

# **Working Memory and Food-Related Decision Making**

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## **Thesis abstract**

Dual-process theories argue that cognitive processes, and executive functions in particular, underpin controlled, goal-directed, decisions about food intake and choice. A considerable amount of research has been devoted to understanding the role of one executive function, inhibitory control, in appetite control. In addition, there has been interest in whether inhibitory control can be trained to improve dietary decisions. A systematic review and meta-analysis, however, casts doubt over the efficacy of training inhibitory control to change eating behaviour (Chapter 2). The importance of another executive function to eating behaviour, working memory, has been less well-studied. The aim of this thesis was to assess the role of working memory in food-related decision making in healthy volunteers and patients with type 2 diabetes. The results of Study 1 (Chapter 3) suggest that visuospatial working memory is important for decisions about the consumption of low energy dense foods and dieting success. The findings from Study 1 also provide support for the suggestion that dietary restraint has detrimental effects on central executive functioning. Study 2 (Chapters 4 and 5) found that working memory training can improve working memory and non-trained aspects of working memory in adults with type 2 diabetes. Transfer effects to eating behaviour were limited to those high in restraint (the higher the restraint the greater the reduction in saturated fat intake from pre-training to post-training). The results from Study 3 (Chapter 6) suggest that cognition (including one component of working memory) may be less important to food intake decisions in the context of other demographic, physical and psychological health factors. The importance of working memory to food intake decisions can be observed in controlled laboratory experiments. However, further research is needed to establish whether training working memory is a useful strategy to help bring about behaviour change to improve dietary choices.

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## **Chapter 1. Introduction**

This section begins by describing the prevalence and physical health consequences of obesity and diabetes, which are conditions linked to the overconsumption of food. A better understanding of the factors that underlie food intake decisions will aid the development of interventions to help tackle these conditions. Evidence that executive functions such as inhibitory control play an important role in decision making about what and how much to eat will be discussed. The focus then turns to an executive function that has been relatively less studied in relation to food intake decisions, that is, working memory. It will be argued that deficits in cognitive functioning could be contributing to difficulties controlling food intake that are associated with obesity and diabetes. Finally, the concept of dietary restraint is described, and the importance of assessing restraint when investigating the cognitive influences on food intake is discussed.

### **1.1 Overweight/obesity**

Overweight/obesity has become a global crisis that is linked to the development of many health complications (Finucane et al., 2011; Ng et al., 2014). Obesity is defined as a Body Mass Index (BMI;  $\text{kg}/\text{m}^2$ ) of 30 or above, and overweight as a BMI of 25 – 29.9 (National Heart Lung and Blood Institute in cooperation with The National Institute of Diabetes and Digestive and Kidney Disease, 1998). Current trends show that global adult obesity prevalence increased from 3.2% to 10.8% in men from 1975 to 2014, and from 6.4% to 14.9% in women (NCD Risk Factor Collaboration, 2016). In the UK alone, the number of obese men and women rose from 1.7 to 6.8 million, and from 2.1 to 7.7 million from 1975 to 2014, respectively. Across all English-speaking high-income countries, obesity rates currently exceed 30% across men and women. These trends are predicted to continue to rise, along with the resultant health complications (NCD Risk Factor Collaboration, 2016; Wang, McPherson, Marsh, Gortmaker, & Brown, 2011).

Obesity is associated with a number of health problems, including type 2 diabetes, cardiovascular disease, hypertension and some types of cancer (Caballero, 2007; Ogden, Yanovski, Carroll, & Flegal, 2007; Renegan, Tyson, Egger, Heller, & Zwahlen, 2008). Just as rates of obesity are predicted to increase, so are the associated health burdens. For example, Wang et al. (2011) predict an additional 544,000 - 668,000 cases of diabetes, 331,000 - 461,000 of coronary heart disease and strokes, and 87,000 - 130,000 of cancer over the next 20 years. Treating these health complications is costly; for example,



treatment and intervention for type 2 diabetes costs the NHS £1 million every hour (Hex et al., 2012). Obesity also has significant indirect costs to society and the economy, in the form of reduced productivity due to the impact of the above mentioned health problems on morbidity (Fontaine, Redden, Wang, Westfall, & Allison, 2003; Grover et al., 2014). One study showed that years of life lost due to an above ideal weight increased with increasing BMI across both men and women (Grover et al., 2014). These effects were highest in the youngest group (20-39 years) and decreased with age. For example, number of years of life lost due to obesity was 0.8 years in men aged 60-79 years, and 5.9 years in men aged 20-39. In women, life years lost due to obesity were 1.6 years in those aged 60-79, and 5.6 years in those aged 20-39. The highest number of life years lost was 8.4 years in very obese men aged 20-39. Healthy life years lost in this group, however, was 18.8 years. Both the direct and indirect costs of obesity to society and the economy are therefore clear.

Whilst obesity is associated with health complications, it is worth mentioning that not everyone who is obese goes on to develop these problems. An emerging area of research describes the existence of a Metabolically Healthy Obese (MHO) phenotype, which has been used to describe people who, despite being obese, do not display metabolic abnormalities (such as high cholesterol, triglycerides, blood pressure and fasting glucose levels) (Phillips, 2013). In one study, people displaying the MHO phenotype were more likely to go on to develop metabolic abnormalities and diabetes than metabolically healthy normal-weight participants (Appleton et al., 2013). However, some MHO individuals maintained metabolic normality. This paper suggests that the reason for a lack of metabolic problems in this group may be due to less central fat and greater peripheral fat. There are currently no set criteria used to identify MHO, and hence prevalence estimates vary widely depending on the criteria used. For example, in a review by Phillips (2013) prevalence of MHO in obese participants varied between 2.2% and 70.4% across the different criteria used. However, the majority of estimates did not rise above 30-40%. It seems then that while MHO is likely to be an important subset of people to consider, the majority of obese people do go on to develop metabolic abnormalities.

## **1.2 Diabetes mellitus**

Diabetes mellitus is a serious, chronic condition that can cause death if left untreated. Approximately 1 in 16 people currently have diabetes in the UK, with an estimated total of 4 million living with the chronic condition (Diabetes UK, 2015). A further 549,000 people are estimated to have diabetes but have not been diagnosed (Diabetes UK, 2015). There

are two main types of diabetes mellitus: type 1 and type 2. Type 1 diabetes is an autoimmune condition where pancreatic  $\beta$  cells do not produce any insulin. People with type 1 diabetes require insulin and/or insulin analogues for the rest of their life, without which they would die. In type 2 diabetes mellitus (T2DM), there is either insulin resistance (the insulin produced is not used effectively) or insulin hyposecretion (the pancreas does not produce enough insulin) (Alberti & Zimmet, 1998). Type 2 diabetes constitutes approximately 90% of all cases of diabetes (Diabetes UK, 2015).

It is also important to note the existence of impaired glucose tolerance and impaired fasting glucose. These are often called “pre-diabetes”, and are when people have either high fasting glucose levels (impaired fasting glucose) or high glucose levels after eating (impaired glucose tolerance). However, these are not high enough to be diagnosed as type 2 diabetes (International Diabetes Federation, 2013). Many people with impaired glucose tolerance go on to develop T2DM (International Diabetes Federation, 2013). The focus of this thesis is on type 2 diabetes, but research on “pre-diabetes” will be referred to where relevant. T2DM is diagnosed based on any of the following: (1) fasting plasma glucose of  $\geq 7.0$  mmol/l; (2) 2 hour plasma glucose level of  $\geq 11.1$  mmol/l after a 75g oral glucose tolerance dosage; (3) glycated haemoglobin of  $\geq 6.5$  % (48 mmol/mol); (4) random plasma glucose  $\geq 11.1$  mmol/l in the presence of classic diabetes symptoms (Clinical Guidelines Task Force, 2014).

### **1.2.1 Causes of type 2 diabetes**

Twin studies suggest that there is a genetic component to T2DM. Concordance rates for monozygotic twins range from 35-58%, compared to 17-20% in dizygotic twins (Stumvoll, Goldstein, & van Haeften, 2005). Monozygotic and dizygotic twins typically share the same environment, but dizygotic twins share 50% of their genes (whereas monozygotic twins share 100% of their genes). Higher concordance rates in monozygotic than dizygotic twins therefore suggest a genetic component to T2DM. The life time risk of developing type 2 diabetes if one parent has a diagnosis is 38% (Pierce, Keen, & Bradley, 1995). The prevalence increases to 60% if both parents have a diagnosis (Tattersall & Fajans, 1975). More recent work gives an estimate of 30-70% heritability of T2DM (Forouhi & Wareham, 2014). However, the addition of genotypic information improves the ability of risk models to predict occurrence of diabetes by only 5-10%. Type 2 diabetes is therefore a result of interactions between the environment/lifestyles and genes (Romao & Roth, 2008).

### **1.2.2 Consequences of poorly controlled diabetes**

High blood sugar levels (hyperglycaemia) is the main short-term complication of poorly controlled diabetes. The long-term complications are micro- and macrovascular health complications (Cade, 2008). Microvascular complications refer to damage to the small blood vessels, resulting in problems with the kidneys (nephropathy), eyes (retinopathy) and extremities (such as the feet) due to damage to the peripheral nerves (called neuropathy). Macrovascular complications concern the larger blood vessels, and can result in cardiovascular problems, such as stroke and vascular disease (Romao & Roth, 2008). Hyperglycaemia is one of the key risk factors associated with these comorbid conditions, along with obesity, hypertension, duration of diabetes, age, smoking, and dyslipidemia (Cade, 2008). A 1% increase in glycated haemoglobin levels (HbA1c) is associated with a 12-14% increased risk of macrovascular complications (Selvin, 2004) and a 37% increased risk of microvascular complications (Stratton, 2000). A HbA1c below 6% (in the normal range) has the lowest risk of complications (Stratton, 2000). Lowering glucose levels is, therefore, essential to reducing these risks. T2DM is often only diagnosed once these complications arise and become visible (Harris & Eastman, 2000), hence it is often a case of preventing further complications.

### **1.2.3 Guidelines for care**

Current guidelines for diabetes care advocate achieving normoglycaemia as essential to reducing the risk of further health problems, including micro and macrovascular complications. UK guidelines recommend a HbA1c of less than 6.5% (48 mmol/mol) (NICE guideline, 2015), whereas American and international guidelines argue for a HbA1c of 7% or less (53 mmol/mol) (American Diabetes Association, 2014; Clinical Guidelines Task Force, 2014). All guidelines agree that a lower HbA1c should be targeted if safe to do so and there is little risk of hypoglycaemia (blood sugar levels that are too low). Higher target HbA1c levels are recommended for individuals with a short life expectancy (i.e. the elderly) or with extensive health complications (8%/64 mmol/mol or above; American Diabetes Association, 2014). Lifestyle changes are the first line of therapy for reducing hyperglycaemia in T2DM (Clinical Guidelines Task Force, 2014; NICE guideline, 2015). Patients are advised to adopt a high-fibre, low fat, low-glycaemic-index carbohydrate diet and to reduce consumption of foods high in saturated and trans fat (NICE guideline, 2015). Patients are also encouraged to increase their physical activity. If lifestyle changes alone are insufficient to obtain target HbA1c levels after initial diagnosis,

glucose lowering agents are introduced, and ultimately insulin therapy may be recommended (Clinical Guidelines Task Force, 2014). Lifestyle interventions are effective in improving glycaemic control and reducing the incidence of T2DM in those at risk of developing the disorder (Diabetes Prevention Program Research Group, 2002; Lindström et al., 2006). Lifestyle changes have also been shown to be at least as effective as pharmacological interventions (Gillies et al., 2007) or even more effective (Diabetes Prevention Program Research Group, 2002).

#### **1.2.4 Negative effects of intensive glucose control**

The effects of intensive glycaemic control (HbA1c  $\leq$  6%) are not as successful as might be expected. Successful reduction in microvascular complications has been reported, although this appears to be limited to a few microvascular problems, such as a reduction in nephropathy outcomes (Ismail-Beigi et al., 2010; The ADVANCE Collaborative Group, 2008) and some eye and neuropathy complications (Ismail-Beigi et al., 2010). Reviews of this area of research, however, argue that the increased risk of hypoglycaemia outweighs the minimal microvascular benefits found (Boussageon et al., 2011; O'Connor & Ismail-Beigi, 2011).

Randomised control trials have typically either found no reduction in macrovascular risks (Abaira et al., 1997; The ADVANCE Collaborative Group, 2008; UK Prospective Diabetes Study Group, 1998), or increased risk and mortality as a result of intensive therapy compared to standard therapy (Genuth, 1996; Meinert, Knatterud, Prout, & Klimt, 1970; The Action to Control Cardiovascular Risk in Diabetes Study Group, 2008). Recent meta-analyses suggest that intensive glucose therapy has no overall effect on macrovascular complications (Boussageon et al., 2011; Seidu, Achana, Gray, Davies, & Khunti, 2016). The cost versus benefit consideration suggests that it may be better to avoid intensive therapy treatments since some studies have identified an increased risk of mortality and cardiovascular events. These negative effects may relate to the increased risk of hypoglycaemia associated with intensive glucose control, since hypoglycaemia has been associated with both micro and macrovascular events (Zoungas et al., 2010).

Controlling diabetes through lifestyle changes, in particular through the diet, therefore not only remains the recommended first line of defence against diabetes complications, but is also a safer option as it is much less likely to result in hypoglycaemia. However, diabetes is a progressive disease whereby  $\beta$  cell function (the cells that release insulin) declines and

insulin resistance increases over time (Fonseca, 2009). This suggests that while lifestyle changes may be sufficient to achieve near normoglycaemia initially, this is unlikely to be maintained as insulin production decreases and insulin resistance increases. Studies have shown that oral agent therapy fails to maintain target HbA1c levels eventually in most people, requiring insulin initiation (Kahn et al., 2011; Kahn et al., 2006). Many patients with T2DM therefore end up taking oral agents and/or insulin as lifestyle changes are insufficient to counteract diabetes progression. While pharmacological intervention may not be inevitable, dietary changes that improve glycaemic control for a period of time is likely to delay the onset (or worsening) of complications and the need for pharmacological intervention, which could reduce the cost of treatment to the NHS and improve patient quality of life.

### **1.3 Diabetes and overweight/obesity**

Diabetes is highly comorbid with obesity (Guh et al., 2009). Excess adipose tissue that occurs in obesity has been linked to insulin resistance in both human and animal studies (Ross, Aru, Freeman, Hudson, & Janssen, 2002; Wang & Liao, 2012). Research suggests that it is abdominal fat that is of primary importance to insulin resistance (Després et al., 2008), with epidemiological studies extending this to visceral abdominal adipose tissue specifically (Kissebah & Krakower, 1994; Preis et al., 2011). How excess adipose tissue can cause insulin resistance and ultimately the development of diabetes is believed to be due to the functional nature of adipocytes (fat cells) in metabolic regulation (Greenberg & Obin, 2006). Adipocytes are no longer believed to have the sole purpose of energy storage, but are now considered an endocrine organ that releases signalling and mediator proteins (known as adipokines). Over 600 adipokines have been identified and many of these play an important (positive) role in the control of appetite, energy intake and metabolism (Lehr, Hartwig, & Sell, 2012). A number of adipokines, however, are inflammatory in nature and have been linked directly to insulin insensitivity (Greenberg & Obin, 2006; Hardy, Czech, & Corvera, 2012). As weight increases adipocytes enlarge, and it is the inability to expand and enlarge adipocytes appropriately that may result in dysregulation of adipocyte function and inflammatory processes (Greenberg & Obin, 2006). The many inflammatory mechanisms identified are beyond the scope of this introduction chapter, however, some inflammatory cytokines implicated in insulin resistance include tumor necrosis factor (TNF)- $\alpha$  and interleukin (IL)-6 (Hardy et al., 2012). The role of inflammation in the relationship between obesity and diabetes is

supported by reports that taking inflammatory markers and adipokines into account halved the association between obesity and diabetes (Luft et al., 2013). Further, anti-inflammatory drugs have been shown to reduce blood glucose levels (Baron, 1982).

