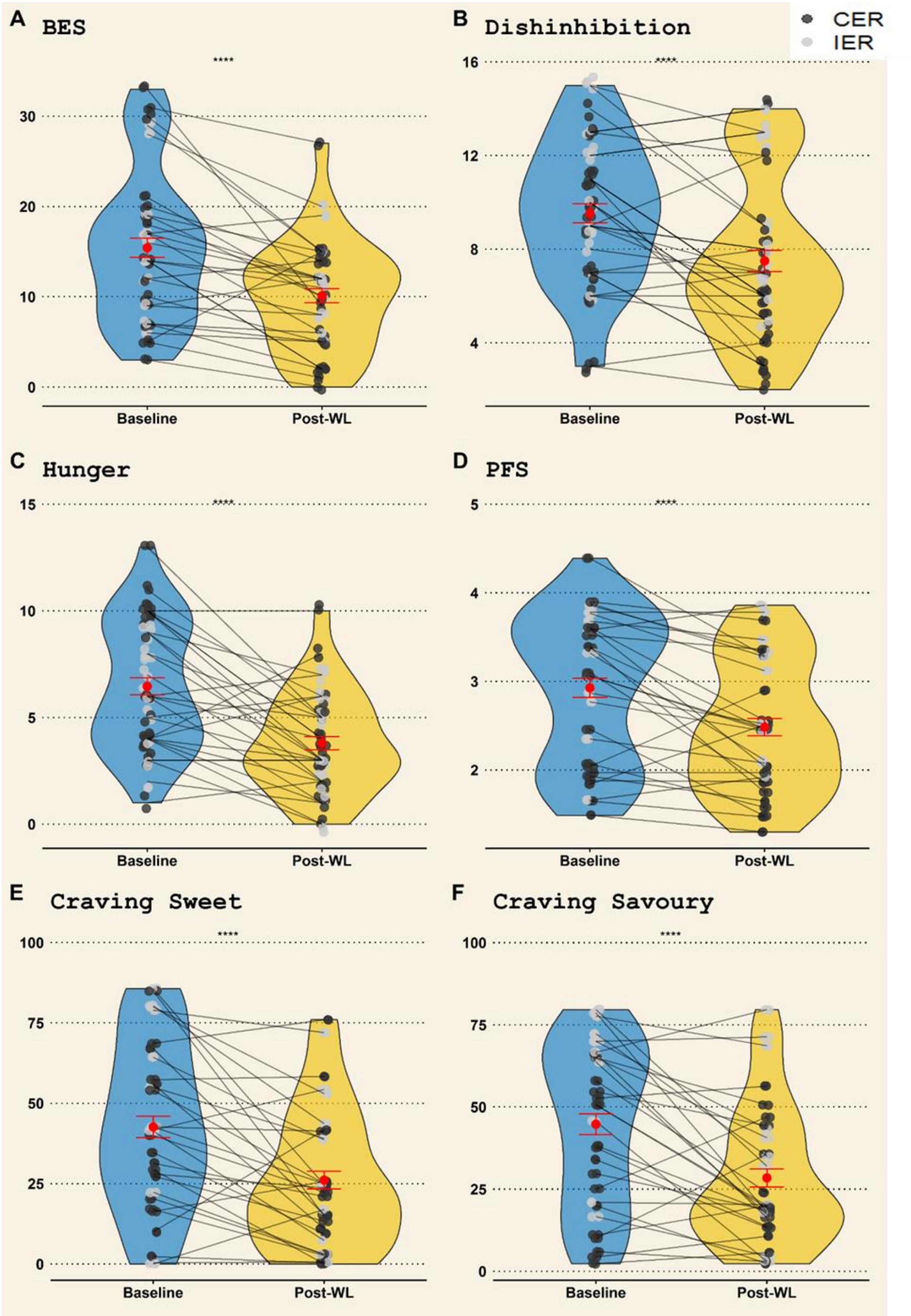

Figure 7-3: Decrease in eating behaviour traits leading to overeating (N = 30)

The individual data are represented by points (light grey for CER and dark grey for IER). Means are represented by red points with error bar (SE). Violin plots represent the variability of the data and the distribution. *significant changes between baseline, post-WL (**p < .01, ***p < .001, ****p < .0001), CER: continuous energy restriction IER: intermittent energy restriction, BES: binge eating scale, Disinhibition (TFEQ), Hunger: Susceptibility to Hunger (TFEQ)

7.3.2.2 Relationship with changes in food reward

There was no association between changes in food reward and any changes in eating behaviour traits. An outlier with a change in liking HFSW that was >3 SD was removed from the analysis. When this participant was removed, the negative moderate association ($r = -.38$, $p = .036$) between Disinhibition and liking for HFSW disappeared, attesting to the weakness of this relationship.

While there was no relationship between changes in food reward, and changes in eating behaviour traits, expected associations between changes in eating behaviour traits were revealed. An increase in Craving Control was associated with an increase in Restraint ($r = .39$) and Intuitive Eating ($r = .46$) and negatively associated with changes in Craving Savoury ($r = -.56$). Lastly, a decrease in PFS was associated with a decrease in BES ($r = .68$). Interestingly MEQ, PFS and IES were associated with BES and TFEQ. See Figure C2 in Appendix C for the correlation matrix of changes in food reward (hungry state) with changes in eating behaviour traits.

7.3.3 Do changes in food reward predict changes in food intake or appetite sensations?

7.3.3.1 Changes in food intake and appetite sensations

Changes in food intake during the test meal pre to post WL are reported in Table 7-3. There was no main effect of time on food intake. Interestingly there was a main effect of diet on yoghurt intake ($p = .02$) with CER having a greater yoghurt intake. It should be noted that CER had a greater intake at baseline.

Table 7-3: Changes in food intake (N = 30)

	Baseline	Post-WL	Changes	P
Risotto-kcal	628.68 ± 203.24	627.40 ± 219.35	-1.28 ± 168.27	0.71
Yoghurt-kcal	273.19 ± 152.51	240.01 ± 131.04	-33.18 ± 94.28	0.12
lunch-kcal	901.86 ± 264.69	867.41 ± 271.78	-34.46 ± 213.06	0.66

Data are mean ± SD

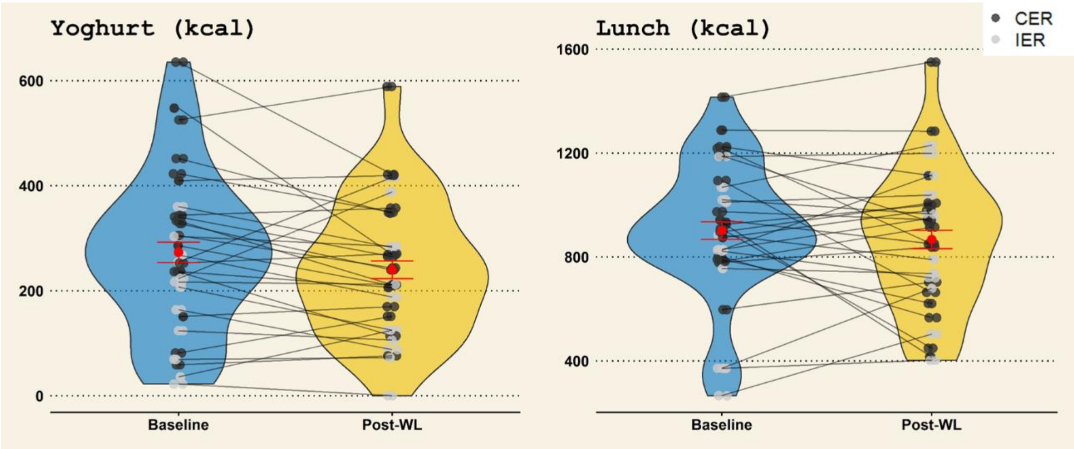

Figure 7-4: Changes in food intake during test meal (N = 30)

The individual data are represented by points (light grey for CER and dark grey for IER). Means are represented by red points with error bar (SE). Violin plots represent the variability of the data and the distribution. *significant changes between baseline, post-WL (**p < .01, ***p < .001, ****p < .0001), CER: continuous energy restriction IER: intermittent energy restriction

Table 7-4 reports changes in appetite sensations pre to post WL. Both the area under the curve (AUC) from breakfast to the test meal (3 hours) and the value at hungry state (pre-lunch) are reported to describe the appetite sensations. Prospective consumption, hunger and desire to eat all decreased (AUC and hungry state) pre to post WL.

Table 7-4: Changes in appetite sensations (N = 30)

	Baseline	Post-WL	Changes	P value
Hunger	59.7 ± 25.2	51.3 ± 23.9	-8.4 ± 18.2	0.009
Fullness	25.5 (12; 34.7)	24.5 (10; 47.7)	-1 (-5. 7: 9.5)	0.347
Desire	69 (51; 78.7)	58 (43.5;68.2)	-10 (-21.5; 5.2)	0.007
P. consumption	53.2 ± 20.9	45.7 ± 20.0	-7.6 ± 19.8	0.045
Hunger (AUC)	5371 ± 2398	4482 ± 2058	-889 ± 1895	0.021
Fullness (AUC)	10521 ± 2456	11089 ± 2886	567 ± 2318	0.122
Desire (AUC)	5909 ± 2609	4894 ± 2139	-1014 ± 2093	0.016
P. consumption (AUC)	4902 ± 2483	4345 ± 1848	-556 ± 2038	0.045

Data are mean ± SD for parametric data and median (IQR) for non-parametric; P. consumption: prospective consumption, AUC: area under the curve

7.3.3.2 Relationship with changes in food reward

No associations were revealed between changes in food reward and changes in food intake and appetite sensations. Other patterns of changes were present such as decrease in desire to eat (AUC) was associated with decrease in prospective consumption (r = .74), decrease in hunger (AUC) (r = .72) and increase in fullness (r = .61) (see Figures C3 and C4 in Appendix C).

7.4 Discussion

This Chapter explored 1) changes in appetite-related variables (body composition, eating behaviour traits, appetite sensations and food intake) pre to post WL; and 2) the relationship between these changes and changes in pre-lunch food reward during the intervention. Diet-induced WL through both CER and IER led to improvements in fat mass, eating behaviour traits associated with overconsumption (i.e. Binge Eating, Disinhibition decreased), in appetite sensations (i.e. desire to eat and hunger decreased) but no change in test meal food intake. Changes in food reward seemed not to be associated with any changes in appetite-related variables and were not associated with changes in appetite sensations or food intake. Interestingly changes in appetite sensations and eating behaviour traits were highly variable compared to the physiological changes, partly due to the study design (i.e. clamped WL). Unfortunately, the high variability and small sample size did not explain the changes in liking during this intervention.

7.4.1 Changes in appetite-related variables

The intervention led to a mean WL of 6.4%, accompanied by a decrease in both fat mass and fat-free mass but not RMR. As per the protocol, the WL was clamped to ≥5% within 12 weeks, the variability was therefore reduced. The range of WL (-4.9% to -8.3%) can be explained by the fact that when participants reached a WL of ~5% at a weekly check-in, they continued the diet for a week to confirm the WL before coming to the final measures' day. There was no difference between diets in terms of fat mass, fat-free mass which is in line with systematic reviews comparing CER and IER (Cioffi et al., 2018; Davis et al., 2016).

In terms of eating behaviour traits, IER and CER led to favourable adaptations in appetite control with an increase in Craving Control, Restraint, Mindful and Intuitive Eating. Similarly, factors associated with susceptibility to overconsumption decreased: Susceptibility to Hunger, Disinhibition, Binge Eating, PFS, and Craving for Sweet and Savoury with no difference between diets. This is in line with Sanchez et al. (2017) and Chaput et al. (2005), showing an improvement in cognitive Restraint measured by the TFEQ pre to post diet-based weight reducing program and progressive WL program both leading to >5 kg WL. While an increase in restraint has been associated with better WL outcomes, the role of restraint in weight management is conflicted. This has led to the definition of flexible and rigid restraint (Westenhoefer et al., 1999), with an increase in flexible restraint being associated with greater WL (Morin et al., 2018) and it remains to be investigated with food reward. Other dietary-WL studies have also reported a decrease in cravings, Disinhibition, Susceptibility to Hunger, Binge Eating, Hedonic Hunger (PFS) and emotional eating (Chaput et al., 2005; Martin et al., 2011; Martin et al., 2006; Mason et al., 2019; Morin et al., 2018; Theim et al., 2013) suggesting an improvement in eating behaviour and relation towards food cues following the dietary intervention.

Interestingly hunger ratings decreased pre to post WL as well as desire to eat and prospective consumption, but no changes in fullness were observed. This improvement in appetite sensations counteracts the potential compensatory adaptations proposed during WL, such as an increase in hunger, that have been suggested to lead to weight regain (Keim et al., 1998; Sumithran et al., 2011). However, in the latter studies, the WL was much higher (∼9-14%) than the one achieved in the current study. As suggested by Sumithran et al. (2011), the state of energy deficit for the last measurements in the present study might have improved appetite. In line with the present study, an 8-week diet-induced WL intervention showed a decrease in appetite sensations (i.e. hunger, desire to eat) and food liking in response to a test meal measured immediately after ~8% WL (Andriessen et al., 2018). These results suggest that diet-induced WL does not always lead to compensatory adaptations in appetite. An interesting issue that remains to be investigated is why WL may lead to either an increase or a decrease in hunger.

While appetite sensations and eating behaviour traits improved, meal food intake did not change pre to post WL. Another 12-week diet-based WL program with probiotic supplementation did not affect food intake and decreased appetite (i.e. lower hunger sensations) and eating behaviour traits (i.e. lower Disinhibition) (Sanchez et al., 2017). On the contrary, Morin et al. (2018) showed a decrease in food intake measured by food frequency questionnaire, from baseline to 16 weeks follow-up, which could be due to the fact that participants improved their eating habits following the WL but the energy intake pre to post WL was not measured. Interestingly in Doucet et al. (2003), a 15-week drug-based WL program coupled with energy restriction resulted in a decrease of measured and reported food intake, and this was not associated with the increase in hunger and desire to eat pre to post WL. Test meals are the gold standard for a controlled measure of energy intake (ad-libitum and calibrated meals in the absence of environmental and social factors). However, the effects of IER and CER on free-living food intake need to be further investigated to measure eating behaviour in real-life settings with a wider range of food available and account for compensation during the day.

7.4.2 Exploring changes in food reward in the context of appetite control

Liking for HFSW decreased during this controlled dietary WL intervention as seen in Andriessen et al. (2018) where it was accompanied by a decrease in appetite sensations. The improvement in appetite, eating behaviour traits, and decreased liking support a reduced interest in food post-WL or greater control over appetite, which does not explain the usual weight regain after WL (Wing & Phelan, 2005). Therefore, possible mechanisms underlying these changes were explored in the current study. However, when correlations were performed between changes in food reward and changes in appetite sensations, eating behaviour traits or body composition, no relationship was observed. Similarly, a 12-week exercise training study measuring changes in the reinforcing value of food found no relationship with changes in body composition (Flack et al., 2020). While food reward has been shown to decrease after different types of interventions (Oustric et al., 2018a), the relationship with psychobiological changes is not always measured (Andriessen et al., 2018). Only a few studies reported associations with body composition (McVay et al., 2016; Stice et al., 2017) or a moderating effect of Disinhibition on wanting pre to post WL (Cameron et al., 2008). A 12-week exercise study that decreased fat mass but not food reward in individuals with obesity, showed no relationship between changes in reward and changes in body composition. However, they reported a relationship between decreased leptin and increased in liking for fat, suggesting a dynamic role of leptin in food reward changes during exercise-induced WL (Hopkins et al., 2014). Therefore, studies with a larger sample size are needed to decipher the mechanisms of changes in food reward during WL (i.e. whether there is a relationship or not to observe).

The relevance of the changes in food reward also relies on their effect on subsequent food intake. However, no significant changes in test meal food intake were reported in the present study. Moreover, no relationship was found between changes in food reward and change in food intake which could be partly explained by the fact that implicit wanting did not change. Or wanting has been shown to have a greater role in predicting food intake (de Araujo et al., 2019). The relationship between food reward and intake during dietary restriction remains to be understood. For example, food intake was only measured at lunchtime and did not consider snacks and or free-living intake. Indeed, it has been shown that 24h energy intake might be a better proxy of habitual diets and that 24h energy intake was associated with WL maintenance, but it was not the case for acute energy intake (Hansen et al., 2019). Also, the test meal was based on two components that were common and could be considered healthy. This questions whether the results would have been different with a test meal design matching the four categories of food presented in the LFPQ.

One might ask how the decrease in liking during this dietary WL intervention can be explained. While the associations between changes in liking and changes in other psychological and biological variables were non-significant, the decrease in liking happened in parallel with the improvement in eating behaviour traits, appetite sensations and body composition. As proposed in chapter 5 and 6, the absence of an association between decrease in liking and WL (measured by %WL, rate of WL, body weight or body composition) lead to the suggestion that the exposure to the diet intervention had a greater effect than the WL per se on liking. The potential mechanisms of these changes in liking (effect of the energy deficit, changes in habits or change in food consumed) remain to be further explored and will be discussed in Chapter 10.

7.4.3 Individual variability

Individual variability is an important feature in this study, exploring changes in psychobiological variables during WL. This individual variability was illustrated in the graphs and made tangible by the individual lines of changes pre to post WL. Interestingly a high apparent variability was observed for food reward, appetite sensations, eating behaviour traits and food intake variables. The variability in body composition variables remained lower than psychological and behavioural variables, partly explained by the study's design. This is in line with Buscemi et al. (2017), who reported a significant variability of craving estimates during WL and Flack et al. (2020), who reported large individual variability in changes in food reinforcement. This raises the point that not every individual has the same eating behaviour response to WL and weight regain (Field et al., 2018).

One might ask what are the implications of inter-individual variability. In the current study, it could explain the small to moderate effect size in the changes during WL and more importantly, why some individuals respond positively to WL while others regain weight. Understanding the causes of this individual variability could help to improve the efficacy of WL interventions. This leads to an exploration of the causes of this individual variability at the genetic (Goltz et al., 2019), and socio-cultural level to distinguish patterns and phenotypes. Multidisciplinary studies (Montesi et al., 2016) investigating the role and causes of individual variability in dietary WL studies are necessary to design WL interventions better.

7.4.4 Limitations and future perspectives

The main limitation of this study is its small sample size which, in addition to the large individual variability, prevents any generalisation of results to a wider population. Larger randomised controlled trials are needed to investigate the effect of diet-induced WL on food reward and to explore the mechanisms of changes in the context of appetite control. The fact that the design was clamped to 5% WL prevents conclusions on the effect of WL percentage on changes in food reward. Other studies need to disentangle the effect of the degree of WL from the effects of the diet on food reward.

Even though there were no significant associations between changes in food reward and changes in other appetite-related variables, the decrease in liking in the context of improvements in appetite sensations and eating behaviour traits suggests that favourable outcomes are possible following diet-induced WL. It remains to be investigated whether these changes are maintained during a no-contact follow-up (see Chapter 8). Also, the absence of significant correlations between changes in the current intervention does not rule out any appetite-related determinant of reward but rather attests to a lack of power, and cross-sectional correlates of food reward remain to be investigated (see Chapter 9).

7.5 Conclusion

Liking but not implicit wanting decreased at pre-lunch after a controlled diet-induced WL intervention via both CER or IER. It was accompanied by improvements in body composition, eating behaviour traits, appetite sensations, but no changes in test meal food intake. This suggests that IER and CER can lead to favourable outcomes that do not explain habitual weight regain following WL. However, changes in food reward seemed to be independent of any changes in appetite sensations, eating behaviour traits, body composition or food intake. Given the high variability of the change estimates and small sample size, this study does not explain the determinants of the decrease in liking during this intervention. Further multidisciplinary studies are needed to investigate the mechanisms of the changes in food reward taking into account the large individual variability and to explore whether these favourable changes are maintained during follow-up.

Chapter 8

DIVA-3: Changes in post-weight loss food reward after 1-year no-contact follow-up

Chapter aims:

1- Explore the changes in pre-lunch food reward after 1-year no-contact follow-up and compare values at follow-up with baseline and post-weight loss (WL) values

2- Compare the potential effect of diet modalities (continuous vs intermittent energy restriction) on food reward changes at follow-up

3- Investigate changes in physiological variables, appetite, eating behaviour traits and food intake at follow-up to contextualise food reward changes

HIGHLIGHTS

► While pre-lunch liking scores decreased during diet-induced WL, food reward scores at 1-year follow-up did not differ from baseline scores. The increase in food reward from post-WL to follow-up were likely non-significant due to the large individual variability and reduced sample size.

► Physiological variables (i.e., body weight, fat mass, fat-free mass) increased from post-WL to follow-up but remained lower than baseline scores.

► Improvements in appetite sensations and eating behaviour traits observed during WL were not sustained at 1-year follow-up, and food intake did not change during WL to follow-up.

► There was no effect of the diet modalities on any variables during WL and follow-up.

► A high degree of individual variability in psychological variables was apparent during WL and follow-up.

8.1 Introduction

After diet-induced WL to ≥5% using continuous or intermittent energy restriction, liking but not implicit wanting decreased with no difference between diets (see Chapter 5). It remains to be discovered whether these changes remain at 1-year of no-contact follow-up when individuals return to their free-living diet. Indeed, heightened hedonic responses (liking, wanting) have been related to overeating and weight regain (Blundell & Finlayson, 2004), and "hedonic hunger" has been proposed as a main barrier to WL during follow-up (Fischer et al., 2020). However, few WL or weight maintenance studies have conducted long-term follow-up measures, and even fewer have reported food reward measures. Anton et al. (2012) showed a decrease in food cravings after a 24-month weight maintenance intervention, while Buscemi et al. (2017) showed a decrease in cravings during 6 months of WL but no significant changes after a 1-year follow-up. To better understand these discrepancies, the characteristics of follow-up and changes in other appetite-related variables such as appetite sensations, eating behaviour traits, or food intake, need to be taken into consideration.

To decipher whether IER and CER could have a differential impact on reward, and appetite-related variables during weight maintenance, differences occurring during WL need to be examined. The effect of IER on appetite sensations and food hedonics seemed not to differ from CER during WL (Beaulieu et al., 2020b; Coutinho et al., 2018) but interestingly individuals who achieved >5% WL with IER showed improved satiety and decreased hunger after 1 year compared to those who lost <5% (Kroeger et al., 2018). IER might result in increased feelings of hunger and CER with increased cognitive restraint after WL (Sundfør et al., 2018; Sundfør et al., 2019), which could suggest more favourable outcomes after CER. However, IER and CER have been shown to have similar results in terms of WL maintenance (Sundfør et al., 2018; Trepanowski et al., 2017). Some reviews suggest that IER might help conserve fat-free mass at the expense of fat mass but it is unclear whether IER offers any benefit over CER in the long term (Alhamdan et al., 2016; Davis et al., 2016; Varady, 2011). The effect of IER and CER on psychobiological variables during follow-up (without contact or a structured weight maintenance intervention) remains to be explored.

The contextual influences on changes in food reward should give a greater understanding of changes occurring during follow-up. Indeed, food reward has been related to other appetite-related variables such as eating behaviour traits and food intake (French et al., 2014; Yeomans et al., 2004). Therefore, investigating changes in appetite, eating behaviour traits and physiological variables during follow-up will shed light on the changes in food reward. Improvements in eating behaviours and appetite sensation (i.e. reduced hunger, Craving and Binge Eating) have been reported after ≥5% WL in women with overweight/obesity, using both CER and IER diets see Chapter 7 (Beaulieu et al., 2020b). There is a need to assess whether these changes are sustained after a year without any contact and whether weight will be regained. It was hypothesised that improvements following WL might weaken during the 1-year period as participants were not aware of the follow-up measures upon initiation of the WL intervention and no-contact was made until invitation to participate in the follow-up measures.

Therefore, this chapter examined changes during follow-up (from post-WL to 1 year later) and differences in follow-up values in comparison to baseline for: 1) liking and implicit wanting; 2) physiological variables, eating behaviour traits, appetite sensations and food intake in order to put in context the hedonic changes; and 3) to explore differences between IER and CER.

8.2 Method

8.2.1 Follow-up: DIVA-3

In DIVA-1, 46 women with overweight/obesity were randomised to IER (ad-libitum day alternating with 75% energy restriction day with LighterLife total diet replacement products provided) or CER (25% daily energy restriction with all foods provided) to ≥5% WL or up to 12 weeks. Thirty-seven women completed the intervention and thirty women reached a WL ≥5%. The 37 completers were invited to return for a follow-up 1-year later (DIVA-3). Probe days were conducted at baseline, post-WL and 1-year post-WL, and included body composition, resting metabolic rate (RMR), test meal energy intake (EI), appetite sensations, and eating behaviour traits (principal: TFEQ, BES, CoEQ, secondary: MEQ, IES, PFS, see Chapter 1). LFPQ was used to assess explicit liking and implicit wanting components of food reward according to 4 categories of food (high-fat savoury, HFSA; low-fat savoury, LFSA; high-fat sweet, HFSW and low-fat sweet, LFSW) at pre-lunch.

At the beginning of the DIVA study, participants were not told that they would be invited for 1-year follow-up measures (the follow-up was implemented in the protocol mid-way through data collection of DIVA-1), but consented to be contacted about future studies. Therefore, participants did not receive recommendations to pursue their diets after the end of the intervention. Having given consent, they were emailed individually 1 month before their expected 1-year measures day to standardise the timeline prior to follow-up testing. Participants were re-screened to confirm eligibility status (i.e., no-WL due to illness or surgical procedures, no pregnancy or breastfeeding, no smoking, no eating disorder, no medical condition or changed health status). Figure 8-1 presents the flowchart of the follow-up study, reporting numbers of individuals invited, consented, lost to follow-up and assessed. As a note, out of the 37 participants contacted, 9 participants did not reply or were not available, 5 moved outside of Leeds or had a scheduling conflict due to work, 4 had health issues and 1 did not want to take part.

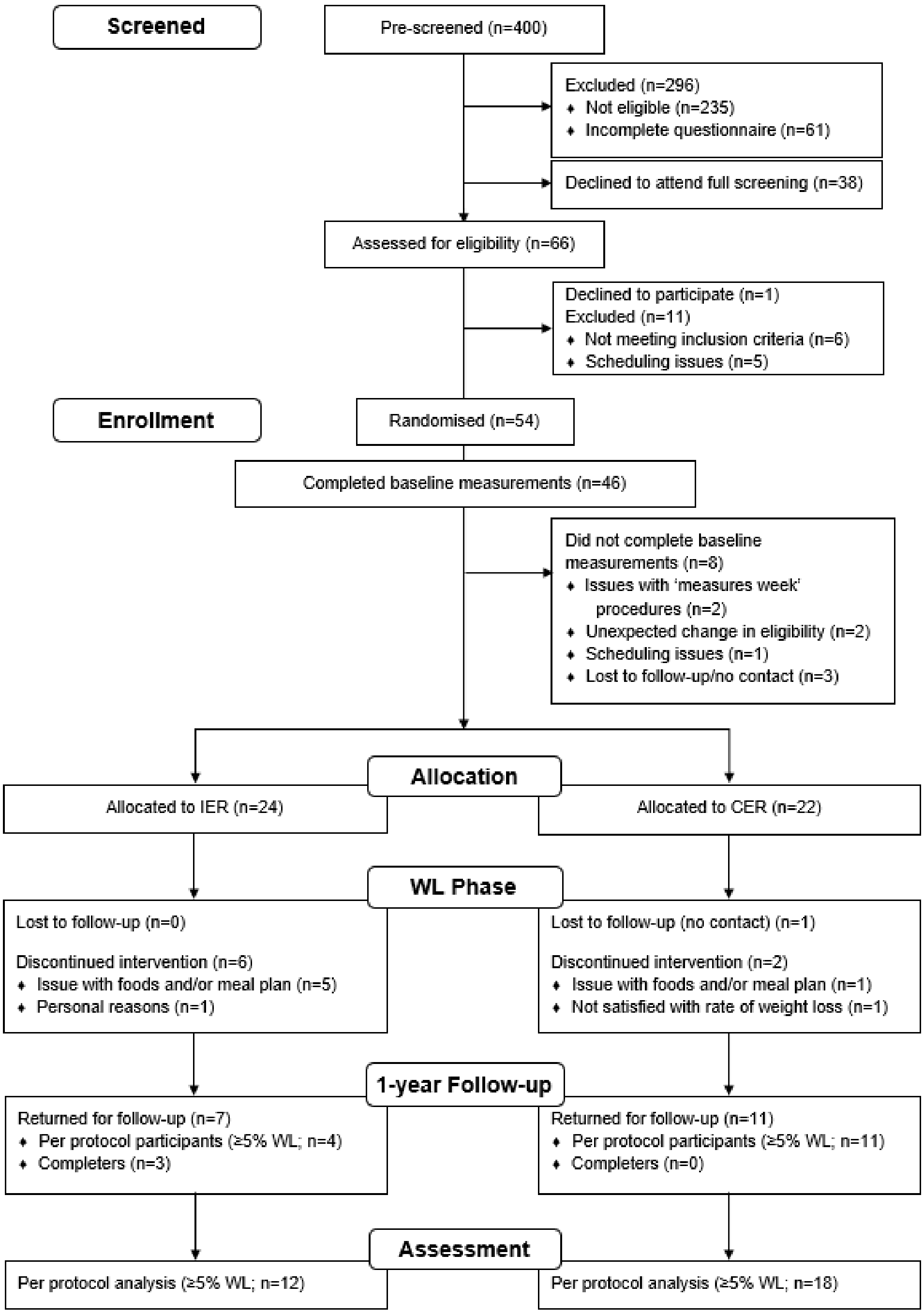

Figure 8-1: Flowchart of participants in DIVA-3 Follow-up

8.2.2 Statistical analysis

To analyse the effect of time (baseline, post-WL, follow-up) and diet (CER vs IER) on food reward and other appetite-related variables, linear mixed models were performed. Mixed models were used to take into account the repeated structure of the data and the effect of missing participants between the post-WL and follow-up time points. Factors of time and diet were considered as fixed effects and the participants were entered as a random effect (with random intercepts only). As there was only one random effect and it was not crossed, the maximum likelihood was used to fit the model. Variable encoding was chosen such that baseline measurement was determined as reference for time and CER as reference for diet. Therefore, post hoc tests were performed to analyse the significance of change between post-WL and follow-up, using the Bonferroni correction.

As the literature is scarce on the effect of diet modalities on food reward, the simplest model without interactions between diet and time was reported as the sample size was small. Residuals plots were visually inspected and did not reveal any deviations from linearity, homoscedasticity or normality. Analyses were performed on R (R Core Team, 2018) using lme4 package (Bates et al., 2015) to run the mixed models, lmerTest package (Kuznetsova et al., 2017) to obtain p-values and performance package (Daniel Lüdecke et al., 2020) to calculate conditional and marginal R2 to assess the quality of the model in accordance with Nakagawa and Schielzeth (2013). The full models for liking and implicit wanting were reported in Table 8-2 and Table 8-3 (formula, fixed effect, random effect and goodness of fit measures).The results are reported using Psycho package (Makowski, 2018). P-values are reported as much as possible as equality with 3 decimals unless too small and then reported as < .001.

Per protocol analyses (≥5% WL within 12 weeks) included 30 (CER N = 18, IER N = 12) out of 37 completers and 15 (CER N = 11, IER N = 4) out of 18 one-year returners. Intent-to-treat analyses in the per protocol participants (N = 30) are reported in coherence with previous chapters.

Detailed data visualisation was performed to explore changes in food reward and changes in appetite control variables from baseline to follow-up. This allowed to investigate individual changes and, therefore, to visualise the apparent individual variability among variables. Data visualisation was complementary to the statistical analysis that reports whether the changes observed were significant or not.

8.3 Results

8.3.1 Preliminary analysis of bodyweight changes during follow-up

Firstly, body weight changes during follow-up were plotted to analyse patterns and outliers (see Figure 8-2). Body weight increased on average by 4.6 ± 5.4% (3.3 kg) ranging from -2.1 to 19.7% in the 15 participants that had achieved ≥5% WL during the intervention. The increase in weight of 19.7% (14 kg) for one participant was considered as an outlier (3.6 SD above the mean), was removed from the mixed models and was examined as case study (see section 8.3.3). Without this outlier, the average change in weight was +3.6 ± 3.6% (2.6 kg) ranging from -2.1 to +8.8%. It can be noticed that 2 individuals decreased their weight (-2.1%, -1.9%) but the effect size of the WL might not be clinically relevant and the sample size was too small to perform a sensitivity analysis between weight gainers and weight losers during follow-up. There was no detectable difference between diets (CER: 3.6 ± 0.9% (2.5 kg), IER: 3.6 ± 1.1% (2.9 kg), p = .69).

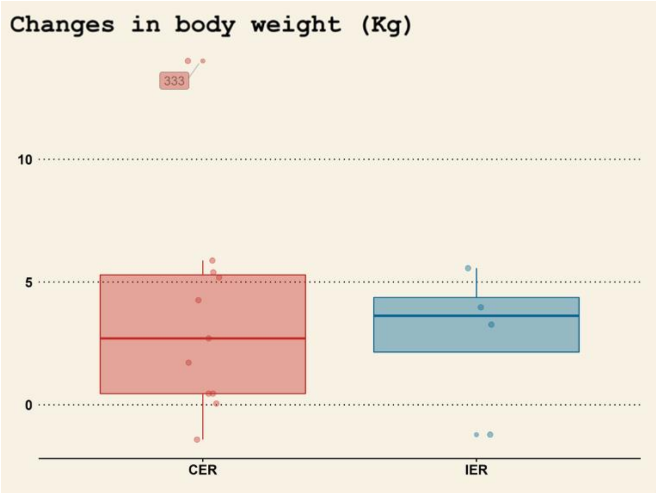

Figure 8-2: Changes in weight during 1-year no-contact after CER or IER (N = 15)

Body weight (kg)

8.3.2 Does food reward remain stable during follow-up?

Table 8-1 represents the mean value of liking and implicit wanting at each time point and the changes during WL and during follow-up.

Table 8-1: Changes in pre-lunch food reward during WL and follow-up

		Baseline (N = 29)	Post-WL (N = 29)	Follow-up (N = 13)	Changes-WL (N = 29)	Changes-FU (N = 13)
Liking (mm)	HFSA	63.0 ± 17.6	55.9 ± 21.2	64.4 ± 12.0	-7.1 ± 15.4	7.1 ± 21.7
	LFSA	53.2 ± 20.4	46.0 ± 20.9	52.7 ± 19.5	-7.2 ± 15.2	0.3 ± 13.4
	HFSW	55.8 ± 25.7	48.3 ± 21.8	53.1 ± 23.0	-7.5 ± 17.6	8.1 ± 13.3
	LFSW	57.0 ± 19.1	50.9 ± 13.9	54.9 ± 17.0	-6.1 ± 16.8	6.4 ± 17.2
Wanting (no unit)	HFSA	18.9 ± 22.1	18.4 ± 22.0	26.9 ± 19.8	-0.5 ± 20.6	4.3 ± 6.8
	LFSA	-2.6 ± 27.5	-3.7 ± 23.0	3.8 ± 20.1	-1.1 ± 21.1	-3.9 ± 11.3
	HFSW	-7.1 ± 29.1	-9.6 ± 25.5	-13.5 ± 21	-2.5 ± 20.0	2.0 ± 12.5
	LFSW	-9.2 ± 27.2	-5.0 ± 25.9	-17.2 ± 6.1	4.13 ± 18.4	-2.4 ± 5.9

Mean ± SD; “Changes-WL” represents changes during the WL (post-WL – baseline); “Changes-FU” represents changes during follow-up (Follow-up – Post-WL). N = 13 for follow-up as there is one missing participant.

8.3.2.1 Changes in liking (pre-lunch)

Changes during WL and Follow-up: Linear mixed models revealed a main effect of time on liking with a significant decrease in all components of liking from baseline to post-WL ($p \leq .047$) and no difference between follow-up and baseline values ($p \geq .251$). There was also no effect of diet modalities ($p \geq .128$) (see Figure 8-3). Post hoc tests showed no significant changes in liking for each food category during follow-up [follow-up – post-WL] ($p \geq .104$). However, the estimates of the changes during WL and follow-up were of similar size (i.e., HFSA: -7.12 ± 3.25 mm for WL and 8.76 ± 4.40 mm for follow-up, HFSW: -7.48 ± 3.15 mm for WL and 5.41 ± 4.32 mm for follow-up) see Table 8-2.