Macronutrient intake has been shown to directly result in cellular oxidative stress and inflammation, suggesting that obesity and excessive food consumption could constitute a pro-inflammatory state (Dandona, Aljada, & Bandyopadhyay, 2004). In a classic study, over-nutrition in lean men resulted in insulin resistance, demonstrating a causal link between weight gain and insulin resistance (Sims & Danforth, 1986). Further, insulin is known to have anti-inflammatory functions, and insulin resistance is therefore likely to reduce these anti-inflammatory effects, ultimately increasing inflammation (Dandona et al., 2004). Insulin treatment to reduce hyperglycaemia causes weight gain in some people (Russell-Jones & Khan, 2007). Over-consumption of foods, obesity, insulin resistance and treatment via insulin injection may therefore be a self-perpetuating cycle of weight gain and insulin resistance.

#### **1.4 Interim summary**

The previous sections have identified obesity and diabetes as serious problems that negatively impact upon health and life expectancy. These physical consequences have both direct and indirect effects on the economy and society. Obesity and diabetes are intricately linked, and while the underlying mechanisms are not fully understood yet, excess high energy dense food intake leading to weight gain and insulin resistance may result in a cycle of weight gain and hyperglycaemia. Overconsumption of high energy dense foods is likely to be an important factor linking obesity and diabetes, and so dietary interventions may help in breaking the cycle. However, a better understanding of the factors that influence food intake decisions is required to help identify novel means of bringing about dietary behaviour change. The next section will briefly describe the wide range of factors known to influence food intake decisions. Recent research on the role of executive functions, such as working memory, in food-related decision making will be discussed in the context of dual-process theories and the suggestion that cognitive processes constitute a novel target for dietary interventions will be evaluated.

#### **1.5 Influences on eating behaviour**

The processes that underlie eating behaviour can be dichotomised into internal and external influences. Research into external influences on food intake has demonstrated the

importance of both the environment in which we eat (Wansink, 2004) and with whom we eat (Herman, Roth, & Polivy, 2003). Environmental influences include the dining atmosphere, such as music and lighting (Biswas, Szocs, Wansink, & Chacko, in press), the way food is presented, such as plate and food packaging sizes (Wansink, 2004), and suggested eating norms (Higgs, 2015b). Eating in a group tends to facilitate food intake (Herman, 2015), whereas eating in the presence of an observer, or someone we would like to impress, tends to reduce food intake (Herman et al., 2003). People also tend to match/model the intake of an eating partner who consistently eats a lot or a little (Cruwys, Bevelander, & Hermans, 2015; Herman et al., 2003).

Internal influences on eating behaviour include physiological regulation of food intake (Assanand, Pinel, & Lehman, 1998), mood (Macht & Simons, 2000) and cognitive processes including learning and memory (Higgs, Robinson, & Lee, 2012; Robinson et al., 2013). The physiological regulation of food intake is well studied and typically centres on the notion that we eat in response to physiological need: that is, the body signals a state of depletion, which triggers food seeking (Assanand et al., 1998). There is a vast array of research suggesting that mood affects food intake, for example people have been shown to eat more when in a negative or positive mood relative to a neutral mood (Evers, Adriaanse, de Ridder, & de Witt Huberts, 2013; Macht & Simons, 2000).

The role of memory and learning in food intake has been less well studied. Implicated learning processes include simple learning in the form of habituation (a reduction in the desire to eat foods as they are consumed; Epstein, Temple, Roemmich, & Bouton, 2009), incentive salience attribution (whereby food acquires the ability to trigger food intake due to learnt associations between cues and the pleasurable taste of foods; Robinson & Berridge, 1993), and learning about the post-ingestive consequences of food (e.g. creamy or sweet tastes signal high fat and sugar, and hence calories; Woods & Ramsay, 2000). For a review of memory and learning processes in food intake see Higgs et al. (2012). As for memory, both memory for recent eating episodes and remembered liking of foods eaten affect subsequent food intake (Higgs, Robinson, et al., 2012). For example, disrupting the encoding of memories of recent meals (such as by watching TV while eating lunch) increases snack food intake later (Higgs & Woodward, 2009). Focusing on food, thereby enhancing memory for a meal, reduces snack food intake later (Higgs & Donohoe, 2011). Other internal factors believed to play an important role in food intake are higher-order cognitive functions, such as executive functions, and their role in top down control of food

intake behaviour (Higgs, Robinson, et al., 2012; Hofmann, Friese, & Strack, 2009; Hofmann, Friese, & Wiers, 2008; Hofmann, Gschwendner, Friese, Wiers, & Schmitt, 2008; Hofmann, Schmeichel, & Baddeley, 2012). The role of cognition and executive functions in food intake has been elaborated with reference to dual-process theories of behavioural control (e.g. Strack & Deutsch, 2004).

### **1.5.1 Dual process theories**

Dual-process theories have been applied to multiple areas of social, personality and cognitive psychology, including persuasion (Chen & Chaiken, 1999; Petty & Cacioppo, 1986), attitude access (Fazio, Sanbonmatsu, Powell, & Kardes, 1986), person perception (Brewer, 1988), correspondent inference (Gilbert, Pelham, & Krull, 1988), social judgement (Martin, Seta, & Crelia, 1990), stereotyping (Devine, 1989), problem-solving (Epstein, 1990; Sloman, 1996), reasoning (Sloman, 1996), and memory (Smith & DeCoster, 2000). However, it has only relatively recently been applied to health behaviours including excessive alcohol consumption (Wiers et al., 2007) and high energy dense food intake (Hofmann, Friese, & Strack, 2009; Hofmann, Friese, et al., 2008).

The basis of all dual-process theories is that there are two competing cognitive systems that influence behaviour (Smith & DeCoster, 2000; Strack & Deutsch, 2004). One system promotes controlled, thought-out, reflective behaviour whereas the other promotes impulsive, automatic behaviours. The balance between the two systems determines behavioural outcomes. Applied to eating behaviour, the impulsive system may be more associated with desires for tasty food and immediate satisfaction, whereas the reflective system is able to incorporate long-term health goals into behavioural decisions. The reflective system can exert inhibitory control over the impulsive system, and may suppress its effects on behaviour (although not fully). The reflective impulsive model (RIM; Strack & Deutsch, 2004) is one dual-process model that considers how the processes and interactions of each system contribute to the overt expression of behaviour. In this model both the reflective and impulsive systems are believed to result in actual behaviour via activation of behavioural schemata, but the path each system takes to the behavioural schemata varies. The impulsive system operates via spreading activation of connected elements that are created based on simple temporal and spatial associations. These associations are therefore based on simple frequent co-occurrence, but they do not hold any semantic value (e.g. banana-good). The reflective system invokes a process of deliberation that weighs the positives and negatives of behaviour, taking into account



future plans. Connections within the reflective system are based on assigned truth values and propositional representations. Propositional representations are representations based on whether things are true or false. They are assigned a value of true only if they are true, often incorporating visual input into this decision (e.g. the banana is good). Once a behavioural outcome is decided upon, the appropriate behavioural schemata are activated. Specific tasks have been devised that are believed to measure automatic and non-automatic behaviours. For example, reaction time based Implicit Association Tests and self-report measures, respectively (Frieze, Hofmann, & Wänke, 2008; Hofmann, Gschwendner, et al., 2008).

The reflective system is heavily influenced by cognitive capacity. When cognitive resources are low, behaviour is more likely to follow the automatic activation of easily accessible behavioural schemata. The impulsive system does not require cognitive capacity, and can therefore occur very quickly and without conscious awareness. It is heavily influenced by perceptual input, but can also be influenced by reflective processes. The impulsive system has a low threshold for processing information, whereas the reflective system has a high threshold. Accessibility is also important: schemata that have recently been activated require a lower threshold for reactivation, and so the behaviour associated with that schemata is facilitated. The impulsive system is considered to be relatively inflexible because connections between links are stable and only change through the slow process of learning, perhaps reflecting what are commonly known as “habits”. Representations in the reflective system are readily changed, yet are slower to be activated.

Both systems are believed to be able to operate simultaneously although the impulsive system is argued to be constantly active whereas the reflective system is not always active. Hence, behavioural schemata that are incompatible with each other can be activated. In this situation, factors such as cognitive capacity, basic needs and motivation will influence which schema “wins”. Stronger basic needs and motivation will favour the impulsive system, whereas higher cognitive capacity will favour the reflective system. In a real-life situation, this may be hunger (basic need) and a desire for tasty foods (motivation) versus having resisted tasty food all day (depleted cognitive and self-control resources). This notion of cognitive resources as having a limited capacity has been conceptualised in psychology in a number of ways, including delay of gratification and the notion of hot and cold systems (Metcalfe & Mischel, 1999; Mischel, Shoda, & Rodriguez, 1989) and as ego-

depletion or willpower that resembles a muscle that can be strengthened (Baumeister, Bratslavsky, Muraven, & Tice, 1998; Muraven & Baumeister, 2000; Muraven, Baumeister, & Tice, 1999).

### **1.5.1.1 How dual-process theories can inform behavioural interventions**

In the context of resisting immediate food desires and making food choices that are more in line with long-term goals (such as weight loss), the balance between the reflective and impulsive systems is very important. A stronger reflective system or a weaker impulsive system would favour behaviour in line with long-term health goals. Dual-process theories can therefore inform understanding of the cognitive processes that underlie behaviour, and ultimately how behaviour may be changed. One approach to changing behaviour would be to target the impulsive system by, for example, altering associations between stimuli and affect to reduce the motivational orientation towards stimuli. Evaluative conditioning has been reported to change implicit affective evaluations of alcohol and reduce alcohol consumption (Houben, Havermans, & Wiers, 2010; Houben, Schoenmakers, & Wiers, 2010). Similarly, evaluative conditioning has been reported to reduce rated liking of foods and consumption (Brunstrom, Downes, & Higgs, 2001; Haynes, Kemps, & Moffitt, 2015). Alternatively, interventions could target the reflective system by, for example, changing personal standards, attitudes and expectancies (Frieze, Hofmann, & Wiers, 2011). According to Frieze and colleagues, there is a third way of changing behaviour that involves targeting ‘boundary conditions’ such as motivation to self-control, self-control strength, working memory capacity and inhibition (Frieze et al., 2011). It has been argued that this approach may address the cognitive resource and/or capacity issues that limit the operation of the reflective system (Strack & Deutsch, 2004). According to Frieze et al. (2011) interventions could target either trait self-control and/or executive functions. Targeting self-control can involve 1) conserving self-control resources, allowing self-control resources to replenish after depletion (Tyler & Burns, 2008); 2) by-passing self-control resources by using implementation intentions (Webb & Sheeran, 2003) and 3) improving basic self-control capacity (based on the assumption that self-control is a muscle that can be trained (Muraven & Baumeister, 2000). Executive functions are the cognitive processes that allow the reflective system to override impulsive processes and for self-control to occur.

## 1.5.2 Executive functions

Executive functions are a set of higher order cognitive abilities that are recruited when behaviour is effortful and deliberate, and not automatic (Diamond, 2013). Executive functions such as inhibition may be a key determinant of the strength of reflective processes in the dual-process theories of behaviour control (Hofmann et al., 2012; Strack & Deutsch, 2004). Current consensus is that there are three core executive functions: inhibition, working memory and cognitive flexibility/set-shifting (Diamond, 2013; Miyake et al., 2000). Enhanced executive function has been repeatedly associated with more healthful eating habits (Allom & Mullan, 2014; Hall, Fong, Epp, & Elias, 2008; Hall, 2012).

### 1.5.2.1 Inhibitory control and overeating/obesity

Inhibitory control is one executive function that has been extensively researched in relation to eating behaviour. People with high impulsivity/weak inhibitory control are more likely to overeat (Guerrieri et al., 2007; Guerrieri, Nederkoorn, Schrooten, Martijn, & Jansen, 2009) and be overweight/obese (Nederkoorn, Jansen, Mulken, & Jansen, 2007; Sutin, Ferrucci, Zonderman, & Terracciano, 2011). Other work has specifically demonstrated that when inhibitory control is low, eating behaviour is more strongly guided by impulsivity (Hofmann & Friese, 2008; Hofmann, Rauch, & Gawronski, 2007; Nederkoorn, Houben, Hofmann, Roefs, & Jansen, 2010). Further, training inhibitory control has been reported to suppress automatic, motivational, impulsive responses to food and improve the ability to resist consumption of desirable food items and aid weight loss (Lawrence, O'Sullivan, et al., 2015; Veling, Koningsbruggen, Aarts, & Stroebe, 2014). The efficacy of inhibitory control training to reduce food intake, aid weight loss and reduce food cravings is assessed in the systematic review and meta-analysis described in Chapter 2.

### 1.5.2.2 Working memory

Working memory, the second of the three core executive functions, is a person's ability to keep information active and in mind, as well as the ability to manipulate this information (Diamond, 2013). Working memory is therefore distinct from short-term memory by virtue of the fact that it involves the manipulation of information and not just short-term storage of information. Baddeley's (1986) tripartite model of working memory argues that

there are three main components to working memory, namely the central executive, and two sub-systems; the phonological loop and visuospatial sketchpad.

The central executive is a system responsible for the control and allocation of attention and resources to the two sub-systems (A Baddeley, 2000, 2007). These abilities are underlined by four processes: (1) the ability to focus attention; (2) divide attention; (3) switch attention; and (4) interact with and retrieve information from long-term memory (via the episodic buffer). The central executive is considered a key player when behaviour cannot rely on automatic, habitual responses, and hence new thought and planning is required (A Baddeley, 2007). The central executive of working memory therefore appears to be very similar to the notion of executive functions and indeed could contribute to functioning of the reflective system in dual-process theories (Strack & Deutsch, 2004).

The first sub-system of working memory, the phonological loop, is responsible for holding verbal and acoustic information for a short period of time (A Baddeley, Lewis, & Vallar, 1984). The phonological loop can be broken down into the phonological store and articulatory control processes. The phonological store is a passive component that simply holds traces of verbal information for a brief time before it fades. The articulatory control process is characterised by rehearsal of verbal material and also converts visual information into verbal information. The rehearsal component functions to restore and maintain information held in the phonological loop. The second sub-component of working memory, the visuospatial sketchpad, is responsible for holding visual (what), spatial (where), and perhaps even kinaesthetic (movement sequence) information for brief periods of time (A Baddeley, 2007). This sub-system of working memory is again passive, with no manipulation abilities. There may even be sub-components for processing visual and spatial information separately (Darling, Della Sala, & Logie, 2007), however this has been much less studied than the phonological loop sub-components.