Comparison between follow-up and baseline: Liking for all food categories after 1-year follow-up did not differ from baseline scores. For example, in the model for liking HFSW, the fixed effects explained 3.80% of the variance, the effect of follow-up compared to baseline was not significant (beta = -2.07, SE = 4.32, 95% CI [-10.72, 6.60], $t(44) = -0.48$, $p = .635$) and can be considered as very small (std. beta = -0.09, std. SE = 0.18), the effect of diet was not significant (IER: beta = 6.21, SE = 7.94, 95% CI [-9.94, 22.23], $t(29) = 0.78$, $p = .440$) and can be considered as small (std. beta = 0.26, std. SE = 0.34). See Table 8-2 for coefficients, SE, P-values, CI of the fixed effects with baseline and CER as reference.

Random effect and variability: For each food category, the high variance of the random effects for participants show large variability between individuals: liking HFSA (SD = 12.15), LFSA (SD = 16.80), HFSW (SD = 19.47), LFSW (SD = 11.71). For example, for liking HFSW, it means that 73% of the variability in the model is explained by the individual variability when the fixed effects have been accounted for.

Figure 8-3 illustrates individual and mean changes after ≥ 5% WL and 1-year follow-up and Table 8-2 reports the estimates, SE, P-values, CI of the fixed effects with baseline and CER as reference, variance and SD for random effects, and goodness of fit measures.

Table 8-2: Mixed model for pre-lunch liking after ≥ 5%WL and 1-year follow-up

	Model for HFSA	HFSA_PreLunch ~ MD + Condition_5percent + (1 | PPID)						
Fixed effect	*Variables*	*Estimate*	*SE*	*t-value*	*df*	*p-value*	*CI_lower*	*CI_higher*
	(Intercept)	59.49	3.95	15.06	44.21	< .001	51.58	67.41
	Post-WL	-7.12	3.25	-2.19	42.78	0.034	-13.64	-0.60
	Follow-up	1.64	4.39	0.37	46.98	0.711	-7.11	10.5
	IER	8.65	5.52	1.56	30.46	0.128	-2.56	19.82
Random effect		*Variance*	*SD*					
	PPID	147.5	12.15					
	Residuals	153.2	12.38					
	Number of obs	Groups: 71; PPID: 29						
Goodness of fit measures	Conditional R^2: 0.537; Marginal R^2: 0.091; AIC: 605.2; BIC:619.2							
	Model for LFSA	LFSA_PreLunch ~ MD + Condition_5percent + (1 | PPID)						
Fixed effect	*Variables*	*Estimate*	*SE*	*t-value*	*df*	*p-value*	*CI_lower*	*CI_higher*
	(Intercept)	50.87	4.60	11.07	35.49	< .001	41.62	60.14
	Post-WL	-7.20	2.62	-2.75	42.26	0.009	-12.47	-1.95
	Follow-up	-4.19	3.60	-1.16	44.08	0.251	-11.35	3.12
	IER	5.62	6.81	0.82	29.59	0.416	-8.19	19.41
Random effect		*Variance*	*SD*					
	PPID	282.29	16.80					
	Residuals	99.81	9.99					
	Number of obs	Groups: 71; PPID: 29						
Goodness of fit measures	Conditional R^2: 0.751; Marginal R^2: 0.046; AIC: 599.9; BIC: 613.5							
	Model for HFSW	HFSW_PreLunch ~ MD + Condition_5percent + (1 | PPID)						
Fixed effect	*Variables*	*Estimate*	*SE*	*t-value*	*df*	*p-value*	*CI_lower*	*CI_higher*
	(Intercept)	53.20	5.37	9.91	35.47	< .001	42.40	64.04
	Post-WL	-7.48	3.15	-2.37	41.85	0.022	-13.81	-1.16
	Follow-up	-2.07	4.32	-0.48	43.80	0.635	-10.72	6.60
	IER	6.21	7.94	0.78	29.19	0.440	-9.94	22.23
Random effect		*Variance*	*SD*					
	PPID	379.3	19.47					
	Residuals	144.2	12.01					
	Number of obs	Groups: 71; PPID: 29						
Goodness of fit measures	Conditional R^2: 0.735; Marginal R^2: 0.038; AIC: 624.2; BIC: 637.8							
	Model for LFSW	LFSW_PreLunch ~ MD + Condition_5percent + (1 | PPID)						
Fixed effect	*Variables*	*Estimate*	*SE*	*t-value*	*df*	*p-value*	*CI_lower*	*CI_higher*
	(Intercept)	55.30	3.73	14.82	41.93	< .001	47.83	62.81
	Post-WL	-6.12	2.99	-2.05	41.41	0.047	-12.11	-0.13
	Follow-up	-0.60	4.04	-0.15	45.40	0.883	-8.7	7.48
	IER	4.14	5.25	0.79	29.04	0.437	-6.56	14.74
Random effect		*Variance*	*SD*					
	PPID	137.2	11.71					
	Residuals	129.3	11.37					
	Number of obs	Groups: 71; PPID: 29						
Goodness of fit measures	Conditional R^2: 0.536; Marginal R^2: 0.044; AIC: 595.5; BIC: 609.1							

MD: Measures Days with 3 levels “Baseline” [ref], “Post-WL” and “Follow-up”; Condition_5percent stands for the diets conditions either IER or CER [ref]; PPID: participant identification; (SE): standard error; (SD): standard deviation; (df): degree of freedom

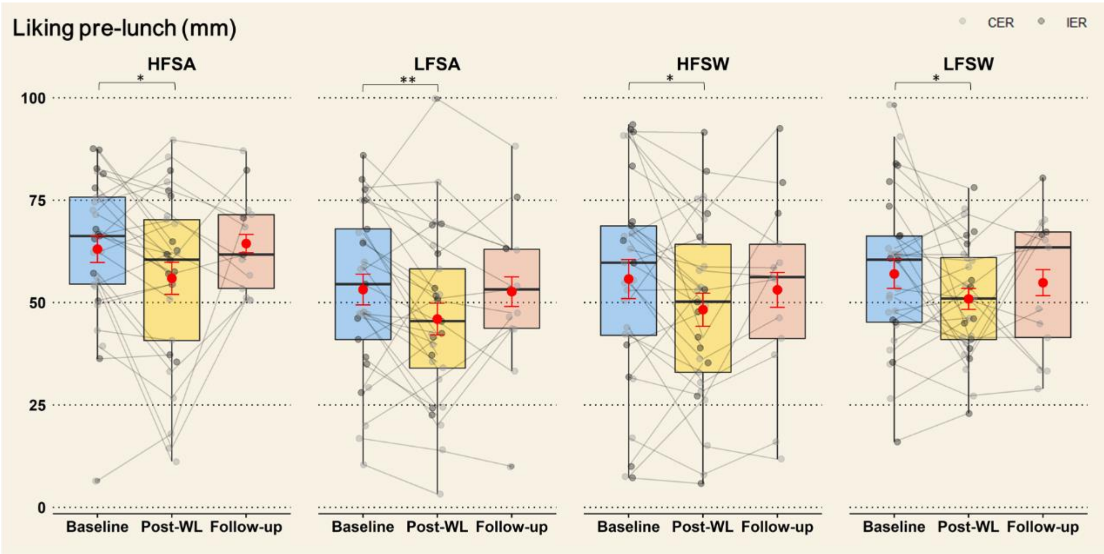

Figure 8-3: Liking for all food categories at baseline, WL (N = 28) and follow-up (N = 13)

The individual data are represented by points (light grey for CER and dark grey for IER) and showed that there was no difference between diets. Means are represented by red points with error bar (SE). Boxplots represent the variability of the data with the median (black line), interquartile range (coloured box) and whiskers representing minimum/maximum (Q ± 1.5*IQR). *Significant changes between baseline, post-WL and follow-up (*p < .05, **p < .01) CER: continuous energy restriction IER: intermittent energy restriction, HFSW: high-fat sweet, HFSA: high-fat-savoury, LFSW: low-fat sweet, LFSA: low-fat-savoury, WL: weight loss.

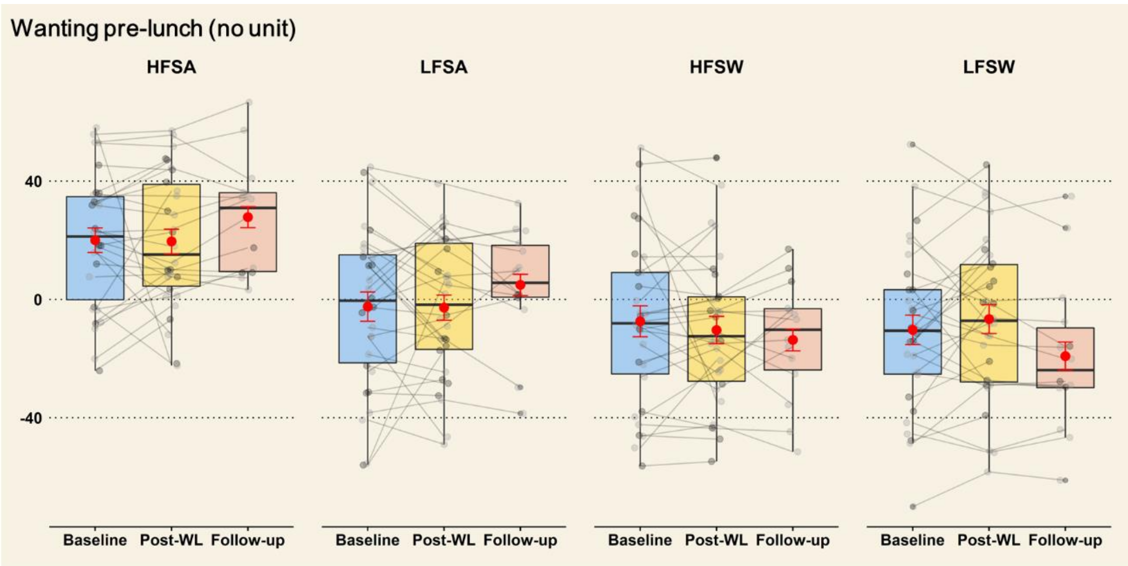

Figure 8-4: Wanting for all food categories at baseline, WL (N = 28) and follow-up (N = 13)

The individual data are represented by points (light grey for CER and dark grey for IER) and showed that there was no difference between diets. Means are represented by red points with error bar (SE). Boxplots represent the variability of the data with the median (black line), interquartile range (colored box) and whiskers representing minimum/maximum (Q ± 1.5*IQR). CER: continuous energy restriction IER: intermittent energy restriction

8.3.2.2 Changes in implicit wanting (pre-lunch)

Changes during WL and Follow-up: Linear mixed models showed no effect of time or diet on implicit wanting for the four food categories ($p \geq .171$). Implicit wanting at follow-up did not statistically differ from baseline and this was the case for each food category ($p \geq .222$). Post hoc analysis showed no significant changes in implicit wanting for each food category during follow-up [follow-up – post-WL] ($p > .381$).

Comparison between follow-up and baseline: For example, in the model for implicit wanting for HFSW the fixed effects explained 0.56% of the variance, with no effect of follow-up compared to baseline (beta = -0.51, SE = 4.61, 95% CI [-9.83, 8.67], $t(43) = -0.11$, $p = 0.913$) and no effect of diet (IER: beta = 2.92, SE = 9.41, 95% CI [-16.20, 21.94], $t(29) = 0.31$, $p = 0.759$).

Random effect and variability: Random effects for participants revealed a large variability between individuals for implicit wanting for each food category: HFSA (SD = 17.40), LFSA (SD = 20.27), HFSW (SD = 23.45), and LFSW (SD = 22.68). In other words, for implicit HFSW the variability between individuals explained 96% of the variability of the model when accounting for the fixed effect.

Figure 8-4 illustrates individual and mean changes after ≥5% WL and 1-year follow-up and Table 8-3 for mean changes, coefficients, SE, p-value and CI of the fixed effect and variance, SD for random effect by food category and goodness of fit measures.

Table 8-3: Mixed model for pre-lunch implicit wanting after WL and follow-up

	Model for HFSA	HFSA_PreLunch ~ MD + Condition_5percent + (1 | PPID)						
Fixed effect	*Variables*	*Estimate*	*SE*	*t-value*	*df*	*p-value*	*CI_lower*	*CI_higher*
	(Intercept)	18.99	4.95	3.84	37.20	< .001	9.01	28.93
	Post-WL	-0.50	3.19	-0.16	42.02	0.876	-6.90	5.90
	Follow-up	5.40	4.36	1.24	44.42	0.222	-3.29	14.20
	IER	-0.22	7.23	-0.03	29.44	0.973	-14.82	14.49
Random effect		*Variance*	*SD*					
	PPID	302.7	17.40					
	Residuals	147.5	12.15					
	Number of obs	Groups: 71; PPID: 29						
Goodness of fit measures	Conditional R2: 0.676; Marginal R2: 0.011; AIC: 619.7; BIC: 633.3							
	Model for LFSA	LFSA_PreLunch ~ MD + Condition_5percent + (1 | PPID)						
Fixed effect	*Variables*	*Estimate*	*SE*	*t-value*	*df*	*p-value*	*CI_lower*	*CI_higher*
	(Intercept)	-1.13	5.68	-0.20	36.02	0.843	-12.58	10.32
	Post-WL	-1.11	3.52	-0.31	41.59	0.755	-8.16	5.95
	Follow-up	-1.88	4.82	-0.39	43.78	0.699	-11.44	7.99
	IER	-3.58	8.35	-0.43	28.97	0.671	-20.51	13.34
Random effect		*Variance*	*SD*					
	PPID	411.1	20.27					
	Residuals	179.4	13.40					
	Number of obs	Groups: 71; PPID: 29						
Goodness of fit measures	Conditional R2: 0.698; Marginal R2: 0.006; AIC: 636.3; BIC: 649.9							
	Model for HFSW	HFSW_PreLunch ~ MD + Condition_5percent + (1 | PPID)						
Fixed effect	*Variables*	*Estimate*	*SE*	*t-value*	*df*	*p-value*	*CI_lower*	*CI_higher*
	(Intercept)	-8.31	6.30	-1.32	33.61	0.196	-21.02	4.42
	Post-WL	-2.52	3.35	-0.75	41.31	0.456	-9.25	4.20
	Follow-up	-0.51	4.61	-0.11	42.9	0.913	-9.83	8.67
	IER	2.92	9.40	0.31	28.6	0.759	-16.20	21.94
Random effect		*Variance*	*SD*					
	PPID	549.9	23.45					
	Residuals	163.0	12.77					
	Number of obs	Groups: 71; PPID: 29						
Goodness of fit measures	Conditional R2: 0.772; Marginal R2: 0.005; AIC: 639.2; BIC: 652.8							
	Model for LFSW	LFSW_PreLunch ~ MD + Condition_5percent + (1 | PPID)						
Fixed effect	*Variables*	*Estimate*	*SE*	*t-value*	*df*	*p-value*	*CI_lower*	*CI_higher*
	(Intercept)	-9.49	6.00	-1.58	33.90	0.123	-21.61	2.61
	Post-WL	4.13	2.97	1.39	42.35	0.171	-1.82	10.08
	Follow-up	-2.22	4.08	-0.54	43.68	0.589	-10.49	5.91
	IER	0.76	9.01	0.08	29.60	0.933	-17.48	19.02
Random effect		*Variance*	*SD*					
	PPID	514.6	22.68					
	Residuals	127.8	11.30					
	Number of obs	Groups: 71; PPID: 29						
Goodness of fit measures	Conditional R2: 0.803; Marginal R2: 0.010; AIC: 626.5; BIC: 640.1							

MD: Measures Days with 3 levels “Baseline” [ref], “Post-WL” and “Follow-up”; Condition_5percent stands for the diets conditions either IER or CER [ref]; PPID: participant identification; (SE): standard error; (SD): standard deviation; (df): degree of freedom

8.3.3 Individual differences in food reward during WL and follow-up

The random effects for the participants showed large individual variability in liking and implicit wanting responses. This variability can be illustrated by plotting the individual changes for each food category during WL and follow-up. Figure 8-5 and Figure 8-6 showed that not all individuals were increasing their liking or wanting for food during follow-up and some were indeed decreasing. However, it can be noticed that the variability of the changes during follow-up is larger than the variability during WL. In addition, with the small sample size during WL, this could explain why mixed models revealed that liking and wanting at 1-year follow-up did not differ from baseline while the changes from post-WL to follow-up were not significant. Larger sample sizes are needed to investigate this high individual variability and explore the relationship between changes in liking and wanting and changes in other psychobiological variables during weight management.

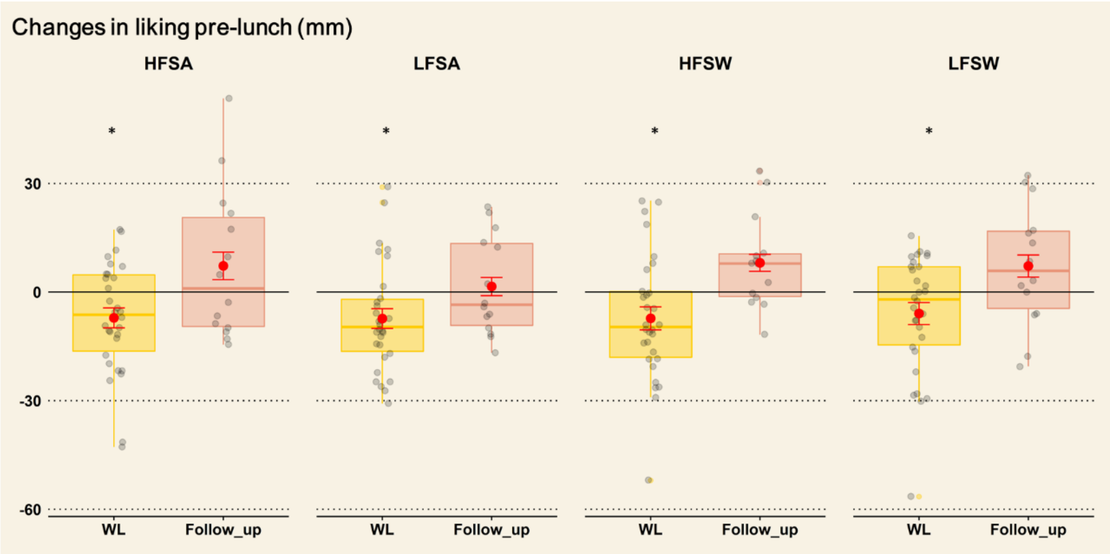

Figure 8-5: Individual changes in liking for all food categories during WL (N = 28) and follow-up (N = 13)

Boxplots represent the variability among changes in pre-lunch liking during WL and follow-up. The individuals' data are represented by points. Points above 0 represent an increase in liking whereas points below represent a decrease in liking. Both increase and decrease in liking can be observed during WL and follow-up but only decreases during WL were significant. Means are represented by red points with error bar (SE). *significant changes during WL and follow-up (*p < .05)

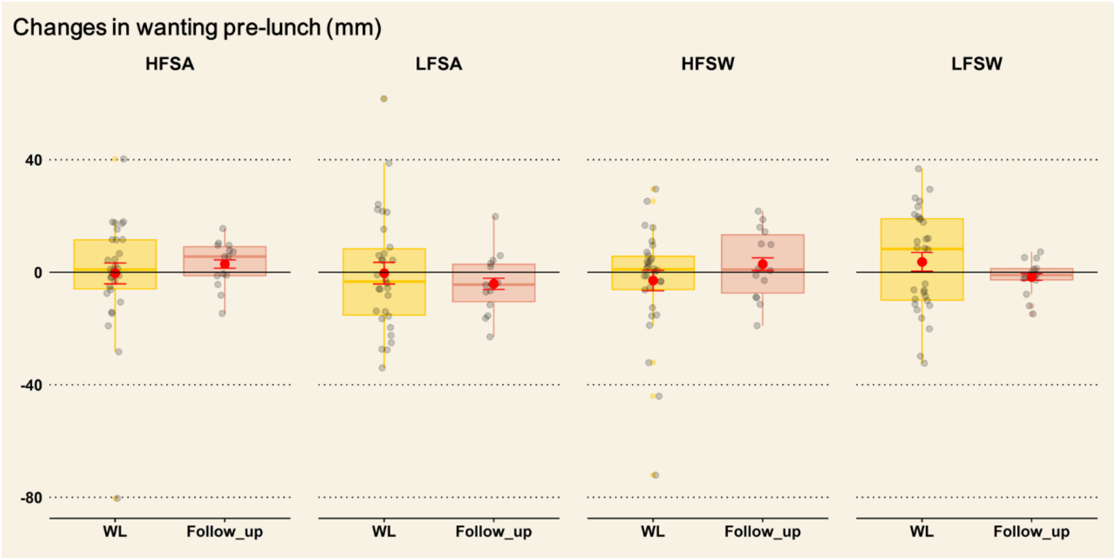

Figure 8-6: Individual changes in wanting for all food categories during WL (N = 28) and follow-up (N = 13)

Boxplots represent the variability among changes in pre-lunch implicit wanting during WL and follow-up. The individuals' data are represented by points. Points above 0 represent an increase in wanting whereas points below represent a decrease in wanting. Both increase and decrease in wanting can be observed during WL and follow-up but none were significant. Means are represented by red points with error bar (SE).

There was interest in exploring the case study of the outlier who increased her weight by nearly 20% to generate hypotheses explaining her large weight gain in comparison with the whole sample. She was allocated to the CER diet during WL. Figure 8-7 presents the changes in the main variables for eating behaviour traits (TFEQ, BES, CoEQ), body composition and food reward during WL and follow-up.

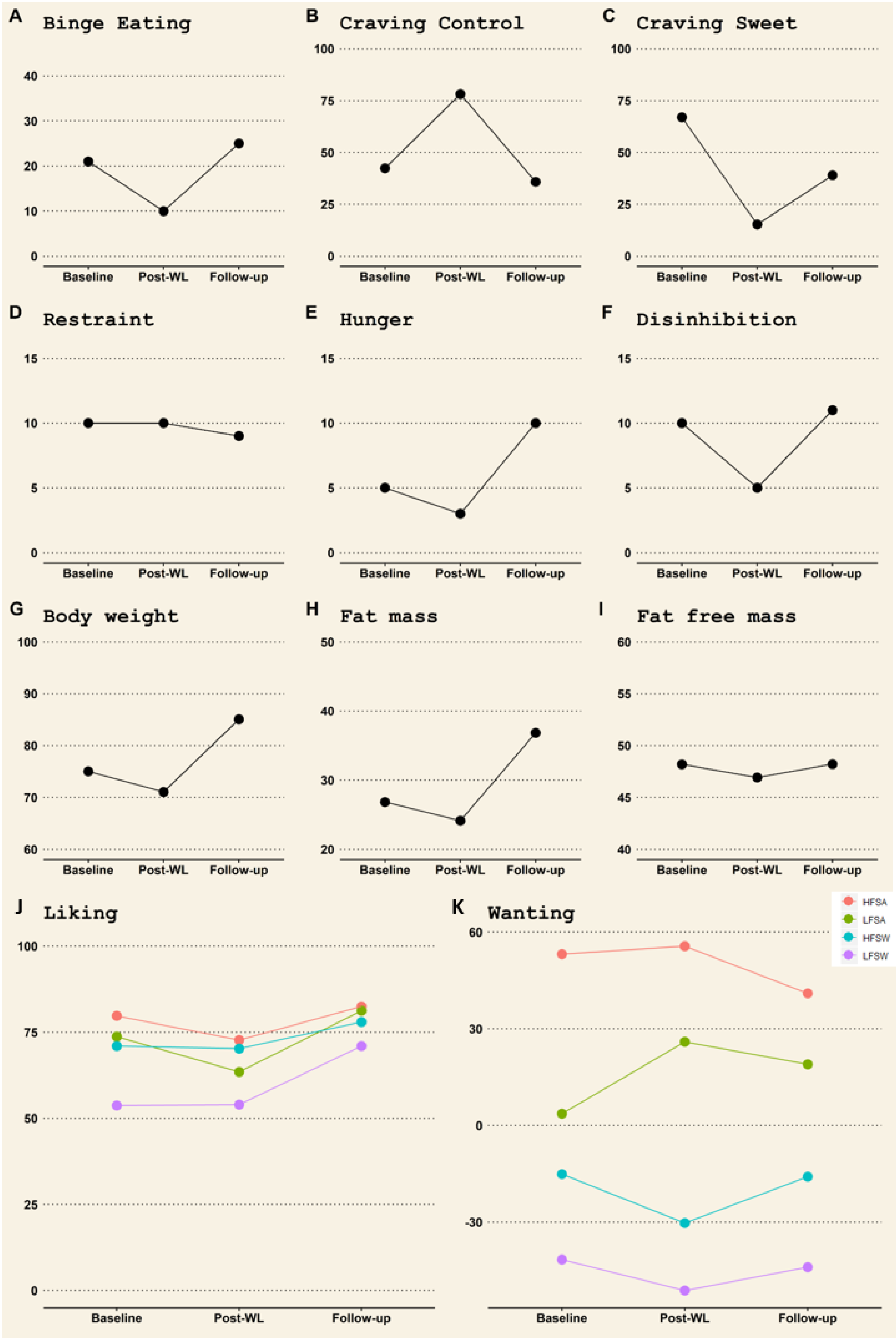

Figure 8-7: Changes in eating behaviour traits, body composition and reward from baseline to follow-up in the case study of the outlier

Body weight (kg), fat mass (kg), fat-free mass (kg), liking (mm), implicit wanting (no unit)

In terms of body composition, this woman was considered overweight at baseline (BMI = 27.73 kg/m^2) and obese at follow-up (BMI = 31.43 kg/m^2), her fat mass decreased by 2.7 kg during WL but increased by 12.7 kg during follow-up (outlier in comparison with the whole sample) while her fat-free mass did not change from baseline. Similarly, her RMR barely decreased during WL but increased by 267 kcal during follow-up.

Regarding appetite sensations, interestingly, her hunger (AUC) did not significantly decrease (-180 mm*min) during WL compared to the average decrease of -914 mm*min and came back to baseline value after follow-up. Moreover, her baseline hunger (AUC) did not differ from the average baseline hunger of the whole sample (5198 vs 5377 ± 2440 mm*min). Her changes in eating behaviour traits followed the pattern seen for the whole sample: decrease in Binge Eating, Susceptibility to Hunger, Disinhibition, Craving for Sweet and increase in Craving Control. However, her Restraint did not increase during WL compared to the whole sample (+4), and slightly decreased during follow-up. It should be noticed that she can be considered as an outlier (value >3*SD) for her change in Binge Eating, Craving Control and Disinhibition during follow-up.

Concerning food reward, this participant increased her scores for liking and implicit wanting for sweet foods at follow-up. Interestingly she was not an outlier in terms of changes in liking as her changes did not differ from the average changes at follow-up (e.g., change liking HFSW = 7.75 vs mean changes are 8.10 ± 13.35) but she already scored high in liking for fat from baseline (>70/100) and reached 80 after follow-up. Interestingly, in terms of changes during WL, liking almost did not change.

To conclude, most of her WL improvements were weakened or lost by the follow-up as values did not differ from baseline or were even higher. Her baseline characteristics suggest a phenotype with susceptibility to overconsumption with moderate Binge Eating (21), high Disinhibition (10), high liking for HFSW (71), high implicit wanting for HFSA (53.1) and low Craving Control (42.4).

8.3.4 Changes in other psychobiological variables during follow-up

8.3.4.1 Changes in physiological variables during follow-up

Changes during WL and Follow-up: Linear mixed models were performed on body weight, %fat mass, fat-free mass, RMR and BMI to evaluate the effect of time and diet during WL and follow-up (Table D4 in Appendix D). There was a main effect of time but no effect of diet on any of the physiological variables. Values at post-WL and at follow-up differed from baseline. Post-hoc tests showed significant changes from post-WL to follow-up for all the physiological variables ($p \leq .027$).

Comparison between follow-up and baseline: Fixed effects at follow-up report differences with baseline scores. Body weight (beta = -2.53, SE = 0.46, 95% CI [-3.46, -1.61], $t(43) = -5.48$, $p < .001$), %fat mass (beta = -1.01, SE = 0.36, 95% CI [-1.73, -0.29], $t(43) = -2.80$, $p < .01$), fat-free mass (beta = -0.74, SE = 0.24, 95% CI [-1.22, -0.26], $t(43) = -3.06$, $p < .01$, and BMI (beta = -0.86, SE = 0.17, 95% CI [-1.21, -0.51], $t(43) = -4.93$, $p < .001$) decreased during WL then increased during follow-up but stayed significantly lower than the baseline scores (i.e. negative coefficients). RMR (beta = 209.51, SE = 29.95, 95% CI [148.94, 269.16], $t(44) = 7.00$, $p < .001$) did not change during WL but increased during follow-up and was significantly higher than baseline.

Figure 8-8 illustrates significant changes during WL or follow-up and the individual changes are drawn to display the individual variability. The left panel of the figure shows the 29 individuals (whole sample) while the right panel presents the 14 that returned for follow-up. The comparison of both panels enables the identification of participants that did not return for follow-up measurements. It can be noticed that the "missing participants" are located in the third quartile of the boxplots for body weight, fat mass and fat-free mass, which means those with the higher weight, fat mass and fat-free mass. Consequently, as the missing data are not random, these are distorting the graphs (i.e. giving the impression of a decrease during follow-up) and therefore graphs using only the individuals coming back for follow-up have been drawn to illustrate WL and then weight regain half-way to baseline levels. Figure 8-8 also shows that the individual variability in the physiological changes was smaller than the variability in the food reward changes.

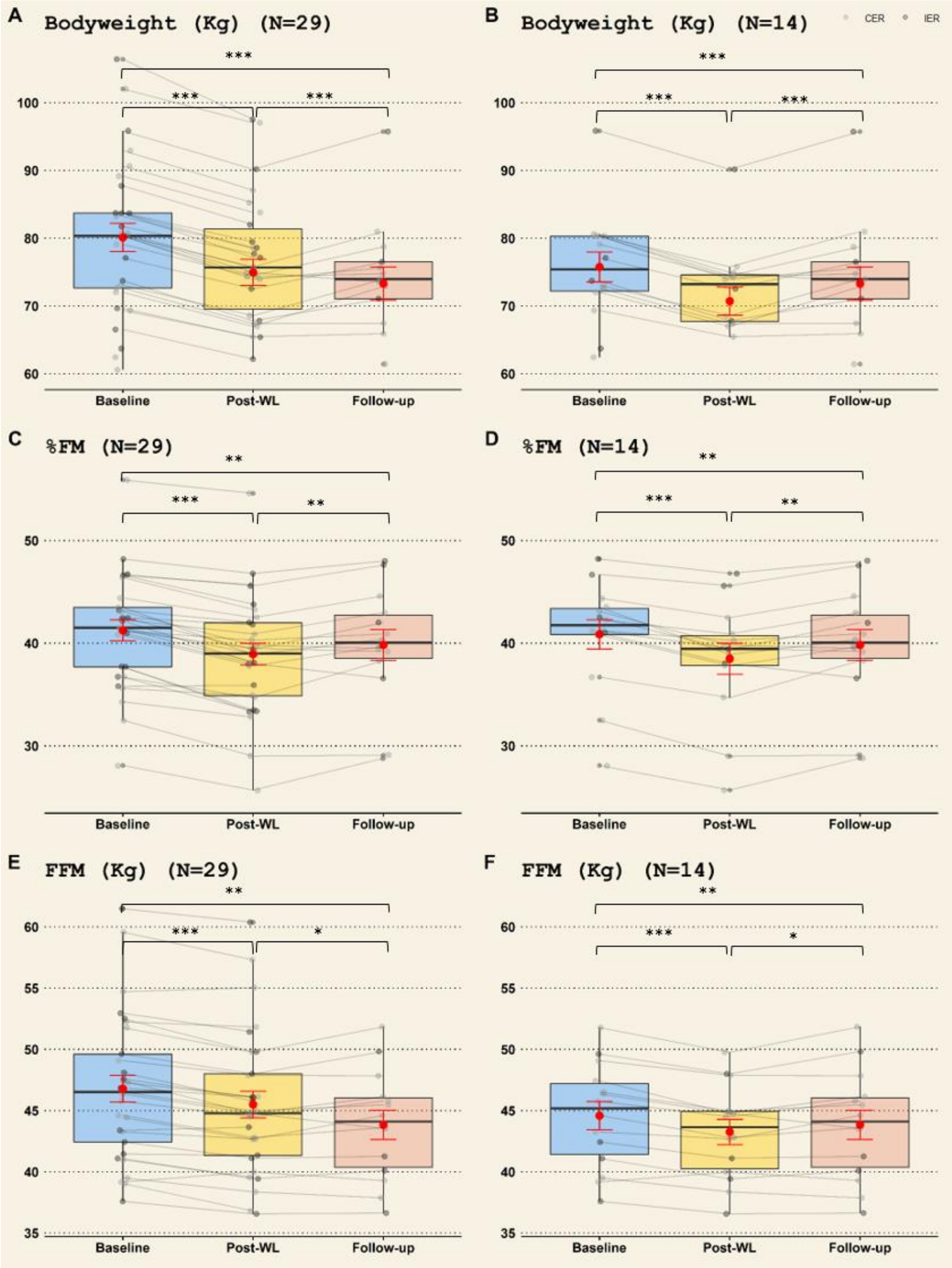

Figure 8-8: Changes in physiological variables during WL (N = 29) and follow-up (N = 14)

The left panel of the figure shows changes in physiological variables during WL and follow-up on the 29 participants, whereas in the right panel figures displayed the 14 participants that return for follow-up to account for the visual distortion due to missing data. FM: fat mass, FFM: fat free mass

8.3.4.2 Changes in psychological variables during follow up

Changes during WL and Follow-up: Linear mixed models were performed on eating behaviour traits to evaluate the effect of time and diet during WL and follow-up (Table D5 in Appendix D). There was a main effect of time but no effect of diet on any of the psychological variables. Post-hoc test showed significant decrease from post-WL to follow-up for Craving Control (p = .0002), Restraint (p = .028) and increase for Craving Savoury (p = .039), Susceptibility to Hunger (p = .020), Disinhibition (p = .041), but no significant changes for Craving Sweet (p = .163), MEQ (p = .348), IES (p = .172), BES (p = .250) and PFS (p = .339).

Comparison between follow-up and baseline: In terms of differences between scores at follow-up with baseline (p-values [follow-up – baseline] are reported): Binge Eating decreased during WL and was the only eating behaviour trait variable remaining significantly lower than baseline scores at follow-up (beta = -3.45, SE = 1.42, 95% CI [-6.31, -0.63], t(44) = -2.44, p = .019). Indeed, Binge Eating decreased from 15.24 ± 8.42 to 10.13 ± 6.30 during WL and remained at 10.84 ± 5.73 at follow-up. Craving Control (p = .673), and Restraint (TFEQ) (p = .054) increased during WL and decreased back to baseline at follow-up. Craving for sweet (p = .163), Craving for Savoury (p = .455), Susceptibility to Hunger (p = .325) and Disinhibition (p = .682) decreased during WL and did not differ from baseline scores at follow-up. Intuitive Eating (p = .086) and Mindful Eating (p = .112) increased during WL and did not differ from baseline scores at follow-up.

Figure 8-9 and Figure 8-10 showed the individual changes during WL and follow-up. Interestingly Binge Eating and Craving Control have less individual variability during follow-up than the other eating behaviour traits and the latter seemed more variable than the physiological changes.

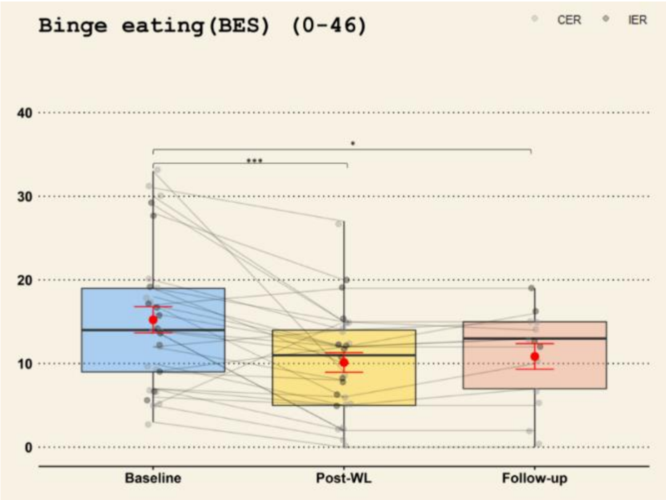

Figure 8-9: Changes in Binge Eating during WL (N = 29) and follow-up (N = 14)

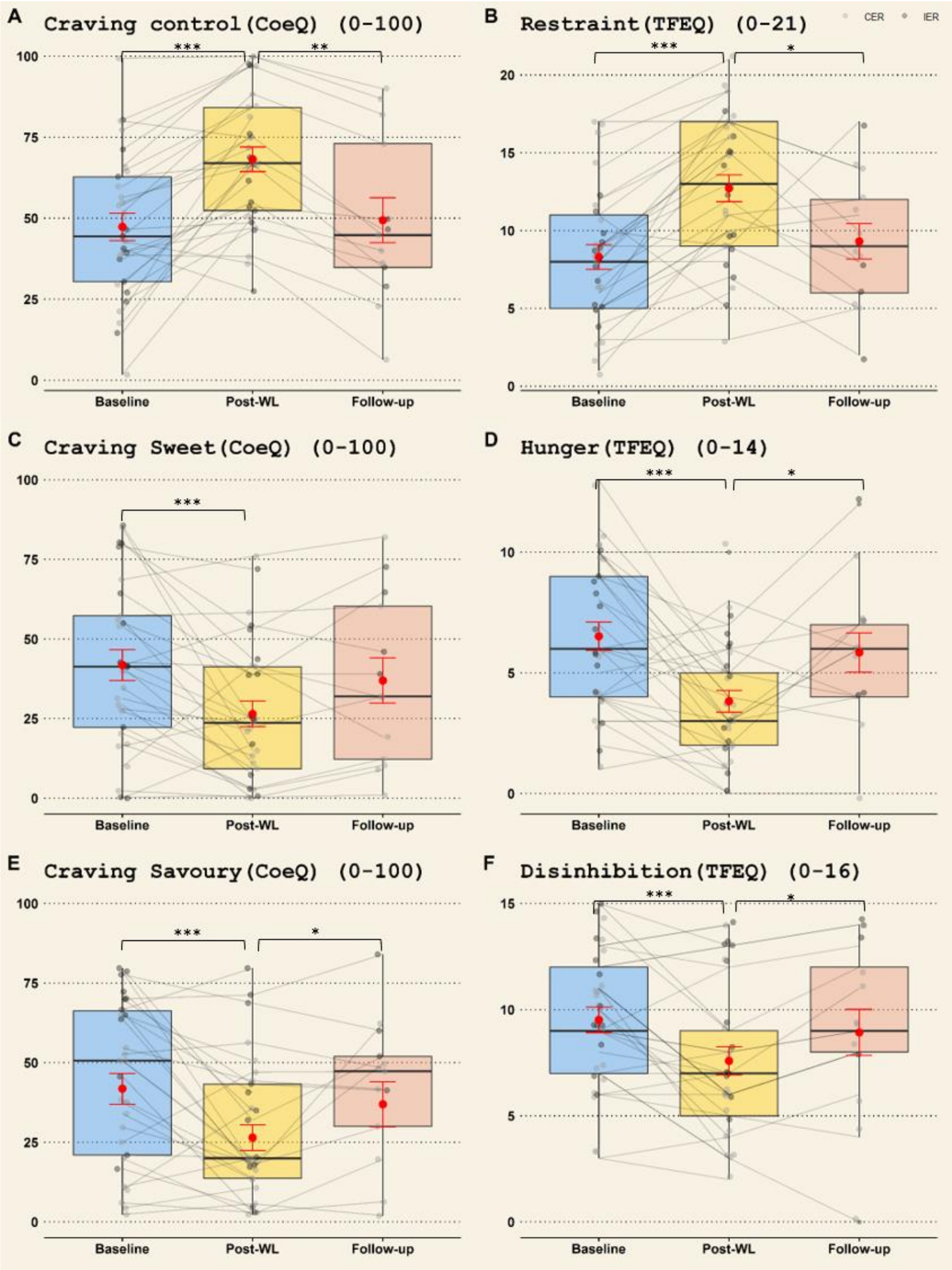

Figure 8-10: Changes in eating behaviour traits during WL (N = 29) and follow-up (N = 14)

8.3.4.3 Changes in appetite sensations and food intake during follow-up

Changes during WL and Follow-up: Linear mixed models were performed on subjective appetite variables (AUC) and food intake during the test meal to evaluate the effect of time and diet during follow-up and WL (Table D6 in Appendix D). There was a main effect of time for hunger, fullness and desire to eat and no effect of diet. Post hoc test showed no significant changes from post-WL to follow-up for desire to eat (p = .480), fullness (p = .367), hunger (p = .491) or prospective consumption (p = .779).

Comparison between follow-up and baseline: In comparison with baselines scores, mixed models showed that: desire to eat and hunger decreased during WL but did not differ from baseline scores at follow-up respectively p = .177 and p = .194. Prospective consumption did not change during WL and did not differ from baseline value at follow-up (p = .590). Interestingly fullness did not differ from baseline during WL but differed from baseline at follow-up (beta = 1191.08, SE = 516.73, 95% CI [148.43, 2220.27], t(46) = 2.31, p = .026) and can be considered as small effect (std. beta = 0.45, std. SE = 0.19). This might be an artefact that individuals with lower fullness did not return for follow-up measurements (see Figure 8-11).

Figure 8-11 illustrates the individual variability in the appetite sensations changes and attests that individuals are following different patterns of changes.

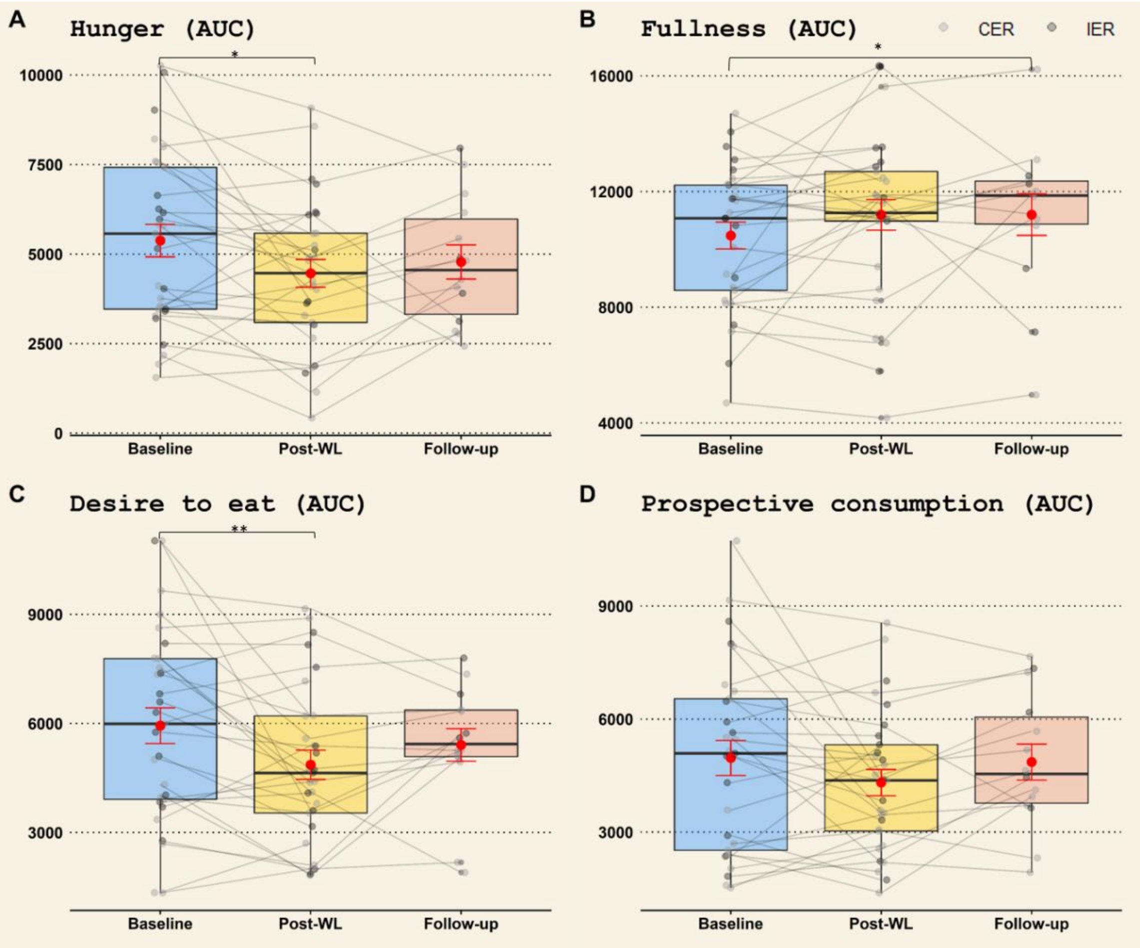

Figure 8-11: Changes in appetite sensations during WL (N = 29) and follow up (N = 14)

AUC: Area under the curve

Changes during WL and Follow-up: With regards to energy intake, there was no main effect of time and diet. Post hoc tests showed no significant changes from post-WL to follow-up.

Comparison between follow-up and baseline: The energy intake from risotto did not change during WL but was approaching a higher score than baseline at follow-up (beta = 88.92, SE = 51.85, 95% CI [-14.22, 196.46], t(48) = 1.71, p = .093) with no effect of diet. The energy intake from yoghurt decreased during WL but did not differ from baseline scores at follow-up. As for total lunch energy intake there was no changes during WL and no differences between follow-up and baseline scores. See Table D7 in Appendix D for coefficients, SE CI and p-values.

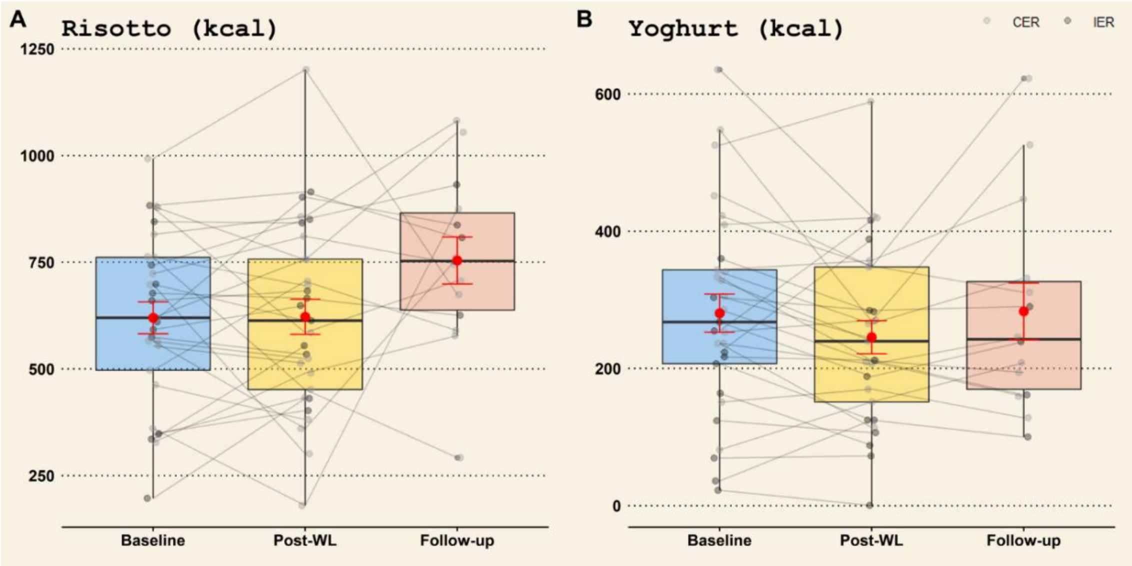

Figure 8-12: Changes in food intake (test meal) during WL (N = 29) and follow-up (N = 14)

8.4 Discussion

This Chapter aimed to explore 1) changes in pre-lunch food reward after 1-year follow-up without contact compared to baseline and post-WL, 2) changes in physiological variables, eating behaviour traits, appetite sensations and food intake in order to put in context the hedonic changes, 3) the potential effect at follow-up of the diet modalities (CER vs IER) on all these variables.

Liking and implicit wanting (pre-lunch) did not change significantly from post-WL to follow-up with large individual variability of the estimates. Moreover, food reward scores at 1-year follow-up did not differ from baseline scores. This 1-year follow-up was associated with an average of 3.6% weight regain, 1.3% increase in %fat mass and fat free mass staying lower than baseline scores. Improvements in eating behaviour traits were not maintained during follow-up and scores returned to baseline; with the exception of Binge Eating which remained lower than baseline scores and did not change during follow-up. Appetite sensations and energy intake did not change during follow-up and follow-up scores did not differ from baseline scores. This appeared to be independent from the modality of WL (CER vs IER), although limited sample size precludes any strong inferences. Thorough data analysis illustrated the high individual variability in psychological variables but did not help to understand the mechanisms of changes taking place during follow-up.

8.4.1 Changes in pre-lunch food reward during follow-up

It could seem contradictory that liking decreased during WL, then did not significantly change during follow-up and did not differ from baseline at follow-up. However, this could be explained by the lack of power to detect a change in a reduced sample size with large individual variability. Indeed, the size of the estimates were similar during WL and follow-up but the sample size was reduced by half and the variability was larger. To sum up, the decrease in food reward (liking) during WL was not sustained after 1-year without contact which is consistent with the observed weight regain after returning to a free-living diet.

Whilst the literature on food reward during WL maintenance is scarce, Buscemi et al. (2017) showed that food craving decreased in a linear manner during the first 6 months of WL and then did not significantly change during the 1-year follow-up. Interestingly, BMI decreased during WL but increased marginally during follow-up. While in this current study, Craving is considered as a separate construct from food reward (trait vs state), it measures a similar concept of susceptibility to food pleasure and is therefore worth comparing when state measures of food reward are not available in the literature. This result is similar to the current study and the non-significant increase during follow-up could be explained by the high variability in the estimates of food craving (Buscemi et al., 2017) and food reward.

However another study (Anton et al., 2012) found that food craving for fats, sweets and starches decreased up to 2 years of caloric restriction diets, while cravings for fruits and vegetables increased. As participants did regain weight during this follow-up, the maintained decrease in food cravings could be explained by the characteristics of the follow-up interventions in which participants are told to continue their intervention diets. Indeed in Anton et al. (2012) even though the frequency of meetings decreased from 3 out of 4 weeks, to 2 out of 4 weeks for the last 18 months of the study, participants met individually with their assigned dietician every 8 weeks for the whole program and were helped to increase adherence to the diet. While in (Buscemi et al., 2017) participants met twice a month during follow-up but with no specific mention of adherence to the intervention. In the current study, participants were not aware of the follow-up measures and therefore the absence of supervised follow-up might have weakened the benefit from the supervised diet on their food habits.

8.4.2 Changes in physiological variables, eating behaviour traits, appetite sensations and food intake.

It was shown that changes in liking during follow-up were not significant and the values at follow-up did not differ from baseline, suggesting that the decrease in liking during WL was not maintained. One might ask what does it mean clinically? To understand the relevance of the changes in liking during follow-up, there is a need to put these changes in perspective of other psychobiological changes during follow-up.

After 1-year follow-up, nearly 4% weight regain with 1.3% increase in %fat mass on average. On the contrary, an alternate day fasting study showed a WL of 5.5% that remained stable during 3-month follow-up (Kalam et al., 2019). In another study by Sundfør et al. (2018), individuals with obesity lost an average of 8% body weight and regained only about 1% 6 months later with no difference between CER and IER. However, similarly to this study, a 12-week intervention leading to 6.5% WL showed that weight was regained after 1-year follow-up (Ash et al., 2003). These discrepancies in WL maintenance underline the interplay between physiology and behaviour and the importance of addressing automatic eating behaviour processes during the follow-up phase (Stubbs et al., 2019). Indeed, the successful weight maintenance included behavioural strategies and were planned before WL: in Kalam et al.(2019), participants continued to consume three meal replacements, and in Sundfør et al.(2018), there was no face to face counselling during follow-up but participants could contact investigators and were encouraged to monitor their weight and food intake. In contrast, in Ash et al.'s study and in the current study, participants were not informed of the follow-up study at the commencement of the intervention and there was no contact during follow-up. Without regular follow-up, or incentive to keep the new eating habits developed during the diet, the improvements might not be maintained (Evans et al., 2019).

In terms of eating behaviour traits, the improvement seen during WL seemed to be weakened at follow-up. Indeed, during follow-up, Craving Control and Restraint decreased while Craving for Savoury, Susceptibility to Hunger and Disinhibition increased. These changes are in line with the weight regain during follow-up. On the contrary, another energy restriction study showed a maintenance of the improvement observed during follow-up including increased flexible restraint and decreased disinhibition (Morin et al., 2018). This could be explained by the improvement of their eating habits during follow-up reflected by decreased energy intake and WL maintenance. Indeed, higher Disinhibition has been associated with higher energy intake, BMI, fat mass, poor diet quality, Binge Eating, Craving and especially weight regain following

WL (Bryant et al., 2019). The evidence for decreased Restraint and WL maintenance are more conflicting. Higher Restraint has been associated with lower food intake (French et al., 2014), successful WL (Urbanek et al., 2015), better weight regulation and diet quality (Bryant et al., 2019). On the other hand, Restraint can also be related to poorer diet and overeating (Bellisle et al., 2004). This discrepancy could be explained by a conflict between the expectation of weight control and the enjoyment of food in an obesogenic environment (Bryant et al., 2019). Further studies need to investigate the role of eating behaviour traits and especially investigate the distinction between rigid and flexible Restraint in WL maintenance (Westenhoefer et al., 1999).

With regards to appetite sensations and food intake, improvements in appetite sensations (i.e. decrease in hunger and desire to eat) were not maintained at follow-up. Food intake from the test meal did not change during WL but the energy intake from risotto approached a significant increase during follow-up which is in line with weight regain and increased disinhibition. Free-living food intake changes during follow-up remain to be investigated. Only a few studies have measured appetite sensations and food intake during WL maintenance. One found no change in appetite sensations during WL and follow-up but reported a decrease in energy intake assessed by FFQ (Morin et al., 2018) but self-report dietary intake methods have been heavily criticised (Dhurandhar et al., 2015). Another study showed that a reduction in appetite sensations during WL maintenance seems to be associated with improved weight management (Hansen et al., 2019). Mechanisms during WL and WL maintenance contributing to a decrease in hedonics, appetite sensations and energy intake remain to be investigated to prevent weight regain. For example, a recent systematic review reported an effect of food texture (form, viscosity, structural complexity) on satiety which is key for weight management (Stribiţcaia et al., 2020); the effect of food texture on food reward and weight management therefore needs to be explored.

Finally, the analysis of the outlier participant who increased her weight by nearly 20% during follow-up presented the opportunity to explore correlates of weight regain and question whether her weight regain was influenced by physiological or psychological compensatory responses during WL. Indeed, during follow-up this participant increased her Binge Eating, Craving for Sweet, Susceptibility to Hunger, Disinhibition and liking and implicit wanting for sweet while Craving Control decreased. During WL, her fat-free mass did not change and her RMR barely decreased and therefore may not act as compensatory physiological adaptations (Melby et al., 2017); on the contrary the decrease in fat mass could contribute to the weight regain (Turicchi et al., 2019). Behavioural and psychological responses to WL need also to be investigated to understand weight regain (Casanova et al., 2019a; Stubbs et al., 2019). For example, in comparison with the whole sample, her appetite sensations (i.e. hunger) did not decrease during WL, liking barely decreased and her Restraint did not improve. This shows that she responded differently to the dietary WL and this poor response might have led to weight regain. Moreover, her baseline characteristics (Binge Eating, Disinhibition, high liking for sweet and low Craving Control) suggested a poor appetite control (Bryant et al., 2019). Consequently, it could be hypothesised that her behavioural and psychological characteristics led to weight regain.

8.5 Limitations

The limitations to the current study need to be acknowledged. The first one being the high drop-out at 1-year follow-up. This could be explained by the fact that participants were not aware of the follow-up measurements at the end of WL and that no contact was made, and participants reported being no longer available for the last measurement day which could have been influenced by their weight maintenance success. This loss to follow-up is important and therefore, the conclusions made from the follow-up analysis are limited and cannot be generalized to a larger population. However, the fact that the decrease in liking was not maintained during follow-up is consistent with the weakening of other appetite control variables such as eating behaviour traits and appetite ratings that improved during WL. Larger sample sizes are needed to conclude on the role of liking and wanting in weight management and weight regain and its mechanisms and more specifically the effect of CER vs IER remains to be explored.

Unfortunately, the sample size was too small (13 participants in follow-up) to perform further analysis of the relationship between changes in liking during follow-up and changes in other psychobiological variables. It should be noted that the analysis investigating changes in liking during WL was performed (Chapter 7) and showed that the decrease in liking HFSW was not related to any changes in biopsychological variables. These could be explained by the large individual variability and the small sample size, and therefore conclusions about mechanisms behind these changes cannot be drawn.

As suggested by Bryant et al. (2019) it remains to be understood whether the WL itself leads to change in eating behaviour traits and reward, or whether the changes in eating behaviour traits or reward cause the WL, or an interaction between the two. The follow-up was not supervised or planned, which could explain the discrepancies with other studies. It would have been interesting to collect information about participants' eating behaviour at the 1-year follow-up to know whether participants continued their respective diet interventions. This would have informed us about the willingness to follow the intervention in a free-living situation. However, it gave a picture of what might happen in a free-living scenario without any weight management plan post-intervention. Further studies need to compare different types of weight management interventions to analyse their effect on the psychological and behavioural improvements with WL.

8.6 Conclusion

Heightened hedonic responses to food has often been proposed to explain unsuccessful WL or weight regain. However, prior to the current study, changes in liking and implicit wanting had not been explored during follow-up after a dietary intervention that led to clinically significant WL. This study explored changes in pre-lunch food reward alongside changes in appetite, eating behaviour, food intake and body composition in order to get a better picture of the control of appetite during a free-living follow-up. Changes in liking during follow-up were not significant but were accompanied by weight regain, an increase in Disinhibition, and food Cravings, and a decrease in Restraint and Craving Control. Consequently, beneficial post-WL changes in appetite control did not remain after 1-year follow-up with no contact. Detailed data analysis showed the high individual variability in psychological variables but did not help to explain any mechanism of changes, largely due to the reduced sample size. It could be proposed that the maintenance of dietary strategies to maintain healthy eating habits would help to sustain appetite control after WL (Evans et al., 2019). Further studies with larger sample size need to elucidate the role of liking and implicit wanting during follow-up, which should compare structured follow up with contact, versus no contact as per the current study.

Chapter 9

DIVA-1-2: Food reward and appetite control in women with or without overweight/obesity

Chapter aims:

1. Compare food reward and appetite control in women with overweight/obesity to women within the normal range of BMI

2. Examine the relationship between food reward and appetite control

HIGHLIGHTS

Part 1: Comparisons between groups

► Liking did not differ between women with or without overweight/obesity. Only fasted implicit wanting for low-fat sweet food was higher in women within the normal range of BMI.

► Women with overweight/obesity had higher Disinhibition, Susceptibility to Hunger, Binge Eating, and lower Craving Control, Mindful and Intuitive Eating. However, there was no difference in appetite sensations, food intake or Cravings for Sweet or Savoury foods.

Part 2: Correlations on the whole sample

► Food reward was associated with food intake, appetite sensations, eating behaviour traits and fat mass in women with and without overweight/obesity. These relationships seemed to differ depending on fasted and pre-lunch measures and food categories.

► Implicit wanting and liking for high-fat food (fasted and hungry) were associated with poorer appetite control (less Craving Control, more Binge Eating) and larger body weight, while implicit wanting for low-fat food seemed to be associated with the opposite pattern.

9.1 Introduction

While the role of exposure to food cues in overeating has been well documented, the question remains as to why some individuals manage to stay within the normal range of BMI. It is often proposed that individuals with obesity have greater reward from food taste than individuals within the normal range of BMI (i.e. reward surfeit theory) (Devoto et al., 2018). It has also been argued that individuals with obesity have weaker brain responsivity to food (i.e. reward deficit theory), causing overeating (Stice et al., 2015). Beyond the “Goldilocks principle” of obesity (i.e. reward surfeit vs deficit theory) (Stoeckel, 2010), five neurocognitive models of obesity have been proposed to explain what differs in terms of reward and cognition between individuals with and without obesity (Devoto et al., 2018; Stice & Yokum, 2016). Most fMRI studies tend to favour the incentive sensitisation theory of obesity to explain the hyperactivity of reward brain regions following food cues (Devoto et al., 2018; Stice & Yokum, 2016). However, a recent meta-analysis found no difference in brain activity in individuals within the normal range of BMI vs. individuals with obesity (Morys et al., 2020).

This evidence is mainly based on neuroimaging studies. However, fMRI studies do not reveal the specific role of behavioural liking and wanting (Devoto et al., 2018). Indeed, the reward surfeit theory implies an increase in liking (pleasure when eating the food). In contrast, the incentive sensitisation theory focuses on enhanced wanting (motivation to eat induced by a food cue). While some behavioural studies have reported greater liking (Rissanen et al., 2002), or greater wanting (Giesen et al., 2010) in individuals with obesity, the comparison of behavioural liking and implicit wanting for food cues varying in fat and taste in women with and without obesity has never been explored. Moreover, the difference between individuals with and without obesity seems to be affected by hunger state (fasted, fed) (Blundell et al., 2005) and requires further investigation.

As obesity is a complex phenomenon involving multiple systems (environmental, genetic, neuronal homeostatic, etc.), it cannot solely be explained by differences in a single variable. Therefore, food reward should be investigated in the context of broader markers (Berthoud et al., 2017) of appetite control, also referred to as control of food intake behaviours. The latter covers the whole field of food intake, appetite sensations, food preferences, motivation (Blundell et al., 2010) but also refers to all the variables that modulate food intake, such as body composition (especially fat-free mass) (Hopkins et al., 2018), energy expenditure (Blundell et al., 2020) and eating behaviour traits (e.g. restraint) (Yeomans et al., 2004). Exploring appetite-related variables is crucial in understanding obesity better.

It has been shown that individuals with obesity consume a greater variety of energy-dense food than their counterparts within the normal range of BMI (McCrory et al., 1999) and that obesity tends to be associated with impairment in inhibitory control (Devoto et al., 2018). In terms of appetite sensations, individuals with obesity seem to have a greater sensitivity to hunger and weaker satiation (Blundell et al., 2005; Devoto et al., 2018). Regarding eating behaviour traits, Binge Eating (BES) and Food Addiction (YFAS) have been characterised as behavioural phenotypes of obesity (Dalton et al., 2013c; Davis et al., 2011). High disinhibition has been consistently associated with obesity, while the association with restraint is less clear (Bryant et al., 2019). Similarly, mindful and intuitive eating seem to be negatively associated with BMI (Framson et al., 2009; Ruzanska & Warschburger, 2019) while Hedonic Hunger (PFS) appears to be more strongly associated with food intake than with BMI (Cappelleri et al., 2009). It remains to be investigated whether specific patterns of appetite control are found in individuals with obesity compared to individuals within the normal range of BMI.

Cross-sectional relationships between food reward and food intake (Dalton & Finlayson, 2014), fat mass (Hopkins et al., 2014), eating behaviour traits (Dalton & Finlayson, 2014) have been investigated in specific populations. However, the relationship between food reward and appetite-related variables for women varying in weight status has only been investigated in the Brazilian population and for binge eating solely (Carvalho-Ferreira et al., 2019). The associations between appetite-related variables and food reward components remain to be explored, as well as the effect of weight status. For example, Craving Control (Dalton et al., 2015), Mindful and Intuitive Eating (Dyke & Drinkwater, 2014) and Hedonic Hunger (Espel-Huynh et al., 2018) translate different facets of the reaction towards food cues but have never been explored in relation to liking and implicit wanting measured by the LFPQ.

Therefore, the analyses in this Chapter aimed to 1) Compare measures of food reward and appetite control in women with or without overweight/obesity, and 2) Explore the relationship between food reward and appetite control. To do so, these cross-sectional analyses first investigated the difference in appetite control and food reward between 46 women with overweight/obesity and 46 women within the normal range of BMI. Secondly, correlations were performed on the whole sample and then by group as a preliminary exploration of potential differences in the relationship between women with or without overweight/obesity. According to the incentive sensitisation theory, it was hypothesised that implicit wanting, but not liking, for high-fat food would be higher in individuals with overweight/obesity. Secondly, reward for high-fat food would be mainly associated with weakened appetite control in individuals with overweight/obesity.

9.2 Method

9.2.1 Cross-sectional data from DIVA-1 and 2

This analysis included 92 healthy women combined from two separate studies designed to follow the same experimental procedures in women with overweight/obesity (DIVA-1, N = 46, BMI = 25.0-34.9 kg/m^2) and women within the normal range of BMI (DIVA-2, N = 46, BMI = 18.5-24.9 kg/m^2). Studies were completed from February 2018 to September 2018 (DIVA-1) and from February 2019 to October 2019 (DIVA-2). DIVA-1 recruited participants with overweight/obesity to take part in a study examining “the effects of a personalised WL meal plan on body composition and metabolism”. This Chapter analysed DIVA-1 baseline data before diet allocation. DIVA-2 was designed to provide a baseline comparison group within the normal range of BMI for DIVA-1 (matched as possible for age) to assess the effect of weight status on appetite control and food reward (see Chapter 4 for details on eligibility criteria, recruitment and outcome measures).

The following outcomes were measured: food reward, appetite sensations (hunger, fullness, desire, prospective consumption) food intake during a test-meal, eating behaviour traits (primary: BES, TFEQ, CoEQ; secondary: MEQ, IES, YFAS, PFS[4]), body composition, RMR, energy expenditure and physical activity [daily minutes of total and moderate-to-vigorous physical activity measured by the SenseWear Armband (see Chapter 4) and physical activity level (PAL; daily energy expenditure divided by measured RMR)]. The LFPQ was used to assess explicit liking and implicit wanting components of food reward according to 4 categories of food (high-fat savoury: HFSA, low-fat savoury: LFSA, high-fat sweet: HFSW and low-fat sweet: LFSW). Liking and implicit wanting were measured 1) after an overnight fast (fasted reward before consuming breakfast); 2) before and 3) after an *ad libitum* test lunch that had a savoury and sweet food item (see Chapter 4) and consumed 3 hours after an individually-fixed breakfast (25% RMR).

9.2.2 Statistical analysis

Exploratory analyses were performed on the main variables of interest to assess normality (Shapiro Wilcoxon’s test, qqplot and density), determine outliers (boxplot), understand distribution and pattern (raw data, boxplot and density). For clarity and homogeneity, all descriptive statistics are reported as median and interquartile range (IQR) as most of the

4 As explained in Chapter 1, MEQ, IES, YFAS and PFS have never been compared to reward measured by the LFPQ and were therefore explored as a secondary aim to give an overview of the main eating behaviour traits involved with food reward, appetite control and obesity.

variables were non-parametric when analysing the whole sample (N = 92) (see Appendix E, Table E1).

To explore whether appetite control variables differed in women with or without overweight/obesity, each variable was plotted (density, boxplot and individual points) and a comparison was made between groups. The graphical representations go beyond the average and display the overlap between groups. The median age was 34 (17) years. Mann-Whitney-Wilcoxon test and t-test were performed to assess the differences between groups for each variable and Cohen's d was reported as a measure of effect size with d = .2 small effect, d = .5 medium effect and d = .8 large effect size (Cohen, 1988).

To investigate the relationship between food reward and appetite control according to weight status, correlations were performed for each appetite control variable, strength and direction of the relationship were illustrated by scatter plots (by group when significantly different). Summary tables outline the correlations by food reward variables (see Appendix E, Tables E7 to E10). Spearman's correlations (r_s) were performed on the whole sample between liking and implicit wanting for all food categories in the fasted state, pre- and post-lunch with all the appetite-related variables. Given the exploratory nature of this analysis (wide range of appetite-related variables) and the moderate sample size, a p-value of .01 instead of .05 was chosen to consider the multiple outcomes testing for each food reward component. All correlations were reported and the analysis took into account the multiple outcome comparison. Pearson's correlations (r) were performed to assess specific correlations within each group. Missing data for eating behaviour questionnaires were due to participants not returning the questionnaires in DIVA-2 or missing some questions in the questionnaires.

9.3 RESULTS PART-1: Comparison between groups with or without overweight/obesity

9.3.1 Body composition and energy expenditure

The two groups differed for all body composition variables with large effect sizes of the difference, except for fat-free mass, whose difference was of medium effect size with a larger overlap between groups (see Figure 9-1 and Table 9-1).

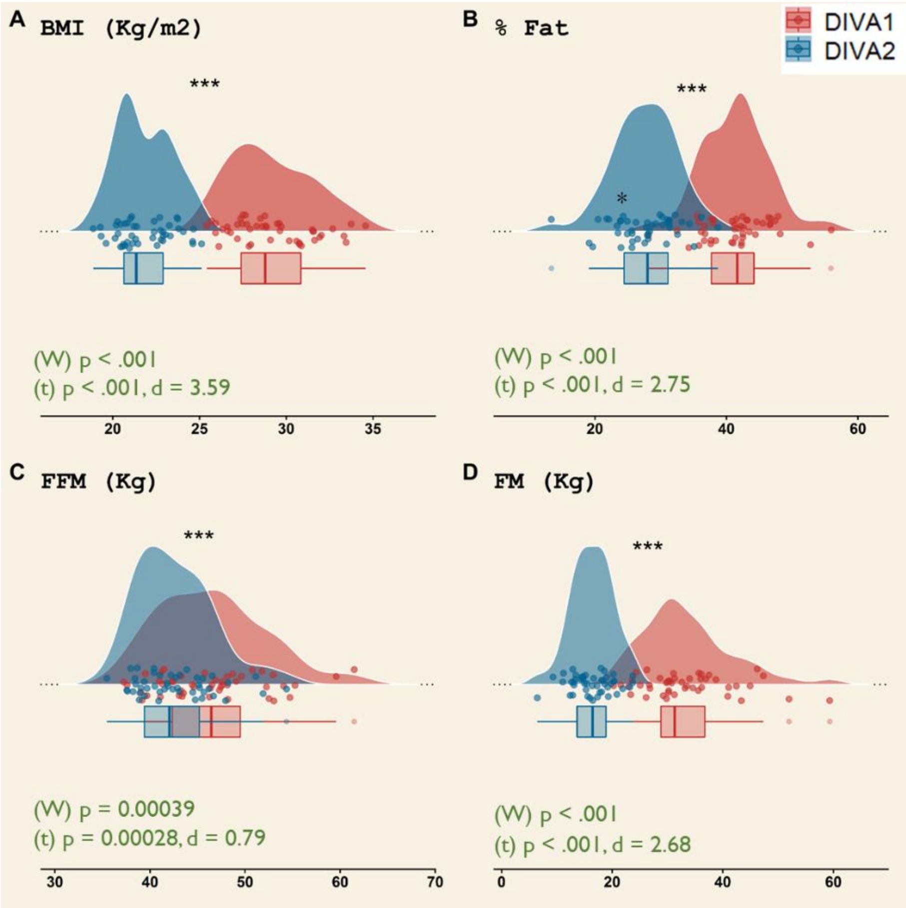

Figure 9-1: Body composition in women with or without overweight/obesity

Density[5], boxplots and individual points visualise differences between groups beyond the average and potential heterogeneity. ***p<.001, (t) t-test, (W) Wilcoxon test, (d) effect size Cohen's d, DIVA-1: women with overweight/obesity, DIVA-2: women within the normal range of BMI

Table 9-1: Difference in body composition between groups

Study	N	BMI (kg/m^2)	%Fat	FM (kg)	FFM (kg)
DIVA1	46	28.8 (3.4)***	41.6 (6.5)***	31.3 (7.9)***	46.4 (7.1)***
DIVA2	46	21.3 (2.2)***	28 (6.7)***	16.4 (5.2)***	42.0 (5.8)***

Data are median and interquartile range (IQR), differences between group assessed by t-test and Wilcoxon test. FM: fat mass, FFM: fat-free mass***p<.001

The two groups were matched as close as possible for physical activity (self-reported less than three days a week), but objectively measured physical activity was higher in the

[5] Densities are displayed to check both the normality and the dispersion of each variable per group. However, due to an artefact of the graphical representation of the tails, they seem to overlap more than they should (e.g, BMI do not overlap). A more precise overlapping of the data is illustrated by the boxplots and the individual points.

group within the normal range of BMI (large effect size). However, physical activity level (total daily energy expenditure divided by RMR) and RMR did not differ (see Figure 9-2 and Table 9-2).