### 1.5.2.3 Working memory and eating behaviour

Working memory capacity has more recently been considered an important executive function, alongside inhibitory control ability, that plays a role in the reflective processes that are believed to influence eating behaviour (Hofmann, Friese, & Strack, 2009; Hofmann, Friese, et al., 2008; Hofmann, Gschwendner, et al., 2008; Hofmann et al., 2012). Important components of working memory relevant to self-regulation of behaviour include not only the amount of information that can be held active at any given time, but

also the ability to hold in mind information stored in long-term memory and to maintain focused attention on currently active information while preventing the interference of other potentially distracting information (Hofmann, Gschwendner, et al., 2008). Applied to eating behaviour, working memory capacity may therefore be important in retrieving long-term memories and holding these active in working memory (e.g. dieting goals); resisting attending to eye-catching stimuli in the environment (e.g. tempting foods); protecting active goals from distracting stimuli by maintaining focused attention on the active goals; and down-regulating emotions (e.g. cravings) (Hofmann et al., 2012). It is clear from this how working memory may therefore be an important executive function contributing to the reflective processes of behaviour.

Working memory capacity has been shown to moderate impulsive processes in predicting health behaviours. In people with low working memory capacity (compared to those with high working memory capacity) impulsive processes are better predictors of alcohol consumption (Grenard et al., 2008; Thush et al., 2008), cigarette use (Grenard et al., 2008) and high energy dense food consumption (Hofmann, Friese, & Roefs, 2009; Hofmann, Gschwendner, et al., 2008). For example, Hofmann and colleagues (2008) conducted three studies investigating the role of working memory capacity in regulating the influence of impulsive processes on sexual interest behaviour (study 1), consumption of sweets (study 2) and anger expression (study 3). Implicit attitudes were assessed in these studies using a variant of the Implicit Association Task. Working memory capacity was assessed with a computation span task, which involved presenting participants with a series of equations, and they had to remember the answer to each one and then recall these answers in the correct order at the end of the series of equations (up to 8 equations in a series). Across the three studies, working memory capacity moderated the effect of implicit associations (interpreted as impulsive processes influencing behaviour) on subsequent sexual interest, eating and anger expression behaviour. More specifically, in those with low working memory capacity, automatic associations better predicted sexual interest behaviour, sweet consumption and anger expression. In those with good working memory capacity however, reflective process behaviours better predicted behaviour in these three domains (reflective process behaviours included explicit attitudes and self-regulatory goals). These findings suggest that working memory capacity may moderate the relationship between automatic processes and behaviour.

Hofmann, Friese, and Roefs (2009) found that all three measures of executive control (executive attention/working memory, inhibitory control and affect regulation) independently moderated the impact of impulsive processes (automatic affective reactions) on consumption of sweets. More concretely, in those with low levels of executive control, impulsive processes had a stronger influence on consumption of sweets, compared to those with high levels of executive control. These data suggest that a high level of one executive control may be sufficient to reduce the influence of impulsive processes on eating behaviour.

Other research has differentiated the influence of working memory on high and low energy dense food intake (Allom & Mullan, 2014; Riggs, Chou, Spruijt-Metz, & Pentz, 2010; Riggs, Spruijt-Metz, Sakuma, Chou, & Pentz, 2010). In two studies, Riggs and colleagues found that executive cognitive functions were negatively correlated with snack food intake as measured by a food frequency-type questionnaire (Riggs, Chou, et al., 2010; Riggs, Spruijt-Metz, et al., 2010). Riggs and colleagues also reported that executive cognitive function was correlated with greater fruit/vegetable intake, and baseline executive function significantly predicted greater fruit/vegetable intake four months later, but not snack food intake (Riggs, Chou, et al., 2010). However, in another study by the same authors, no relationship was observed between executive functioning and fruit/vegetable intake (Riggs, Spruijt-Metz, et al., 2010). Executive functioning in these studies was measured via self-report on the Behavioural Rating Inventory of Executive Functioning, using the subscales “emotional control”, “inhibitory control”, “working memory” (e.g. “I forget what I’m doing in the middle of things”), and “organisation of materials” (Guy, Isquith, & Gioia, 2004) but in both studies the scores on each scale were combined to form a composite executive function score. Therefore, little can be said about the contribution of the working memory assessment to these relationships. In fact, other studies suggest working memory does not relate to high energy dense food intake.

Allom and Mullan (2014) measured executive functioning in undergraduate students and then measured saturated fat and fruit/vegetable intake one week later using a food frequency-type questionnaire. They reported that working memory ability only predicted fruit and vegetable intake, and not saturated fat intake. Another study by Sabia et al. (2009) found that poorer working memory was associated with eating less than two portions of fruit and/or vegetables a day. This study did not measure high energy dense food intake. The results from these studies suggest that working memory ability relates to

fruit and/or vegetable intake, and not to high energy dense food intake. Indeed, Allom and Mullan (2014) concluded that for behaviours that improve health, inhibitory control is not needed. Instead, updating, or working memory is necessary for such behaviours, as updating may support active representations of self-regulatory goals and the associated means by which these goals can be obtained (Kruglanski et al., 2002; Miller & Cohen, 2001). Specifically, a superior updating ability may enable the management of attentional resources, which in turn, results in individuals seeking out opportunities to eat fruit and vegetables.

#### 1.5.2.4 Working memory and eating behaviour in diabetes

Few studies have examined whether impaired cognitive functioning in diabetes relates to dietary intake or dietary self-care (Asimakopoulou & Hampson, 2002; Coker & Shumaker, 2003). Compeán-Ortiz et al. (2010) found that immediate and delayed visual recall predicted the extent to which participants with type 2 diabetes followed their prescribed diet (7% and 8% respectively). Asimakopoulou (2001) found that dietary self-care (as measured by the Summary of Diabetes Self Care Activities scale; Toobert, Hampson, & Glasgow, 2000) correlated positively with both number and quality of diabetes-specific problem solving strategies. Dietary self-care was related to the ability to modify behaviour in response to feedback (measured by the Wisconsin Card Sorting Task) even when controlling for possible confounds (e.g. depression levels). Stepwise multiple regression revealed that 45% of the variance of dietary self-care was predicted by both depression and the quality of diabetes-specific problem solving strategies. Diabetes is associated with various alterations in brain structure that have been linked with several cognitive impairments, including inhibition, working memory and mental flexibility (Asimakopoulou, 2001; McCrimmon, Ryan, & Frier, 2012). However, little research has linked this to problems following a diet apart from the above mentioned dietary self-care questionnaire studies (also see neuroimaging studies discussed in section 1.8). In addition, the sample sizes in most studies is small and it is unclear whether significant associations would be observed when controlling for confounding factors.

## 1.6 Interim summary

Many internal and external factors influence decisions around food, the current thesis focuses on one internal factor, cognition. Dual-process theories on the cognitive controls of behaviour can inform understanding of how cognition influences food intake decisions,

and ultimately inform interventions for changing eating behaviour by changing cognition. Executive functions, including inhibitory control and working memory, are an important set of cognitive functions. Inhibitory control is one executive function that has been researched extensively in relation to eating behaviour, however, less is known about the role of working memory in food-related decision making. Studies have begun to investigate the importance of working memory to food intake in both healthy adults and children. The next section will describe the cognitive consequences of obesity and diabetes. Considering the importance of cognition to eating behaviour (as described in the previous section), the negative effects of overweight/obesity and diabetes on cognition are important, as these may contribute to and exacerbate difficulties controlling food intake.

### **1.7 Obesity and cognition**

Identifying the effects of obesity on cognitive functioning independently of the many health problems typically comorbid in overweight/obese is no easy feat, and hence little research exists on this topic. A review of research on the relationship between obesity and cognitive functioning, excluding studies looking at obesity with other conditions, found that obesity is associated with poorer cognitive functioning across the lifespan (Smith, Hay, Campbell, & Trollor, 2011). In adults (19-65 years) 14 out of 15 studies found that obesity was related to poorer cognitive functioning. This included both cross-sectional and prospective studies. The most consistent cognitive deficit found was in executive functioning. These effects were independent of other factors, including socioeconomic status, depression and cardiovascular disease. This review therefore demonstrates that obesity is associated with cognitive deficits, particularly executive functioning.

A more recent review was able to assess the relationship between obesity and specific domains of cognitive functioning across 17 studies in adults (Prickett, Brennan, & Stolwyk, 2015). The authors concluded that after taking obesity-related comorbid conditions into account, there was no strong evidence of a relationship between obesity and any specific cognitive domain. There was some evidence of an independent effect of obesity on psychomotor performance and speed, visual construction, verbal memory, concept formation and set shifting decision making, delay discounting and inhibition. However, they concluded that there was no evidence for an independent relationship between obesity and general cognitive performance, intellectual function, time estimation, visual memory, verbal fluency, and working memory.



Evidence also exists to support the notion that cognitive impairments may precede overweight and obesity, suggesting that cognitive impairments may also contribute to causing overweight/obesity. Prospective longitudinal studies show that early cognitive abilities predict subsequent weight gain and BMI. Lower childhood IQ was related to BMI a few years later (Halkjaer, Holst, & Sørensen, 2003) and in adulthood (Batty, Deary, Schoon, & Gale, 2007; Chandola, Deary, Blane, & Batty, 2006; Lawlor, Clark, Davey Smith, & Leon, 2006). Although Halkjaer et al. (2003) found these effects were no longer significant when controlling for educational level. Fine motor control at ages 7 and 11 years predicted obesity at age 33 years, adjusting for various demographic factors (Osika & Montgomery, 2008).

Research has also considered executive functions more specifically. Studies have shown that childhood poorer executive functioning predicts overweight at age 6 (Guxens et al., 2009) and into adolescence (Francis & Susman, 2009; Goldschmidt, Hipwell, Stepp, McTigue, & Keenan, 2015). Even in toddlers self-regulatory skills have been associated with obesity 8 years later (Graziano, Kelleher, Calkins, Keane, & Brien, 2013). Research therefore supports the notion that cognitive abilities predict and contribute to overweight/obesity. The mechanism here may be that cognitive function impacts health-related behaviours, such as physical activity and food intake, as suggested in section 1.5.

While it is interesting and important to consider cognitive domains separately, it may be that this has been done too early in reviews, as some areas of cognition have received less research focus. This means that in reviews, conclusions about cognitive sub-domains are based on the findings of a very small number of studies. For example, in the review by Prickett et al. (2015), only two studies were identified as having assessed working memory performance and both found no difference between overweight/obese and normal weight controls across three measures of working memory (Ariza et al., 2012; Gonzales et al., 2010). Further, these were three different measures of working memory (WAIS-III digit span subtest – forwards and backwards, verbal N-back and Letter-Number Sequencing). While all three tasks assess working memory, they are measuring different functions and sub-components. Digit span forwards is simple recall of verbal information, whereas digit span backwards requires manipulation of the information in order to recall it in reverse order. The verbal N-back task requires updating of verbal information, and the letter-number sequencing experimental condition requires manipulation to reorganise and recall letters and numbers in ascending order. Overall, these tasks involve the

phonological loop sub-component of working memory and in some cases the central executive sub-component where updating and manipulation are required (A Baddeley, 2007). Little can therefore be concluded from these studies about the relationship between overweight/obesity and working memory as only two studies have been conducted, and nothing can be said about the relationship between overweight/obesity and other working memory sub-components (e.g. visuo-spatial working memory). Overall, both reviews (Prickett et al., 2015; Smith et al., 2011) appear to concur that obesity is related to executive function deficits, but any relation to working memory specifically is unclear.

The relationship between adiposity and cognition is likely to be bidirectional, where food intake and obesity impairs cognition, and impaired cognition promotes overeating and overweight/obesity (Kanoski & Davidson, 2011). Consumption of certain foods and dietary patterns can positively affect cognition. For example, consumption of a Mediterranean diet high in unsaturated fats and anti-oxidants can improve cognition and help protect against age-related cognitive decline (Panza et al., 2007; Valls-Pedret et al., 2015). Further, Omega-3 supplementation in children increased learning, memory and school performance (Gómez-Pinilla, 2008). Flavanoid supplementation increased indicators of synaptic density and hippocampus-dependent memory in mice (Gómez-Pinilla, 2008; van Praag et al., 2007) and improved cognitive function in elderly humans (Letenneur, Proust-Lima, Le Gouge, Dartigues, & Barberger-Gateau, 2007). On the other hand, too much of some macronutrients can have negative effects on cognition. For example, higher intake of saturated fats, trans fats and sucrose have been linked to greater general cognitive impairments (Devore et al., 2009; Eskelinen et al., 2008) and specific memory and learning impairments in rodents (Goldbart et al., 2006; Stranahan et al., 2008). Deficits in working memory specifically have also been shown to be a consequence of such diets (Granholtm et al., 2008; Kanoski & Davidson, 2010). It is possible then that just as overconsumption of certain foods impairs cognition, these deficits in cognition subsequently impact upon food-related decision making (Davidson, Kanoski, Schier, Clegg, & Benoit, 2007; Davidson, Kanoski, Walls, & Jarrard, 2005). Reports that learning and memory deficits caused by a Western diet precede obesity support this notion (Kanoski & Davidson, 2010; Murray et al., 2009). It is believed that these effects occur via damage to brain structures utilised during food-related decision making, such as the hippocampus (Clifton, Vickers, & Somerville, 1998).

## 1.8 Diabetes and cognition

Separate to the relationship between cognition and weight, diabetes is also associated with cognitive deficits. An early review identified cognitive deficits in people with T2DM in the areas of verbal memory, and to a lesser extent psychomotor ability and frontal lobe functioning (Strachan, Deary, Ewing, & Frier, 1997). A more recent systematic review by van den Berg and colleagues (2009) identified 27 studies looking at the effect of diabetes on cognitive functioning. While the included studies tended not to distinguish between type 1 and type 2 diabetes, the age of the included samples suggest it is likely to be predominately type 2 diabetes. Diabetes was associated with poorer attention in 50% of studies, poorer memory in 44% of studies, poorer cognitive flexibility in 38%, poorer processing speed in 63%, poorer language in 33%, poorer general intelligence in 31%, and poorer perception and construction in 22%. While the findings vary across domains, this review shows that there are some consistent cognitive deficits in those with diabetes. A strength of this review is that it included both cross-sectional and longitudinal studies, and therefore supports a causal relationship between diabetes and cognition. The studies discussed in the review by van den Berg and colleagues (2009) examined a variety of short-term and long-term memory abilities, including working memory.

Evidence of cognitive deficits in a pre-diabetes group compared to controls would provide further evidence for a causal relationship between cognition and diabetes, as it would suggest cognitive impairments even in those with impaired glucose tolerance or metabolism. Van den Berg et al. (2009) also assessed studies in a pre-diabetes sample, but they reported much less consistency in the results than in studies with a diabetes sample. There are few reports of poorer cognitive performance in pre-diabetes (cross-sectional and longitudinal studies), and one report of better performance in the impaired glucose tolerance group than controls (Fuh, Wang, Hwu, & Lu, 2007). Further research conducted since this review does however support that pre-diabetes is associated with cognitive deficits. In one study, insulin resistance was associated with poorer declarative memory, whereas HbA1c was associated with deficits in executive functioning and working memory (Bruehl, Sweat, Hassenstab, Polyakov, & Convit, 2010).