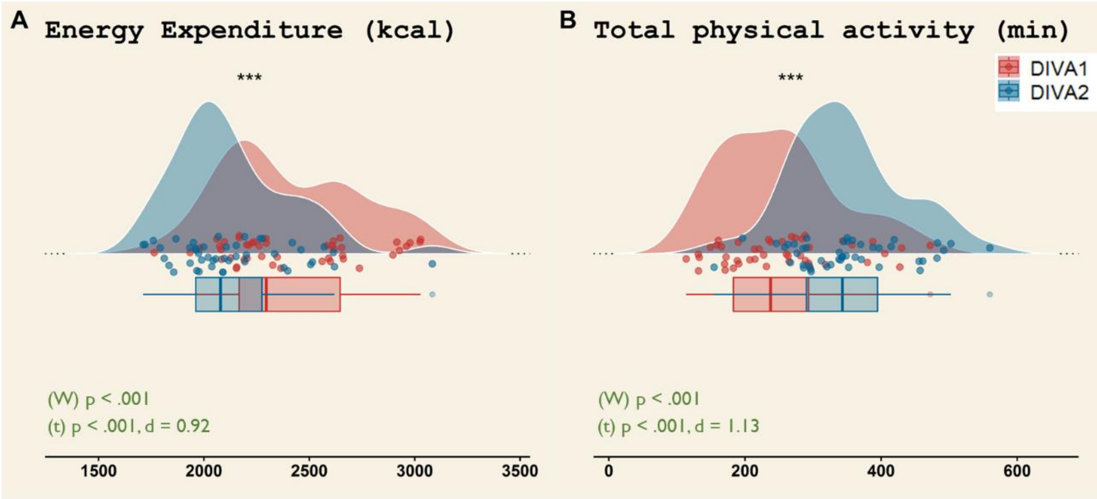

Figure 9-2: Energy expenditure in women with or without overweight/obesity

Density, boxplots and individual points visualise differences between groups beyond the average and potential heterogeneity. ***p<.001, (t) t-test, (W) Wilcoxon test, (d) effect size Cohen's d, DIVA-1: women with overweight/obesity, DIVA-2: women within the normal range of BMI

Table 9-2: Difference in energy expenditure between groups

Study	N	Total EE (kcal)	Total PA (min)	MVPA (min)	PAL	RMR (kcal)
DIVA1	46	2296 (479)***	238 (110) ***	76 (42)***	1.51 (0.17)	1451 (274)
DIVA2	46	2079 (315)***	343 (104) ***	110 (48)***	1.53 (0.15)	1398 (195)

Data are median and interquartile range (IQR), differences between group assessed by t-test and Wilcoxon test. ***p<.001, EE: Total energy expenditure, PA: physical activity, MVPA: medium to vigorous physical activity, PAL: physical activity level, RMR: resting metabolic rate, DIVA-1: N = 45 for EE, PA, MVPA and PAL

9.3.2 Eating behaviour traits

In terms of control over eating (CoEQ), only Craving Control differed between groups, with women within the normal range of BMI having a greater Craving Control than women with overweight/obesity (large effect size). Craving for Sweet and Savoury and Positive Mood did not differ between groups (see Figure 9-3, Table 9-3).

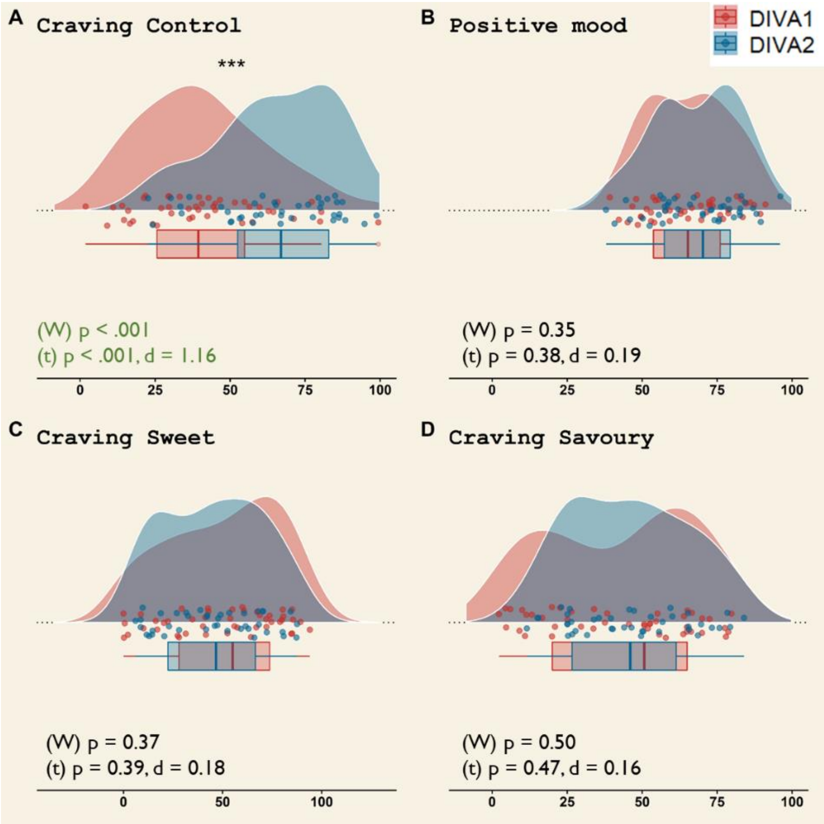

Figure 9-3: Craving in women with or without overweight/obesity

Density, boxplots and individual points visualise differences between groups beyond the average and potential heterogeneity. ***p<.001, (t) t-test, (W) Wilcoxon test, (d) effect size Cohen's d, DIVA-1: women with overweight/obesity, DIVA-2: women within the normal range of BMI

Table 9-3: Difference in control of eating between groups

Study	N	Craving Control	Craving Sweet	Craving Savoury	Positive Mood
DIVA1	45	39.4 (29.2)***	55 (45.7)	50.7 (45)	65.2 (22.2)
DIVA2	40	66.9 (30.4)***	46.67 (44.1)	46 (34.7)	70.2 (22)

Data are median and interquartile range (IQR), differences between group assessed by t-test and Wilcoxon test. ***p<.001

Women with overweight/obesity had greater Binge Eating (BES), Food Addiction Symptoms (YFAS), and less Mindful Eating (MEQ) and Intuitive Eating (IES). While, there was an overlap between groups for those variables, the effect size of the difference was large. There was no difference in Hedonic Hunger (PFS) (see Figure 9-4 and Table 9-4).

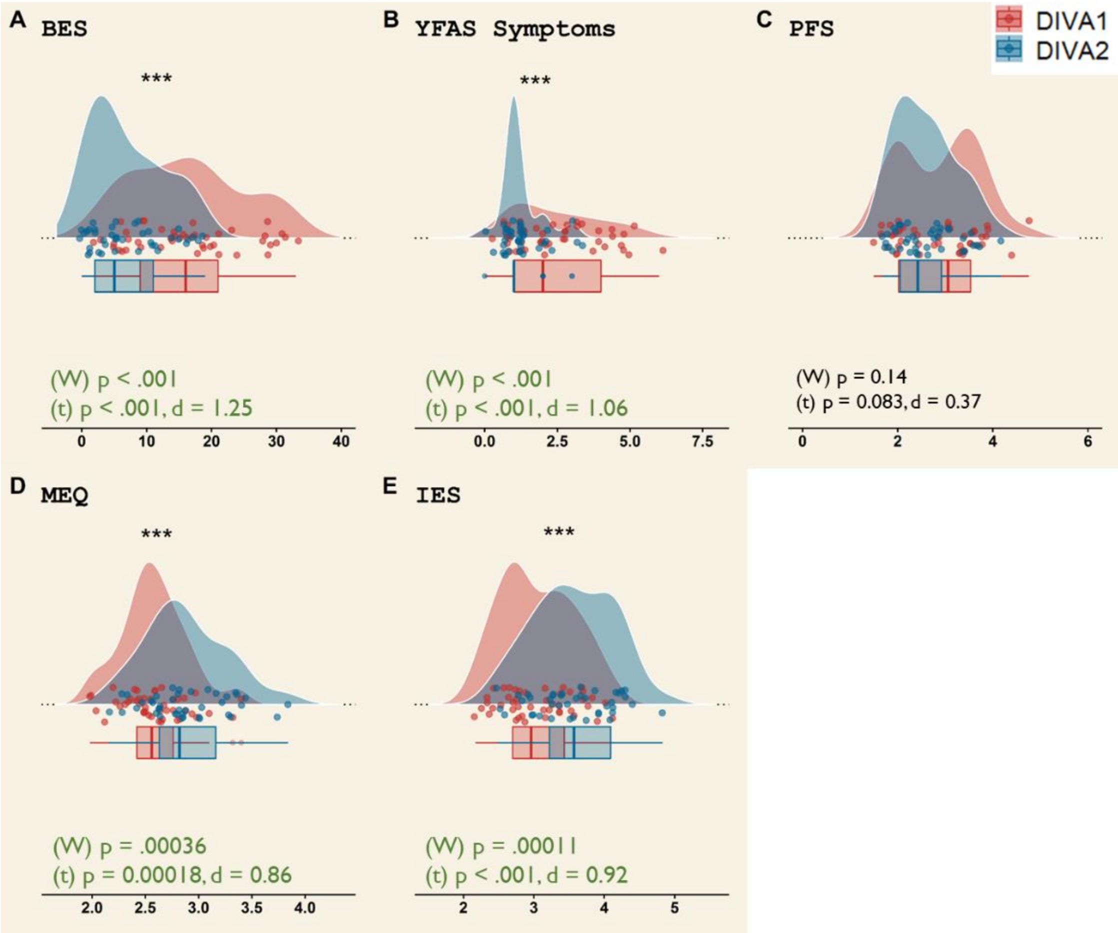

Figure 9-4: Eating behaviour traits in women with or without overweight/obesity

Density, boxplots and individual points visualise differences between groups beyond the average and potential heterogeneity. ***p<.001, (t) t-test, (W) Wilcoxon test, (d) effect size Cohen's d, DIVA-1: women with overweight/obesity, DIVA-2: women within the normal range of BMI

Table 9-4: Differences in eating behaviour traits between groups

Study	N	BES	YFAS	PFS	MEQ	IES
DIVA1	45	16 (12)***	2 (3)***	3.1 (1.5)	2.6 (0.3)***	2.9 (0.7)***
DIVA2	41	5 (9)***	1 (0)***	2.4 (0.9)	2.8 (0.5)***	3.6 (0.9)***

Data are median and interquartile range (IQR), differences between group assessed by t-test and Wilcoxon test. ***p<.001 DIVA-2 N = 40 for BES and YFAS

For TFEQ, only Disinhibition and Susceptibility to Hunger differed and were greater (large and medium effect size) in women with overweight/obesity (see Figure 9-5 and Table 9-5).

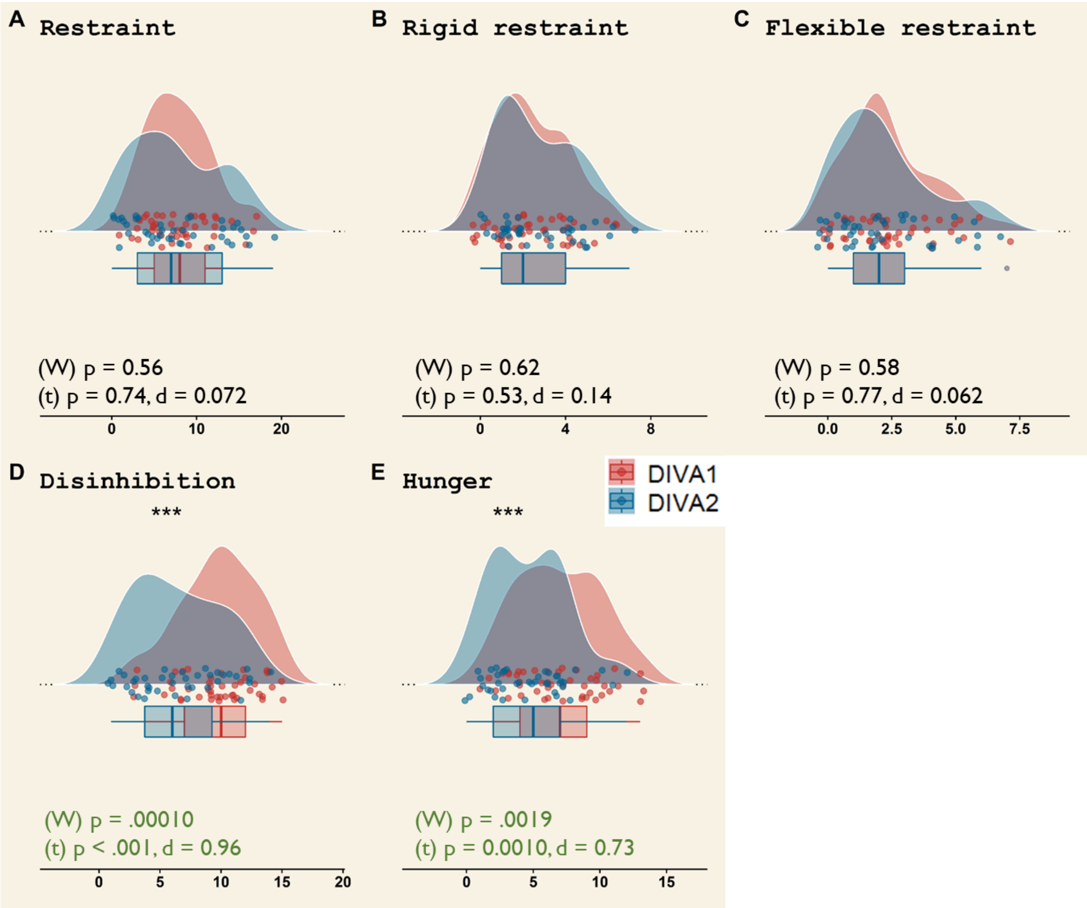

Figure 9-5: TFEQ in women with or without overweight/obesity

Density, boxplots and individual points visualise differences between groups beyond the average and potential heterogeneity. ***p<.001, (t) t-test, (W) Wilcoxon test, (d) effect size Cohen's d, DIVA-1: women with overweight/obesity, DIVA-2: women within the normal range of BMI, Hunger: Susceptibility to Hunger

Table 9-5: Differences in eating behaviour traits (TFEQ) between groups

Study	N	Restraint	Rigid Restraint	Flexible Restraint	Disinhibition	Susceptibility to Hunger
DIVA1	45	8 (6)	2 (3)	2 (2)	10 (5)***	7 (5)***
DIVA2	41	7 (10)	2 (3)	2 (2)	6 (6)***	5 (5)***

Data are median and interquartile range (IQR), differences between group assessed by t-test and Wilcoxon test. ***p<.001 DIVA-2: N = 40 for Restraint and Disinhibition N = 39 for Rigid Restraint

9.3.3 Appetite sensations

In terms of appetite sensations measured by VAS (area under the curve from pre-breakfast to post-lunch), there was no difference between groups for desire to eat, fullness, hunger or prospective consumption (see Figure E1 in Appendix E and Table 9-6).

Table 9-6: Differences in appetite sensations between groups

Study	N	Desire (mm*min)	Fullness (mm*min)	Hunger (mm*min)	Prospective consumption (mm*min)
DIVA1	46	6450 (4095)	10879 (3465)	5816 (4225)	5303 (4206)
DIVA2	46	6236 (4749)	10496 (2832)	6034 (4217)	5771 (3515)

Data are median and interquartile range (IQR), differences between group assessed by t-test and Wilcoxon test.

9.3.4 Food intake

Food intake objectively measured in the laboratory (test meal at lunch) did not differ between groups (see Figure E2 in Appendix E and Table 9-7).

Table 9-7: Differences in food intake between groups

Study	N	Lunch (kcal)	Risotto (kcal)	Yoghurt (kcal)
DIVA1	46	835 (280)	603 (279)	270 (170)
DIVA2	45	841 (284)	610 (281)	199 (204)

Data are median and interquartile range (IQR), differences between group assessed by t-test and Wilcoxon test.

9.3.5 Food reward

Differences between groups were only apparent in the fasted state for implicit wanting with a small to medium effect size. Only fasted implicit wanting for low-fat sweet differed between groups with women within the normal range of BMI wanting more low-fat sweet food than women with overweight/obesity. Based on the graphs and effect size, fasted implicit wanting for high-fat savoury seemed to be higher in individuals with overweight/obesity but was not statistically different.

No other difference in food reward appeared between groups (See in Appendix E, Figure E3 to Figure E7 and Tables E2 to E6)

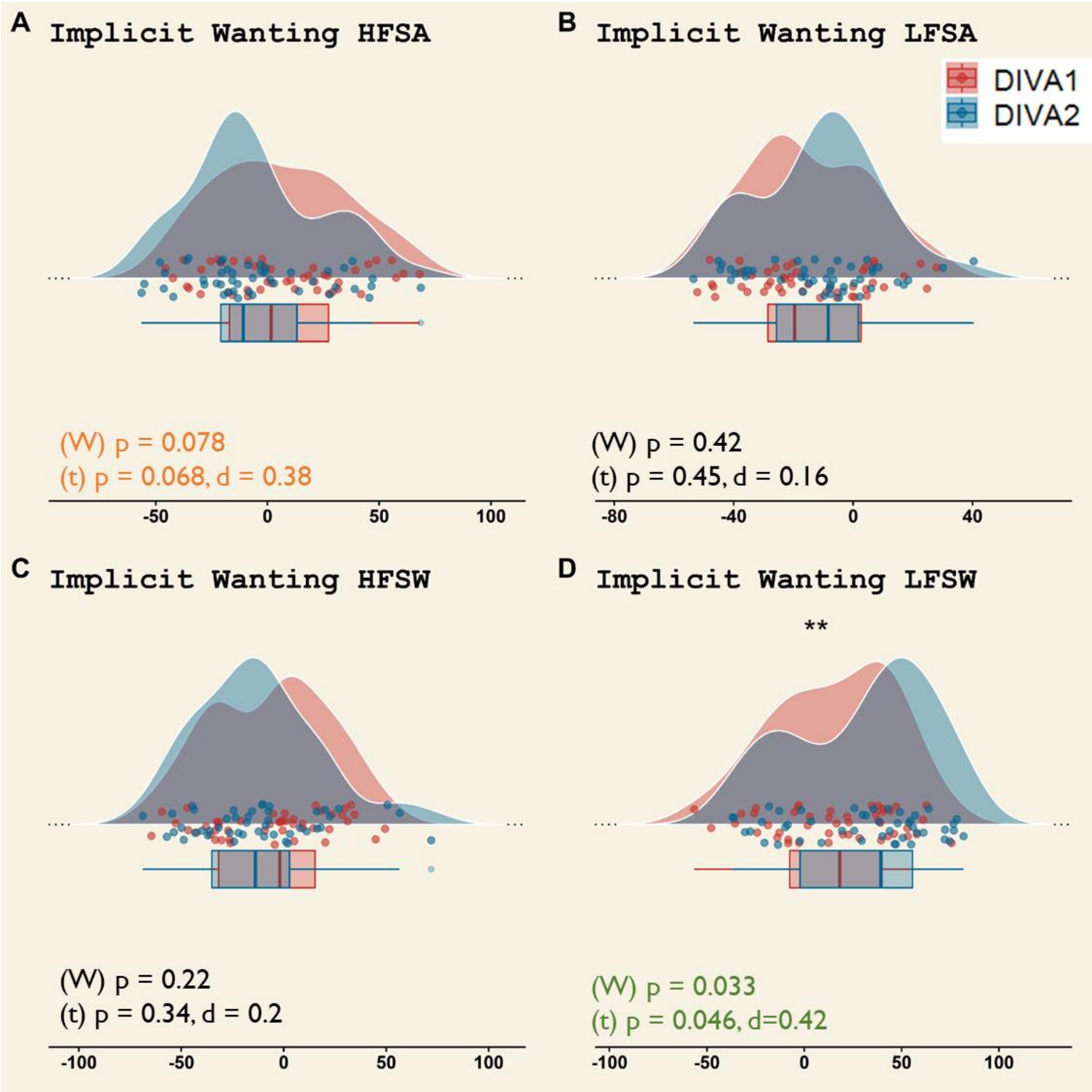

Figure 9-6: Implicit wanting fasted in women with or without overweight/obesity

Density, boxplots and individual points visualise differences between groups beyond the average and potential heterogeneity. ***p<.001, (t) t-test, (W) Wilcoxon test, (d) effect size Cohen's d, DIVA-1: women with overweight/obesity, DIVA-2: women within the normal range of BMI

Table 9-8: Differences in implicit wanting fasted between groups

		Implicit Wanting fasted			
Study	**N**	**HFSA**	**LFSA**	**HFSW**	**LFSW**
DIVA1	46	1.7 (44.4)	-19.6 (31.2)	-1.9 (47.1)	18.1 (47.3)**
DIVA2	46	-10.9 (34.1)	-8.4 (27.4)	-13.9 (37.8)	39.2 (57.7)**

Data are median and interquartile range (IQR), differences between group assessed by t-test and Wilcoxon test. **p<.01

9.3.6 Interim Summary

Figure 9-7 summarises the difference in appetite control between individuals with or without overweight/obesity. As expected, physiological factors such as body composition and energy expenditure were higher in women with overweight/obesity. Eating behaviour traits in women with overweight/obesity were characteristic of overconsumption (e.g. more Binge Eating, Disinhibition and less Craving Control). In terms of food reward, only implicit wanting for low-fat sweet differed and was higher in women within the normal range of BMI with a small to medium effect size. Interestingly there was no difference in appetite sensations, food intake, cravings for sweet or savoury or other food rewards.

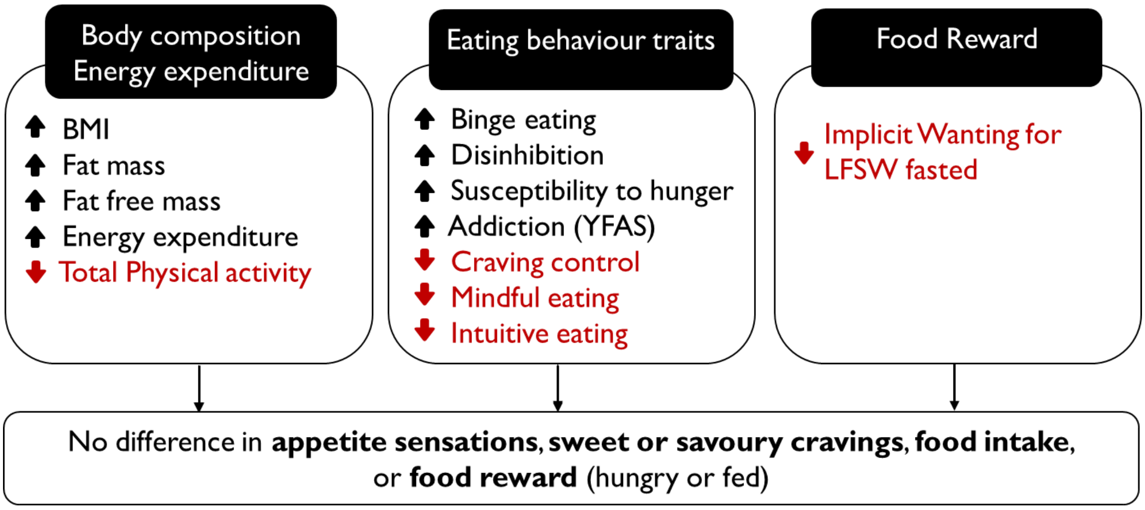

Figure 9-7: Summary of appetite control and food reward differences in women with overweight/obesity compared to women within the normal range of BMI

Arrows reflect women with overweight/obesity compared to women within the normal range of BMI, “Energy Expenditure” refers to total energy expenditure

9.4 DISCUSSION – PART-1: Food reward and appetite control in women with or without overweight/obesity

This cross-sectional study aimed to compare behavioural dimensions of liking and implicit wanting and other appetite-related variables in women with or without overweight/obesity to better characterise individual susceptibility to overeating.

Contrary to expectations, only fasted implicit wanting for low-fat sweet food differed between groups and was higher in women within the normal range of BMI in the current study. This result makes sense given the fact that the low-fat sweet food presented in the LFPQ task were mostly fruits and perceived as healthy. On the whole, food reward mostly did not differ between women with or without overweight/obesity; but, as food reward is not a unitary concept, differences need to be further explored in terms of liking and implicit wanting and according to fasted and lunchtime measures.

9.4.1 Liking

In the current study, liking did not differ between groups (at fasted, hungry or fed state). This result is in line with Snoek et al. (2004), who reported no difference in liking or sensory-specific satiety between women within the normal range of BMI and women with overweight/obesity and speculated that the desire to eat, a subjective measure of wanting, might differ. Those results favour the incentive salience theory reporting differences in wanting in the absence of changes in liking (Devoto et al., 2018) and are consistent with reviews suggesting that liking does not distinguish participants with or without obesity (Mela, 2006). On the contrary, a few behavioural studies have reported increased preferences for high-energy food in individuals with overweight/obesity compared to individuals within the normal range of BMI. A higher preference for fat has been reported in twins with obesity than their co-twin within the normal range of BMI and was acquired independent of genetic background (Rissanen et al., 2002). Drewnowski et al. (1992) reported a high preference for fat in adults with obesity, but there was no control within the normal range of BMI. Findings on the relationship between liking and overweight/obesity remains mixed (Spinelli & Monteleone, 2021) and need to be further explored using larger sample sizes with consistent methodology taking into account physiological state, time of day, and the food category being rated.

9.4.2 Wanting

Previous behavioural studies comparing individuals with or without overweight/obesity are all in favour of greater wanting being associated with obesity (Clark et al., 2010; Giesen et al., 2010; Saelens & Epstein, 1996; Temple et al., 2009; Temple et al., 2008), which is not observed in the current analysis. The discrepancy in the results could first be explained in terms of differences in the methodology used. Previous studies used the relative-reinforcing value of favourite snacks as a proxy for wanting, whereas the current analysis used a forced-choice task for food varying in fat and taste. The LFPQ has been compared to the willingness to work for a food through a grip force task (Arumäe et al., 2019), and to the reinforcing value of food via a computer game to obtain a snack (French et al., 2014; Griffioen-Roose et al., 2010). The difference could be explained by the fact that the LFPQ presents pictures of common food while the reinforcing value task uses rather specific snacks and compares the value of these snacks to another activity (often non-food related). Along the same line, fMRI studies showed increased activity in brain areas related to salience network, food reward and overeating in individuals with obesity compared to individuals within the normal range of BMI but brain activation does not always translate into behavioural outcomes (Devoto et al., 2018; García-García et al., 2013; Pursey et al., 2014; Stoeckel et al., 2008). A comparison between methods would help to assure that the same concept is measured.

9.4.3 Fasted reward and reward at lunchtime

It can be questioned why only fasted implicit wanting differed between women within the normal range of BMI and women with overweight/obesity, while pre- and post-lunch reward were not different according to weight status.[6] It is important to keep in mind that fasted reward and reward at lunchtime are based on a different set of pictures to correspond to the time of day, so they are not directly comparable. Food reward might vary across time of day (Beaulieu et al., 2020d) but the relationship between food reward, obesity and time of day remains to be investigated. Fasted reward might be a more stable state than lunchtime reward (See Results part 2, where fasted reward correlate with eating behaviour traits) but their role with obesity status remains to be investigated. To sum up, the difference in food reward between the groups is modest (only one food category at fasted state) and remain to be further explained.

9.4.4 Appetite control

Is appetite control different in women with overweight/obesity compared to women within the normal range of BMI? As expected, women with overweight/obesity had higher BMI, fat mass, fat-free mass, energy expenditure, but no difference in RMR and lower objectively-measured total physical activity. In terms of eating behaviour traits, women with overweight/obesity had heightened susceptibility to overeat with increased Binge Eating, Food Addiction Symptoms, Disinhibition, Susceptibility to Hunger and less Craving Control, which is consistent with previous literature (Bryant et al., 2019; Dalton & Finlayson, 2014; Flint et al., 2014). Studies have usually explored food cravings with obesity but Craving Control has also been shown to be related to better weight loss (Dalton et al., 2017), and this study concurs that it is a meaningful factor to consider in preventing obesity. As in previous studies, Mindful Eating (Camilleri et al., 2015; Framson et al., 2009) and Intuitive Eating (Dyke & Drinkwater, 2014; Tylka & Kroon Van Diest, 2013) were associated with obesity (here BMI) while Hedonic Hunger as

[6] Changes pre to post lunch between individuals with or without overweight/obesity were investigated through linear mixed models but there was no group-related effect on liking or wanting

conceptualised by the PFS was not (Espel-Huynh et al., 2018). This raises some doubt about whether all eating behaviour traits involved in overeating are related to obesity status.

Interestingly there were no differences in appetite sensations, Cravings for Sweet or Savoury foods, or food intake. This contrasts with other studies showing that individuals with obesity reported consuming a greater variety of energy-dense foods (McCrory et al., 1999) or craved more high-energy food at non-eating moments (Roefs et al., 2019). The lack of difference in food intake between women with or without overweight/obesity could be attributed to the specific sample of this study (women with overweight/obesity seeking to lose weight) and that food intake was measured in the laboratory only at lunch. Food reward, food Cravings and appetite sensations did not differ between groups and are usually associated (Andriessen et al., 2018; Dalton et al., 2013c; Yang et al., 2019a), suggesting that obesity entails different phenotypes leading to overconsumption. Even so the literature is mixed, it seems that women with overweight/obesity have a weakened appetite control and that several appetite-related variables are needed to explain obesity. Lastly, previous work on food preferences in obesity suggested a great diversity of behaviour among individuals with obesity making it difficult to establish differences with individuals within the normal range of BMI (Bellisle, 1995). This was in line with the substantial overlaps between groups (densities) even for variables significantly different between women with or without overweight/obesity. These graphical representations are another illustration of the need to go beyond averages and to investigate the heterogeneity of obesity.

9.4.5 Limitations and future implications

Contrary to expectations, food reward did not differ greatly between women with or without overweight/obesity: how can this be explained? Firstly, the definition of obesity was based on BMI category, which does not take into account the heterogeneity of obesity, nor accurately represents body fatness (Prentice & Jebb, 2001). Indeed, BMI might not reflect overconsumption phenotypes. For example, Hedonic Hunger (PFS) has been associated with overeating but not with BMI, and Food Addiction is rather associated with eating pathology than BMI (Davis et al., 2011). As for Hedonic Hunger, food reward might act in combination with other appetite-related variables to predict overconsumption and weight gain (Espel-Huynh et al., 2018). Obesity is not a single entity and rather a heterogeneous system, including different phenotypes (Dalton et al., 2013c). However, a PCA on the fasted food reward variables did not reveal any food reward patterns between individuals with or without overweight/obesity (See Appendix E, Figure E8). Moreover, while participants within the normal range of BMI were recruited following the same exclusion criteria than the group with obesity (e.g. not dieting to lose or maintain weight, no health problem, no eating disorders, no supplement affecting appetite, no recent changes in body weight or physical activity), but less was known about their weight management history. However, it was important to note that they did not differ from the group with obesity for either flexible or rigid restraint and were at low level of restraint. While the LFPQ has been shown to be a relatively reliable tool (in term of test-retest reliability) (Oustric et al., 2020), fluctuations in its measurements might depend for example on eating behaviour traits, chronotype, culture or physical activity (Beaulieu et al., 2020d).Secondly, these results are limited to this study's sample, which is moderate in size and half of which is motivated to lose weight. Finally, a cross-sectional analysis does not allow an understanding of whether the difference in food reward could be a consequence rather than a cause of obesity. Lastly, comparing groups with and without overweight/obesity assumes that the relationship between reward and obesity is linear, which is not resolved yet (Davis & Fox, 2008). Further studies should test for the non-linear relationship between liking, wanting and obesity.

Going beyond the group comparison and the limitation of BMI as a classification for obesity, the next part of the analysis, considered the whole sample, using BMI as a continuous variable to analyse the relationships between reward and appetite control components.

9.5 RESULTS PART-2: Relationships between food reward and appetite control

All correlations between food reward at breakfast, pre-lunch and post-lunch with appetite-related variables were performed in this exploratory analysis. Consequently, a p-value of .01 instead of .05 was chosen to consider the multiple outcomes testing for each food reward component. Scatter plots illustrate the correlations of interest and specify whether the correlation was driven by one group. Summary tables summarised the correlations by food reward variables (see Appendix E, Tables E7 to E10).

9.5.1 Food reward and body composition

Body composition was mainly associated with pre-lunch reward, and only once with post-lunch reward. Fat mass, %fat, and body mass were weakly associated with wanting and no correlation with fat-free mass.

Implicit wanting for LFSA was negatively associated with fat mass (r_s (91) = -.26, p = .013), body mass (r_s (91) = -.26, p = .012), and to a lesser extent to %fat (r_s (91) = -.23, p = .024) and BMI (r_s (91) = -.24, p = .023). On the contrary, implicit wanting HFSW was positively associated with body mass (r_s (91) = .27, p = .011), and to a less extent to fat mass (r_s (91) = .24, p = .021), and %fat (r_s (91) = .21, p = .045). Interestingly the relationship with wanting HFSW and fat mass or %fat was stronger in the group with overweight/obesity as shown in Figure 9-8.

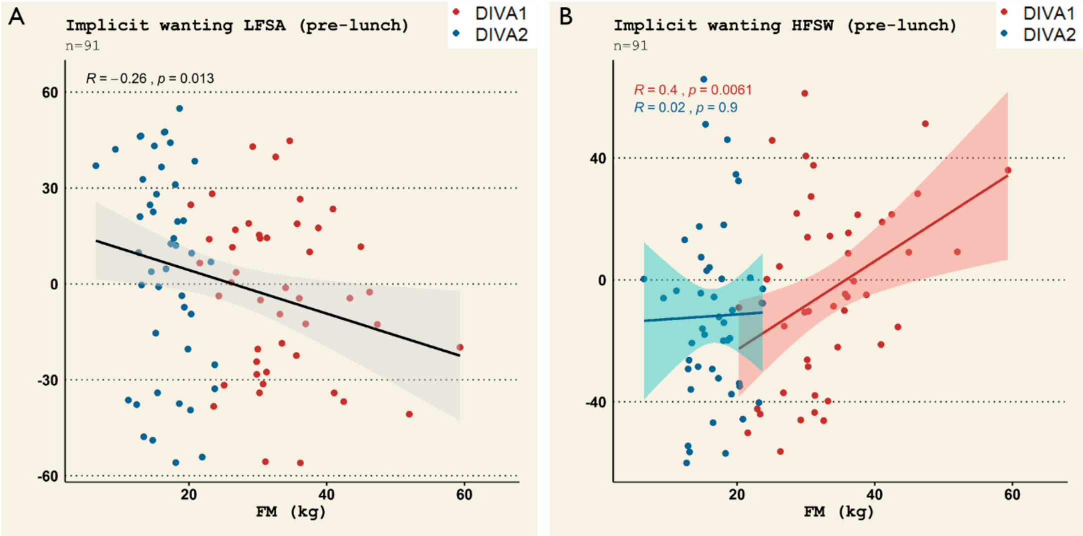

Figure 9-8: Pre-lunch implicit wanting and fat mass

(R) Spearman's correlation coefficients (whole sample analysis in A) and Pearson's correlation coefficients for group analysis in B, DIVA-1: women with overweight/obesity, DIVA-2: women within the normal range of BMI

9.5.2 Food reward and energy expenditure

Energy expenditure variables were weakly associated with food reward: total energy expenditure was mostly associated with food reward at pre-lunch, and RMR with liking for sweet pre-lunch. Physical activity level (PAL) was weakly associated with liking for savoury.

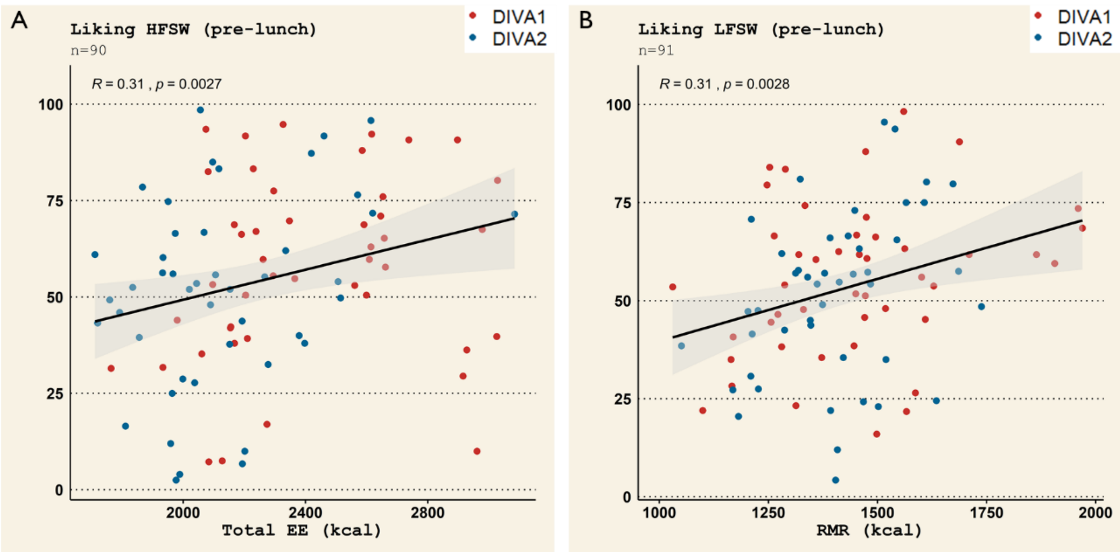

Figure 9-9: Pre-lunch liking, total energy expenditure (EE) and RMR

(R) Pearson's correlation coefficients for group analysis, DIVA-1: women with overweight/obesity, DIVA-2: women within the normal range of BMI

Total energy expenditure was positively associated with liking for HFSW (r_s (90) = .31, p = .003), LFSW (r_s (90) = .29, p = .006), and implicit wanting for HFSW (r_s (90) = .28, p = .009), but negatively and to a lesser extent with implicit wanting for LFSA (r_s (90) = -.24, p = .03), As shown in Figure 9-9, RMR was also positively associated with Liking for LFSW and to a lesser extent to HFSW (rs (90) = .22, p = .034). Physical activity level (PAL) and total physical activity were only correlated with liking for savoury (see Appendix E, Tables E7 to E10)

9.5.3 Food reward and eating behaviour traits

9.5.3.1 Food reward and Craving (CoEQ)

Craving was mainly associated with fasted food reward (breakfast) and correlations were weak to moderate.

Craving Control was negatively with HFSA (r_s (85) = -.29, p = .006), and to a less extent positively associated with implicit wanting for LFSW (r_s (85) = .24, p = .03) see Figure 9-10. There was no association with Craving for Savoury. Food reward pre-lunch; implicit wanting (r_s (84) = .46, p < .001) and liking HFSW (r_s (84) = .44, p < .001); were moderately and positively associated with Craving for Sweet and this association was driven by the group with overweight/obesity (see Figure 9-11).

With other appetite-related variables, Craving Control was moderately and inversely associated with %fat (r_s (85) = -.42, p < .001) and strongly to BES (r_s (84) = -.71, p < .001).

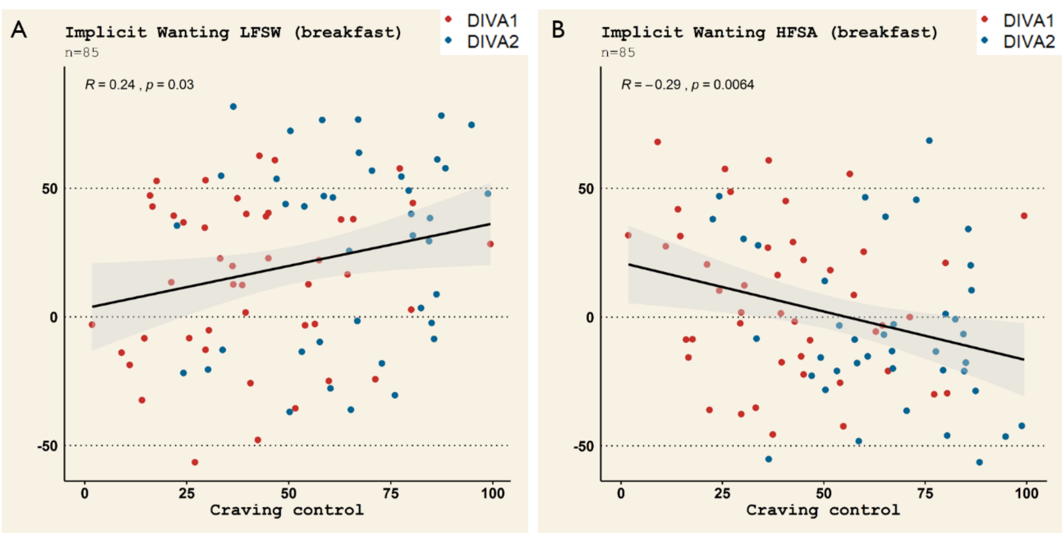

Figure 9-10: Fasted reward and Craving Control

(R) Spearman's correlation coefficients (whole sample analysis in A and B), DIVA-1: women with overweight/obesity, DIVA-2: women within the normal range of BMI

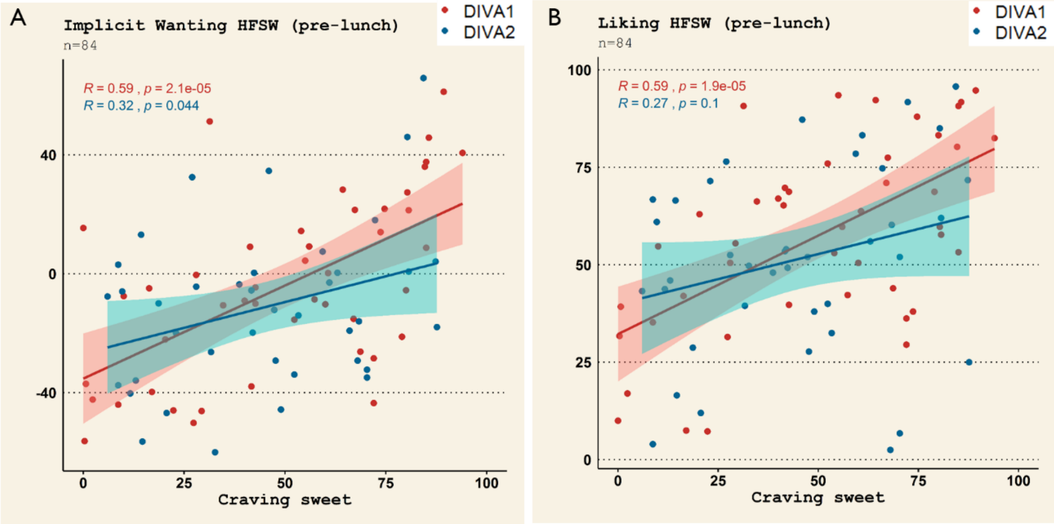

Figure 9-11: Pre-lunch reward and Craving sweet

(R) Pearson's correlation coefficients for group analysis, DIVA-1: women with overweight/obesity, DIVA-2: women within the normal range of BMI

9.5.3.2 Food reward and disinhibition, Restraint and hunger (TFEQ)

Eating behaviour traits measured by TFEQ were associated only with fasted reward with small effect sizes. Disinhibition was positively associated with fasted implicit wanting for HFSA ($r_s(85) = .28$, $p = .010$) and to a less extent negatively associated with implicit wanting LFSW (r_s (85) = -.22, $p = .045$) , both correlations were driven by the group with overweight/obesity as shown in Figure 9-12. Restraint was weakly and negatively associated with implicit wanting LFSA (r_s (85) = -.24, $p = .003$) and positively with liking LFSW (r_s (85) = .25, $p = .002$). Susceptibility to Hunger was positively associated with liking HFSW (r_s (86) = .26, $p = .015$). and to a lesser extent to wanting HFSA (r_s (86) = .23, $p = .031$). With other appetite-related variables, Disinhibition was the most strongly associated with BES and %fat.

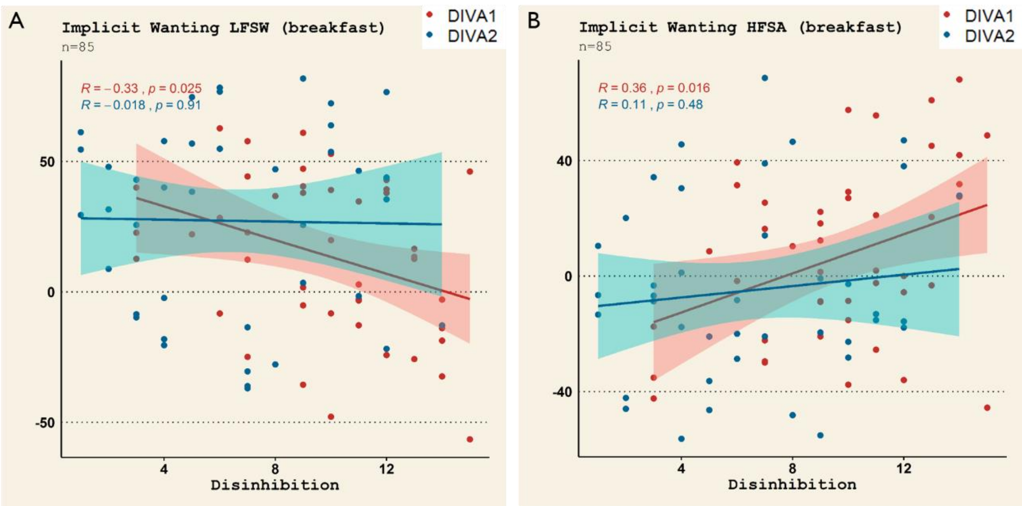

Figure 9-12: Fasted food reward and Disinhibition

(R) Pearson's correlation coefficients for group analysis in A and B, DIVA-1: women with overweight/obesity, DIVA-2: women within the normal range of BMI

9.5.3.3 Food reward and binge eating (BES)

Binge eating was only associated with fasted implicit wanting with a small effect size.

BES was positive associated with HFSA (r_s (85) = .34, p = .0016) and to a less extent negative association with implicit wanting LFSW (r_s (85) = -.23, p = .031). The association with high-fat reward was driven by the group with overweight/obesity (see Figure 9-13). With other appetite-related variables, BES was positively associated with %fat and strongly and negatively with Craving Control.

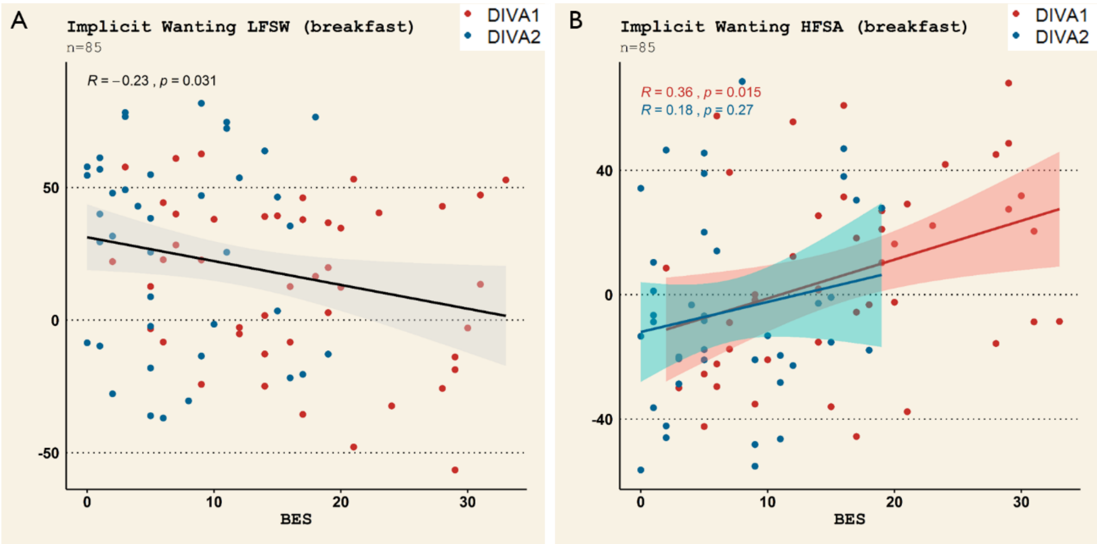

Figure 9-13: Fasted implicit wanting and BES

(R) Spearman's correlation coefficients (whole sample analysis in A) and Pearson's correlation coefficients for group analysis in B, DIVA-1: women with overweight/obesity, DIVA-2: women within the normal range of BMI

9.5.3.4 Food reward and addiction (YFAS) Hedonic, Mindful or Intuitive Eating (PFS, MEQ, IEQ)

Food addiction symptoms count measured by YFAS was not associated with food reward. IES and PFS were weakly associated with fasted reward, and MEQ was weakly and only associated with one pre-lunch reward component.

The association between components of food reward and PFS, IES and MEQ were scarce and above the significant threshold of p = .01. Fasted implicit wanting for HFSA was positively associated with PFS (r_s (86) = .22, p = .047) and negatively with IES (r_s (86) = -.23, p = .033) with a stronger association in the group with overweight/obesity (see Figure 9-14). Liking for HFSW was associated with PFS, and the association was driven by the group with overweight/obesity (see Appendix E, Tables E7-E8). Only pre-lunch wanting for HFSW was associated with MEQ (r_s (85) = -.22, p=.048).

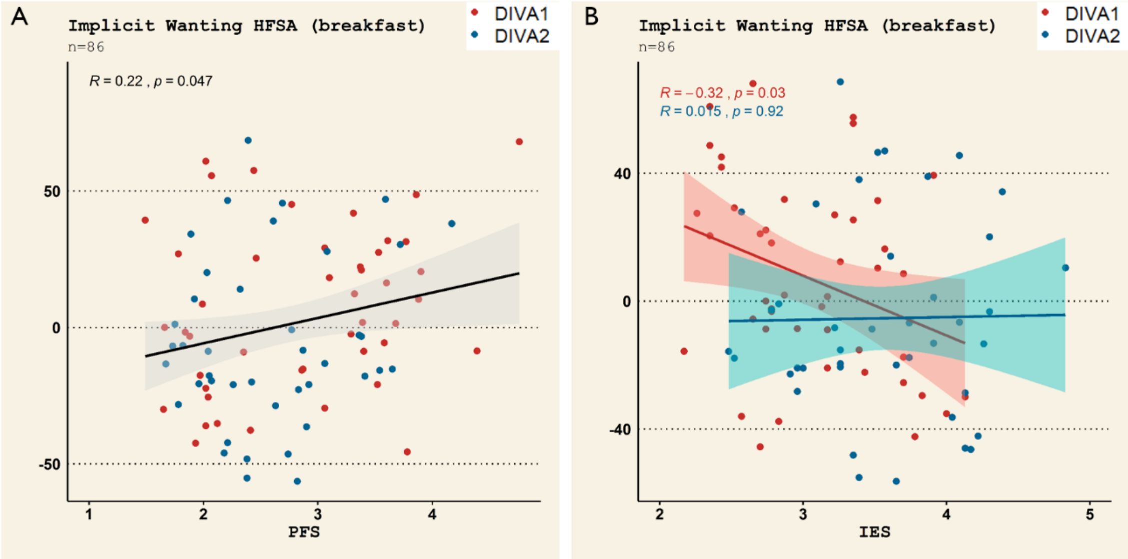

Figure 9-14: Fasted implicit wanting with PFS and IES

(R) Spearman's correlation coefficients (whole sample analysis in A) and Pearson's correlation coefficients for group analysis in B, DIVA-1: women with overweight/obesity, DIVA-2: women within the normal range of BMI

9.5.4 Food reward and appetite sensations (VAS)

Appetite sensations (AUC) were mostly associated with fasted and pre-lunch reward and liking compared to wanting (weak to moderate). Desire to eat, hunger and prospective consumption were positively associated with high-fat food reward while fullness was negatively associated. For example, liking HFSW was positively associated with desire to eat (r_s (91) = .28, p = .008) but negatively with fullness (AUC) (r_s (91) =-.33, p = .002), both associations were driven by the group with overweight/obesity (see Figure 9-15).

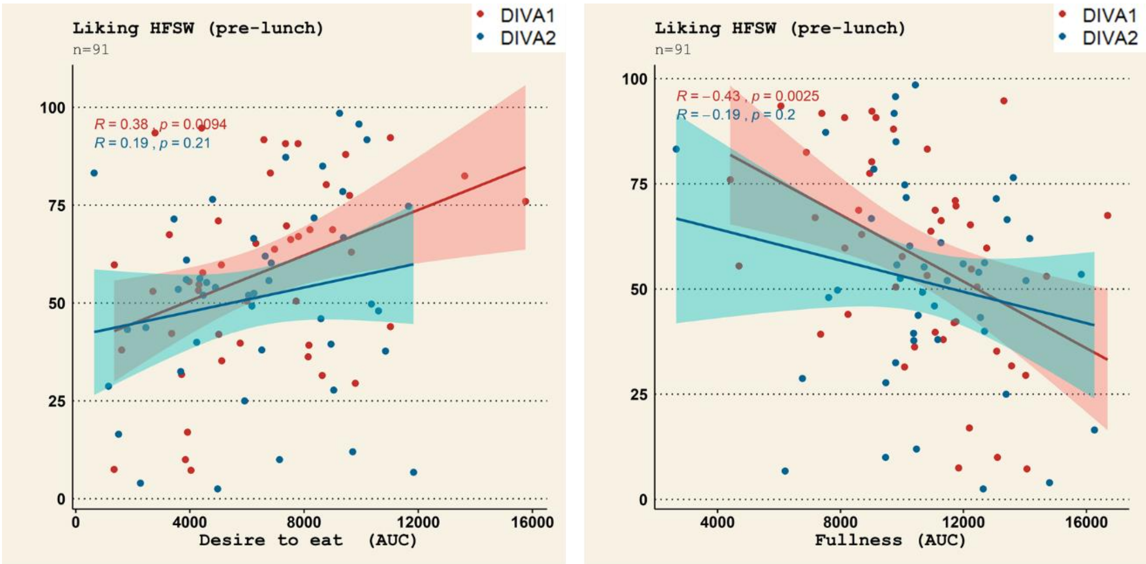

Figure 9-15: Fasted liking with appetite sensations (AUC)

(R) Pearson's correlation coefficients for group analysis; AUC: Area under the curve, DIVA-1: women with overweight/obesity, DIVA-2: women within the normal range of BMI

9.5.5 Food reward and food intake

Fasted food reward and lunchtime food reward were associated with test-meal food intake with a small effect size.

Fasted food reward for LFSA was negatively associated with yoghurt intake at lunch (r_s (91) = -.28, p = .008) and this was stronger in the group of women within the normal range of BMI (see Figure 9-16). Both liking and implicit wanting pre-lunch were weakly to moderately associated with energy intake at lunch. For example, liking LFSW was positively associated with yoghurt intake (r_s (91) = .36, p=.0005), and this relationship seemed to be stronger in the group within the normal range of BMI. Liking for LFSA was positively associated with risotto intake (r_s (91) = .27, p = .01). Associations were weak or non-significant between pre-lunch food reward and total intake at lunch.

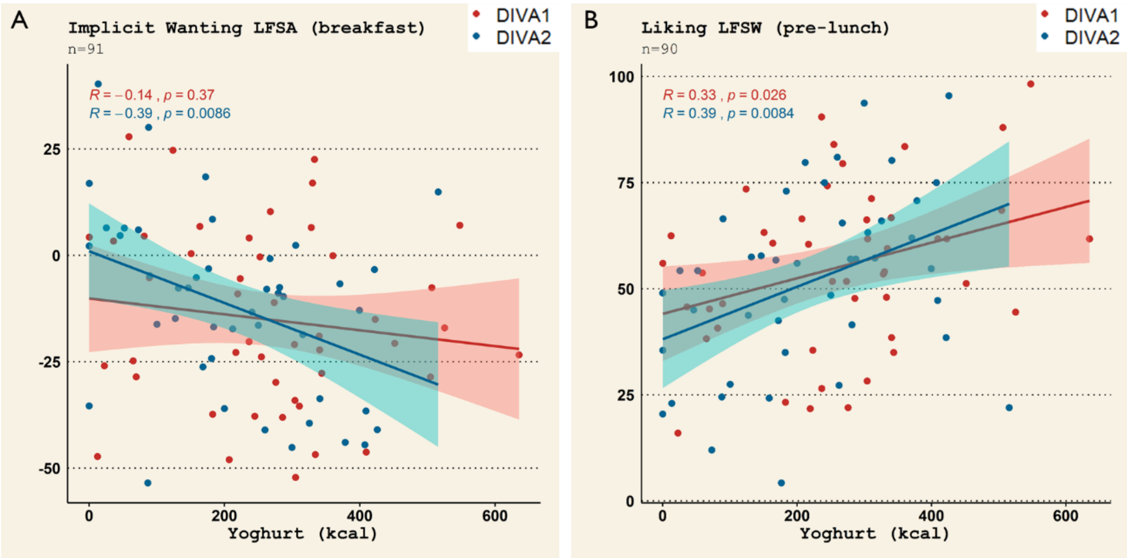

Figure 9-16: Food reward and food intake

(R) Pearson's correlation coefficients for group analysis in A and B, DIVA-1: women with overweight/obesity, DIVA-2: women within the normal range of BMI

9.5.6 Interim Summary

Food reward components were associated with food intake, eating behaviour traits, appetite sensations, energy expenditures and body composition, but effects were weak to moderate and dependant on food categories, physiological state and weight status. Figure 9-17 summarises the associations in fasted vs pre-lunch and high- vs low-fat reward depending on their impact on appetite control. For instance, eating behaviour traits and appetite sensations were more associated with fasted food reward. Similarly, only implicit wanting pre-lunch was associated with fat mass with an opposition between LFSA, which was negatively associated and HFSW, positively associated. As expected, reward for high-fat food was associated with weakened appetite control and interestingly, fasted implicit wanting for low-fat sweet was associated with improved appetite control. See Appendix E (Tables E7 to E10) for the summary tables of the relationships between food reward and appetite control. When considering multiple comparisons, the associations between reward for low-fat food and appetite control were weaker than those with reward for high-fat food.

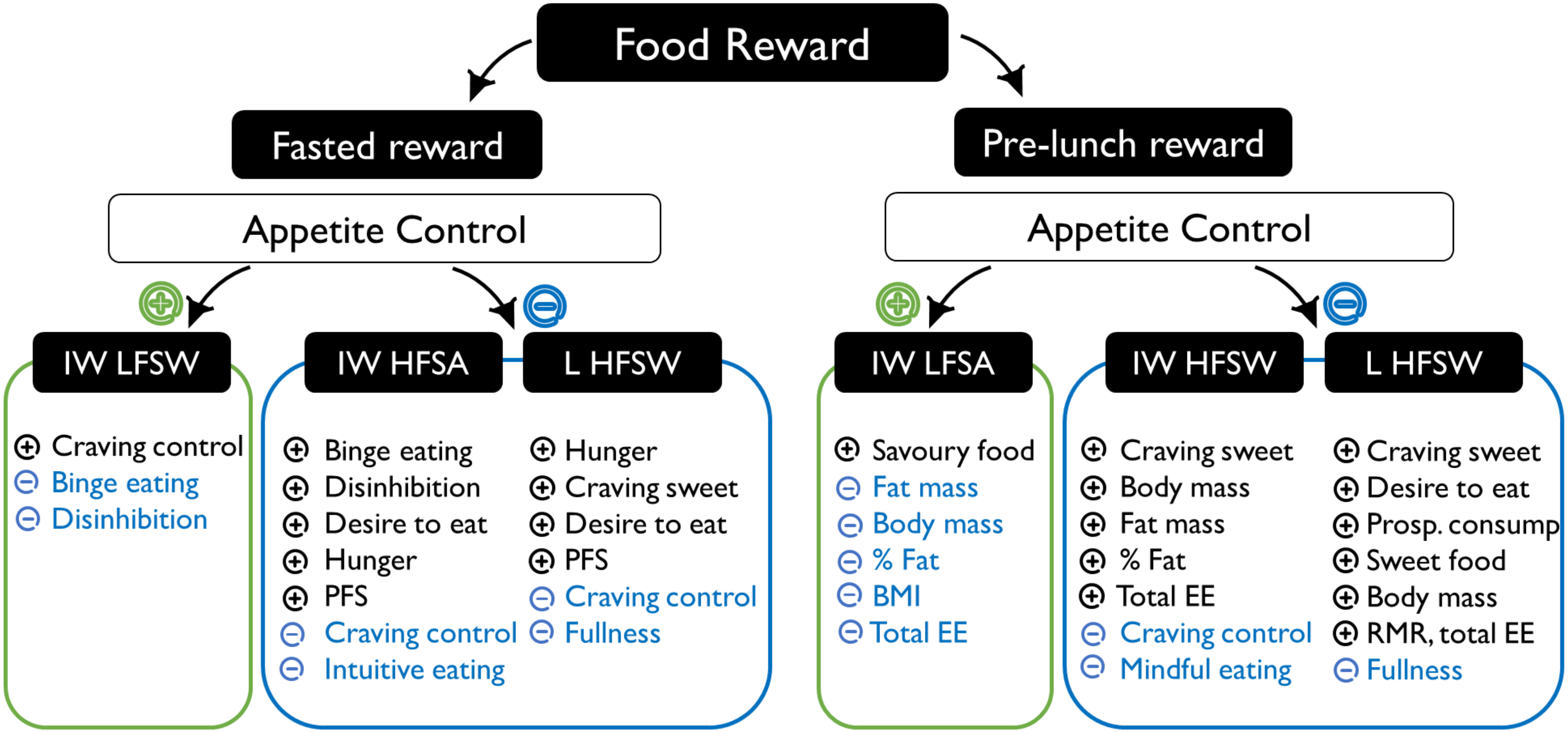

Figure 9-17: Summary of the associations between food reward and appetite control

EE: energy expenditure; IW: implicit wanting; L: liking, Prosp. Consumption: prospective consumption; RMR: resting metabolic rate

9.6 DISCUSSION – PART-2 Relationship between food reward and appetite control

This cross-sectional study was designed to analyse the associations between behavioural measures of liking and implicit wanting for food varying in fat and taste with appetite-related variables taking into account weight status.

9.6.1 Liking, implicit wanting and appetite control

Components of food reward were associated with appetite-related variables such as energy expenditure, body composition (fat mass but not fat-free mass), eating behaviour traits (BES, TFEQ, PFS, IES, MEQ but not YFAS), appetite sensations (hunger, desire to eat, fullness, prospective consumption), and food intake (test meal). Importantly, these associations supported the conceptual differentiation between liking and wanting.

9.6.1.1 Implicit wanting but not liking was associated with fat mass

Interestingly, implicit wanting was associated with fat mass but not fat-free mass with a difference in direction between LFSA (negatively associated) and high-fat sweet (positively associated). Fat mass and fat-free mass are involved in the tonic inhibition and drive to eat while food reward is involved in the episodic processes involved in appetite control. Several mechanisms underpinning the interaction between these tonic and episodic signals can be suggested. Firstly, increased fat mass could be the result of heightened implicit wanting for HFSW food. Indeed, the implicit motivation for high-fat food has been related to energy intake in individuals with and without obesity (Dalton & Finlayson, 2014; French et al., 2014). Secondly, the increased fat mass could result in leptin resistance affecting brain reward by increasing wanting. Leptin resistance in animal models counter-regulates leptin's inhibitory role on brain reward, thus increasing food reward (Scarpace & Zhang, 2009). Both mechanisms could feed each other by creating a vicious cycle favouring obesity as proposed with the dynamic vulnerability model of obesity (Stice & Yokum, 2016). Similar to this study result, Carvalho-Ferreira et al. (2019) reported an association between implicit wanting for high-fat and BMI in the Brazilian population, while Rissanen et al. (2002) suggested an effect of body fatness on liking. It remains to be understood which component of body composition (i.e. fat mass or fat-free mass) is associated with which component of food reward (i.e. liking or wanting). For example, Hopkins et al. (2014) showed an association between liking and fat-free mass. This will allow a better understanding of the role of food reward in the physiological drive to eat (Blundell et al., 2020).

9.6.1.2 Liking and implicit wanting were associated with energy expenditure

While only implicit wanting was associated with fat-mass, liking and implicit wanting were associated with total energy expenditure. These weak associations were mostly explained by relationships between liking and RMR, and only a few associations of liking and PAL, which could be explained by the low level of physical activity in this sample (i.e. PAL < 1.7 (World Health Organization, 2004). This is coherent with the conceptual model of the impact of habitual physical activity on food reward processes proposed in a recent review: a lower level of physical activity is associated with higher reward. In contrast, moderate to vigorous physical activity is associated with lower reward for high-fat food (Beaulieu et al., 2020c; Beaulieu et al., 2020e; Oustric et al., 2018b).

9.6.1.3 Liking and implicit wanting for high-fat food, marker for increased binge eating, cravings, disinhibition

In line with the current study, Davis et al. (2009) and Dalton et al. (2013b) showed that binge eating was associated with elevated reward based on genetic (genotype frequencies for the dopamine D2 receptor and the opioid mu receptor) and behavioural indicators, especially in individuals with obesity. Similarly, Yeomans et al. (2004) reported that individuals with low restraint and high disinhibition were more responsive to palatable food and more prone to obesity. Regarding Food Addiction, this study revealed no relationship with food reward. On the contrary, other studies described how individuals with self-perceived Food Addiction had higher food reward, but this may be attributable to high disinhibition and low restraint (Ruddock et al., 2017). As expected, reward for high-energy food seemed to be associated with overconsumption traits (Binge Eating, high Disinhibition, low Restraint) – a cluster that could constitute a phenotype to be further analysed to prevent obesity. This study also adds to the literature by exploring the relationship between Craving Control and components of food reward. Interestingly wanting for low-fat food was associated with heightened Craving Control while the inverse relationship was shown for reward for high-fat food. Investigating control of eating in association with food reward is novel and brings new insight to appetite control.

9.6.1.4 Liking and implicit wanting for high-fat food weakly associated with hedonic eating, less intuitive and mindful eating

In contrast to Binge Eating, Disinhibition and Food Addiction; Hedonic Hunger (PFS), Intuitive Eating (IES) and Mindful Eating (MEQ) had never been compared to food reward measured by the LFPQ. Hedonic Hunger had previously been associated with heightened brain responsivity to food cues (Espel-Huynh et al., 2018). Similarly, the current results revealed associations between liking and implicit wanting for high-fat food with Hedonic Hunger, which makes sense given the availability of high-energy food in the environment (Lowe et al., 2009). Mindful and intuitive eating illustrate the relationship individuals have with both food and body cues. They have been previously investigated with food intake and food choice (Allirot et al., 2018; Arch et al., 2016; Dyke & Drinkwater, 2014; Fisher et al., 2016), and the relationship between mindful eating and enjoyment of food or liking seems unclear (Allirot et al., 2018; Arch et al., 2016). Indeed, most of the studies investigate the effects of heterogenous interventions aiming at improving mindful or intuitive eating on appetite factors but without measuring intuitive or mindful eating concepts directly. In this study, MEQ and IES were scarcely and negatively associated with implicit wanting for high-fat food, which seems logical given the fact that paying attention to food or body cues might be related to less external eating (Daubenmier et al., 2011). Further studies need to investigate their relationship with food reward components to unveil whether targeting mindful or intuitive eating could attenuate reactions to energy-dense food cues via reducing food reward.

9.6.1.5 Liking and implicit wanting are associated with food intake and appetite sensations

Consistent with the current study, food reward has been previously related to subsequent food intake (Fay et al., 2015) independent of energy need (Yeomans et al., 2001). While food intake is mostly driven by implicit wanting (de Araujo et al., 2019), this study showed that both pre-lunch liking and implicit wanting were associated with test meal food intake, especially to the sweet component (strawberry yoghurt), possibly the most palatable. Regarding appetite sensations, it is important to note that their association with food reward was mostly significant in the fasted and pre-lunch states. Similarly, Erlanson-Albertsson (2005) suggested that palatable foods could disrupt appetite sensations by increasing hunger signals and decreasing satiety however, the strength of this narrative review was limited. Liking and wanting measured by the LFPQ translated into food consumption and are useful in understanding the control of appetite in women with or without overweight/obesity.

Interestingly, the associations reported differed according to liking vs implicit wanting, low vs high fat, and the physiological state (mostly fasted and pre-lunch), requiring further investigation as detailed in the following sections.

9.6.2 Reward in the fasted and pre-lunch state

Most of the significant associations were found in the fasted or pre-lunch states. Fasted liking and wanting were mainly associated with eating behaviour traits and appetite sensations which was not the case for pre and post meal reward, raising the question of the conceptual status of fasted reward as traits tend to be associated (Blundell et al., 2005). On the contrary, body composition was only associated with pre-lunch wanting and not post-lunch. It has previously been suggested that hunger influences food reward by increasing both liking and food-cues incentive salience (Berridge, 2009). For instance, elevated appetite sensations and ghrelin led to increased hedonic response to food pictures (Kroemer et al., 2013a). It can be suggested that a hungry state is necessary to stimulate the association between food reward components and appetite-related variables. Consequently, the role of food reward components in the initiation of eating could partly explain the stronger associations at fasted or hungry (pre-lunch) states, as described by Nijs et al. (2010).

On the contrary, individuals susceptible to weight gain have been shown to maintain a higher preference for high-fat food over low-fat food when fed compared to their counterparts who remained women within the normal range of BMI (Blundell et al., 2005). This suggests a role of food reward components in the post-ingestive state in driving eating beyond satiation. To conclude, food reward components might have a role both in the initiation and the consummatory phase. Indeed, in the absence of hunger, liking and wanting might have a role in the amount of food eaten. Lastly, one study found that sensitivity to reward did not differ between individuals initiating snacking or not (Fay et al., 2015), suggesting that reward might act in relation with other factors to lead food intake during the consummatory phase (Kroemer et al., 2013b). Indeed, women with binge eating and obesity were shown to have enhanced implicit wanting in the fed state compared to women with obesity but without binge eating (Dalton et al., 2013b).

9.6.3 Reward for high-fat and low-fat foods

The association between food reward components and appetite-related variables revealed patterns that were reinforcing appetite control and others that were weakening appetite control. Both implicit wanting for low-fat sweet fasted and LFSA pre-lunch were associated with characteristics strengthening appetite control such as stronger Craving Control and less Binge Eating, Disinhibition or fat mass. On the contrary, liking and implicit wanting for high-fat sweet fasted and pre-lunch were associated with weakened appetite control such as higher Binge Eating, Disinhibition, desire to eat, hunger, Hedonic Hunger, Craving for Sweet, fat mass, and lower Craving Control, Intuitive Eating or fullness. There was a clear opposition between reward for high-fat and low-fat in terms of the effect on appetite control. This is in line with previous studies showing that women with a higher reward for high-fat sweet food have greater adiposity and binge eating (Carvalho-Ferreira et al., 2019; Dalton et al., 2013b). It remains to be understood whether it constitutes on its own a phenotype of risk for overeating and whether interventions could specifically reduce reward for high-fat food to prevent overeating,

Interestingly, the relationship between appetite-related variables and food reward for high-fat sweet tends to be driven by the group with overweight/obesity. For example, the relationship between fat mass and implicit wanting for HFSW or Craving for sweet and liking for high-fat sweet was only significant in the group with overweight/obesity. This was consistent with other studies showing that elevated liking and wanting are markers of overconsumption phenotypes (Finlayson & Dalton, 2012b). More specifically, Hedonic Hunger (PFS) was associated only with rewards for high-fat and not low-fat food. This constitutes another argument in favour of the influence of the "obesogenic" environment on reward, with more energy-dense food having greater influence than less energy-dense food. And this raises the need to tailor environmental interventions reducing the access to high-energy foods.

9.6.4 Limitations and future perspectives

This analysis has some limitations that need to be discussed. First, the sample size consisting exclusively of women was relatively moderate, and the study needs to be replicated in a larger sample size to interpret the results in terms of population. The exploratory nature of this correlational study explored components of food reward with a high number of appetite-related variables. When considering the multiple comparisons, associations with low-fat food were weaker than those with high-fat food. However, a larger study should replicate this analysis using Benjamini and Hochberg corrections to account for false positives, and false negatives (Jafari & Ansari-Pour, 2019) which was not possible here due to the number of outcomes and the small sample size.

While previous studies have shown that the relationship between reward for high-fat sweet and BMI seemed not to be influenced by sex (Carvalho-Ferreira et al., 2019), there is a need to evaluate the moderating effect of sex on the relationship between food reward components and other appetite-related variables. Secondly, this study was an exploratory analysis of the effect of weight status on the association between women within the normal range of BMI and women with overweight/obesity. Correlations were run first on the whole sample and then by group to estimate whether the association was driven by one group. Larger studies could replicate this study and specifically assess the moderation by weight status. Importantly, it was the first time Craving Control was explored in relation to food reward and overweight/obesity. It revealed the importance of craving control to prevent overeating and obesity, and further studies should investigate how to reinforce craving control and its impact on appetite control.

9.7 GENERAL DISCUSSION

Taken together, the results of this chapter illustrate a bigger picture of the role of food reward in appetite control and overweight/obesity. Firstly, do food reward components differ between women with or without overweight/obesity? Contrary to expectations, only implicit wanting for low-fat sweet was higher in women within the normal range of BMI than women with overweight/obesity. This can be understood, given that implicit wanting for low-fat sweet was also associated with improved appetite control. However, this result might be less frequently evaluated as most studies tend to focus on the effect of snack or highly palatable and energy-dense food (Stoeckel et al., 2008) and the role of low-energy food might be overlooked. Indeed, the food environment is largely characterised by high-energy food and this study showed that the influence of the food environment on food reward was driven mainly by high-fat food. As reward for high-energy food was similar between women within the normal range of BMI and women with overweight/obesity, food reward alone may not be responsible for obesity. It can be suggested that food reward components act in combination with other appetite-related variables such as Craving Control or Disinhibition, especially in a hungry state, to generate overeating (Dalton et al., 2013c).