As with the relationship between obesity and cognition, the relationship between diabetes and cognition is likely to be bidirectional. That is, cognitive abilities may also precede the development of diabetes. Lower cognitive ability at age 11 years was a significant predictor of a diagnosis of diabetes and HbA1c levels at 70 years of age (Möttus, Luciano,

Sarr, McCarthy, & Deary, 2015; Möttus, Luciano, Starr, & Deary, 2013). Lower general cognitive ability and reading comprehension (adjusted for sex, birth weight, gestational age, parental social class, maternal smoking during pregnancy, age mother left school, mother's age at delivery, presence of mild or severe mental retardation, disability, and ethnic origin) were associated with a greater risk of type 2 diabetes at both 16 and 42 years of age (Olsson, Hultin, & Montgomery, 2008). However, Cheng, Treglown, Montgomery and Furnham (2015) found no association between cognitive ability at age 11 and T2DM at 50 years of age, using the same dataset as Olsson et al. (2008). As argued by the authors, it is possible that the longer time-frame used in their study explains the results (Cheng et al., 2015). Two other studies did not find lower childhood cognitive ability to predict subsequent diabetes diagnosis later in life (Batty, Deary, & Macintyre, 2007; Batty, Deary, Schoon, et al., 2007).

The prospective relationship between young adult cognitive functioning and subsequent T2DM has been less studied than childhood cognitive ability. The results, however, are similarly contradictory. One study in men found that poorer cognitive ability at age 22 was associated with a higher risk of type 2 diabetes at age 55 (Schmidt et al., 2013). Using the National Longitudinal Study of Youth 1979, those with poorer cognitive ability aged 14-21 years were more likely to have diabetes at age 40 (Der, Batty, & Deary, 2009) and 50 (Wraw, Deary, Gale, & Der, 2015). However, no association between cognitive ability in men aged 20 years and glucose tolerance at aged 61 years was found in another study (Paile-Hyvärinen et al., 2009). Educational level was however associated with prevalence of T2DM at 61 years in the study conducted by Paile-Hyvärinen and colleagues. The evidence for cognitive impairments prior to indicators of type 2 diabetes is clearly very contradictory, and this may be due to the factors controlled for across studies and the outcome measures used (e.g. onset of T2DM or glucose tolerance). The major limitation to this area of research is the intense focus on one aspect of cognitive functioning, namely IQ. The results of these studies therefore say very little about the role of executive functions in the development and maintenance of T2DM. Nevertheless, the findings overall suggest that diabetes may negatively impact upon cognition, and poorer cognition may also promote diabetes.

Neuroimaging research supports the link between diabetes and poorer cognition. A recent meta-analysis (Moulton, Costafreda, Horton, Ismail, & Fu, 2015) found that people with diabetes not only have significant volumetric reductions in total brain volume and grey

matter, but also region specific impairments, including the orbitofrontal cortex, hippocampus, basal ganglia and frontal and temporal volumes. Voxel based morphometric analysis identified significant reductions in the bilateral hippocampus in type 2 diabetes. These regions play an important role in the reflective and impulsive cognitive processes (cortical and subcortical regions, including frontal regions, the orbitofrontal cortex and the hippocampus) as well working memory capacity functions, such as retrieval of long-term memories from the hippocampus (Bechara, 2005). Hence, there is evidence that diabetes is associated with reductions in brain areas essential to the ability to exert self-control over eating behaviour.

As in obesity, the evidence for deficits in working memory specifically in diabetes is unclear. In the review by van den Berg et al. (2009), of the 25 studies that assessed memory, only 10 assessed working memory specifically (Atiea, Moses, & Sinclair, 1995; Brands et al., 2007; Elias, Elias, Sullivan, Wolf, & D'Agostino, 2005; Fuh et al., 2007; Hassing et al., 2004; Kilander, Nyman, Boberg, & Lithell, 1997; Lindeman et al., 2001; Reaven, Thompson, Nahum, & Haskins, 1990; Ryan & Geckle, 2000; Vanhanen et al., 1997). Eight of these ten studies found non-significant differences between those with and without diabetes on working memory. One study found that the number of diabetes years was not related to working memory performance (Elias et al., 2005), and another found a significant difference on forwards digit span but not on backwards digit span (Fuh et al., 2007). These null results are relatively consistent, despite the range of tasks used (e.g. Forward and Backward Digit Span tasks, Forward and Backward Corsi Block Span tasks, Brown–Peterson task and the Four-Word Short Term Memory task). As noted by van den Berg et al. (2009), many of the non-significant effects included in their review had large effect sizes and is difficult to tell then whether non-significant effects are true effects, or are due to small sample sizes.

Cognitive deficits in diabetes could be contributing to difficulties controlling food intake (Knopman et al., 2001). This suggestion is supported by findings from neuroimaging research that brain responses to food pictures in people with diabetes in brain regions important for executive functions are linked to dietary self-care (Chechlacz et al., 2009). People with type 2 diabetes (compared to body weight matched healthy controls) showed greater neural activity in response to food cues in subcortical areas of the brain that form part of the brain's impulsive system (Chechlacz et al., 2009). There was also greater activity in response to food pictures in cortical areas, including the orbitofrontal cortex and

insula, which form part of the reflective system and as such are important for executive functions and restraining immediate desires in favour of long term outcomes (Chechlacz et al., 2009). Most importantly, Chechlacz and colleagues also reported that increased activity in cortical areas was associated with better self-reported dietary self-care, whereas activity in subcortical areas was associated with poorer dietary self-care. These data support the potential role of the reflective system and executive functions (such as inhibitory control and working memory) in food intake choices in people with type 2 diabetes.

### **1.9 Interim summary**

Both obesity and diabetes are associated with cognitive deficits. There is evidence that these deficits may precede these conditions but also may develop as a consequence. There is also evidence that obesity and diabetes are associated with deficits in executive functions specifically. The evidence for working memory in particular, however, is unclear. It is important to consider how obesity and diabetes are associated with cognition, as cognitive deficits may impair food-related decision making. The next section will describe the concept of dietary restraint. Dietary restraint is a psychological eating style that affects responses to internal and external cues to eating behaviour. It also has negative effects on cognition, including working memory. Dietary restraint is therefore an important concept to consider when assessing the importance of cognition to food intake decisions.

### **1.10 Dieting and the concepts of dietary restraint and tendency towards disinhibition**

Dietary restraint is the conscious and deliberate attempt to restrict food intake for the purposes of weight loss or avoiding weight gain. Food intake therefore becomes controlled by cognitive rather than physiological processes (Herman & Mack, 1975; Herman & Polivy, 1975, 1980). The theory of dietary restraint originally developed following the theories by Schachter (1968, 1971) and Nisbett (1972), both of which aimed to explain the differences in eating behaviour observed between obese and normal-weight people. Schachter argued that the eating habits of overweight/obese people was guided by external, environmental cues rather than internal hunger cues. Nisbett provided his “set-point” theory to explain the reliance of overweight/obese people on external cues, arguing that each person has a biologically defined ideal body weight. This is called their personal set-point and they are homeostatically driven to maintain this set-point. However, due to

societal emphasis on and preferences for slimness, overweight/obese people try to override their set-point weight in order to maintain a lower weight. People could therefore be underweight and deprived compared to their biologically determined set-point, but overweight by views of society. In sum, Schachter argued that externally driven eating behaviour was a correlate of obesity, whereas Nisbett argued it was a consequence of deprivation in overweight/obese. Herman and colleagues extended this to argue that the eating behaviour of obese people is a consequence of dietary restraint that leads to overreliance on external food cues (Herman & Polivy, 1980).

The 1984 boundary model by Herman and colleagues further argued that dietary restraint could underlie eating disorder pathologies, including binge eating and anorexia (Herman & Polivy, 1984; Polivy & Herman, 1985). The application of restraint theory to binge eating is based on the disinhibition hypothesis of restraint theory. If the cognitive control of food intake is disrupted in a restrained eater, disinhibited eating occurs. Events that cause this temporary lapse in self-control are known as “disinhibitors”. Classic psychological experiments have shown that when restrained eaters believe they have overeaten, their subsequent food intake increases (Heatherton, Strieppe, & Wittenberg, 1998; Herman & Mack, 1975; Hibscher & Herman, 1977; Knight & Boland, 1989; Polivy, 1976; Spencer & Fremouw, 1979). In one study, normal weight participants were identified as either high or low in restraint, and were given a “pre-load” of either none, 1 or 2 milkshakes to consume (Herman & Mack, 1975). Participants were then asked to taste and rate some ice cream. Consumption of the ice cream by unrestrained eaters decreased as the number of milkshakes consumed increased, supposedly following internal satiety signals. High restraint participants behaved in the opposite way, and ate more ice cream if they had 1 or 2 milkshakes than if they had none. Colloquially, this was coined the “what the hell effect”, whereby restrained eaters overconsume and “binge” if they surpass their cognitively determined level of intake. This is believed to stem from an all-or-nothing attitude where cognitions similar to “I’ve blown it – I might as well continue to eat” occur (Ruderman, 1986).

Further research has shown that there are many types of disinhibitors that can cause restrained eaters to overeat. Firstly, restrained eaters only need to believe they have overeaten (e.g. told the food was high calorie vs low calorie) (Polivy, 1976; Spencer & Fremouw, 1979) or anticipate that they will overeat (Knight & Boland, 1989; Ruderman, Belzer, & Halperin, 1985) in order to disinhibit. Negative mood, including emotional

distress and anxiety can induce overeating in restrained eaters (Heatherton et al., 1998; Herman, Polivy, Lank, & Heatherton, 1987). Further, substances such as alcohol that sedate and relax people also induce overeating in restrained eaters (Polivy & Herman, 1976). A high cognitive load has also been shown to cause overeating in restrained but not unrestrained eaters (Ward & Mann, 2000).

Considering the wealth of research demonstrating that people who try to restrain their food intake typically overeat, it became widely believed that dietary restraint was counterintuitive for weight loss. Evidence that dietary restraint is associated with weight gain supports this hypothesis (Field et al., 2003; French et al., 1994; Klesges, Isbell, & Klesges, 1992; Klesges, Klem, & Bene, 1989; Schur, Heckbert, & Goldberg, 2010; Stice, Cameron, Killen, Hayward, & Taylor, 1999; Stice, Presnell, Shaw, & Rohde, 2005). Restraint is also associated with stronger implicit preferences for food (Hoefling & Strack, 2008; Houben, Roefs, & Jansen, 2012, 2010), greater salivary responses towards palatable food (Brunstrom, Yates, & Witcomb, 2004; Klajner, Herman, Polivy, & Chhabra, 1981), and attentional bias towards food (Hollitt, Kemps, Tiggemann, Smeets, & Mills, 2010; Papiés, Stroebe, & Aarts, 2008b). This early school of thought that dietary restraint is solely detrimental to weight loss attempts is now outdated, and has been replaced by an understanding of the importance of taking into account a person's tendency towards disinhibition as well. Advancements in the development of better tools for measuring restraint and associated concepts, including tendency towards disinhibition, have been used to demonstrate that, in fact, restraint may be associated with greater weight loss. This is discussed in the next section.

### **1.10.1 Measurement of dietary restraint**

Restrained eating was originally measured and assessed using the Restraint Scale (RS; Herman & Polivy, 1975). However, the RS is now known to select for unsuccessful dieters, considering that it assesses both restraint and tendency towards disinhibition (Heatherton, Herman, Polivy, King, & McGree, 1988). Therefore, anyone scoring high on the RS scale is high in both restraint and disinhibition, which is likely to constitute unsuccessful dieting. This calls into question many of the research findings in relation to so called dieters and restrained eaters, as many studies identified their sample as high scorers on the restraint scale.

Two alternative measures of dietary restraint were subsequently developed, that allowed



researchers to separate restraint and tendency towards disinhibition, namely the Three Factor Eating Questionnaire (TFEQ; Stunkard & Messick, 1985) and the Dutch Eating Behaviour Questionnaire (DEBQ; van Strien, Frijters, Bergers, & Defares, 1986). Studies implementing the pre-load design have failed to demonstrate the “what the hell” effect in dieters when using the restraint subscales of the TFEQ and DEBQ (Lowe & Kleifield, 1988; Wardle & Beales, 1987). Further, one study showed that counter-regulation only occurred in those high in both restraint and disinhibition (Westenhoefer, Broeckmann, Munch, & Pudel, 1994). These findings are further supported by an examination of the construct validity of all three scales (RS, DEBQ, TFEQ), which found that the restraint sub-scales of the DEBQ and TFEQ are associated with less calorie intake, and the RS was associated with disinhibition of food intake (Laessle, Tuschl, Kotthaus, & Pirke, 1989).

Longitudinal studies assessing both restraint and disinhibition also suggest that these are differentially associated with weight. In one study, baseline restraint was associated with a lower body weight, whereas disinhibition was associated with more binge eating (Foster et al., 1998). At the end of the weight loss treatment, higher restraint was associated with a greater reduction in weight. Studies using the National Weight Control Registry have found that disinhibition was associated with weight gain over time (Bond, Phelan, Leahey, Hill, & Wing, 2009), and that successful weight losers had higher restraint, as well as paid more attention to their weight and eating behaviour, compared to normal weight participants (Phelan et al., 2008).

Overall, research suggests that the Restraint Scale identifies those high in both restraint and disinhibition, and hence selects for unsuccessful dieters. The TFEQ and DEBQ however allow researchers to separate these constructs and identify successful dieters (those high in restraint but low in disinhibition) and unsuccessful dieters (high restraint, high disinhibition). Considering the large variation in findings when the RS is used compared to the restraint sub-scales of the TFEQ and DEBQ, researchers should be aware of these issues and select the scales measuring the constructs most in line with their research aims, as argued by Heatherton et al. (1988). While this has been addressed in the use of the pre-load design and longitudinal studies of the correlates of weight gain/loss, this has been relatively neglected in the literature investigating the relationship between dieting/restraint and cognition. This literature is summarized in the next section, but is criticized in relation to the measures used to assess dietary restraint in the introduction in Chapter 2.

### **1.10.2 Dieting and cognition**

The consequences of dieting on cognition have been well studied, and there is sufficient research to allow a focus on working memory in particular. Early research found dieters to show deficits in sustained attention (Rogers & Green, 1993), along with poorer immediate recall and slower reaction times (Green, Rogers, Elliman, & Gatenby, 1994). These deficits have been found in the same people when they are dieting and not when they were not dieting, suggesting these impairments may be related specifically to dieting and not pre-existing differences between dieters and non-dieters (Green & Rogers, 1995). Green and colleagues also identified these cognitive impairments to be specifically working memory capacity related rather than being due to poor ability to sustain attention (Green, Elliman, & Rogers, 1997).

Subsequent research focused on identifying which components of working memory are impaired in dieters, identifying the phonological loop and central executive as areas showing deficits (Green & Rogers, 1998; Kemps, Tiggemann, & Marshall, 2005). The visuo-spatial sketchpad component however has consistently been found to be intact in dieters (Green & Rogers, 1998; Kemps & Tiggemann, 2005; Kemps, Tiggemann, & Marshall, 2005; Shaw & Tiggemann, 2004; Vreugdenburg, Bryan, & Kemps, 2003). Further breakdown of the sub-components of the phonological loop have produced contradictory findings. Some researchers have found deficits in the articulatory control processes of the phonological loop (Shaw & Tiggemann, 2004), while others have found deficits in the phonological store (Vreugdenburg et al., 2003). Two studies however only found deficits in the central executive and not in the phonological loop (Green et al., 2003; Kemps & Tiggemann, 2005).

The sub-components of the central executive that are impaired in dieters have also been investigated. Baddeley (1996) identified four subcomponents of the central executive; (1) the ability to coordinate performance of two simultaneous tasks (dual-task performance); (2) the ability to inhibit stereotyped responses (random generation); (3) the ability to switch attention between two tasks (task switching); and (4) the ability to hold and manipulate information in long-term memory (activation of long-term memory). Kemps, Tiggemann and Marshall (2005) identified deficits in 3 out of 4 of these functions in dieters, namely the ability to perform two simultaneous tasks, switching of attention between tasks and ability to maintain and manipulate information retrieved from long-term memory. Preoccupying thoughts with food, eating, weight and body shape have

consistently been found to mediate the relationship between dieting status and impaired working memory functions (Green et al., 1997; Kemps, Tiggemann, & Marshall, 2005; Shaw & Tiggemann, 2004; Vreugdenburg et al., 2003). The suggestion is that these preoccupying thoughts use up limited working memory resources. Food cravings in particular have been shown to negatively affect cognitive functioning and consume working memory resources.

### **1.10.3 Dieting and food cravings**

Both dieting (food deprivation) and restrained eating have been linked to greater food cravings. Low calorie or restricted diets have been related to greater food cravings (Massey & Hill, 2012; Overduin & Jansen, 1996; Warren & Cooper, 1988). In those high in dietary restraint, exposure to food cues increases food cravings and desire to eat that food more than in unrestrained eaters (Fedoroff, Polivy, & Herman, 1997, 2003). Similarly, deprivation of a specific food (chocolate) resulted in more cravings for chocolate in restrained than unrestrained eaters (Polivy, Coleman, & Herman, 2005). In this study, restrained eaters were also more likely to eat the craved food, and to spend less time on a mentally taxing task when they believed chocolate would be available in the next task. Some research has extended these findings to show that the experience of food cravings varies with dieting success. In one study, trait food cravings were able to distinguish between successful and unsuccessful dieters. Specifically, unsuccessful dieters reported more food cravings in relation to difficulties in self-control around the food and intention to eat that food than successful dieters (Meule, Lutz, Vögele, & Kübler, 2012). State food cravings in this study, however, did not distinguish between successful and unsuccessful dieters, suggesting that momentary food cravings are a problem for both groups, but perhaps successful dieters are better able to deal with these in some way. Another marker of dieting success, flexible versus rigid dieting, shows differences in food cravings. Food cravings mediated the relationship between greater rigid control of food intake and poorer dieting success, yet did not mediate the relationship between flexible dieting and dieting success (Meule, Westenhofer, & Kubler, 2011), again suggesting that cognitive differences between successful and unsuccessful dieters influence how cravings are processed. However, this area of research is not without contradictory evidence, with studies showing that low calorie diets are associated with decreases in food cravings (Harvey, Wing, & Mullen, 1993; Martin, O'Neil, & Pawlow, 2006). Some early studies also suggested that dietary restraint is not associated with the number, frequency or types

of food cravings (Hill, Weaver, & Blundell, 1991; Rodin, Mancuso, Granger, & Nelbach, 1991). These early studies measured everyday experiences of cravings outside of the laboratory. The more recent studies by Polivy, Herman and colleagues were well controlled lab-based studies that investigated the effects of manipulating exposure to food cues and depriving participants of specific foods. It may be that only under strict laboratory conditions where other factors are controlled, can the relationship between dietary restraint and food cravings be seen.

The nature of food cravings is widely considered to be visual. Questionnaire studies found that reports of food cravings often involve imagery and seeing the food e.g. “I am visualising it” (May, Andrade, Kavanagh, & Penfound, 2008; May, Andrade, Panabokke, & Kavanagh, 2004), with visual, gustatory and olfactory modalities described as most frequently involved in food cravings, and auditory and tactile modalities the least involved (Tiggemann & Kemps, 2005). The strength of food cravings also appears to be positively related to the vividness of this imagery (Harvey, Kemps, & Tiggemann, 2005; Tiggemann & Kemps, 2005). Evidence from experimental research shows that asking people to imagine and visualise foods increases experiences of food cravings (Harvey et al., 2005). A recent theory, the elaborated intrusion theory, argues based on this evidence, that imagery is the key element in food cravings (May, Kavanagh, & Andrade, 2015).

Cravings have been shown to negatively affect cognitive functioning and consume working memory resources. Induced food cravings were found to slow simple reaction times in dieters but not in non-dieters in one study (Green, Rogers, & Elliman, 2000). Kemps and colleagues replicated this effect and also demonstrated impaired working memory capacity after chocolate craving induction (Kemps, Tiggemann, & Grigg, 2008). Further work found impaired visuo-spatial working memory specifically after craving induction, but no effects on the central executive or phonological loop sub-components of working memory (Tiggemann, Kemps, & Parnell, 2010). A study in low and high trait cravers found that all participants showed slower reaction times and more omission errors on an N-back task involving pictures of food (Meule, Skirde, Freund, Vögele, & Kübler, 2012). State cravings were equal across the groups at baseline, supporting that state cravings are better predictors of working memory performance than trait cravings. The strongest effect was found for savoury foods in this study, extending previous research which has only considered the effect of cravings for sweet foods on working memory. The authors of this study argue that considering the visual nature of the task, the findings

support that cravings negatively affect visuo-spatial working memory. While true, it should also be noted that the N-back task involves central executive functioning, due to the updating component involved in remembering the picture 2 items previous (for example), and hence the effects found cannot be interpreted as solely visuo-spatial working memory impairments.

A further line of evidence for the visual nature of food cravings, and the involvement of working memory in food cravings, comes from research showing that concurrent visual processing reduces food cravings. If food cravings consume limited visuospatial working memory resources, then concurrent visual processing should compete for these limited resources, and reduce food cravings. In students, holding images of highly desired food items in mind while simultaneously completing a task known to load the visuo-spatial sketchpad reduced the vividness of the images held in mind and the intensity of cravings for these foods (Kemps, Tiggemann, Woods, & Soekov, 2004). Two follow-up studies showed that these effects are mostly specific to loading the visuo-spatial sketchpad and not the phonological loop component of working memory (Harvey et al., 2005; Kemps, Tiggemann, & Hart, 2005). While these studies did find that performing a task that loaded the phonological loop reduced cravings, loading the visuospatial sketchpad reduced cravings and vividness ratings more than did the phonological loop task. This finding suggests that food cravings may incorporate some auditory elements (such as the sound of sizzling food), but it also supports the idea that visuospatial processing is the key element in cravings. Loading the visuospatial sketchpad has been shown to reduce cravings both in those hungry and not hungry (Steel, Kemps, & Tiggemann, 2006). Personalising the procedure by asking participants to imagine their favourite foods, and using a more naturalistic tasks to load the visuospatial sketchpad also proved to effectively reduce craving vividness (Andrade, Pears, May, & Kavanagh, 2012; McClelland, Kemps, & Tiggemann, 2006). Olfactory imaging is also effective in reducing general food cravings (study 1) and chocolate cravings (study 2) and chocolate cravings when induced without visual imagery (i.e. chocolate deprivation and exposure to chocolate cues) (Kemps & Tiggemann, 2007). Finally, the efficacy of loading the visuospatial sketchpad to reduce food cravings has also been demonstrated in a community sample of adults on the “weight watchers” weight loss programme (Kemps, Tiggemann, & Christianson, 2008).

Overall, the evidence suggests that cravings are associated with dieting and dietary restraint. Cravings appear to be visual in nature, and hence consume visuospatial working

memory resources. Concurrent visuospatial processing seems to reduce food cravings, further supporting their visual nature. The three sub-components of working memory are therefore closely associated with dieting behaviour, with an apparent direct relationship between dieting and central executive and phonological loop components, and an indirect relationship between dieting and visuospatial sketchpad functioning via food cravings.

### **1.11 Summary and aims of thesis**

Rates of obesity and diabetes are increasing across the world, which is a cause for concern due to their associated physical health consequences. Less attention had been paid to the cognitive consequences of obesity and diabetes, which is a significant omission because cognitive deficits may be contributing to a further increase in the prevalence of obesity and diabetes, due to the importance of executive functions in food intake decisions. Executive functions appear to play a key role in the reflective processes that underlie deliberate, controlled, thought-out behaviour that is in line with healthy eating and long-term health goals. The involvement of inhibitory control in eating behaviour is clear: greater inhibitory control is typically associated with more healthful food choices (i.e. consumption of less high energy dense food and/or greater consumption of low energy dense foods). The efficacy of inhibitory control training to change eating behaviour is formally assessed in a systematic review and meta-analysis in Chapter 2. The role of working memory in eating behaviour is less clear. The aim of this thesis is to add to the existing empirical literature and further clarify the role of working memory processes in food intake choices, both in those with and without type 2 diabetes. Chapter 3 describes an experimental, laboratory based study that examined the role of working memory sub-components in food intake in a student sample. The moderating role of individual differences on the relationship between working memory and food intake (namely restraint and tendency towards disinhibition) is also assessed in Chapter 3. Chapters 4 and 5 describe an NHS-based double-blind randomised controlled trial designed to investigate whether working memory training can improve dietary habits and diabetes control in a sample of adults with type 2 diabetes. The aim of this study was to test the causal relationship between working memory and food intake, and investigate whether working memory training could be an effective intervention to change eating habits. Chapter 6 moves beyond the constraints of laboratory-based controlled experimental research to assess the importance of cognition (including working memory) to food intake by analysing a large data set from a representative population (using the UK Biobank cohort).

Chapter 7 provides a general discussion of the results of the studies presented in this thesis, an evaluation of their strengths and limitations and provides suggestions for future research.

## **Chapter 2. Inhibitory Control Training in Eating Behaviour: A Systematic Review and Meta-Analysis.**

### **2.1 Introduction**

Obesity is a global concern linked to the development of many health complications, including type 2 diabetes and cardiovascular disease (Ng et al., 2014). Treating these resultant complications is costly; for example, treatment and intervention for type 2 diabetes in the UK costs the NHS £1 million every hour (Hex et al., 2012). Reducing energy consumption is one way obesity can be reduced. However, changing ingrained food consumption habits is not easy for many people. Automatic impulsive responses towards food may undermine long-term health goals. Inhibitory control has been identified as a key executive function essential to controlling these impulsive responses (Hofmann, Friese, et al., 2008; Strack & Deutsch, 2004) and has been shown to influence behaviour. People with high impulsivity/weak inhibitory control are more likely to overeat (Guerrieri et al., 2007, 2009) and be overweight/obese (Nederkoorn et al., 2007; Sutin et al., 2011). Other work has specifically demonstrated that when inhibitory control is low, eating behaviour is more strongly guided by impulsivity (Hofmann & Friese, 2008; Hofmann et al., 2007; Nederkoorn et al., 2010).

A number of computer-based tasks described collectively as “inhibitory control training” have emerged in recent years as a method for improving control over habitual, automatic behaviours. These have been employed to promote a range of health behaviours, including reduced alcohol consumption (Jones & Field, 2013), smoking cessation (Kerst & Waters, 2014) and resisting consumption of high energy dense foods (Houben, 2011). These types of inhibitory control training are typically modified versions of tasks originally used to assess inhibitory control or attentional bias/action tendencies, and have included the go/no-go task, stop-signal task, visual dot-probe task and approach-avoidance task.

The original go/no-go task requires participants to either respond (e.g. press the space bar) or withhold a response (e.g. not press the space bar) to pictures of different types of stimuli presented on a screen. Responding to a stimulus erroneously suggests poorer inhibitory control for that type of stimulus. The modified training go/no-go task repeatedly pairs the signal to withhold a response with a condition-relevant category of stimuli (e.g. junk foods). Participants are therefore trained to withhold responses to food. Pairing all stimuli in one type of category with no-go signals is considered consistent mapping, and this differs from some versions of the stop signal task described below.



The stop-signal task (SST) is similar to the go/no-go task, except that participants are instructed to respond to all stimuli that they see. For a subset of the stimuli, (typically 25%; Logan, Schachar, & Tannock, 1997) a signal is presented which indicates to the participants that they should withhold their response on this trial. The modified training version of the SST typically involves pairing stop-signals with condition-relevant stimuli (e.g. junk foods). The belief here is that practising withholding responses towards condition-relevant stimuli will train inhibition toward that stimulus (Lawrence, Verbruggen, Morrison, Adams, & Chambers, 2015). The key difference between no-go and stop-signal training is that cues to withhold responses and condition-relevant stimuli are presented simultaneously in the no-go task (requiring inhibition of initiating a response), and shortly after the condition-relevant stimuli in the stop-signal task (requiring inhibition of an already initiated response). The no-go task therefore requires inhibition of behaviour at an earlier stage of processing than the stop-signal task. A further difference is that stop-signal tasks have previously used either consistent or inconsistent mapping. Inconsistent mapping between stimuli and signals is when only a subset of one category of stimuli is paired with signals to withhold a response. A stop-signal task that uses consistent mapping is therefore very similar to a no-go task, and indeed this consistent mapping has been shown to be an important factor in the effectiveness of inhibitory control training tasks (Allom, Mullan, & Hagger, 2015).

The assessment version of the visual dot-probe task involves presenting two stimuli (pictures or words typically) simultaneously on a screen for a brief period. These stimuli then disappear from the screen and a probe appears in the place of one of the stimuli (e.g. either the letter F or G). Participants then have to identify which letter is presented. Attention is biased when participants respond faster to probes that appear in the place of a particular type of stimuli (e.g. junk foods) than to probes replacing another type of stimuli (e.g. stationary). In the modified training version of this task (often called attentional bias modification; ABM), the probe repeatedly replaces condition-neutral stimuli (e.g. stationary), requiring participants to divert their gaze away from condition-relevant stimuli (e.g. junk foods). This is likely to require inhibitory control in order to direct attention away from otherwise attention-grabbing stimuli. As argued by Giel, Schag, Plewnia and Zipfel (2013), attention bias modification training paradigms may be training top-down volitional control of gaze direction, and hence tapping into higher executive functions. Further to this, neurocognitive studies have demonstrated that attention bias modification training recruits brain areas known to be involved in top-down control of behaviour (Browning, Holmes, Murphy, Goodwin, & Harmer, 2010). Similarly, Eldar and Bar-Haim

(2010) found greater N2 amplitude after ABM training in socially anxious people. The N2 potential is a marker of attentional control processes, therefore suggesting greater attentional control in participants after ABM training.

In the assessment version of the approach-avoidance task, participants are instructed to push a joystick away from them when they see pictures in a certain format (e.g. landscape) and pull it towards them when they see pictures in another format (e.g. portrait). Positive stimuli have been shown to facilitate approach (pull) movements, whereas negative stimuli facilitate avoidance (push) movements (Cacioppo, Priester, & Berntson, 1993). Therefore, faster pulling than pushing in response to one type of stimulus suggests an approach bias towards that stimulus. In the training version of this task, “push” signals are paired with condition-relevant stimuli. There is a close connection between valence and action, such that negative evaluations of stimuli are associated with inhibition of behaviour, and positive evaluations of stimuli are associated with activation of behaviour (Verbruggen, Best, Bowditch, Stevens, & McLaren, 2014; Verbruggen, McLaren, & Chambers, 2014). The idea behind the approach-avoidance training task is that pushing something away from you is associated with more negative evaluations than pulling something towards you, and therefore practising pushing something away from you may increase negative evaluations and this may in turn train inhibition of behaviour towards the condition-relevant stimuli (Wiers, Rinck, Kordts, Houben, & Strack, 2010).