While the reward for high-fat sweet food did not differ between women with or without overweight/obesity, it was positively associated with fat mass and body mass. Moreover, this association was stronger in the group with overweight/obesity, where there was also more variability in fat mass. Similarly, the associations between reward for high-fat-food and appetite-related variables were stronger in women with overweight/obesity. This could suggest that for some women, a higher reward for high-fat sweet is a marker of weakened appetite and could characterise a phenotype of obesity alongside Binge Eating (Dalton et al., 2013b), high Disinhibition (Finlayson et al., 2012) as previously studied but also lower Craving Control, higher Susceptibility to Hunger and lower Intuitive and Mindful Eating as raised for the first time by this study.

What is the role of food reward in appetite control? As expected, liking and implicit wanting for high-fat food was associated with weakened appetite control, especially in the group with overweight/obesity. Furthermore, liking and implicit wanting for low-fat food seemed to be protective for appetite control. Therefore, food reward seems to be a meaningful variable to better understand phenotypes of obesity and should be investigated in conjunction with appetite-related variables. Further longitudinal studies need to explore food reward and appetite-related variables in individuals prone to obesity to understand the direction of causality between weakened appetite control and heightened food reward with obesity.

9.8 Conclusion

Food reward components are often considered as worsening factors responsible for obesity. Contrary to expectations, this cross-sectional analysis showed that women with overweight/obesity did not have higher reward for high-fat food. Rather, women within the normal range of BMI had higher implicit wanting for low-fat sweet food when fasted, which was also associated with improved appetite control. While the difference in implicit wanting was modest, women with overweight/obesity had higher Binge Eating, Disinhibition, and lower Craving Control, Mindful and Intuitive Eating suggestive of a weakened appetite control. Moreover, the effect of food reward on appetite control depended on the food category: fasted implicit wanting for low-fat sweet (e.g. fruits, yoghurt) seemed to be favourable for appetite control, while implicit wanting for high-fat sweet (e.g. doughnuts, pastries) was related to greater body fat. Therefore, heightened food reward for high-fat sweet combined with lower Craving Control or high Disinhibition, especially in the hungry state, could be implicated in overeating. Exploring food reward alongside appetite control is necessary to understand phenotypes of obesity and may help the development of personalised treatments or preventing obesity. Further studies should explore the potential for non-linear relationships between food reward and markers of obesity, such as fat mass, to conclude on the role of food reward across the spectrum of obesity.

The work in this chapter was deliberately undertaken to exhaustively analyse interactions between sets of variables of varying logical status; including objectively quantified physiological measures; hypothetical constructs (factors), rated psychological perceptions and numerical physical choice behaviour. The intention was to show the potential of a statistical and descriptive approach to explore the inter-relationships among a complex network that forms the landscape of human appetite. The approach is therefore deliberately exploratory in order to showcase the power of a form of data analysis to try to understand the complexity of multiple interacting variables rather than present each variable one at a time. The picture that has emerged is therefore complex yet realistic.

Chapter 10
General Discussion

10.1 Summary of thesis findings

This thesis examined the role of liking and implicit wanting during weight management, diet-induced weight loss (WL), no-contact follow-up, and BMI status in women. Furthermore, these relationships were investigated alongside appetite-related variables such as body composition, eating behaviour traits, appetite sensations and food intake to contextualise the role of liking and wanting.

These aims were explored in a series of experiments called the DIVA studies, including a diet-induced WL randomised controlled trial, a one-year no-contact follow-up and a cross-sectional study comparing women with and without overweight/obesity. The originality of the thesis was twofold. First, the use of behavioural measures of liking and implicit wanting for food varying in taste and fat using all the outputs from the LFPQ within a psychobiological approach of appetite control in the context of weight management was novel. Second, multivariate analyses and data visualisation enabled the individual variability to be summarised beyond the often-misleading average. Together, these raised the importance of studying both the large individual variability in reward and the separate role of liking and implicit wanting for low- and high-fat food in overweight/obesity and weight management. Importantly, these findings emerged from a small dataset contrasting with the ambitious aims and therefore, interpretations must be approached with caution.

More specifically, this thesis contributed to undermine the belief that food reward is inevitably greater in obesity and that it increases during food restriction. On the contrary, liking and wanting decreased after different weight management interventions (Ch.2) and liking decreased with a small effect size during diet-induced WL to ≥5% (Ch.5). There were also minimal differences in food reward among BMI categories (Ch.9). Exploring individual variability revealed different patterns of decreases and increases in food reward, showing that the same dietary intervention affected women differently (Ch.6). The decrease in liking occurred in the context of improved appetite control but was not correlated with WL per se (Ch.7). After 1-year of no contact, weight was regained, appetite control weakened and liking returned to baseline levels (Ch.8). Lastly, women with overweight/obesity did not have higher implicit wanting for high-fat sweet (HFSW) but lower implicit wanting for low-fat sweet food (LFSW) than women within the normal range of BMI, which was associated with improved appetite control (Ch.9). See Figure 10-1 for a summary of the main questions and results developed in this thesis.

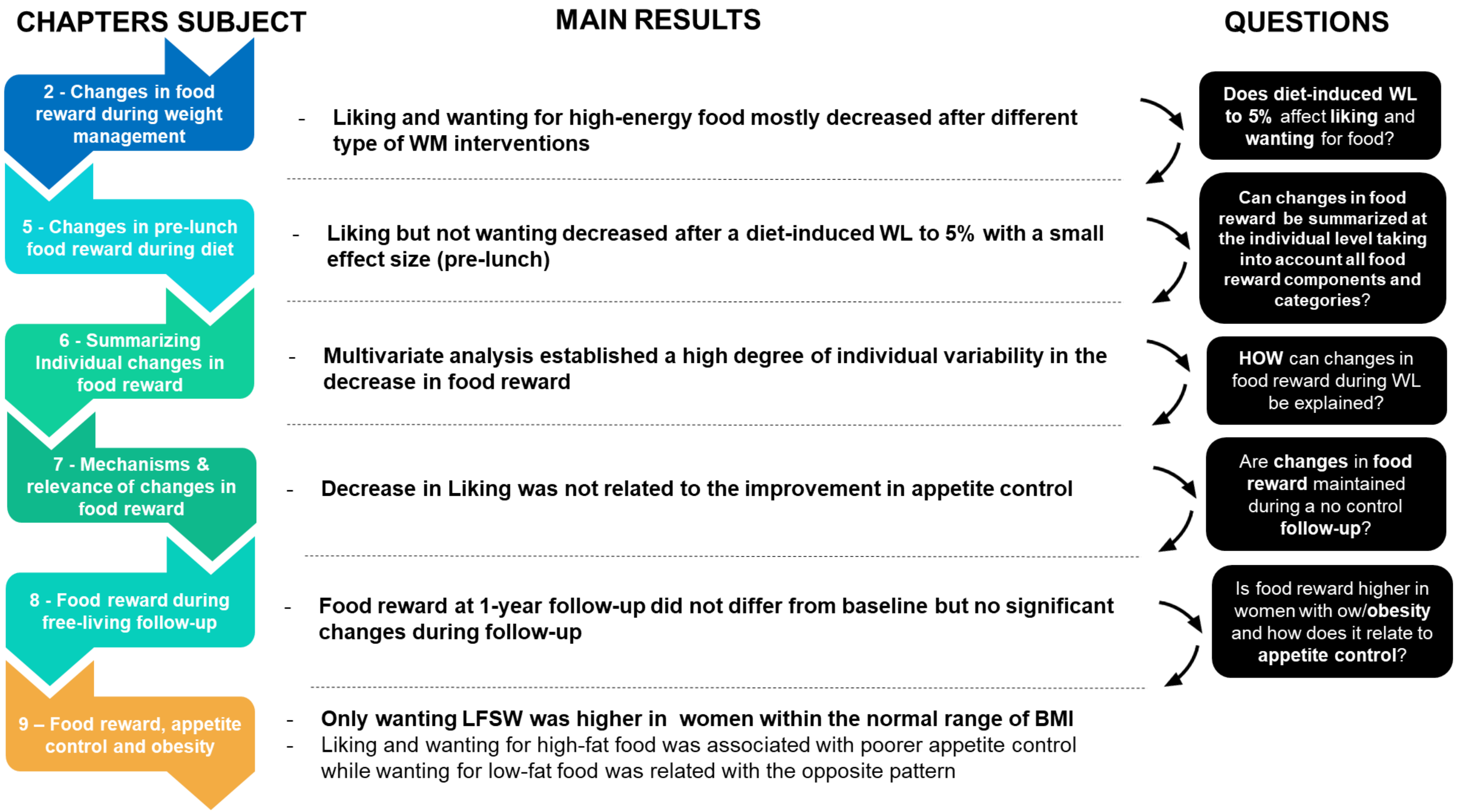

Figure 10-1: THESIS SUMMARY: Effect of dietary induced-WL and obesity on components of Food Reward

Wanting: implicit wanting; HFSW: high-fat sweet, LFSW: low-fat sweet, ow: overweight

10.2 Implication of food reward components for weight management and obesity

10.2.1 Why does liking decrease during diet-induced WL?

One of the most important findings from this thesis was the decrease in liking for all food categories during the diet-induced WL intervention. This finding contradicts the common idea of hedonic compensatory mechanisms by which energy restriction could lead to increased reward in responses to food cues (Hintze et al., 2017). As explained in Chapters 2 and 5, these contradictory findings might be due to differences in methodology used to assess components of food reward and the duration of the energy restriction, with short-term energy restriction tending to increase reward while longer-term decreasing reward (Kahathuduwa et al., 2017; Oustric et al., 2018a). However, less is known about why this decrease in liking might happen.

10.2.1.1 Effect of WL

It has been proposed that WL (i.e. the decrease in body weight) is associated with a decrease in liking during energy restriction (Andriessen et al., 2018; Ledikwe et al., 2007; Martin et al., 2011). It is important to note that one strength of the DIVA-1 study was the intention to match WL between participants and diet modalities to ≥5% WL as it was shown to affect compensatory responses (Nymo et al., 2017; Nymo et al., 2018). Therefore, this study was not designed to assess the effect of the degree of WL per se. However, Chapter 5 showed that the decrease in liking was not associated with the percentage of WL or rate of WL. Chapter 6 added that the individual changes in liking in the seven women who did not lose more than 5% WL did not differ from those who achieved clinically significant WL. Lastly, Chapter 7 showed that the decrease in liking was not associated with changes in body weight or changes in body composition, as shown in another study (Hopkins et al., 2014). Altogether, these findings were consistent with the results from Martin et al. (2006), showing no relationships between the decrease in food cravings and percentage WL during a food-based low-energy diet and a liquid-based very-low-energy restriction. According to the authors, the decrease in craving was not explained by a decrease in food variety, but energy restriction could account for the suppression of food cravings. As a note, craving is different from liking and wanting but is the closest comparator investigated.

Another study from these authors (Martin et al., 2011) reproduced these findings during a 2-year diet intervention, reporting a decrease in cravings and food preferences for the food targeted by the restriction (low-fat vs low-carbohydrate diet). Again, there was no relationship between changes in food preferences and percentage WL, and as the sample size was quite large, this cannot be explained by a lack of power. Importantly, the characteristics of the intervention (long-term free-living food restriction) suggest that the mechanisms underlying the effect of restricting energy or specific food on liking decrease need to be further studied. Similarly, another study (Ledikwe et al., 2007), using the Fat Preference Questionnaire, also reported a decrease in fat preferences following a reduced-fat diet, and WL was associated with a decrease in fat consumption but not with a decreased preference for fat. To conclude, it seems that WL (in terms of body weight or body composition) might not be directly related to changes in liking during energy restriction, and other mechanisms remain to be explored.

10.2.1.2 Effect of energy restriction or exposure to diet

If the relationship between changes in food reward and WL is not robust, then how can the decrease in liking be explained? Several hypotheses can be suggested. First, the previous paragraph raised the possible effect of energy restriction or food restriction on changes in liking, with the mechanism remaining to be explained. However, to distinguish the effect of the energy restriction from the exposure to the diet (e.g. change in eating habits, healthy food exposure, change in the food environment), studies would need to have a control arm with the same diet exposure without the energy restriction. Based on children's literature, increasing the exposure to healthy food such as vegetables increased the liking of those foods without energy restriction (Anzman-Frasca et al., 2012; Appleton et al., 2018). However, the effect of taste exposure has been reported especially on specific food types such as single and unfamiliar vegetables in children (Nekitsing et al., 2018). Similarly, in adults, the effect of the repeated exposure to food on liking is also modulated by the type of food, such that a staple food appears to be resistant to monotony (i.e. liking stable over time) compared to more liked and less frequently eaten food, which tends to decrease with repeated exposure (Hetherington et al., 2002). Less is known about the repeated exposure to a variety of low-energy foods in the context of meals in adults.

Moreover, while the dietary interventions investigated in this thesis did not have a control arm without energy restriction, they all showed a decreased liking for low and high-energy food (Andriessen et al., 2018; Martin et al., 2011; McVay et al., 2016; Oustric et al., 2021). These findings suggest that energy restriction might interact with cognition and WL goals to attenuate liking for the food used to lose weight (Oustric et al., 2018a). As a note, the 12-week exercise study by Beaulieu et al. (2020c) reduced wanting for high-fat food while there were no changes in the control (without intervention), showing that the decrease in wanting was not an effect of time. More work is needed to disentangle the effect of energy restriction from food exposure on specific food categories such as high-fat and low-fat food.

10.2.1.3 Effect of change in eating behaviour and conditioning

Secondly, the dietary intervention could change the eating habits previously established, which could attenuate liking (Meule, 2020). Based on conditioning principles, decoupling the consumption of high-energy food with the stimuli generating consumption of this food (e.g. state, specific environment, etc.) has been shown to reduce food cravings in adults (Kahathuduwa et al., 2017) and to affect food preferences in children (Birch, 1998). Indeed, associative learning plays a key role in shaping food preferences in children with associative conditioning resulting in increased liking for food in positive social and environmental contexts. Conversely, using high-fat food as a reward to increase the consumption of low-fat food (which can be seen as negative context) has been shown to increase the liking for the high-fat food and the dislike for the low-fat one (Birch, 1998). More recently, using a sweet food as a reward (for completing a cognitive task) has been shown to increase the liking for this reinforcing food in both children and rats (Bauer et al., 2021). Interestingly the food used in children was a dried apple, which after conditioning, was preferred against other tasted healthy snacks and against hypothetical French fries and gummy bears, which suggests the use of this technique to increase the liking for healthy low-energy food with different taste (Bauer et al., 2021). This mechanism remains to be proven in adults but suggests that learning and conditioning might be mechanisms by which liking decreases in adults.

Finally, several mechanisms might probably interact to decrease liking. Even though liking does not seem to predict WL changes, understanding how liking is amenable to change could contribute to better eating behaviour and sustained weight management (Stubbs et al., 2021).

10.2.2 What about changes in liking during follow-up?

This thesis was the first to examine changes in food reward during a no-contact 1-year follow-up after diet-induced WL and showed that liking returned to baseline at follow-up. In contrast, two other weight management studies (Morin et al., 2018; Watson et al., 2018) reported decreased food cravings during diet-induced WL and maintenance of this decreased craving during weight stabilisation. Anton et al. (2012) reported decreased cravings after 2 years of caloric restriction while weight was regained during the follow-up. All these studies have in common that eating habits acquired during the dietary interventions were maintained during the follow-up, in addition to moderate-intensity exercise in Watson et al. (2018). In Morin et al. (2018), it was proposed that exposure to a highly satiating low-energy-density diet favoured the adherence to a healthier food pattern. In the current study, it can be suggested that the return to a completely free-living diet during follow-up where participants were free to choose their diet allowed them to return to their habitual conditioned responses with food (Meule, 2020). Consequently, to maintain the decreased liking for high-energy food observed after the WL intervention, which would contribute to improve appetite control, maintenance of the eating habits acquired during the intervention seems necessary, raising the need for research to increase adherence to healthier dietary patterns (Stubbs et al., 2021).

To conclude, some might hypothesise that liking is not a good predictor of WL and weight regain and might not be related to WL. However, while there was no statistical relationship between changes in liking and changes in weight during WL and follow-up, the fact that liking and other appetite-related variables decreased during WL and increased during follow-up shows that components of food reward have a role to play during weight management. Moreover, this was further supported by the cross-sectional analyses from Chapter 9 showing the role of liking and implicit wanting for high- vs low-fat food in appetite control. Therefore, both the dietary intervention and follow-up confirm the findings from the systematic review in Chapter 2 - that liking and wanting can be modulated by different types of interventions - and the mechanisms of these changes (changes in eating behaviour or physiological factors, conditioning, diet exposure …) remain to be investigated. Also as explained in Chapter 6 and 9, it might be that food reward is important for WL in some individuals but not for others, and other appetite-related variables are necessary to understand WL and obesity.

10.2.3 Can we target food reward to improve weight management outcomes?

This thesis poses the question as to whether components of food reward could be viable targets to improve weight management strategies (Finlayson & Dalton, 2012b). The fact that liking did not increase during either continuous (CER) or intermittent (IER) energy restriction suggests that liking for food can be positively modulated by a diet intervention. As a whole, changes in food reward during WL did not result in compensatory responses weakening appetite control. However, several points need to be raised to better understand the role of food reward in weight management.

10.2.3.1 The need to distinguish liking, wanting and food categories

A major message raised by this thesis is the importance of distinguishing between liking and implicit wanting. Both the randomised controlled trial and the cross-sectional studies supported making the distinction between liking and wanting: only liking decreased during energy restriction while only implicit wanting differed between women with or without overweight/obesity. This distinction between liking and wanting with the LFPQ was also for the first time validated via a PCA statistical approach. These findings emphasise the Incentive Salience model from Berridge showing separate underpinning of liking and wanting in the brain and possible dissociation of these processes under specific conditions such as eating disorders or obesity (Berridge & Robinson, 2016; Morales & Berridge, 2020). These findings also have consequences in terms of weight management strategies. While most of the studies assessing the effect of dietary interventions on food reward did not assess wanting, this thesis was the first to suggest that liking but not wanting decreases after two types of dietary energy restriction, which now remains to be confirmed using larger dataset and a non-interventional control arm.

A second question raised by the review in Chapter 2 (Oustric et al, 2018) was whether different types of weight management strategies would affect food reward differently. More recently, a 12-week exercise training study led to reduced wanting for high-fat food but not liking (Beaulieu et al., 2020c). How might these opposite responses to WL between diet and exercise be explained? One possibility is that exercise affects cognition and executive function, while dieting directly modulates eating habits (Beaulieu et al., 2020c). During a diet, the relationship with food is externally affected, whereas the individual's intrinsic motivations are probably not. On the contrary, during exercise, the strengthening of cognitive processes such as inhibitory control could have a moderating effect on wanting rather than liking (Joseph et al., 2011). Furthermore, it has recently been suggested that chronic exercise could decrease wanting for high-energy food while increasing liking for low-energy food. The mechanisms of change in food reward such as cognitive processes, modulation of brain reward systems or other mechanisms (Beaulieu et al., 2020e) remain to be deciphered. Importantly understanding how to increase liking for low-energy food, could improve appetite control for future weight management strategies.

Along the same lines, this thesis, and especially the last chapter, showed the importance of measuring liking and wanting for high-fat and low-fat food. Not only was wanting for low-fat sweet food the only food reward variable differentiating between women with or without overweight/obesity, it was also associated with improved appetite control. This finding is in line with two recent studies, measuring components of food reward with different methodologies, also reporting higher reward for low-fat food in different samples of mainly normal-weight women (Kahveci et al., 2021; Pedersen et al., 2021). In Pedersen et al. (2021), liking and wanting measured by a culturally adapted version of the LFPQ were higher for low-fat food than high-fat food, which was associated with an increased attentional response (measured by eye tracker) and intake of low-fat food. Similarly, Kahveci et al. (2021) showed that participants had an approach bias towards low-energy food but not high-energy food, which was related to increased desire for low-fat foods. This challenges the common idea that high-energy foods are more rewarding than low-energy foods. Moreover, the authors suggest that other factors such as cognition, learning, expectations could enhance reward for low-energy food in specific contexts.

To conclude, both studies and this thesis showed that individuals within the normal range of BMI focus more on low-energy food, which could be a strategy to maintain their healthy body weight. It could also relate to the samples being predominantly female, who are known to give more importance to healthy eating and to avoid high-fat food compared to males (Wardle et al., 2004). As a note, in this thesis, women within the normal range of BMI did not have higher restraint than the women with overweight/obesity, which might have explained the higher wanting for low-fat food. These results raise the importance of assessing reward for low-fat foods, which are often underrepresented with research focusing mainly on high-energy food conceived as an innate reward. Now, it remains to be understood how the reward for low-fat food can be manipulated in women with overweight/obesity to reinforce appetite control and weight management (e.g. via exposure, conditioning, cognitive strategies (Boswell et al., 2018)).

10.2.3.2 The need to take into account the individual variability

Individual variability was a recurring feature of this thesis exploring psychobiological variables during WL, follow-up and overweight/obesity. The visualisations of both individual changes and variable densities have highlighted the need to go beyond the mean, which often fails to reflect the reality of true variability between people. Indeed, the phenomenon of individual variability has for years been ignored by researchers who favoured a dependence on the mean value of groups (Dilnot, 2007). The importance of focussing on the variability in outcome rather than the mean value was previously highlighted in a fully supervised 12-week exercise intervention on appetite control, body weight and fat mass (King et al., 2008). However, to ascertain the true nature of the individual variability, as alleged by Atkinson and Batterham (2015), further studies with a non-intervention control group are needed to determine whether the observed inter-individual variability is due to random effects of the intervention, rather than to true differences between individuals. Moreover, resolution of this issue requires not only statistical arguments but also a consideration of biological principles.

In this thesis, the exploration of individual changes during WL and follow-up has underlined potential individual patterns of responses to dietary interventions. Chapter 6 proposed a clustering approach based on the variables summarising changes in food reward, but a larger sample size would be necessary to test the clinical validity and utility of such phenotypes. For example, this multivariate approach could be reproduced using a much larger dataset from a weight loss maintenance trial in adults who have achieved significant weight loss (Scott et al., 2019). The final aim is to personalise the dietary interventions based on the individual characteristics or responses to go beyond the unsuited 'one size fits all' approach (Butland et al., 2007). Lastly, the variability and the overlap between groups with or without overweight/obesity highlight the concept of a family of "obesities" proposed by Butland et al. (2007), recognising the complexity of obesity and the need to go beyond univariate analysis.

10.2.3.3 The need to investigate food reward within appetite control

Considering individual variability leads to the recognition that a range of solutions will be needed to solve the multifactorial condition of obesity. Indeed, this thesis showed the importance of exploring food reward within the context of appetite control using a biopsychological approach as described previously (Caudwell et al., 2011). Even though food reward alone was not expected to distinguish between women with and without overweight/obesity, the work in this thesis is in contrast with the common idea that reward for high-energy food characterises women with overweight/obesity. Chapter 9 illustrates the high overlap in reward for high-fat sweet food between women with and without overweight/obesity, therefore there is a need to identify and investigate phenotypes of overconsumption based on different appetite-related variables which may help to better characterise obesity. Indeed, Berthoud et al. (2020) summarised different behavioural phenotypes such as "the ability to resist high energy-dense snack foods when not metabolically hungry, the willingness to work for food reward, and the ability to resist the drive towards palatable food items". They recognised that it is not yet known how to modulate reward processes, but it is more likely that a combination of strategies targeting different appetite-related variables will be most efficient to tackle obesity (Berthoud et al., 2017).

The main study in this thesis did not permit inferences to be made about causal mechanisms between food reward and weight management or weight loss. However, a number of candidate mechanisms can still be implicated in changes in food reward during weight loss. While it is still debated whether obesity is a cause or consequence of changes in food reward, the dynamic vulnerability model (Devoto et al., 2018) integrates in a sequential theory both susceptibility to, and consequences of obesity once developed on food reward. First, a predisposition to obesity might involve a hyper-responsivity to taste generating overconsumption and contributing to greater cue-reward sensitisation. Next, repeated overeating can lead to weight gain which may contribute to blunted food reward responses (Devoto et al., 2018). Dietary fat has been shown to affect the dopamine pathway and food intake via inflammatory pathways (Wallace & Fordahl, 2021). In addition to inflammatory processes, insulin and leptin resistance have been associated with obesity (Leite & Ribeiro, 2020). Dysregulation in these pathways has been shown to impact reward processing in the brain (Berthoud et al., 2011). Yet, little is known about the mechanisms by which weight loss, diet or behavioural components of weight management might be responsible for the changes in food reward. More research is needed to explore these potential mechanisms.

10.3 Methodological considerations

This thesis is centred on women, which questions the generalization of the findings to the general population. Indeed, Wardle et al. (2004) showed a gender difference in food choices, health beliefs, and dieting status, confirming that women report trying to follow healthy eating recommendations (such as avoiding fat) more than men. While this was a self-reported study, the large sample size and the cross-cultural nature of this study suggest that gender might influence eating behaviour and adherence to dietary interventions. However, this thesis focused on women, reducing the variability due to gender, and showing that other factors account for the variability observed. In the future, it would be interesting to study the possible effect of gender on changes in food reward during dietary interventions.

Moreover, both animal and human studies have raised the impact of oestrogen and progesterone on food reward, intake and binge eating (Ma et al., 2020; McNeil et al., 2013). However, the menstrual cycle was not taken into consideration in the studies within this thesis. Indeed, the matched WL design of the study implied that the final measures day was fixed at 5% WL (and not to a specific intervention duration), which did not allow the timing of the menstrual cycle with the measures day. Consequently, the menopausal status (in which the ovarian hormone balance changes) might have affected food reward results (Thomas et al., 2014). However, the per-protocol analyses included only one post-menopausal woman and excluding this woman did not reveal a differential effect on food reward see (Beaulieu et al., 2020b).

As mentioned in the thesis, the relatively small number of women in DIVA-1 (WL study) without a non-interventional control group implied that the results might not be generalisable to larger, longer, and more intensive interventions and a larger randomised controlled trial is warranted to confirm the findings. The effect of the diet-induced WL intervention on liking was small, which was expected, as the intervention was not purposely designed to modulate liking or wanting but to reach ≥5% WL. However, the clinical threshold for changes in food reward remains to be determined, especially considering the large individual variability identified in this thesis. One might ask whether this study was underpowered to detect the changes in implicit wanting. Indeed, in DIVA-1 the effect sizes of the changes in liking were small ($\eta^2_G \geq .02$) but the actual power to detect the changes was ≥ 63%, while for implicit wanting the changes were non-significant with negligible effect sizes ($\eta^2_G \leq .005$) and an actual power ≤ 10% depending on the food categories. Based on these effect sizes (using G*Power v3.1), 42 participants (for liking) and 342 participants (for wanting) would have been necessary to detect changes with a power of 80%. This analysis is consistent with the argument that dietary interventions might affect liking more than wanting. As a note, the analysis in Chapter 5 showed a significant increase in implicit wanting for LFSW only from week 3 to post-WL. This result raises the fact that the power also depends on the food category. Interestingly LFSW food was the least wanted food category at pre-lunch (data not reported) and was also less wanted in women with overweight/obesity compared to women within the normal range of BMI in the fasted state. Therefore, the only wanting category approaching an increase during the WL was the one associated with improved appetite control.

In DIVA-2 (cross-sectional study), the same question could apply whether the study was powered to detect a difference in food reward components between women with or without overweight/obesity. The effect size of the difference in wanting between groups was small to medium (d = .42), and the actual power was 70%. Based on this sample size and a two-tailed t-test, 90 participants per group would have been necessary to reach a power of 80%. Also, it should be noted that the control group in DIVA-2 was not collected at the same time as participants with overweight/obesity in DIVA-1 and they were not motivated to lose weight which might have added to the variability in the comparison. However, participants in DIVA-1 were restricted to overweight or class 1 obesity to reduce the variability in the sample with overweight/obesity. Further studies should test whether individuals with a higher level of obesity might have different food reward responses compared to individuals in the normal range of BMI.

In terms of DIVA-1 design, the highly controlled and personalised dietary intervention assured greater control and adherence. Indeed, all the food was ordered from the local supermarket, was pre-portioned and provided to the participants every week (except for the alternating *ad libitum* ‘feeding days' in IER) and tailored to individual food preferences by a registered dietician. Moreover, energy intake was assessed in the laboratory with an *ad libitum* meal carefully tailored to offer a sweet and savoury component matched for energy density and reduce the effect of food diversity on intake (Embling et al., 2021). While laboratory *ad libitum* test meals are the gold standard to measure energy intake, they might not reflect less controlled, free-living behaviour (Gibbons et al., 2014). Indeed, large portion sizes are also known to increase energy intake, especially in the laboratory (Hetherington & Blundell-Birtill, 2018), which might decrease the sensitivity to detect changes in energy intake between women with or without overweight/obesity or during WL. However, the results from this thesis illustrate energy intake in a specific scenario where too much food is provided, which might also happen in this “obesogenic” food environment. Moreover, this test meal was not specifically designed to explore the effect of liking and wanting using the LFPQ. It would have been interesting to design a lunch matching the food categories present in the LFPQ to investigate the food selection per category as in Pedersen et al. (2021).

Eating behaviours are inherently influenced by culture (Alonso-Alonso et al., 2015), with craved food (Komatsu, 2008), explicit and implicit perception of tasty food (Werle et al.,

2013) or the importance of social and sensorial pleasure (Fischler & Masson, 2008; Rozin et al., 1999) varying among countries. These cultural differences question to what extent food pleasure and motivation can be modulated by food culture and how this could have affected the present results. This thesis used a validated measure of food reward validated for the British culture (see post-script). While participants were not screened based on their nationalities, participants had to be fluent in English and the food stimuli used in the LFPQ were individually screened to make sure they were frequently eaten and liked. To conclude, the influence of culture, environment and cognitive factors on food reward was not the purpose of this thesis but remain key components of appetite control that should be explored in further studies (Higgs et al., 2017).

One defining feature of the LFPQ is that liking is an absolute measure (aggregated scores for different food categories from VAS ratings) while wanting is a relative measure (aggregated food category scores from amalgamation of reaction times and choice frequency from the forced choice task). Participants are required to choose between the presented pair of foods and consequently cannot express "no wanting" for one stimulus. There is no absolute zero for "no wanting" but implicit wanting does quantify both the degree and the direction of participant's motivation. Moreover, the task measures "wanting" for each food category by comparing reaction times and choice frequency to that of the foods from the other food categories. This allows an understanding of participants' response patterns for meaningful dimensions (fat vs taste) over multiple trials (N = 96 pairs). One might ask, if a participant has the same degree of preference for both stimuli in one trial, the reaction time will be longer and it could be questioned whether the algorithm will reflect a lower wanting for both stimuli. However, a slower response in one trial is only a proxy of the ease of each choice decision and not a direct measure of low wanting per se. The wanting for each food category can only be inferred after all food pairs from that category have been accounted for in the calculation.

Moreover, it can be debated whether wanting from the LFPQ should be labelled as "implicit" or "indirect" for example, according to the definitions by De Houwer (2006). It can be accepted that the wanting task in the LFPQ is an indirect measure as its scores are calculated from the accumulation of choices and reaction times after all trials in the task have been performed. Participants are made aware that the goal of the task is to measure "food preferences" and they are explicitly instructed to "choose the food [they] most want to eat right now". However, participants are not aware that their reaction times are being recorded and that these are key to the calculation of the scores in the task. Indeed, participants are instructed to work as "quickly as possible" in the task and mean reaction times are usually less than 1,000ms, limiting the opportunity for reflective processes to affect the outcome. Moreover, during the task there is no verbalisation or linguistic reasoning required to complete the trials. It is also unlikely that participants would be able to bias their responses or control the outcome to present a particular health identity such as preferring low-fat foods. Firstly, participants are unaware of the 4 categories of food being measured and that each food choice will be representative of a food category. Secondly, the required speed and repetition of responding in the task makes it very difficult (and easy for the researcher to spot) to produce an intentional pattern of responses that diverges from the participant's true preferences. In future research, it would be interesting to run data simulations by adjusting the weight of reaction time in the algorithm compared to choice frequency and to test the predictive and convergent validity of these different algorithms for "implicit wanting".

A main strength and originality of this thesis was to analyse components of food reward for food varying in fat and taste using all the output from the LFPQ. Indeed, usually, authors limit the analysis to fat appeal bias (i.e. mean low-fat scores are subtracted from the mean for high-fat scores) (Beaulieu et al., 2020c; Hopkins et al., 2016c; Martins et al., 2017; McNeil et al., 2017), which is simpler but lowers the sensitivity. This multivariate analysis of food reward allowed the possibility of reflecting the importance of the different food categories within appetite control. Moreover, this analysis was performed within a multisystem approach of appetite control to provide a more comprehensive investigation, which is often a limitation in other studies studying one component of appetite control in isolation. Importantly, these multivariate analyses would require a larger dataset to enable the generalisation, confirms or challenge these findings.

10.4 Conclusion

This thesis provides novel evidence for the strength and direction of the relationship between food reward, appetite control and weight loss. The systematic review in Chapter 2 (Oustric et al., 2018) was the first to comprehensively examine changes in food reward during weight management. Contrary to expectations, findings revealed that liking and implicit wanting for high-energy food decreased after different interventions including dietary, behavioural, cognitive and pharmaceutical interventions. Secondly, this thesis extended these findings by showing that liking but not implicit wanting decreased with a small effect size after two types of highly controlled dietary interventions (Oustric et al., 2021), and multivariate analyses established a high degree of individual variability in the decrease in food reward, which could explain why individuals respond differently to the same dietary intervention. Thirdly, this thesis adds to theory by suggesting that food reward does not seem to differ greatly between women with or without overweight/obesity. This is an important finding with regards to the current debate concerning reward surfeit or deficit (Devoto et al., 2018; Morys et al., 2020) and suggests that other appetite control factors need to be taken into consideration. As a whole, this thesis contributed to improving the sensitivity and comparability of measurements of food reward. It underlined that food reward is not a unitary concept, and the term cannot be used with precision since its components may vary separately. In order to target liking and implicit wanting to improve weight management strategies, future research needs to focus on underpinning the different mechanisms modulating components of food reward in association with other appetite-related variables.

POST-SCRIPT

Measuring food reward and further research

"Design methods are like toothbrushes. Everyone uses them, but no one likes to use someone else's" (Harrison & Rutström, 2008).

A protocol to improve measures of food reward with the LFPQ

This thesis raised the importance of standardising methods to measure food reward components to facilitate comparison between studies and test the reproducibility of the findings in different samples of the population. This is not to advocate for the sole use of the LFPQ, as different operationalisations are necessary to picture the different facets of implicit wanting (e.g. attentional processing vs instrumental responding). This being said, there is a need to standardise the methods used between laboratories and especially to take into account the food culture beyond a simple linguistic translation.

The use of food pictures in the LFPQ is both a strength and a limitation as it requires both nutritional and perceptual validation of the food stimuli. Food pictures are a reproducible and simple operationalisation of food cues and have been shown to generate reward in the brain, as humans contrary to animals do not necessarily require the presence of actual physical food cues (Berridge, 2018). The limitation mentioned earlier about the measure of expected liking instead of liking from the actual taste of food could be minimised by a double validation of the set of pictures. Before the study, the pictures need to be validated in the population of interest so that the food pictures represent foods that are highly recognised, frequently eaten, liked, appropriate to the culture and time of day and identified as high or low in fat and perceived as sweet or savoury. Then before the task, each participant needs to complete a screening process such that the foods on the pictures are known and eaten. Therefore, to facilitate the validation of both a cultural adaptation and its application in the laboratory, a protocol was developed based on lessons learned from this thesis to facilitate and standardise good research practice using the LFPQ (Oustric et al., 2020).

The design of this protocol has led to the publication of the Danish version of the LFPQ (Pedersen et al., 2021) and its comparison with biometrics. I have initiated collaboration with French laboratories (Institut Paul Bocuse, Laboratory of the Metabolic Adaptations to Exercise under Physiological and Pathological Conditions of Clermont Ferrand, Hospital CHU Dijon-Bourgogne and the French Armed Forces Biomedical Institute), as well as Spanish and Quebec laboratories to develop and validate culturally appropriate versions of the LFPQ in various contexts (i.e. bariatric surgery, obstructive sleep apnoea, physical activity, dietary restrictions, obesity, cold or extreme environments). I have specifically coordinated the French and Spanish LFPQ validation, from the picture selection, statistical validation, to the validation of the task in the laboratory. This protocol has since been taken up by researchers in China, Japan, Germany and Australia.