This collection of cognitive training tasks is frequently referred to as inhibitory control training (ICT). There is some evidence to support top-down mechanisms of action, such as the involvement of brain areas known to be important for executive functions (Browning et al., 2010) and improved Stroop task performance, a measure of inhibitory control, after stop-signal training (Allom & Mullan, 2015). However, evidence is accumulating to suggest that the key mechanism underlying the effectiveness of these types of training is in fact associatively mediated improved inhibitory control. That is, practising effortful inhibition of one’s behaviour leads to habitual and less effortful, automatic inhibition of behaviour (Verbruggen & Logan, 2008). Inhibition therefore becomes a prepared or learned reflex as a result of these types of training (Verbruggen, Best, et al., 2014). Evidence supports improvement in typically automatic behaviours across all four tasks, such as reduced automatic action tendencies towards alcohol mediating avoidance training effects on alcohol consumption (Sharbanee et al., 2014), reduced attentional bias for chocolate following attention bias modification training (Kemps, Tiggemann, & Elford, 2015), devaluation of stimuli after stop-signal training (Wessel, Tonnesen, & Aron, 2015)

and increased implicit associations between stopping and chocolate after no-go training (Houben & Jansen, 2015).

A recently published meta-analysis (Allom et al., 2015) examined the effectiveness of no-go and stop-signal training on reducing food intake and alcohol consumption. An overall small to medium effect size was found (Cohen's  $d = 0.378$ ), indicating that no-go and stop-signal inhibition training were moderately effective in changing behaviour. When split by type of training, no-go training had a significant effect on behaviour, whereas stop-signals had a marginally significant effect. Behaviour-specific training also appeared more effective than neutral inhibition training. The total number of training trials did not significantly predict ICT effects. The effect of ICT on behaviour measured at follow-up time points was less successful than behaviour measured immediately after training, but both effects were still significant.

Another review by Jones et al. (2016) extended Allom et al.'s (2015) review by including additional studies and another type of inhibitory control training (namely oculomotor inhibition training, called attentional bias modification in the current review; ABM). Overall, ICT reduced food choices/consumption ( $p < .001$ ,  $SMD = 0.33$ ). When split by type of training used, no-go training was successful in reducing food choice/consumption, whereas the effect of stop-signal training was only marginally significant and ABM was not effective. Neither the number of training trials nor the training contingency predicted training effects, but successful inhibition on critical trials did. That is, the more successful participants were at inhibiting their behaviour, then the greater the effect of training was on food and alcohol consumption/choice. The authors also investigated the mechanisms underlying ICT effects. Stimulus devaluation did not occur as a result of inhibition training. ICT had an effect on behaviour in participants scoring high in dietary restraint but not those scoring low in restraint, yet the test for subgroup differences was not significant.

The current review aimed to extend these two reviews in a number of ways. First, a novel type of training was included, namely approach-avoidance training. Second, the effect of ICT on food intake/consumption and food choice/selection and on weight loss and food cravings was assessed; the latter two outcome measures have not been considered previously. One goal of inhibitory control training is to create changes in food intake that will facilitate weight loss, and there are now a number of studies that have investigated weight loss after ICT. Food cravings have been linked to indexes of overeating, including

unsuccessful dieting, binge eating, emotional eating and food-addiction (Crowley et al., 2012; Davis et al., 2011; Meule, Lutz, et al., 2012). Reducing food cravings may therefore change eating habits and so cravings should be considered. The type of comparison group used in ICT has previously been commented on, but has not yet been considered in a meta-analysis of training effects (Jones et al., 2016). Many studies have compared inhibitory control training to attend/approach training, which could be overestimating ICT effects. The effect of two different types of comparison group: 1) control groups, and 2) attend/approach training groups, were therefore assessed.

A number of potential moderators were also examined, including the type of training task used, the type of stimuli used, the number of training sessions used, when the outcome behaviour was assessed and the effect of dietary restraint on training effects. Finally, a rigorous analysis of the quality of published work was conducted and used to make recommendations about the conduct of future research.

## **2.2 Methods**

### **Search Strategy**

This review was conducted in accordance with the PRISMA guidelines (Moher, Liberati, Tetzlaff, & Altman, 2009). Three electronic databases were searched using the controlled indexing terms specific to each database: Ebsco Psychinfo, Ebsco Medline and Embase (as well as additional keys terms where necessary). See Appendix A for the search terms used. Searches took place at the beginning of March 2015, and were re-run at the beginning of January 2016 to identify new articles. There was no limit on publication time frame, but only English language articles published in journals were searched. Due to errors in database indexing, vital articles were excluded from the results when “human only” was an inclusion criteria in the PsychInfo and Medline searches, therefore, this was removed as a search limiter in the initial searches of these two databases and the authors manually sorted incorrectly indexed human studies relevant to the review topic. Unpublished work was not sought.

### **Selection criteria**

- 1) Experimental studies investigating the effect of inhibitory control training (using the no-go, stop-signal, approach-avoidance or attentional bias modification training tasks) in adults (18 years +) to change responses towards food (excluding eating disorders).

- 2) Any eating behaviour related outcome measures, such as actual consumption of food in/outside the laboratory, as well as other measures such as weight loss, self-reported food consumption, cravings and hypothetical food choices.

### **Data Extraction**

A standardised data extraction template was developed, and the following data was extracted from each study. Data was extracted by VW and cross-checked by SH. There were no disagreements on extracted information.

### **Study details**

We recorded the author details, year of publication and the country where the study was conducted.

### **Sample characteristics**

We extracted the type of sample used, key selection criteria, baseline characteristics of the sample (mean age and BMI, where reported), gender and final sample size for the primary outcome measure (food intake, choice or weight loss). Where baseline characteristic information was presented for each condition, these were averaged to provide an overall mean for the total sample.

### **Training**

We recorded the type of training used, along with the conditions and experimental design employed (between or within-subjects), and type of stimuli used. The number of training sessions, number of trials and over what time period this was implemented if more than one training session was used were also extracted. Only the conditions (as labelled by the authors) relevant to this review are described in the study characteristics tables (Tables 1 and 2).

Studies were coded as one of the four different types of inhibitory control training: go/no-go task, stop-signal task, approach-avoidance task and attentional bias modification. More specifically, studies were coded as using no-go training where stimuli and the cue to withhold responses were presented simultaneously. Studies were coded as using stop-signal training when the cue to withhold responses was presented after/following the stimuli. Study 1 and 2 by Veling, Aarts and Stroebe (2013b) were therefore coded as stop-signal training as the tone indicating to withhold a response was presented 500ms after the

stimuli. Veling et al. (2014) was coded as go/no-go training, as the cue to withhold responses was presented 100ms after task stimuli, and was therefore deemed likely to be perceived before the action was initiated.

### **Relevant outcome measures**

Outcome measures relevant to the review were extracted and coded as either food intake/consumption (e.g. grams of food consumed in a taste-test), food choice/selection (e.g. computer-based choice between 4 food pictures), weight loss/BMI change and food cravings. How these were measured (e.g. weight measured by researchers, kcal from a taste-test) and when they were measured i.e. post-training only, or both pre- and post-training, were also recorded.

### **Synthesis of results**

#### Meta-analyses

We extracted means and standard deviations of the appropriate outcome measures. Authors were contacted for this information when it was not available in the published paper. A pre-post change score (mean and SD) was calculated where the outcome measure was assessed both pre and post-training. To ensure that the data entered in the meta-analyses were as consistent as possible, where studies provided post-training and follow-up measures, those assessed immediately post-training were extracted for the meta-analyses (for example, Lawrence, O'Sullivan, et al., 2015). The current review, therefore, did not assess the longevity of training effects, as this has been done elsewhere (Allom et al., 2015). Revman (Review Manager, version 5.3) was used to calculate the standardised mean difference (SMD) between experimental and comparison conditions (Hedge's adjusted *g*). A negative SMD indicates that the ICT group ate less than the comparison group, and a positive SMD indicates that the ICT group ate more than the comparison group. Despite efforts to combine outcome measures into homogenous groups, some heterogeneity remained, therefore random effects models were used as a more conservative test of the effects of ICT (DerSimonian & Laird, 2015). Stata (version 12) was used to conduct sensitivity analysis and to examine funnel-plot asymmetry (95% confidence intervals) around the pooled random-effects effect size. Studies using a within-subjects design were treated like between-subjects studies, as has been done in other meta-analyses (Robinson et al., 2013).

Four separate meta-analyses were conducted: food intake/consumption – ICT vs control group; food intake/consumption – ICT vs attend/approach training group; weight loss; and cravings. A number of studies utilised both a control and an attend/approach comparison group. To include both comparison groups in a single meta-analysis would have required dividing the experimental group sample size by the number of comparisons being entered, resulting in a smaller sample size for the experimental group, and only partially overcoming the unit-of-analysis error (section 16.5.4, Higgins & Green, 2011). As this had to be done to look at some moderators (e.g. non-food vs food-specific training), instead, two separate meta-analyses for control and attend/approach comparison groups were conducted.

Inhibition training was identified as when participants were required to withhold responses (no-go and stop-signal tasks) or avoid target stimuli with either hand or eye movements (approach-avoidance and attentional bias modification tasks). Attend/approach/go training was identified as the opposite to inhibition training; where participants had to go, approach or attend to target stimuli (palatable high energy dense food typically) when defined as such by the authors. In the studies by Lawrence and colleagues (Lawrence, Verbruggen, et al., 2015), the “double-response” group was identified as an attend/approach group, due to the nature of the task involving making 2 responses towards target food stimuli. Control groups were identified as such when described as a control/sham group by the authors. This included for example, when participants had to make an equal number of avoid (with hand or eye movements) and approach/attend movements in response to energy dense foods pictures (attention bias modification and approach-avoidance training); or high energy dense foods were paired with go and no-go/stop-signals equally often (no-go/stop-signal training). These are just one example of each and the types of control groups used varied widely. These are discussed in more detail in the quality analysis section, as is the potential impact of these on the meta-analyses results.

The food choice/selection outcome measures were heterogeneous. For example, the number of healthy foods chosen when asked how participants would behave in different scenarios was used in Becker, Jostmann, Wiers, and Holland (2015 - studies 1 & 2), whereas choosing 8 foods out of 16 food pictures presented on a computer screen for taking home after the study was used in Veling et al. (2013b). Therefore, these studies were reviewed in a narrative form and were not entered into a meta-analysis, in a similar fashion to previous reviews identifying a large amount of heterogeneity in food selection/choice outcome measures (Robinson et al., 2013).

## Subgroup and sensitivity analyses

Subgroup analyses were used to assess potential moderators, and in line with Cochrane recommendations these were only investigated where 10 or more comparisons were available (Higgins & Green, 2011). Information on training type (no-go, stop-signal, attention modification, avoidance-training), stimuli type (food-specific, non-food), restraint levels (low, high), number of training sessions (single or multiple) and when the outcome measure was assessed (post-training only or pre- and post-training) were extracted for subgroup analyses. Leave-one-out sensitivity analysis was conducted to assess the robustness of effects and to help identify causes of heterogeneity (Greenhouse & Iyengar, 2009). Assessing training type subgroups is particularly important, as it is not clear whether these types of training all operate via the exact same underlying mechanisms, and hence it is important to understand which are the most effective.

## Quality Assessment

The quality of studies was assessed using the risk of bias tool recommended by the Cochrane Collaboration (Higgins & Green, 2011). Risk of bias considers 7 ways bias can affect a study's outcomes: random sequence generation (selection bias: specifically how participants were randomised to conditions e.g. computer generated random sequence); allocation concealment (selection bias: method used to prevent researchers foreseeing which condition participants would be allocated to e.g. a single URL link provided to participants at the end of the testing session that allocated them to training conditions); blinding of study personnel (performance bias: evidence that researcher blinding was protected after condition allocation e.g. online studies with no researcher involvement); blinding of outcome assessment (detection bias: how/whether those measuring the outcome were kept blind to condition, e.g. awareness probes, use of a cover story, or self-report measures), incomplete outcome data (attrition bias: e.g. appropriate explanations for attrition or exclusion of data), selective reporting (reporting bias: assessed where a published protocol was available to help identify selective reporting of results) and whether groups were comparable on baseline characteristics (other bias). Two authors (VW, KvD) independently judged the included studies on each of these domains based on the information reported in the published papers and made judgements on the extent to which the outcome measure was likely to have been influenced by the methods reported (risk of bias). For each domain, a judgement of low risk, high risk or unclear risk was made. Disagreements were resolved by discussion. This was repeated for each outcome



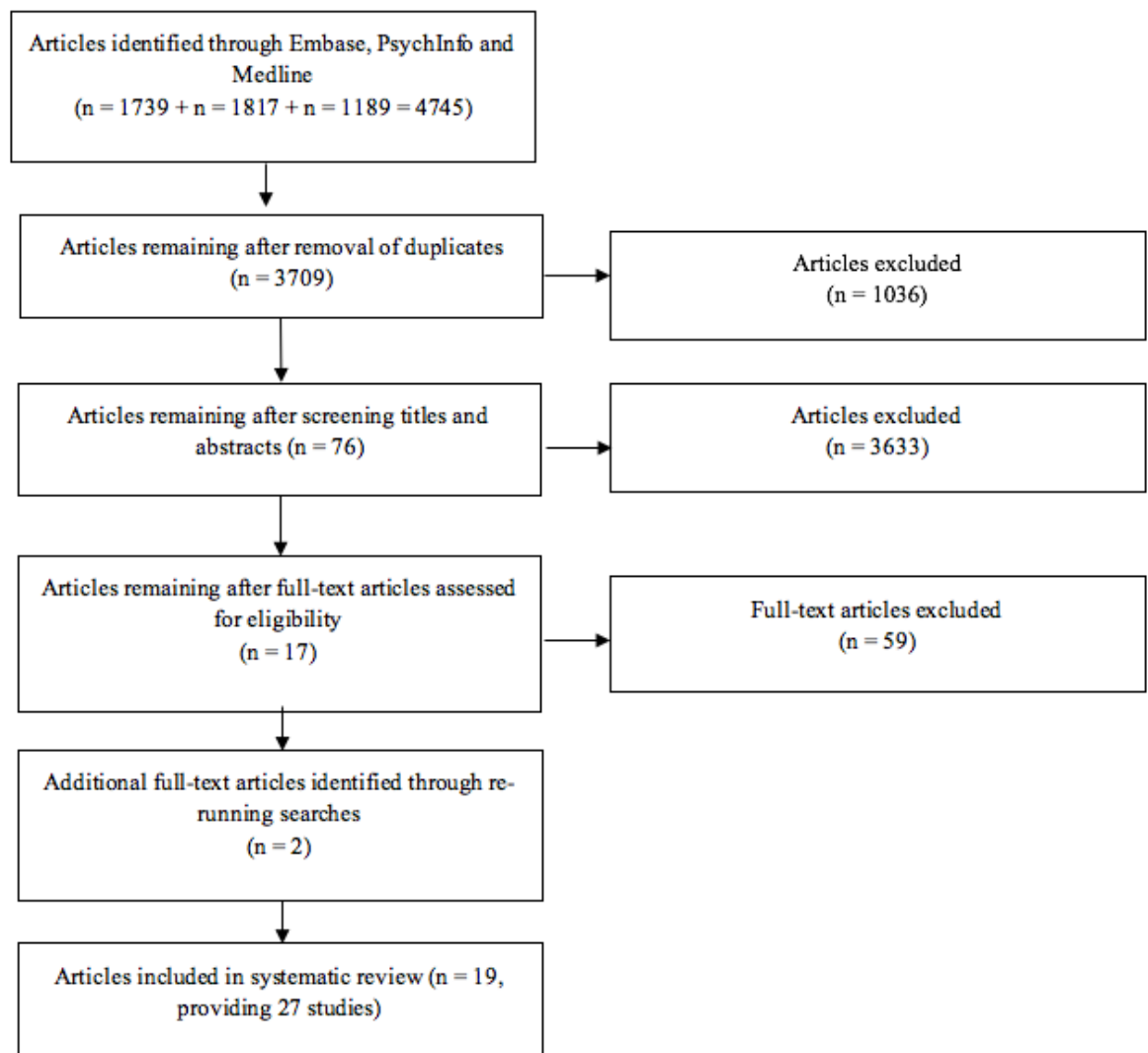
measure (food intake/consumption, food choice/selection, weight loss, food cravings). A summary risk of bias graph was developed from this and used in decisions about the strength of conclusions made from the meta-analyses and narrative reviews, and in drawing conclusions and recommendations about the conduct of future research. An in-depth consideration of the types of control and comparison groups used in studies was also conducted, such as how likely the comparison group was to train behaviour away or towards food.