In this protocol, I proposed a visual methodology (Cluster Plot) to statistically validate the perception of taste and fat categories by the participants and this approach has raised cultural differences between perceptions of food pictures. For example, the validation of the French food pictures revealed that both vanilla and fruit flavoured yoghurt were misleadingly perceived as high-fat-sweet, which prevented them from being used as food cues in their original low-fat-sweet categories (see Figure 10-2). In the future, this methodology could be used for cross-cultural comparisons of food reward and explore the role of food culture in the development of food reward.

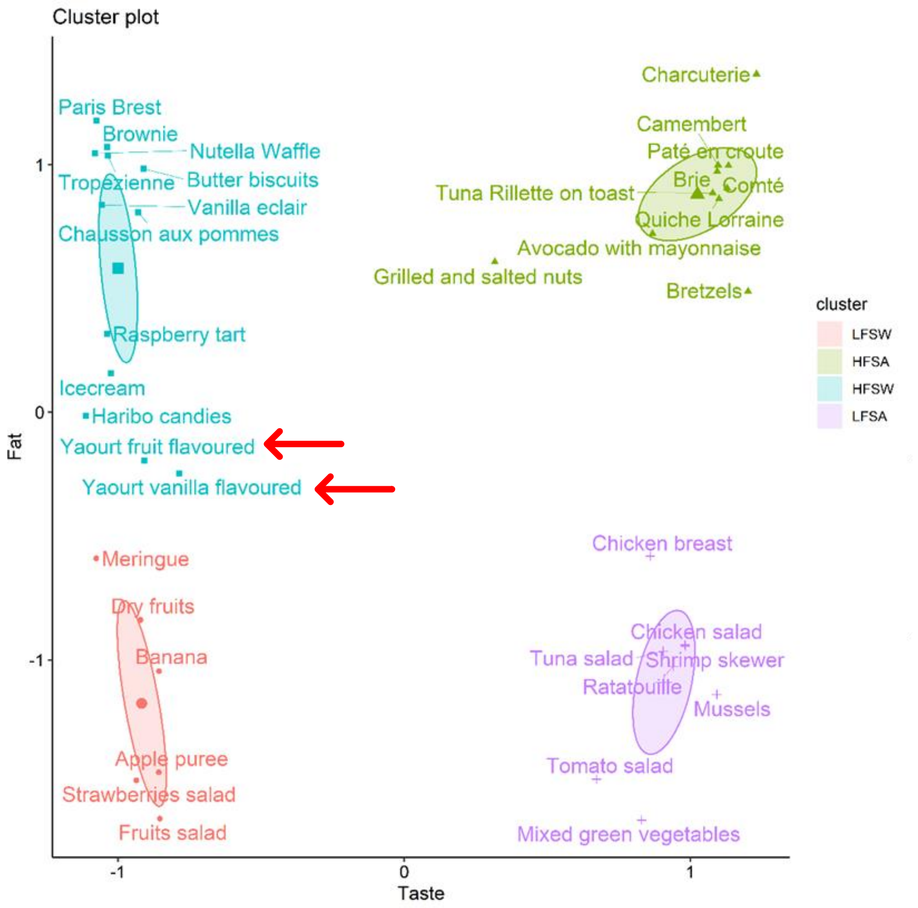

Figure 10-2: Cluster plot to validate the LFPQ French food on taste/fat perception

Scatter plot depicting the results of the hierarchical clustering by taste and fat from a French LFPQ. Mean results of the survey for taste and fat have been scaled and the foods have been projected according to their new fat and taste coordinates. Positive ratings represent savoury taste or high-fat, respectively. Smaller points represent the foods and larger points depict the centre of the cluster. The smaller the ellipse of the cluster, the more homogenous the cluster (e.g. HFSA). The further the foods are from zero, the more separate are the clusters. This scatter plot demonstrates four distinct groups of food and allows to indicate which food are closer to other clusters. Plot performed on R version 3.5.1 (R Core Team, 2013) using factoextra v1.0.5 package and enhanced hierarchical clustering. See Oustric et al. (2020) for comparison with the British LFPQ. Red arrows indicate that yoghurt, a low-fat food, was actually perceived to be high-fat by the participants in the validation survey.

Finally, based on this protocol, I also developed a diurnal-LFPQ adapted to the British culture to measure food reward across the day, co-designed and supervised a study to assess the effect of meal timing and chronotype on food reward, which has been recently published (Beaulieu et al, 2020). This diurnal-LFPQ allows the comparison of reward across the day, which was not statistically possible with the LFPQ in the current thesis as a different set of pictures was used for fasted breakfast and pre to post-lunch. Consequently, this diurnal-LFPQ could be used in future research to explore the effect of time of day on reward in specific populations to personalise and improve health-related interventions.

An app for wider applications of the LFPQ

This thesis has shown the potential of using the LFPQ to detect individual variability in food reward during weight management and the role of liking and wanting in appetite control. While it remains unknown how to modulate components of reward to improve appetite control, the next steps would be to track them in free-living situations and analyse the potential of this tool at the individual level. This progress could be enabled by developing an online version of the LFPQ (the Leeds Food Preference Platform) that will improve the features of the current tool and foster a wider use. Therefore, I initiated a project to evaluate and generate impact for the LFPQ within and beyond academia. This 3-month impact project was organised in three parts:

First, I evaluated the past and ongoing impact of the LFPQ beyond academia by interviewing collaborators and users of the LFPQ (semi-structured interview according to Reed (2018)). The LFPQ is currently used by the French and US militaries to track the food preferences of soldiers during field training. Deployments and field operations demand a properly fuelled body to maintain optimal performance, which can mean the difference between the success and failure of missions. These military testimonials show that this tool has already improved the awareness and understanding of soldiers' eating behaviour during missions and will inform changes in military ration policy. For example, soldiers exposed to intense cold temperature experienced a shift towards sweet food preferences showing that LFPQ could inform policy on rationing in extreme environments. Altogether it shows the impact of this research-grade tool when taken up as a digital platform, adaptable to contexts and goals beyond academia for health and societal impact.

Secondly, I generated a potential future impact of the LFPQ by showcasing the platform to a business audience and interviewing health professionals and investors. Regarding business impact, I created a 45-sec video, pitched the platform at various start-up events and was invited as a guest on the Impact Sessions Podcast about collaboration between academia and business using the LFPQ platform as a case study[7]. In terms of health impact, an interview with Dr. Helen McCarthy (Consultant Clinical Psychologist) to further explore the applicability of the Leeds Food Preference Platform in her consultancy suggested that the tool could help establish diagnoses on the motivation to eat and be used as a tool to raise awareness. A discussion of the platform with two other nutritionists showed that the tool could be useful, especially for improving the uptake with teenagers and improve their awareness of healthy eating. Further research is needed to test the usefulness of improving awareness of the motivation to eat in weight management in different population.

Finally, I initiated and designed a prototype Leeds Food Preference Platform (https://lfpq.co.uk/) that consists of a website showcasing the digital version of the LFPQ within and beyond academia. The interviews and networking raised the need for a digital version that will be easier to use and offer more features (e.g. free-living, pre-analysed results, user-friendly, real-time access to high-quality data, multi-device with intuitive touchscreen interface). Consequently, I worked on improving the tool's efficiency to make the platform fully customisable, cross-cultural, easy to use with pre-processed analysis and data visualisation, and able to use on different devices. I designed a website enabling better visibility and access to the tool that conveys a long-term impact vision: *A solution to assess food preferences that will help people lead healthier lives.* In future, I would like to fine-tune and validate this platform and especially for use with dietitians, nutritionists and clinicians to help patients understand and change their food reward and nutritional choices.

In terms of technical improvement, I developed eye-catching and intuitive visualisation of the results and won a prize from Leeds Institute of Cardiovascular and Metabolic Medicine for the visualisation of the platform results for patients (see Figure 10-3). This platform will improve data quality and security, reinforce standardisation and comparability of the results and will be an asset for multidisciplinary work and translational research. However, the new features of the LFPQ platform such as an admin portal to customise the task depending on needs or configurable questions to generate metadata on the individual/population, remain to be fully developed and validated in research before being used beyond academia. Therefore, I would like to validate this platform and foster its use in healthy and patient populations to understand and improve eating behaviour and health in the field of appetite control and hedonics.

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[7] Interview on the Impact Sessions Business Podcast Available on YouTube at https://www.youtube.com/watch?v=HICYiqldVrE&t=1287s

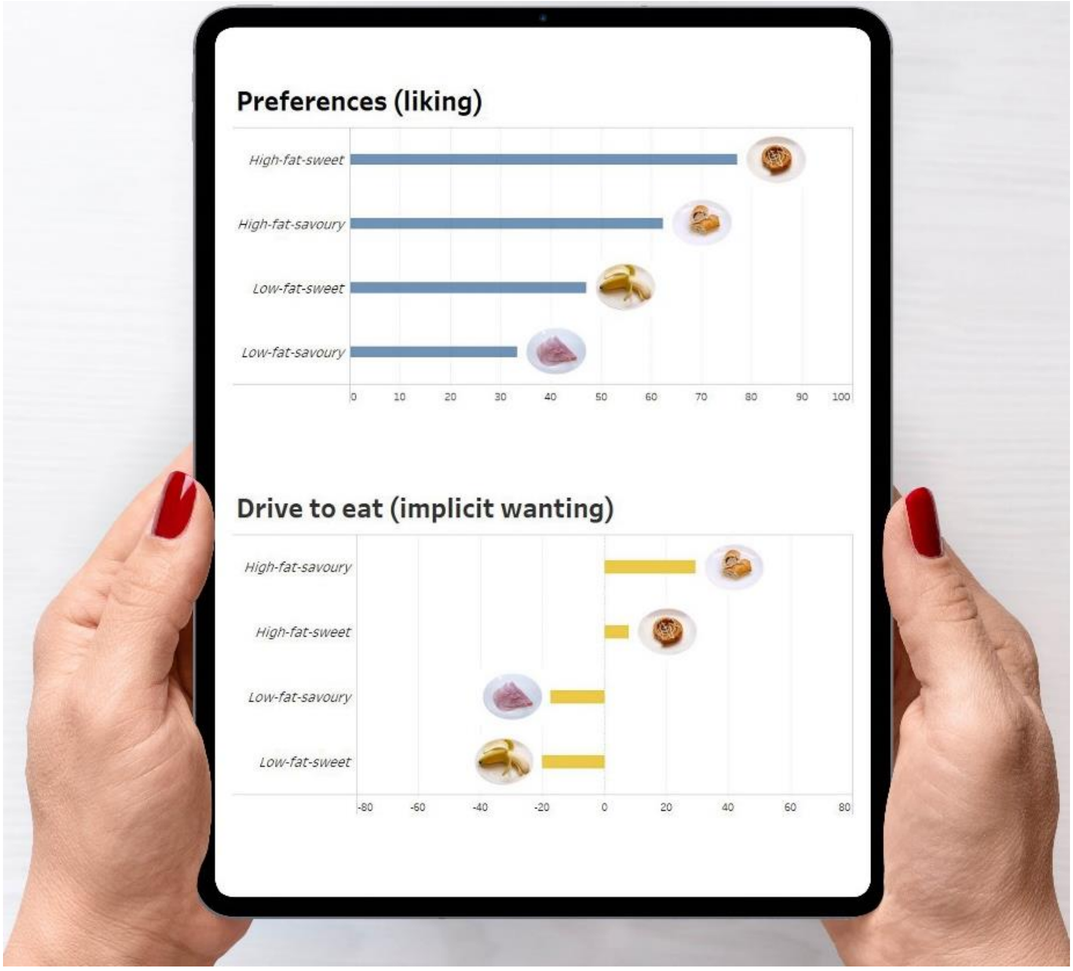

Figure 10-3: Visualisation of results using the Leeds Food Preference Platform

Visualisation performed on Tableau to facilitate the understanding of the results

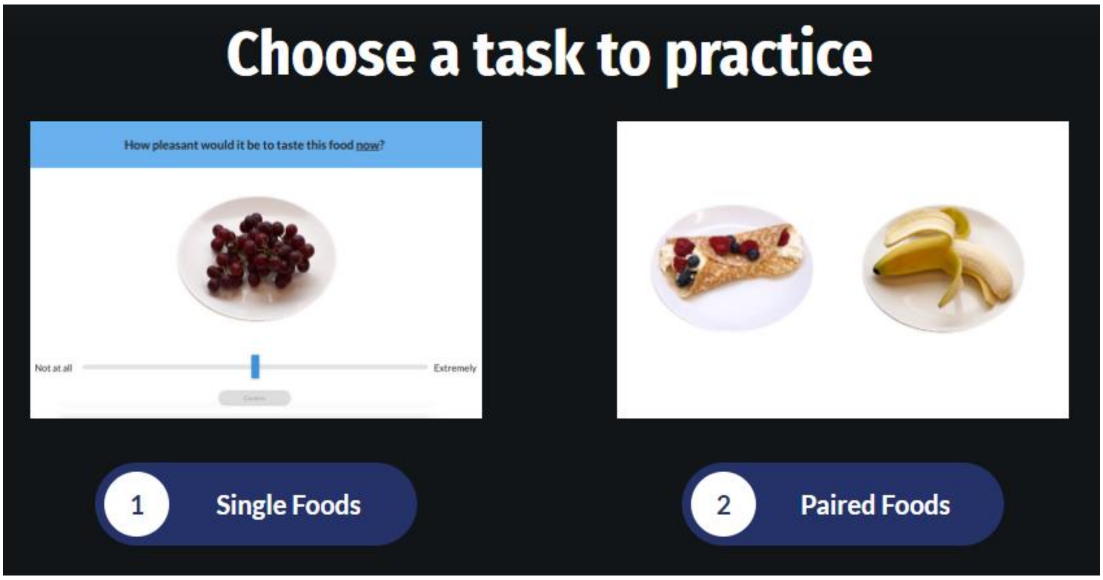

Figure 10-4: User friendly design of the task

Screenshot of the app representing training for liking (single foods) and implicit wanting (paired foods)

APPENDIX A

Chapter 2

Table A1: Keywords used for computerised database search

WEIGHT LOSS	APPETITE	LIKING	WANTING	FOOD REWARD
- weight loss - weight reduction - weight management - weight maintain* - weight maintenance - weight control - prevent* weight regain - energy balance - energy restriction - negative energy balance	- appetite - eating - eating behaviour - food intake - ingestion - food consumption	- food preferences - liking - liking for food - palatability - pleasure-giving value of food - pleasure/food - hedonic value of food - food hedonics - affective pleasure - sensory perception of food - food enjoyment - consummatory reward	- wanting - wanting for food - incentive motivation - disposition to eat - drawn to food - motivational drive to eat - incentive salience - motivation for food - motivation to eat - drive to eat - food craving - food-related motivation - anticipatory reward	- reward - food reward - hedonic* - hedonic driven eating - hedonic hunger - food reinforcement - relative reinforcing value - hedonic eating - hedonically-driven - reward-driven eating - food responses - responses to food cues

APPENDIX B

Chapter 5

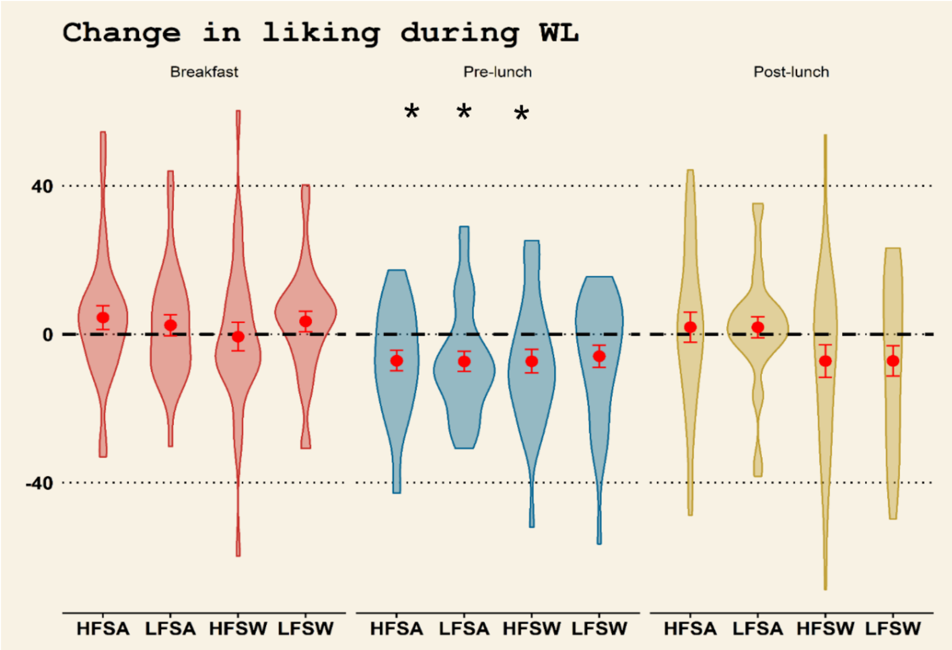

Figure B1: Changes in liking during WL by physiological states

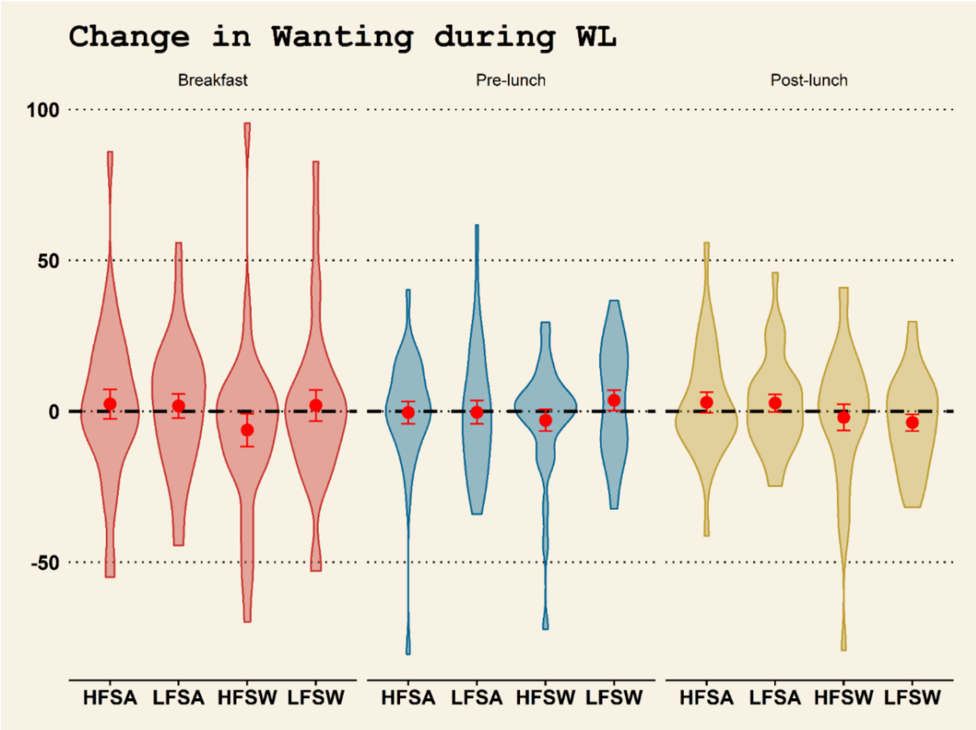

Figure B2: Changes in wanting during WL by physiological states

APPENDIX C

Chapter 7

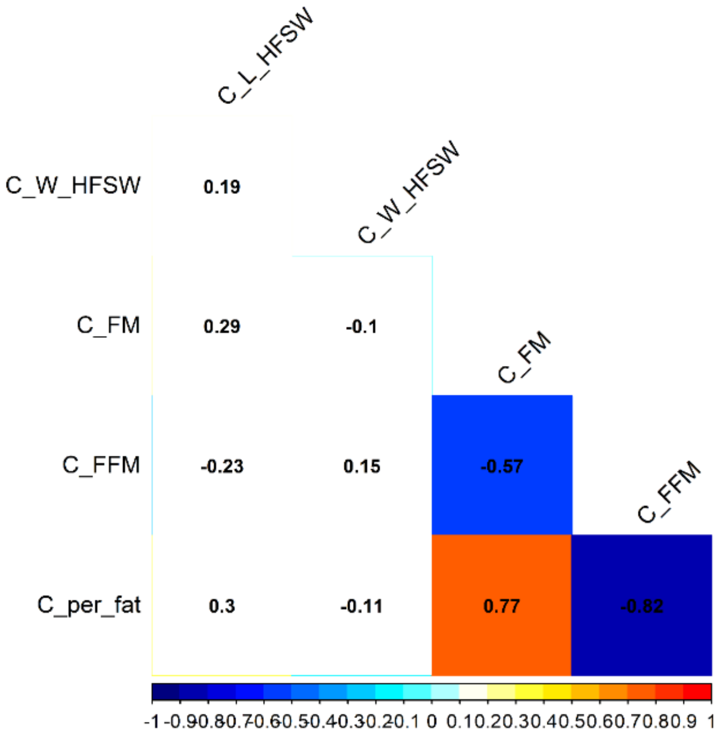

Figure C1: Correlations between changes in food reward (pre-lunch) and changes in body composition from pre to post WL (N = 30)

Pearson's correlation coefficients (r) are reported and colours represent the strength of the correlation when they are significant ($p < .05$). C_W_HFSW: change in wanting HFSW; C_L_HFSW: change in liking HFSW; C_FM: change in fat mass; C_FFM: change in fat-free mass; C_per_fat: change in percentage of fat.

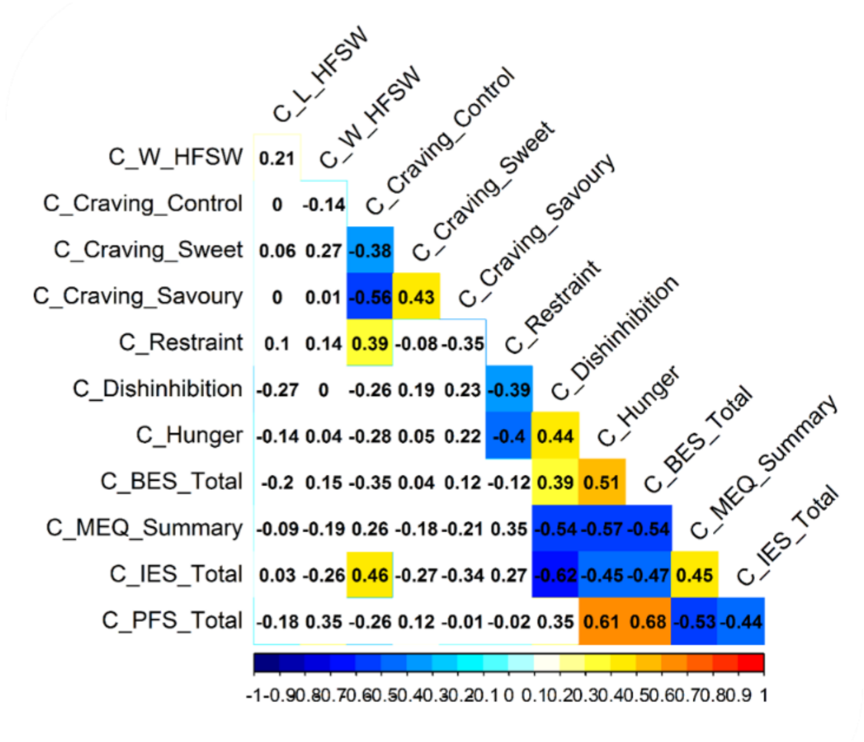

Figure C2: Correlations between changes in food reward (pre-lunch) with changes in eating behaviour traits from baseline to post-WL (N = 29)

Pearson's correlation coefficients (r) are reported and colours represent the strength of the correlation when they are significant (p < .05). C_W_HFSW: change in wanting HFSW; C_L_HFSW: change in liking HFSW; C_: change; C_Hunger: change in susceptibility to hunger (TFEQ), C_BES: change in Binge Eating, C_MEQ: change in mindful eating, C_IES: change in intuitive eating, C_PFS: change in power of food scale

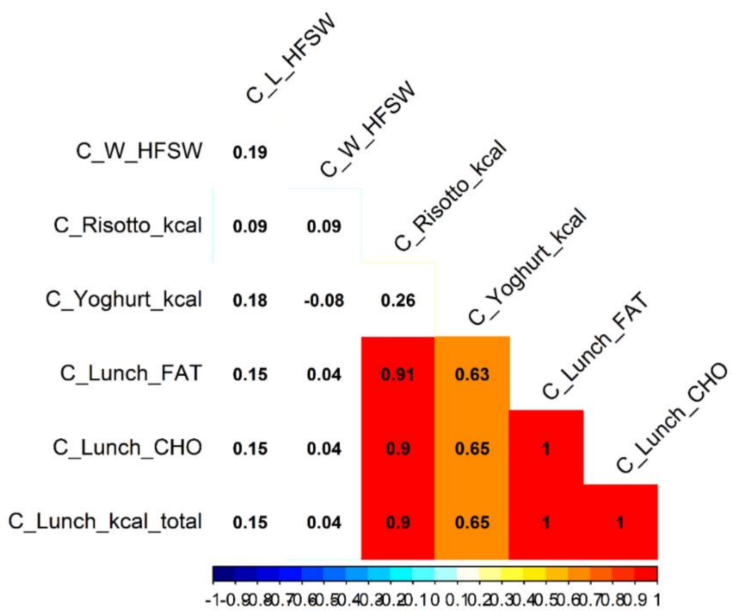

Figure C3: Correlations between changes in food reward (pre-lunch) and changes in food intake from baseline to post-WL (N = 30)

Pearson's correlation coefficients (r) are reported and colours represent the strength of the correlation when they are significant (p < .05). C_W_HFSW: change in wanting HFSW; C_L_HFSW: change in liking HFSW; C_: change

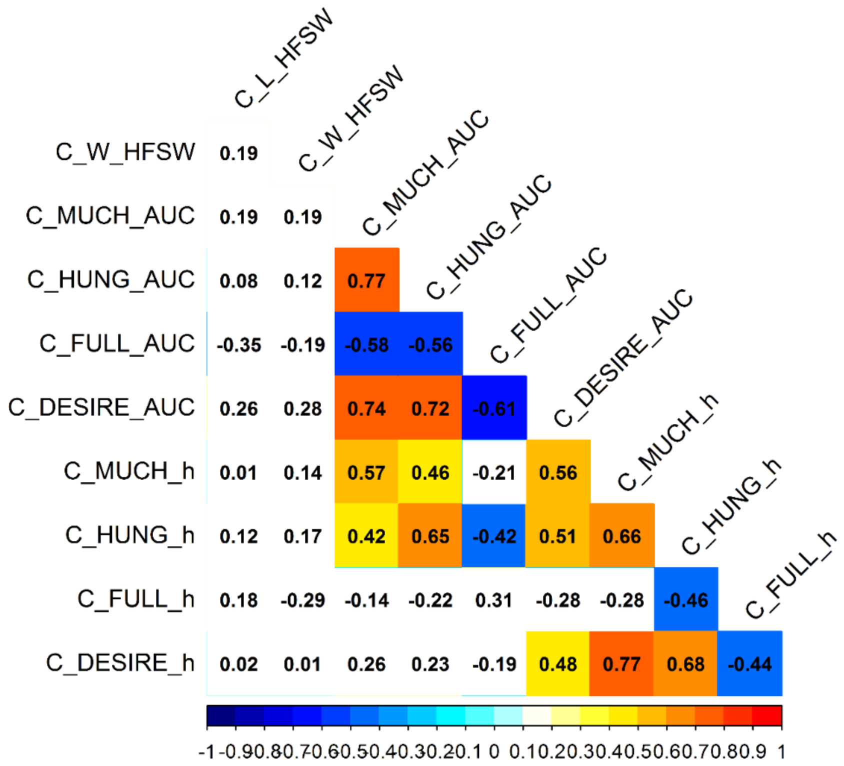

Figure C4: Correlation between changes in food reward (pre-lunch) and changes in appetite sensations from baseline to post-WL (N = 30)

Pearson's correlation coefficients (r) are reported and colors represent the strength of the correlation when they are significant ($p < .05$). C_W_HFSW: change in wanting HFSW; C_L_HFSW: change in liking HFSW; C_: change; C_MUCH: change in prospective consumption, C_HUNG: change in hunger, C_FULL: change in fullness, C_DESIRE: change in desire to eat; AUC: area under the curve; h: hungry state

APPENDIX D

Chapter 8

Table D4: Mixed model for physiological variables – Fixed effect

Model for body weight

Variable	Coef	SE	t	df	p	CI_lower	CI_higher
(Intercept)	79.446	2.601	30.544	29.261	< .001	74.176	84.715
Post-WL	-5.149	0.344	-14.954	42.972	< .001	-5.839	-4.458
Follow-up	-2.532	0.462	-5.48	43.062	< .001	-3.462	-1.608
IER	1.622	4.033	0.402	28.97	> .1	-6.552	9.795

Model for %FM

Variable	Coef	SE	t	df	p	CI_lower	CI_higher
(Intercept)	40.96	1.333	30.728	29.685	< .001	38.261	43.66
Post-WL	-2.314	0.268	-8.62	42.982	< .001	-2.852	-1.776
Follow-up	-1.009	0.36	-2.802	43.191	< .01	-1.731	-0.288
IER	0.706	2.06	0.343	29.007	> .1	-3.471	4.88

Model for FFM

Variable	Coef	SE	t	df	p	CI_lower	CI_higher
(Intercept)	46.571	1.408	33.065	29.247	< .001	43.717	49.425
Post-WL	-1.288	0.18	-7.17	42.967	< .001	-1.648	-0.928
Follow-up	-0.737	0.241	-3.059	43.051	< .01	-1.222	-0.255
IER	0.522	2.185	0.239	28.978	> .1	-3.905	4.949

Model for BMI

Variable	Coef	SE	t	df	p	CI_lower	CI_higher
(Intercept)	29.18	0.588	49.63	29.896	< .001	27.989	30.37
Post-WL	-1.873	0.13	-14.355	43.04	< .001	-2.134	-1.611
Follow-up	-0.862	0.175	-4.928	43.294	< .001	-1.213	-0.511
IER	-0.044	0.908	-0.049	29.071	> .1	-1.884	1.795

Model for RMR

Variable	Coef	SE	t	df	p	CI_lower	CI_higher
(Intercept)	1432.64	46.795	30.615	32.749	< .001	1338.125	1527.122
Post-WL	0.056	22.46	0.002	42.5	> .1	-44.98	45.091
Follow-up	209.515	29.945	6.997	43.76	< .001	148.942	269.162
IER	27.52	70.321	0.391	28.641	> .1	-115.011	170.14

FM: fat mass, FFM: fat-free mass

Table D5: Mixed models for eating behaviour traits during weight management - Fixed effect

Model for Craving Control

Variable	Coef	SE	t	df	p	CI_lower	CI_higher
(Intercept)	50.958	4.918	10.362	38.204	< .001	41.063	60.844
Post-WL	20.869	3.266	6.389	42.575	< .001	14.32	27.418
Follow-up	1.891	4.456	0.424	45.326	> .1	-7.049	10.796
IER	-8.682	7.15	-1.214	29.736	> .1	-23.148	5.81

Model for Craving Sweet

Variable	Coef	SE	t	df	p	CI_lower	CI_higher
(Intercept)	37.04	5.338	6.939	37.584	< .001	26.317	47.796
Post-WL	-15.345	3.514	-4.367	42.143	< .001	-22.391	-8.298
Follow-up	-6.806	4.795	-1.419	44.855	> .1	-16.356	2.882
IER	11.569	7.77	1.489	29.299	> .1	-4.222	27.267

Model for Craving Savoury

Variable	Coef	SE	t	df	p	CI_lower	CI_higher
(Intercept)	32.843	4.935	6.655	46.525	< .001	22.963	42.723
Post-WL	-9.608	4.487	-2.141	41.605	< .05	-18.609	-0.606
Follow-up	1.227	5.691	0.216	44.593	> .1	-10.17	12.628
IER	27.74	7.672	3.616	46.525	< .001	12.381	43.099
Post-WL: IER	-14.809	6.976	-2.123	41.605	< .05	-28.802	-0.815
Follow-up: IER	-14.091	9.999	-1.409	45.693	> .1	-33.958	6.462

Model for Positive mood

Variable	Coef	SE	t	df	p	CI_lower	CI_higher
(Intercept)	67.929	3.341	20.334	40.323	< .001	61.22	74.639
Post-WL	5.409	2.45	2.208	42.491	< .05	0.496	10.321
Follow-up	-2.779	3.328	-0.835	45.95	> .1	-9.435	3.89
IER	-3.974	4.779	-0.832	29.668	> .1	-13.655	5.703

Model for restraint

Variable	Coef	SE	t	df	p	CI_lower	CI_higher
(Intercept)	8.943	0.998	8.956	38.996	< .001	6.937	10.951
Post-WL	4.414	0.716	6.167	41.742	< .001	2.978	5.849
Follow-up	1.925	0.973	1.978	45.056	= 0.05	-0.07	3.859
IER	-1.528	1.434	-1.065	28.913	> .1	-4.439	1.375

Model for Hunger

Variable	Coef	SE	t	df	p	CI_lower	CI_higher
(Intercept)	6.49	0.633	10.247	44.479	< .001	5.223	7.761
Post-WL	-2.69	0.544	-4.944	41.722	< .001	-3.781	-1.598
Follow-up	-0.729	0.732	-0.995	46.833	> .1	-2.19	0.74
IER	0.067	0.875	0.076	28.896	> .1	-1.715	1.832

Model for Disinhibition

Variable	Coef	SE	t	df	p	CI_lower	CI_higher
(Intercept)	8.882	0.763	11.642	42.907	< .001	7.352	10.412
Post-WL	-2.647	0.63	-4.204	41.746	< .001	-3.91	-1.384
Follow-up	-1.082	0.802	-1.35	44.088	> .1	-2.697	0.517
IER	1.534	1.186	1.294	42.907	> .1	-0.844	3.913
Post-WL: IER	1.73	0.979	1.768	41.746	= 0.08	-0.233	3.694
Follow-up: IER	2.286	1.41	1.621	44.937	> .1	-0.522	5.138

Model for MEQ

Variable	Coef	SE	t	df	p	CI_lower	CI_higher
(Intercept)	2.735	0.064	42.969	42.007	< .001	2.607	2.863

Variable	Coef	SE	t	df	p	CI_lower	CI_higher
Post-WL	0.179	0.052	3.468	41.357	< .01	0.075	0.282
Follow-up	0.113	0.07	1.619	45.795	> .1	-0.028	0.251
IER	-0.208	0.089	-2.326	28.54	< .05	-0.388	-0.026

Model for IES

Variable	Coef	SE	t	df	p	CI_lower	CI_higher
(Intercept)	3.282	0.115	28.494	32.354	< .001	3.05	3.515
Post-WL	0.234	0.05	4.691	41.994	< .001	0.134	0.334
Follow-up	0.121	0.069	1.757	43.084	= 0.09	-0.016	0.259
IER	-0.28	0.174	-1.607	29.072	> .1	-0.633	0.074

Model for Binge Eating

Variable	Coef	SE	t	df	p	CI_lower	CI_higher
(Intercept)	14.507	1.648	8.805	36.013	< .001	11.192	17.83
Post-WL	-5.103	1.035	-4.93	41.44	< .001	-7.18	-3.026
Follow-up	-3.453	1.415	-2.441	43.903	< .05	-6.306	-0.631
IER	1.775	2.414	0.735	28.588	> .1	-3.131	6.657

Model for PFS

Variable	Coef	SE	t	df	p	CI_lower	CI_higher
(Intercept)	2.699	0.18	14.975	38.277	< .001	2.338	3.063
Post-WL	-0.476	0.125	-3.82	41.849	< .001	-0.726	-0.226
Follow-up	-0.312	0.17	-1.837	44.891	= 0.07	-0.65	0.031
IER	0.544	0.26	2.087	29.013	< .05	0.013	1.069

Table D6: Mixed model for appetite during weight management - Fixed effect

Model for prosp. consumption

Variable	Coef	SE	t	df	p	CI_lower	CI_higher
(Intercept)	4805.439	473.93	10.14	40.97	< .001	3854.594	5757.615
Post-WL	-653.015	351.06	-1.86	43.67	= 0.07	-1356.48	50.454
Follow-up	-251.274	462.6	- 0.543	46.91	> .1	-1172.49	680.909

IER	393.105	676.54	0.581	29.97	> .1	-978.752	1760.824

Model for hunger

Variable	Coef	SE	t	df	p	CI_lower	CI_higher
(Intercept)	5303.141	487.74	10.87	39.78	< .001	4324.052	6283.902
Post-WL	-913.713	343.69	-2.659	43.72	< .05	-1602.39	-225.038
Follow-up	-598.547	453.82	-1.319	46.6	> .1	-1506	310.213
IER	179.702	702.42	0.256	30	> .1	-1244.98	1599.278

Model for fullness

Variable	Coef	SE	t	df	p	CI_lower	CI_higher
(Intercept)	10012.58	600.17	16.68	37.49	< .001	8803.921	11219.15
Post-WL	719.919	390.22	1.845	43.14	= 0.07	-62.244	1502.083
Follow-up	1191.083	516.73	2.305	45.56	< .05	148.434	2220.273
IER	1129.809	874.95	1.291	29.38	> .1	-639.758	2905.442

Model for desire to eat

Variable	Coef	SE	t	df	p	CI_lower	CI_higher
(Intercept)	5863.186	515.56	11.37	41.12	< .001	4829.507	6899.575
Post-WL	-1073.538	391.5	-2.742	43.15	< .01	-1858.25	-288.824
Follow-up	-707.008	515.3	-1.372	46.6	> .1	-1733.11	331.92
IER	186.885	732.44	0.255	29.45	> .1	-1301.25	1666.466

Table D7: Mixed model for food intake during weight management - Fixed effect

Model for risotto

Variable	Coef	SE	t	df	p	CI_lower	CI_higher
(Intercept)	612.157	46.561	13.15	44.83	< .001	519.031	705.623
Post-WL	2.428	39.647	0.061	43.09	> .1	-77.043	81.899
Follow-up	88.925	51.854	1.715	47.64	= 0.09	-14.219	196.463
IER	18.69	64.426	0.29	29.43	> .1	-112.44	148.641

Model for yoghurt

Variable	Coef	SE	t	df	p	CI_lower	CI_higher
(Intercept)	346.3	30.902	11.21	38.84	< .001	284.177	408.423
Post-WL	-61.899	22.114	-2.799	42.6	< .01	-106.237	-17.561
Follow-up	-4.377	27.078	-0.162	44.07	> .1	-59.083	49.574
IER	-158.839	48.04	-3.306	38.84	< .01	-255.413	-62.264
Post-WL: IER	65.21	34.377	1.897	42.6	= 0.06	-3.717	134.136
Follow-up: IER	-16.488	49.136	-0.336	44.86	> .1	-114.279	82.977

Model for lunch

Variable	Coef	SE	t	df	p	CI_lower	CI_higher
(Intercept)	982.209	63.942	15.36	50.19	< .001	854.4	1110.018
Post-WL	-109.327	63.096	-1.733	41.79	= 0.09	-235.891	17.238
Follow-up	58.008	76.465	0.759	45.04	> .1	-94.643	211.711
IER	-197.55	99.401	-1.987	50.19	= 0.05	-396.236	1.137
Post-WL: IER	185.694	98.086	1.893	41.79	= 0.07	-11.059	382.447
Follow-up: IER	31	137.98	0.225	46.9	> .1	-243.094	313.836

Measures Days with 3 levels “Baseline” [ref], “Post-WL” and “Follow-up”; with diets conditions either IER or CER [ref]

APPENDIX E

Chapter 9

Table E1: Normality test of appetite control variable in 92 women

Parametric variables (shapiro.test >.05)	**Non-parametric variables (shapiro.test <.05)**
%Fat, WH_ratio	BMI, Body mass, FM, FFM, RMR
Total PA	Total EE, PAL
Craving Control, Positive mood	Craving Sweet, Craving Savoury
MEQ	Restraint, Rigid and flexible Restraint, disinhibition, Susceptibility to hunger
Yoghurt, Risotto, Lunch	BES, YFAS, PFS
Desire, Fullness, Hunger (AUC)	Desire, fullness, Hunger, Prospective consumption (fasted and fed)
Implicit Wanting LFSA, HFSW (fasted)	Implicit Wanting HFSA, LFSW (fasted)
Liking LFSA, HFSW (fasted)	Liking HFSA, LFSW (fasted)
Implicit Wanting HFSA, HFSW, LFSW (pre-lunch)	Implicit Wanting LFSA (pre-lunch)
Liking LFSA, LFSW (pre-lunch)	Liking HFSA, HFSW (pre-lunch)
Implicit Wanting HFSW, LFSW (post-lunch)	Implicit Wanting HFSA, LFSA (post-lunch)
	Liking (post-lunch)

EE: Total energy expenditure, PA: physical activity, PAL: physical activity level, RMR: resting metabolic rate, FM: fat mass, FFM: fat-free mass.