Publication bias was assessed by inspecting funnel plots and using Egger's test of funnel plot asymmetry. Heterogeneity was assessed using the  $I^2$  statistic and Cochrane recommended cut-offs for interpretation purposes (section 9.5.2; Higgins & Green, 2011).

## **2.3 Results**

### **Study Selection**

Initial searches retrieved 4,745 results, with 3,709 remaining after duplicates were removed. Following the PRISMA guidelines, a summary of the search and screening process is shown in Figure 1 (Moher et al., 2009). All screening was conducted separately by two authors (VW and KvD). There were no disagreements regarding exclusion of any articles. Of the 59 articles excluded after screening the full texts, 53 of these were excluded because they did not use one of the 4 types of ICT relevant to this review. The remaining 6 articles were excluded for the following reasons: information for the meta-analyses could not be obtained from the authors (Guerrieri, Nederkoorn, & Jansen, 2012; Guerrieri et al., 2009), the sample consisted of children (Boutelle, Kuckertz, Carlson, & Amir, 2014; Verbeken, Braet, Goossens, & van der Oord, 2013); only "attend" training was used, resulting in no ICT conditions (Smith & Rieger, 2009); and the outcome measure was unrelated to food intake or food choices (Kemps, Tiggemann, & Hollitt, 2014). No additional articles were identified following forwards and backwards searches. The January 2016 re-run of the searches identified 2 additional articles (Allom & Mullan, 2015; Lawrence, O'Sullivan, et al., 2015). Nineteen articles describing 27 studies were included in this meta-analysis and systematic review. See Tables 1 and 2 for the summary of study characteristics for included studies.



**Figure 1. PRISMA flowchart of search and screening processes**

### Meta-analysis decisions

The outcome measure for study 1 (Van Koningsbruggen, Veling, Stroebe, & Aarts, 2013) was classified as a food choice/selection outcome measure, as participants did not actually consume the sweets. To avoid double-counting participants, food intake (kcal) measured by 24-hour recall was extracted from the study by Lawrence, O’Sullivan, et al. (2015), as the pre-post nature of this measure is likely to be a better measure of changes in food intake than the post-training only taste-test measure of calorie intake. Results for the single training session conditions were extracted from Kemps et al. (2015). As all other studies in the meta-analyses used high energy dense food intake, chocolate muffin and not blueberry muffin consumption data was extracted from this study. For Werthmann, Field, Roefs, Nederkoorn and Jansen (2014) ad-libitum food intake and not chocolate search time was extracted. Both the general stop-training and the stimulus-specific stop training conditions

in study 3 (Lawrence, Verbruggen, et al., 2015) used non-food stimuli, and therefore both were counted as non-food inhibition training. Both the food-specific and general inhibition training conditions in the studies by Allom and Mullan (2015) used food stimuli, and therefore both were counted as food-specific inhibition training. Where studies contributed more than one comparison to a meta-analysis, the number of participants in the control condition was divided by the number of experimental conditions (section 16.5.4 of the Cochrane Handbook, Higgins & Green, 2011). The study by Kakoschke, Kemps and Tiggemann (2014) was included in the narrative review of ICT to increase food choices because the outcome measure (amount of healthy snack food consumed as a proportion of the total amount of food consumed) fit this narrative review better than any of the meta-analyses looking at ICT to reduce intake of high energy dense foods.

### **Characteristics of included studies**

Out of the 27 studies included in this review, 8 used no-go training, 9 used stop-signals, 4 used avoidance training and 6 used attentional bias modification training. The total sample size across included studies was 2,201 ( $M = 81.52$ , range = 24-170). The mean percentage of women was 83.5% (range = 53.9-100%). All but one study reported the age of the sample (Fishbach & Shah, 2006 - S5), resulting in a mean age of 22.5 years (range = 19.5-50.5 years). Four studies did not report information about the BMI of the sample (Fishbach & Shah, 2006 - S5 ; Kemps, Tiggemann, Orr, & Grear, 2014 - S1 & 2; Schonberg et al., 2014). Mean BMI across the remaining studies was in the healthy range:  $22.7 \text{ kg/m}^2$  (range =  $21.0\text{-}28.9 \text{ kg/m}^2$ ). The majority of study samples were composed of undergraduate students or other university staff, with only one study using a sample of overweight community-dwelling adults (Lawrence, O'Sullivan, et al., 2015). Two studies implemented 10 training sessions (Allom & Mullan, 2014), two implemented 4 training sessions (Lawrence, O'Sullivan, et al., 2015; Veling et al., 2014), and the remaining 21 studies implemented a single training session. High energy/calorie dense palatable food pictures and non-food objects (e.g. stationary) were the most widely used type of stimuli. Food intake was an outcome measure in 16 studies, food choices in 10 studies, weight loss/change in BMI in 6 studies and food cravings in 3 studies (note that a number of studies had multiple outcome measures, and hence the total number of studies here exceeds the number of included studies, i.e. 27). Sixteen out of the 27 included studies utilised a control or sham condition. The majority of studies measured the key outcome only post-training. Three studies measured food cravings both pre- and post- training, and 4 studies measured weight/BMI pre- and post-training. Tables 1 and 2 summarise the

characteristics of all included studies (Table 1 refers to those in the meta-analyses, Table 2 refers to those in the narrative review). These tables also indicate how author-defined groups were coded for the purpose of this review (AAG = attend/approach/go group; ICT = inhibitory control training group; C = control group) The review by Allom et al. (2015) excluded Veling, Aarts and Stroebe (2013a) over concerns of the generalisability of the study findings because the same stimuli were used in both the training and food choice/selection outcome measure. Here, this paper is included in the narrative review of food choice/selection outcomes and the methodology is commented on. The current review identified 5 more studies testing the effectiveness of attentional bias modification on eating behaviour than did Jones et al. (2016). This may be because the search term used to identify this type of training in the current review (variations of “attentional bias modification”) is more widely used in the keywords and abstracts of these papers than the term used by Jones et al. (“antisaccade”).

**Table 1. Table of study characteristics for food intake/consumption, weight loss and food craving studies.**

	Type of training	Participants (characteristics provided for final sample size for conditions included in review, where provided)	No: of training sessions and trials, and time period implemented	Training conditions	Stimuli	Outcome measures relevant to review	When outcome measures were assessed.
Houben & Jansen (2011). The Netherlands.	go/no-go	Sample = Undergraduate students who were high trait chocolate cravers (score >10 on ACQC) N = 63 (all female) Age = 19.94 y (M) BMI = 22.39 (M)	1; 320 trials	1) chocolate/no-go group <sup>ICT</sup> 2) chocolate/go group <sup>AAG</sup> 3) control group <sup>C</sup>  between-subjects	chocolate snacks, empty plates, snack foods	Food intake (taste-test, grams)	Post training only

Velting, Aarts & Papiés (2011). The Netherlands. Study 2.	go/no-go	Sample = Undergraduate students N = 46 (28 female) Age = 21.16 y (M) BMI = 21.55 (M)	1; 72 trials	1) no-go group <sup>ICT</sup> 2) control group <sup>C</sup>  between-subjects	sweets and everyday objects	Food intake (self-served amount of sweets into sweet bag given to take home and returned the next day, grams)	Post training only
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Veling, van Koningsbruggen, Aarts & Stroebe (2014). The Netherlands.	go/no-go	Sample = Mostly students, but some employed and unemployed. Completed general secondary education, and no severe obesity (BMI > 35kg/m <sup>2</sup> ) N = 55 (50 female) Age = 22.35 (M) BMI = 24.55(M)	4; 800 trials over 4 weeks. 200 trials per session.	1) food no-go and control implementation intentions <sup>ICT</sup> 2) control no-go and control implementation intentions <sup>C</sup>  between-subjects	high calorie/palatable food and non-food pictures	Weight loss (measured by researcher)	Pre and post-training
Houben & Jansen (2015). The Netherlands	go/no-go	Sample = undergraduate students who eat chocolate on a regular basis. N = 41 (all female)	1; 320 trials	1) chocolate/no-go <sup>ICT</sup> 2) chocolate/go <sup>AAG</sup>  between-subjects	chocolate snacks, empty plates, snack foods	Food intake (taste-test, kcal)	Post training only

		Age = 20.13 y (M) BMI = 22.18 (M)					
Lawrence, O'Sullivan et al. (2015)	go/no-go	Sample = adults in the community aged 18-65, BMI $\geq$ 18.5, ate the training foods $\geq$ 3 times a week and reported some disinhibition. N = 83 (65 female) Age = 50.46 y (M) BMI = 28.89 (M)	4; 864 trials over 1 week. 216 trials per session.	1) active (response inhibition) training <sup>ICT</sup> 2) control group <sup>C</sup>  between-subjects	high energy dense foods, healthy foods, non-food pictures	Weight loss (measured by researcher)  Food intake (24-hour recall, calories)	Pre and post- training
Houben (2011). The Netherlands.	stop-signal task	Sample = undergraduate students that liked the study foods N = 29 (all female)	1; 248 trials	1) stop-food <sup>ICT</sup> 2) go-food <sup>AAG</sup> 3) control food <sup>C</sup>	food and non- food pictures	Food intake (taste test, calories)	Post training only



		Age = 21.15 y (M) BMI = 23.12 (M)		within-subjects			
Lawrence, Verbruggen et al. (2015). UK. Study 1.	stop-signal task	Sample = University students and staff. N = 54 (32 female) Age = 24.00 y (M) BMI = 22.90 (M)	1; 480 trials	1) stop-group <sup>ICT</sup> 2) double-response group <sup>AAG</sup>  between subjects	food and non- food pictures	Food intake (taste test, calories)	Post training only
Lawrence, Verbruggen et al. (2015). UK. Study 2.	stop-signal task	Sample = university students and staff. N = 136 (100 female) Age = 24.13 y (M) BMI = 23.53 (M)	1; 512 trials	1) stop-training group (food) <sup>ICT</sup> 2) double-response group <sup>AAG</sup> 3) ignore control group c  between subjects	food and non- food pictures	Food intake (taste test, calories)	Post training only

Lawrence, Verbruggen et al. (2015). UK. Study 3.	stop-signal task	Sample = university students and staff. N = 146 (111 female) Age = 23.50 y (M) BMI = 22.93 (M)	1; 512 trials	1) general stop-training (non-food) <sup>ICT</sup> 2) stimulus-specific double-response group AAG 3) stimulus-specific stop-training (non-food) <sup>ICT</sup>  between subjects	non-food pictures	Food intake (taste test, calories)	Post training only
Allom & Mullan (2015) Study 1.	stop-signal task	Information provided only for baseline sample. Sample = undergraduate students with an intention to change dietary behaviour N = 82 (66 female; Final N = 72)	10; 1920 trials over 10 days (192 trials per session)	1) food-specific inhibition training <sup>ICT</sup> 2) general inhibition training <sup>ICT</sup> 3) control group <sup>C</sup>  between-subjects	sweet and savoury healthy and unhealthy food pictures	BMI change (self-reported weight)  Food intake (Block Food Screener Questionnaire,	Pre and post-training

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Age = 20.43y (M)  
BMI = 22.62 (M)

grams of fat  
intake per day)

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Allom & Mullan (2015) Study 2.	stop-signal task	Information provided only for baseline sample. Sample = staff and students from a variety of disciplines with an intention to change dietary behaviour N = 78 (61 female; Final N = 70)	10; 1920 trials over 10 days (192 trials per session)	1) food-specific inhibition training <sup>ICT</sup> 2) general inhibition training <sup>ICT</sup> 3) control group <sup>C</sup>  between-subjects	sweet and savoury healthy and unhealthy food pictures	BMI change (researcher measured weight)  Food intake (The National Cancer Institute percentage of energy from fat screeener).	Pre and post- training
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Age = 22.97y (M)

BMI = 23.11 (M)

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Becker et al. (2015). The Netherlands. Study 3.	Approach- avoidance training	Sample = students with a strong desire for chocolate and intention to reduce chocolate intake N = 103 (all female) Age = 21.94 Y (M) BMI = 22.04 (M)	1; 320 trials, followed by a refresher manipulation phase of 80 trials after the post- assessment phase	1) experimental condition (avoid unhealthy/approach healthy) <sup>ICT</sup> 2) sham condition <sup>C</sup>  between-subjects	chocolate and stationary pictures	Food intake (taste-test, grams)	Post training only
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Hardman et al. (2013). U.K.	Attentional bias modification	Sample = undergraduate students N = 60 (35 female) Age = 23.2 Y (M) BMI = 22.4 (M)	1; 512 trials	1) attend cake group AAG 2) avoid cake group <sup>ICT</sup> 3) control group <sup>C</sup>  between-subjects	cake and neutral stationary pictures	Food intake (taste-test, % kcal consumed)	post- training only
Werthmann et al. (2014). The Netherlands.	Attentional bias modification	Sample = undergraduate students N = 51 (all female) Age = 19.54 y (M) BMI = 22.13 (M)	1; 320 trials	1) attend chocolate/avoid shoes AAG 2) avoid chocolate/attend shoes ICT  between-subjects	chocolate and shoe pictures	Food intake (free access to a bowl of chocolates, grams)  Cravings (100mm visual analogue scale about general food cravings)	Food intake; post- training only  Cravings; pre and post training

Kemps, Tiggemann, Orr et al. (2014). Australia Study 1.	Attentional bias modification	Sample = undergraduate students N = 110 (all female) Age = 20.43 y (M) BMI = not measured/reported	1; 256 trials.	1) attend chocolate/avoid non- chocolate food <sup>AAG</sup> 2) avoid chocolate/attend non- chocolate food <sup>ICT</sup>  between-subjects	chocolate and non-chocolate highly desired food pictures	Food intake (taste-test, grams)  Cravings (Chocolate specific 100mm visual analogue scale)	food intake; post- training only cravings; pre and post training
Kemps, Tiggemann, Orr et al. (2014). Australia Study 2.	Attentional bias modification	Sample = undergraduate students N = 88 (all female) Age = 19.82 y (M) BMI = not measured/reported reported	1; 256 trials.	1) attend chocolate/avoid non- chocolate food <sup>AAG</sup> 2) avoid chocolate/attend non- chocolate food <sup>ICT</sup>  between-subjects	chocolate and non-chocolate highly desired food pictures	Food intake (taste-test, grams)  Cravings (Chocolate specific 100mm visual analogue scale)	food intake; post- training only cravings; pre and post

Kemps, Tiggemann & Elford (2014). Australia.	Attentional bias modification	Sample = undergraduate students who like chocolate N = 149 (all female) Age = 20.22 y (M) BMI = 23.44 (M)	1 or 5 (across 5 weeks); 224 trials per session	1) attend chocolate/avoid non- chocolate food <sup>AAG</sup> 2) avoid chocolate/attend non- chocolate food <sup>ICT</sup>  between-subjects	chocolate and non-chocolate highly desired food pictures	Food intake (taste-test, grams)	Post, 24- hour and 1-week follow-up
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**Note.** ACQC = Attitudes to Chocolate Questionnaire Cravings Subscale; BMI = Body Mass Index (kg/m<sup>2</sup>); <sup>AAG</sup> = attend/approach/go group; <sup>ICT</sup> = inhibitory control training group; <sup>C</sup> = control group