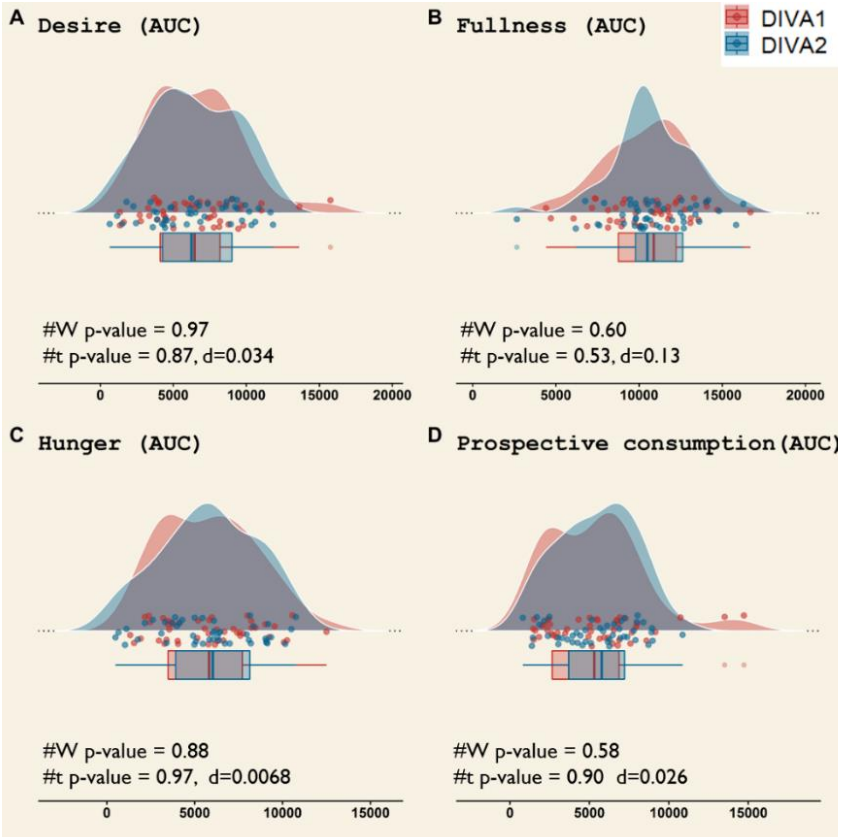

Figure E1: Appetite sensations between groups with and without obesity

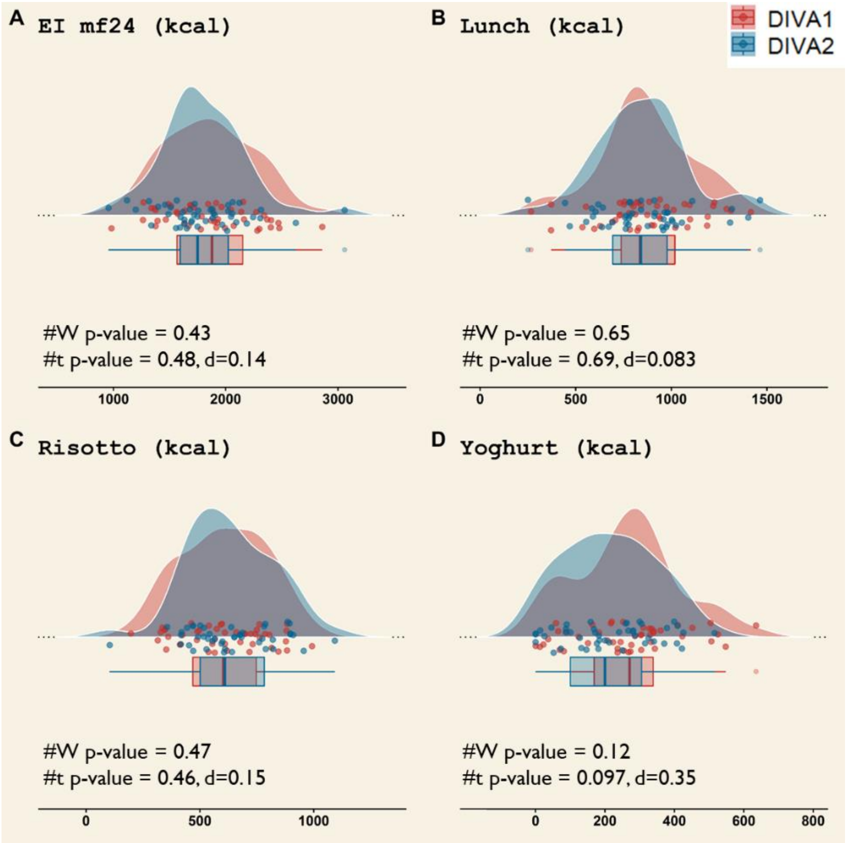

Figure E2: Food intake between groups with and without obesity

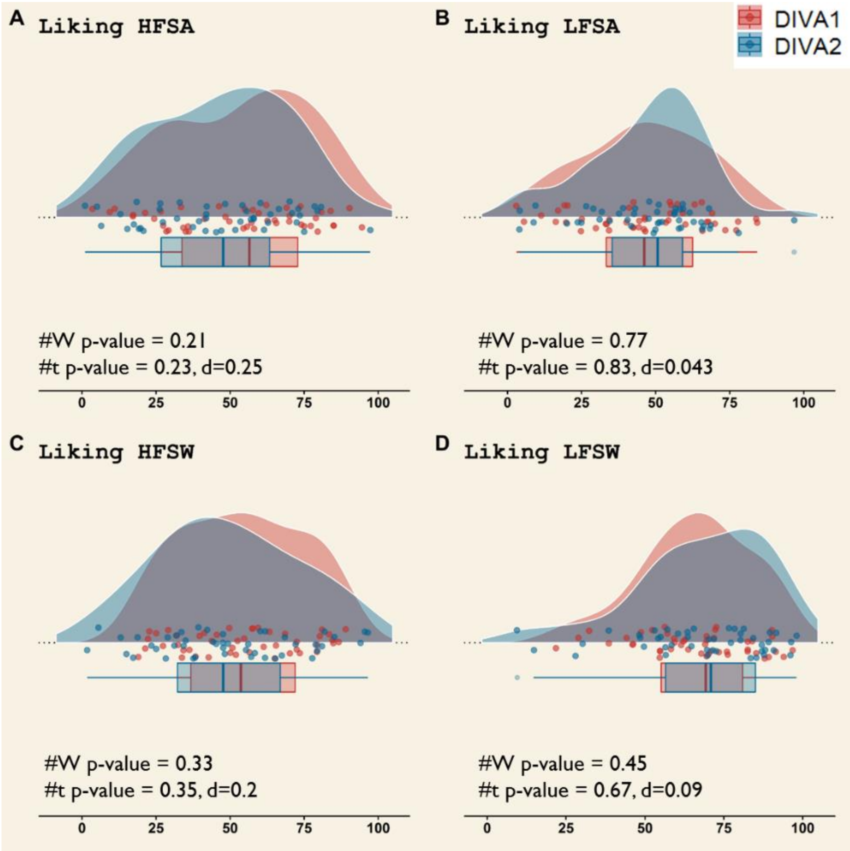

Figure E3: Liking fasted between groups with and without obesity

Table E2: Differences between liking fasted between groups

		Liking fasted			
Study	N	HFSA	LFSA	HFSW	LFSW
DIVA1	46	56.5 (39.1)	46.1 (29.1)	53.6 (35.2)	69.2 (25.8)
DIVA2	46	47.6 (36.6)	50.6 (23.7)	47.6 (34.7)	70.9 (28.5)

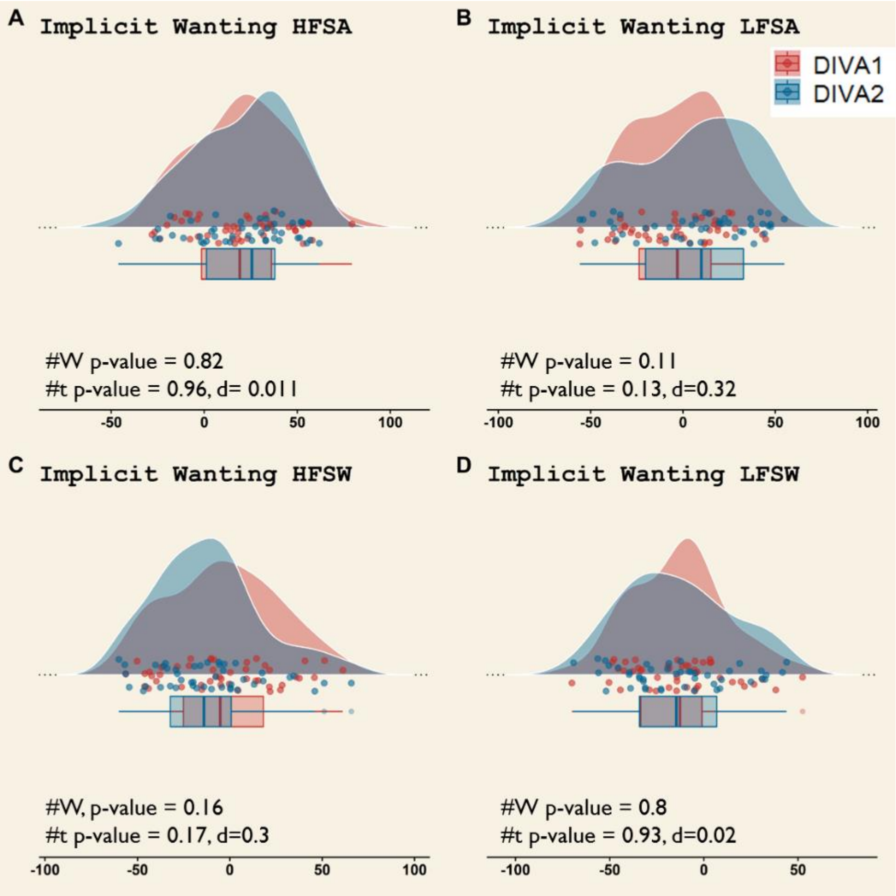

Figure E4: Implicit wanting pre-lunch between groups with and without obesity

Table E3: Differences between implicit wanting pre-lunch between groups

		Implicit wanting pre-lunch			
Study	N	HFSA	LFSA	HFSW	LFSW
DIVA1	46	19.0 (37.7)	-3.1 (38.9)	-5.2 (43.3)	-12.7 (32.4)
DIVA2	46	25.57 (36.7)	9.82 (53.1)	-14.01 (32.9)	-14.63 (41.0)

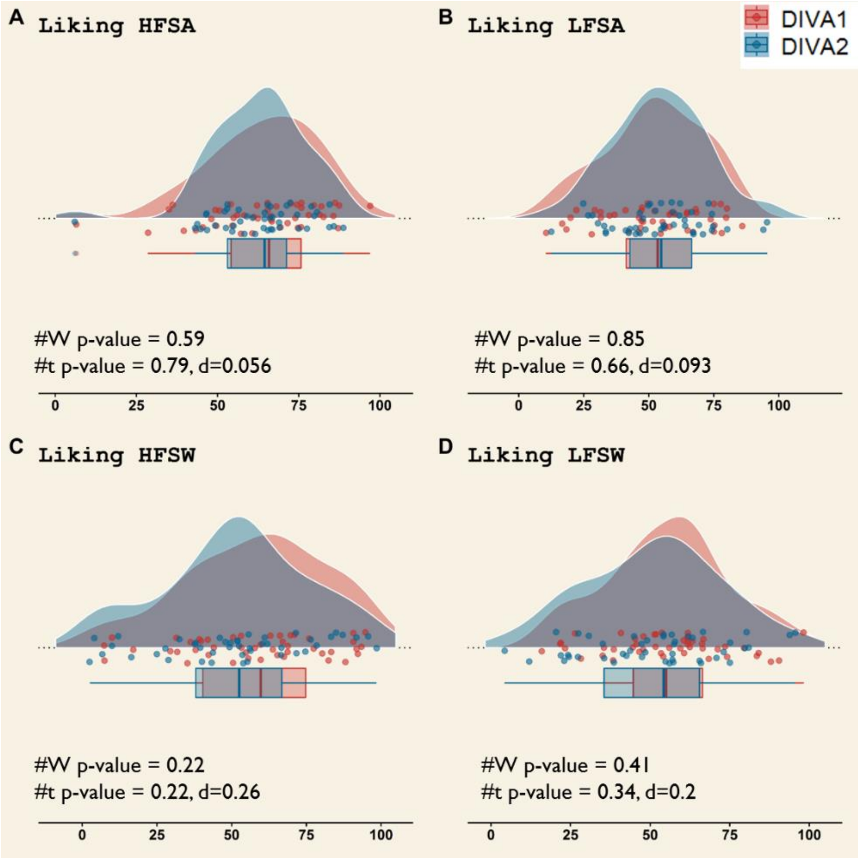

Figure E5: Liking pre-lunch between groups with and without obesity

Table E4: Differences between liking pre-lunch between groups

		Liking pre-lunch			
Study	N	HFSA	LFSA	HFSW	LFSW
DIVA1	46	65.9 (21.6)	53.4 (25.2)	59.7 (34.4)	55 (21.7)
DIVA2	46	64.5 (18.2)	54.7 (23.7)	52.5 (28.7)	54.2 (30)

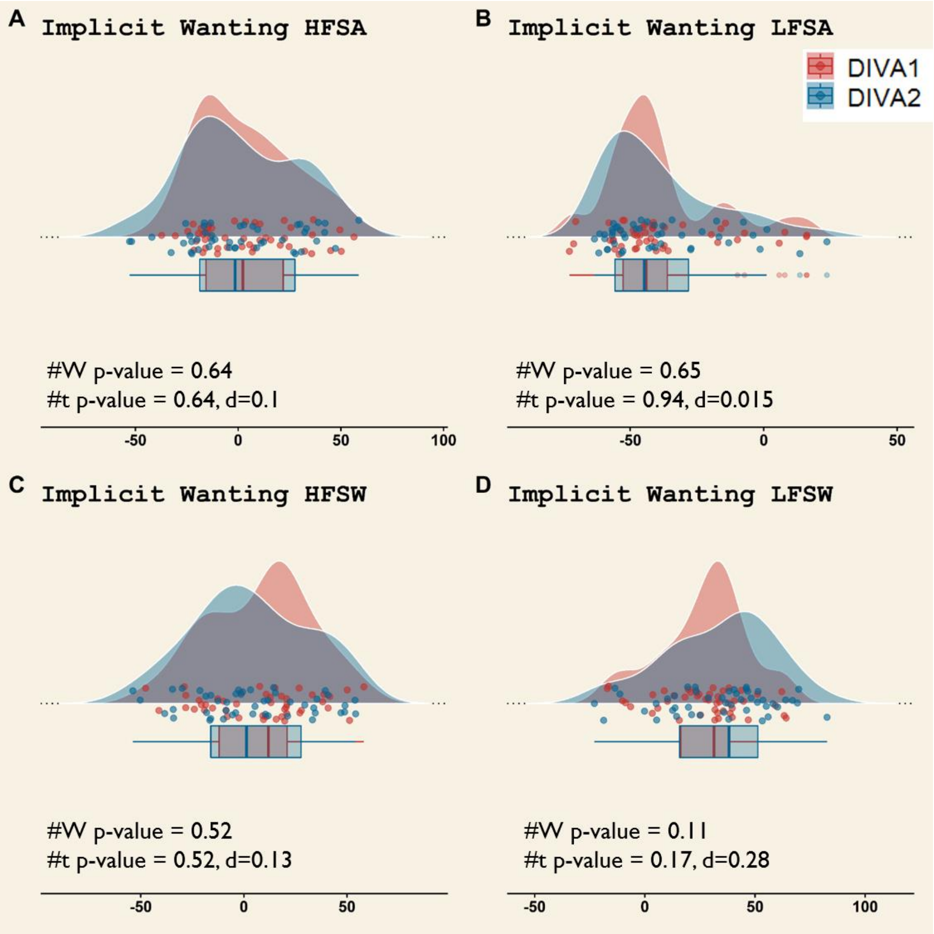

Figure E6: Implicit wanting post-lunch between groups with and without obesity

Table E5: Differences between implicit wanting post-lunch between groups

		Implicit wanting post-lunch			
Study	N	HFSA	LFSA	HFSW	LFSW
DIVA1	46	2.3 (37.6)	-44.0 (16.6)	11.8 (32.9)	31.3 (22.3)
DIVA2	46	-1.5 (46.3)	-44.8 (27.5)	1.31 (43.8)	38.1 (35.6)

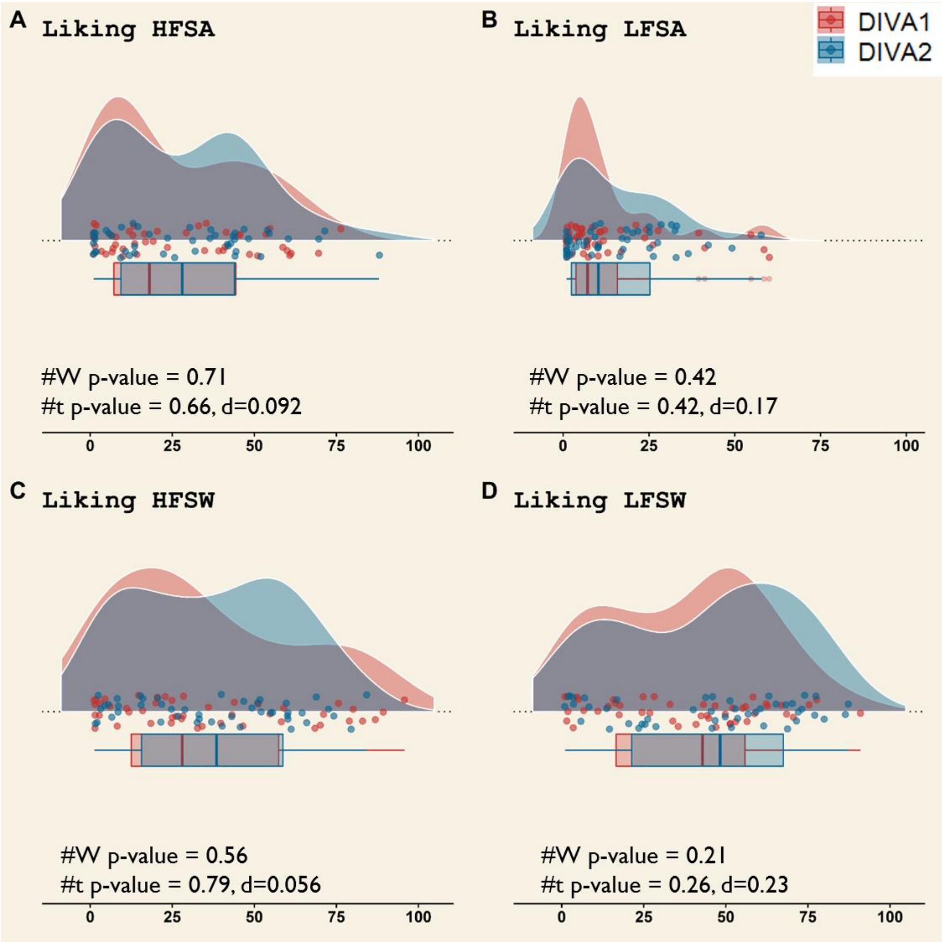

Figure E7: Liking post-lunch between groups with and without obesity

Table E6 Differences between liking post-lunch between groups

		Liking post-lunch			
Study	N	HFSA	LFSA	HFSW	LFSW
DIVA1	46	18 (37.1)	7.12 (12.1)	28 (44.9)	42.9 (39.25)
DIVA2	46	28 (34.7)	10.2 (22.9)	38.5 (43.1)	48.2(46.2)

Table E7: Fasted implicit wanting and appetite control

Implicit Wanting	+	-
IW HFSA	• **BES** (r_s (85) = .34, p =.002) *D1 (r(45)=.36, p=.015)* • **Disinhibition** (r_s (85) = .28, p = .0098) *D1 (r(45) = .36, p = .016)* • **Desire to eat** (AUC) (r_s (92) = .27, p = .008) *D1 (r(46) = .38, p = .0094)* • **Hunger** (AUC) (r_s (92) = .23, p = .027) *D1 (r(46) = .32, p = .03)* • **PFS** (r_s (86) = .22, p = .047)	• **Craving Control** (r_s (85) = -.29, p = .006) • **IES** (r_s (86) = -.23, p = .033) *D1 (r(45) = -.32, p = .03)*
IW HFSW	• **Craving sweet** (r_s (85) = .33, p = .002) *D1 (r(45) = .32, p = .033)*	• **Risotto (kcal)** (r_s (91) = -.23, p = .025) • **Lunch (kcal)** (r_s (91) = -.22, p = .038)
IW LFSA	• **Yoghurt (kcal)** (r_s (91) = - .28, p = .008) *D2 (r(44) = - .39, p = .008)*	• **Restraint** (r_s (85) = -.24, p = .003) *D2 (r(40) = -.33, p = .037)*
IW LFSW	• **Craving Control** (r_s (85) = .24, p = .03)	• **BES** (r_s (85) = -.23, p = .031) • **Disinhibition** (r_s (85) = -.22, p = .045) D1 (r(45) = -.33, p = .025)

All Significant correlations are reported in descending order. Correlations are performed as Spearman correlations (r_s) for the whole sample is non-normally distributed (N = 92) and as Pearson correlation (r) for the correlations by group (D1(N = 46) individuals with overweight/obesity, D2 (N = 46) individuals within the normal range of BMI) when they differ.

Table E8: Fasted liking and appetite control

Liking	+	-
L HFSA	• **Desire to eat** (AUC) (r_s (92) = .43, p < .001) *D2 (r(46) = .51, p = .00031)* • **Hunger** (AUC) (r_s (92) = .41, p < .001) D2 (r(46) = .54, p < .001) • **Prosp. consumption** (AUC) (r_s (92) = .38, p < .001) *D2 (r(46) = .45, p = .002)* • **PAL** (r_s (91) = .32, p = .002) • **Total EE** (r_s (91) = .29, p = .005) *D2 (r(45) = .32, p = .032)*	
L HFSW	• **Hunger** (AUC) (r_s (92) = .4, p < .001) *D2 (r(46) = .43, p = .0032)* • **Craving sweet** (r_s (85) = .37, p = .00053) *D2 (r(40) = .5, p = .001)* • **Desire to eat** (AUC) (r_s (92) = .36, p = .00035) *D1 (r(46) = .42, p = .0037)* • **Prosp. consumption** (AUC) (r_s (92) = .3, p = .004) • **PFS** (r_s (86) = .22, p = .046) *D1 (r(45) = .35, p = .02)*	• **Fullness** (AUC) (r_s (92) = -.25, p = .017) *D1 (r(46) = -.41, p = .0041)* • **Craving Control** (r_s (85) = -.24, p = .024) *D2 (r(40) = -.37, p = .018)*
L LFSA	• **Hunger** (AUC) (r_s (92) = .36, p = .00043) *D2 (r(46) = .45, p = .0015)* • **Desire** (AUC) (r_s (92) = .31, p = .003) *D2 (r(46) = .45, p = .00018)* • **Prosp. consumption** (AUC) (r_s (92) = .29, p = .005) *D2 (r(46) = .4, p = .006)* • **PAL** (r_s (91) = .25, p = .017) *D1 (r(45) = .33, p = .029)*	

	• **Total PA** (r_s (91) = .23, p = .027) *D1 (r(45) = .31, p = .041)* • **Risotto** (r_s (91) = .22, p = .037)
L LFSW	• **Restraint** (r_s (85) = .25, p = .0023) *D2 (r(40) = -34, p = .034)*

EE: Total energy expenditure, PA: physical activity, PAL: physical activity level. All Significant correlations are reported in descending order. Correlations are performed as Spearman correlations (r_s) for the whole sample is non-normally distributed (N = 92) and as Pearson correlation (r) for the correlations by group (D1(N = 46) individuals with overweight/obesity, D2 (N = 46) individuals within the normal range of BMI) when they differ.

Table E9: Pre-lunch food reward and appetite control

Food Reward	+	-
IW HFSW	• **Craving sweet** (r_s (84) = .46, p < .001) *D1: (r(45) = .59, p = 2.1e-05)* • **Total EE** (r_s (90) = .28, p = .009) *D1 (r(45) = .35, p = .02)* • **Body mass (kg)** (r_s (91) = .27, p = .011) *D1: (r(46) = .39, p = .0077)* • **FM** (r_s (91) = .24, p = .021) *D1: (r(46) = .4, p = .0061)* • **%Fat** (r_s (91) = .21, p = .045) *D1: (r(45) = .32 , p = .032)* •	• **Craving Control** (r_s (84) = -.24, p = .027) • **MEQ (**r_s (85) = -.22, p = .048)

IW LFSA	• **Risotto (kcal)** (r_s (90) = .23, p = .026) *D2: (r(45) = .3, p = .05)*	• **FM (kg)** (r_s (91) = -.26, p = .013) • **Body mass (kg)** (r_s (91) = -.26, p = .012) • **Total EE** (r_s (90) = -.24, p = .026) *D1 (r(45) = -.33, p = .02)* • **BMI (kg/m2)** (r_s (91) = -.24, p = .023) • **%Fat** (r_s (91) = -.23, p = .024)
IW LFSW	• **Yoghurt (kcal)** (r_s (90) = .24, p = .021) *D2: (r(45) = .34, p = .022)* • **Fullness** (AUC) (r_s (91) = .21, p = .042) *D1 (r(46) = .33*, p = .018*)*	
L HFSA	• **Desire to eat** (AUC) (r_s (91) = .45, p < .001) *D1 (r(46) = .58*, p < .001*)* • **Hunger** (AUC) (r_s (91) = .44, p < .001) *D1 (r(46) = .58*, p < .001*)* • **Prosp. consumption** (AUC) (r_s (91) = .41, p < .001) *D1 (r(46) = .55*, p < .001*)* • **PAL** (r_s (90) = .29, p = .006) *D1 (r(45) = .32, p = .031)*	• **Fullness** (AUC) (r_s (91) = -.22, p = .033) *D1 (r(46) = -.37*, p = .011*)*
L HFSW	• **Craving sweet** (r_s (84) =.44, p < .001) *D1: (r(45)=.59, p=1.9e-05)* • **Total EE** (r_s (90) = .31, p = .003) *D2 (r(45) = .31, p = .035)* • **Desire to eat** (AUC) (r_s (91) = .28, p = .008) *D1 (r(46) = .38*, p = .009*)* • **Prosp. consumption** (AUC) (r_s (91) = .25, p = .017) • **Yoghurt (kcal)** (r_s (90) =.24, p=.023) • **Body mass (kg)** (r_s (91) =.23, p=.026)	• **Fullness** (AUC) (r_s (91) = -.33, p = .0016) *D1 (r(46) = -.43*, p = .002*)*

	• **RMR** (r_s (90) = .22, p = .034) *D2 (r(45) = .26, p = .086)*
L LFSA	• **Hunger** (AUC) (r_s (91) = .44, p < .001) *D2 (r(45) = .52*, p = .0002*)* • **Desire to eat** (AUC) (r_s (91) = .39, p < .001) *D2 (r(45) = .47*, p = .001*)* • **Prosp. consumption** (AUC) (r_s (91) = .36, p < .001) *D2 (r(45) = .43*, p = .003*)* • **Risotto (kcal)** (r_s (90) = .27, p = .01) *D1: (r(46) = .37, p = .012)*
L LFSW	• **Yoghurt (kcal)** (r_s (90) =.36, p = .00053) *D2: (r(45) = .39, p = .0084)* • **RMR** (r_s (90) = .31, p = .003) *D2 (r(45) = .33, p = .027)* • **Total EE** (r_s (90) = .29, p = .006) *D2 (r(45) = .32, p = .033)* • **Lunch (kcal) (**r_s(90) = .22, p = .041) D1: (r(45) = .37, p = .0012)

EE: Total energy expenditure, PA: physical activity, PAL: physical activity level, RMR: resting metabolic rate, FM: fat mass, FFM: fat-free mass. All Significant correlations are reported in descending order. Correlations are performed as Spearman correlations (r_s) for the whole sample is non-normally distributed (N = 92) and as Pearson correlation (r) for the correlations by group (D1(N = 46) individuals with overweight/obesity, D2 (N= 46) individuals within the normal range of BMI) when they differ.

Table E10: Post-lunch food reward and appetite control

Food Reward	+	-
IW HFSW	• **Craving Sweet** (r_s (85) = .3, p = .006) *D1: (r(45) = .38, p = .011)*	
IW HFSA		• **Lunch (kcal)** (r_s (91) = -.28, p = .006) *D1: (r(46) = -35, p = .016)* • **Risotto (kcal)** (r_s (91) = -.24, p = .024) *D1: (r(46) = -3, p = .04)*
IW LFSW	• **Yoghurt (kcal)** (r_s (91) = .26, p = .013) *D2: (r(45) = -35, p = .018)* • **Lunch (kcal)** (r_s (91) = .23, p = .026)	
L HFSA	• **Prosp. consumption** (AUC) (r_s (92) = .21, p = .049) • **Desire to eat** (AUC) (r_s (92) = .21, p = .049)	
L HFSW	• **Prosp. consumption** (AUC) (r_s (92) = .22, p = .039)	
L LFSA	• **Prosp. consumption** (AUC) (r_s (92) = .22, p = .039) *D2: (r(45) = -33, p = .024)*	
L LFSW	• **%Fat** (r_s (92) = -.22, p = .035) • **Lunch (kcal)** (r_s (91) = .22, p = .040) *D1: (r(46) = -34, p = .021)*	

All Significant correlations are reported in descending order. Correlations are performed as Spearman correlations (r_s) for the whole sample is non-normally distributed (N = 92) and as Pearson correlation (r) for the correlations by group (D1(N = 46) individuals with overweight/obesity, D2 (N = 46) individuals within the normal range of BMI) when they differ.

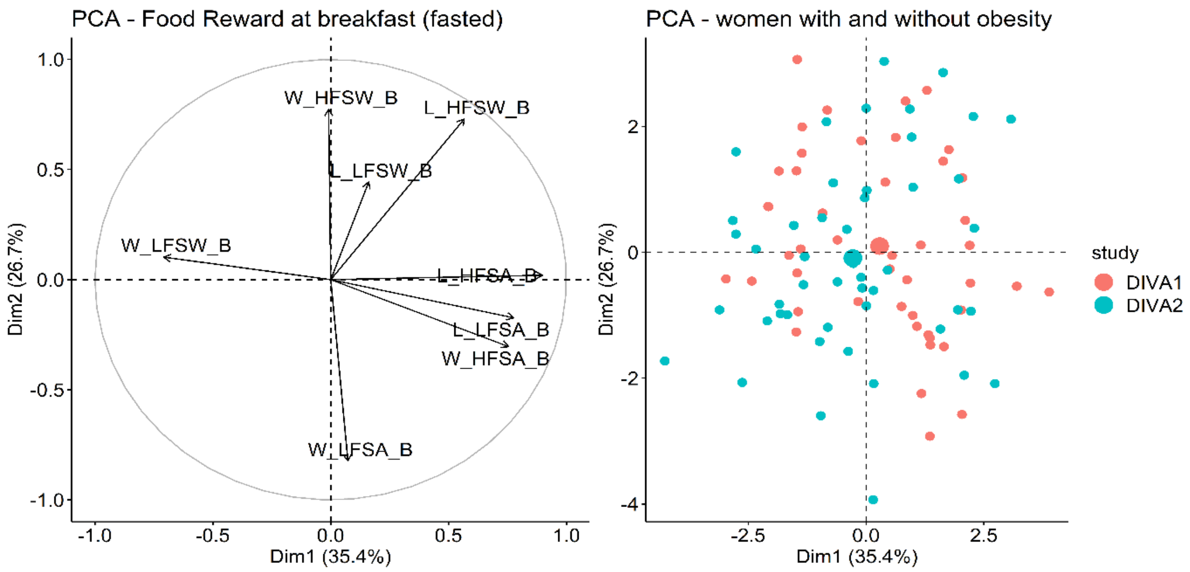

Figure E8: PCA on fasted food reward did not reveal patterns of food reward between individuals with or without obesity

W_: implicit wanting, L_:liking, B_breakfast, DIVA-1: women with overweight/obesity, DIVA-2: women within the normal range of BMI

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