**Table 2. Table of study characteristics and summary of findings for food choice/selection studies.**

Authors, year and country of publication	Type of training	Participants (after exclusions and drop outs where this information is provided)	No: of training sessions and trials, and time period implemented	Training conditions (relevant to review)	Stimuli	Outcome measures relevant to review	When outcome measures were assessed	Results
Velting, Aarts & Stroebe (2013a). The Netherlands	go/no-go	Sample = student and others N = 50 (34 females) Age = 22.00 y (M) BMI = 22.48 (M)	1; 80 trials.	1) no-go group <sup>ICT</sup> 2) go group <sup>AAG</sup>  within-subjects	palatable foods	Food choice/selection (computer-based food choice, scored 0-3 each for go and no-go foods)	Post training only	High appetite participants chose fewer of the no-go (inhibition) trained foods than the go trained foods ( $p < 0.01$ ). Those in the low appetite condition chose as many no-go and go foods.



van Koningsbruggen et al. (2013). The Netherlands. Study 1.	go/no-go	Sample = Psychology and other subject students N = 89 (48 females, N = 46 for the two groups relevant to this review) Age = 21.76 y (M) BMI = 22.08 (M)	1; 72 trials	1) no-go only <sup>ICT</sup> group 2) control group <sup>C</sup>  between-subjects	sweets and everyday objects	Food choice/selection (self-serving of sweets into sweet bag, grams)	Post training only (the day after)	ICT reduced self-serving of sweets in a bag compared to the control group ( $p=.005$ ).
van Koningsbruggen et al. (2013). The Netherlands. Study 2.	go/no-go	Sample = Psychology and other subject students N = 88 (55 females) Age = 21.17 y	1; 72 trials	1) no-go only group <sup>ICT</sup> 2) control group <sup>C</sup>  between-subjects	sweets and everyday objects	Food choice/selection (self-served amount of sweets from computerised	Post training only (same day)	ICT reduced self-serving of sweets using computerised sweet dispenser compared to the

		(M) BMI = 21.63 (M)				snack dispenser, scored 0-500)		control group ( $p=.005$ ).
Veling et al. (2013b). The Netherlands. Study 1.	stop-signal task	Sample = young adults N = 79 (49 females) Age = 21.38 y (M) BMI = 22.00 (M)	1; 96 trials	1) stop-group <sup>ICT</sup> 2) control group <sup>C</sup>  between-subjects	healthy and unhealthy snack food and neutral pictures	Food choice/selection (number of experimental foods chosen in a computer- based food choice task, out of 4)	Post training only	High appetite participants (those who took part before lunch) in the inhibition training group chose fewer experimental palatable foods than those in the control group ( $p<.01$ ). No difference between

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low appetite groups.

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Velting et al. (2013b). The Netherlands. Study 2.	stop-signal task	Sample = young adults N = 44 (27 females) Age = 21.50 y (M) BMI = 21.61 (M)	1; 96 trials	1) stop-group <sup>ICT</sup> 2) control group <sup>C</sup>  between-subjects	healthy and unhealthy snack food and neutral pictures	Food choice/selection (number of experimental foods chosen in a computer-based food choice task, out of 4)	Post training only	Those who frequently consumed the foods used in the inhibitory control training chose fewer of the palatable unhealthy foods after inhibitory control training than the control training
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group ( $p < .01$ ). No effect in those who did not consume the foods frequently.

Schonberg et al. (2014). U.S.A. Comparison between pooled results of studies 1-4 (cue-approach training) and studies 5 and 6 (ICT).	stop-signal task	Sample = students N = 170 (119 female) Age = 20.77 y (M) BMI = not reported	1 training session.  Study 1 & 3 = 720 Study 2 = 480 Study 4 = 960 Study 5 = 720 Study 6 = 960	1) cue-avoidance <sup>ICT</sup> 2) cue-approach <sup>AAG</sup>	appetitive junk food pictures	Food choice/selection (number of "go" foods chosen in a computer-based food choice probe task)	Post training only	Those in the approach training group chose more of the highly valued go food pictures than the inhibitory control training group ( $p < 0.0001$ ). Low valued go items were chosen equally by the inhibition and
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approach training groups ( $p=0.28$ ).

Becker et al. (2015). The Netherlands. Study 1.	Approach-avoidance training	Sample = students N = 51 (all female) Age = 20.47 y (M) BMI = 21.57 (M)	1; 360 trials.	1) experimental condition (avoid unhealthy/approach healthy) <sup>ICT</sup> 2) sham condition <sup>C</sup>  between-subjects	sweet and savoury high and low calorie food pictures	Food selection/choices (number of hypothetical healthy food choices in scenarios, behavioural choice of 3 foods and frequency of	Post training only	Trend for ICT participants to choose more of the healthy foods than those in the control condition on the scenarios assessment ( $p=0.073$ ). Actual food choice (tangerine, granola bar or chocolate
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health behaviour  
over past week)

bar) did not differ  
between training  
groups ( $p=0.164$ ).  
Two-week follow-  
up questionnaire  
found that the ICT  
group consumed  
fewer ready meals  
than the control  
group over the last  
week ( $p=0.021$ ).  
No other  
comparisons were  
significant at this  
time point.

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Becker et al (2015). The Netherlands. Study 2.	Approach-avoidance training	Sample = students N = 104 (all female) Age = 20.77 y (M) BMI = 21.01 (M)	1; 360 trials.	1) experimental condition (avoid unhealthy/approach healthy) <sup>ICT</sup> 2) sham condition <sup>C</sup>	sweet and savoury high and low calorie food pictures	Food selection/choices (number of hypothetical healthy food choices in scenarios)	Post training only	No difference between the inhibition and control groups in healthy food choices on the scenarios assessment (p=0.456).
Fishbach & Shah (2006). U.S.A. Study 5.	Approach-avoidance training	Sample = undergraduate students N = 24 (all female) Age = not reported BMI = not reported	1; 120 trials	1) avoid tasty/approach healthy <sup>ICT</sup> 2) avoid healthy/approach tasty <sup>AAG</sup>	healthy and tasty food words	Food choice/selection (choose one food item out of a pair - one healthy, one fatty food. 3 pairs presented, scored the number of healthy items	Post training only	Participants chose more healthy food items after ICT than approach training (p<0.05)

chosen.  
 Participants  
 received one of  
 their choices at  
 the end of the  
 study)

Kakoschke et al. (2014). Australia.	Attentional bias modification	sample = undergraduate students N = 146 (all female) Age = 20.16 y (M) BMI = 22.2 (M)	1; 256 trials.	1) attend healthy/avoid unhealthy food 2) attend <sup>ICT</sup> unhealthy/avoid healthy food <sup>AAG</sup> between-subjects	healthy, unhealthy and non- food pictures	Food choice/selection (taste test, proportion of total food intake that was the healthy snack, kilojoules)	post- training only	ICT (attend healthy/avoid unhealthy) participants ate a higher proportion of healthy food than the attend unhealthy/avoid healthy training group ( $p = 0.03$ ).
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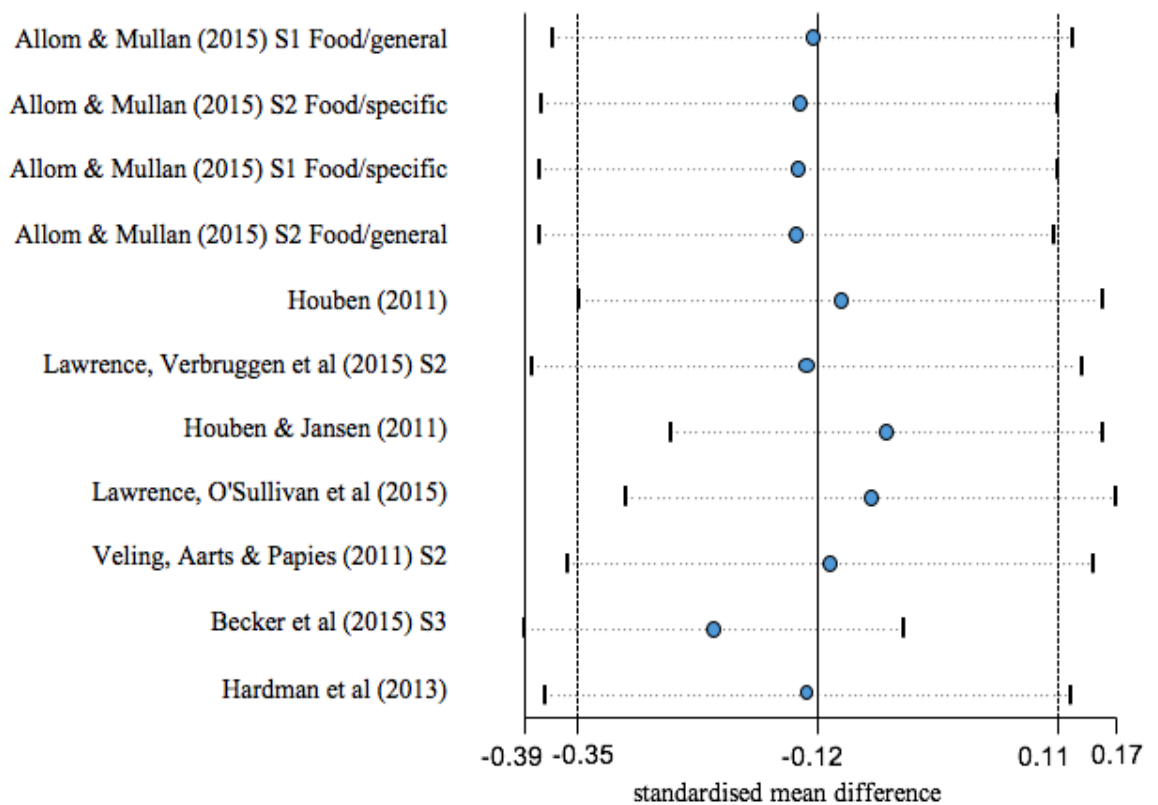
**Note.** BMI = Body Mass Index (kg/m<sup>2</sup>); <sup>AAG</sup> = attend/approach/go group; <sup>ICT</sup> = inhibitory control training group; <sup>C</sup> = control group



## Food intake/consumption studies

Control group as comparison group

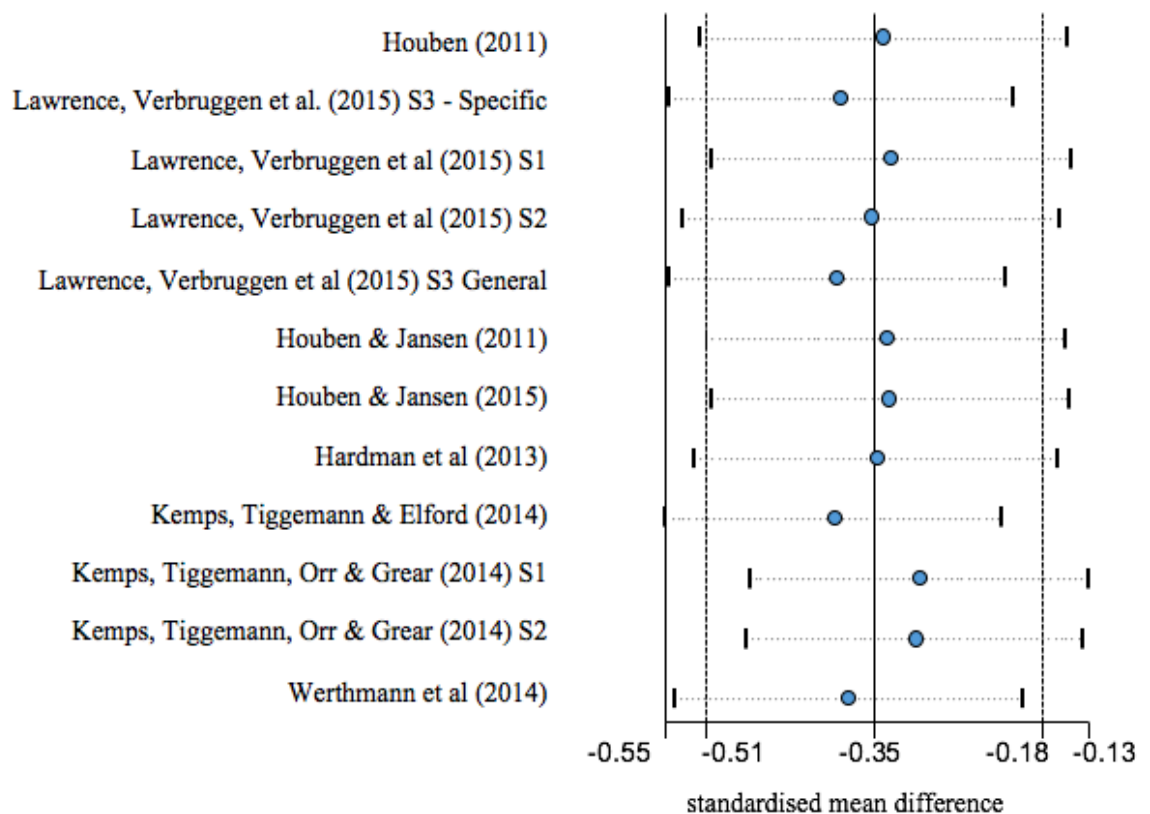
Eight papers contributed 11 comparisons to this meta-analysis. The overall effect of ICT on behaviour was not significant (SMD = -0.12, 95% CIs [-0.35, 0.11];  $Z = 1.01$ ,  $p = 0.31$ ;  $I^2 = 46\%$ ). Leave-one-out analysis (Figure 2) showed that the effect became significant when Becker et al. (2015 - S3) was removed (SMD = -0.21, 95 % CIs [-0.39, -0.04];  $Z = 2.34$ ,  $p = 0.02$ ) and heterogeneity was reduced to zero ( $I^2 = 0\%$ ). This is the only study that found ICT to increase food intake, explaining the heterogeneity caused by including this study. See Figure 3 for a forest plot of the main effects of ICT compared to control groups on food intake.



**Figure 2. Leave-one-out sensitivity analysis for the effects of ICT on food intake compared to a control group. The vertical axis shows the omitted study, and the horizontal axis depicts the pooled estimate (circle) when each study is removed, with 95% confidence intervals.**

## Attend/approach training as comparison group

Eight papers contributed 12 comparisons to this meta-analysis. The overall effect of ICT on behaviour was significant (SMD = -0.35, 95% CIs [-0.51, -0.18];  $Z = 4.05$ ,  $p < 0.0001$ ;  $I^2 = 26\%$ ). The small amount of heterogeneity here is considered unlikely to be important. Leave-one-out analysis showed that omitting any one study had minimal effects on the pooled estimate, demonstrating the robustness of these effects (Figure 4). See Figure 5 for a forest plot of the main effect of ICT compared to attend/approach comparison groups on food intake.



**Figure 4. Leave-one-out sensitivity analysis for the effects of ICT on food intake compared to an attend/approach group. The vertical axis shows the omitted study, and the horizontal axis depicts the pooled estimate (circle) when each study is removed, with 95% confidence intervals.**

## Moderators

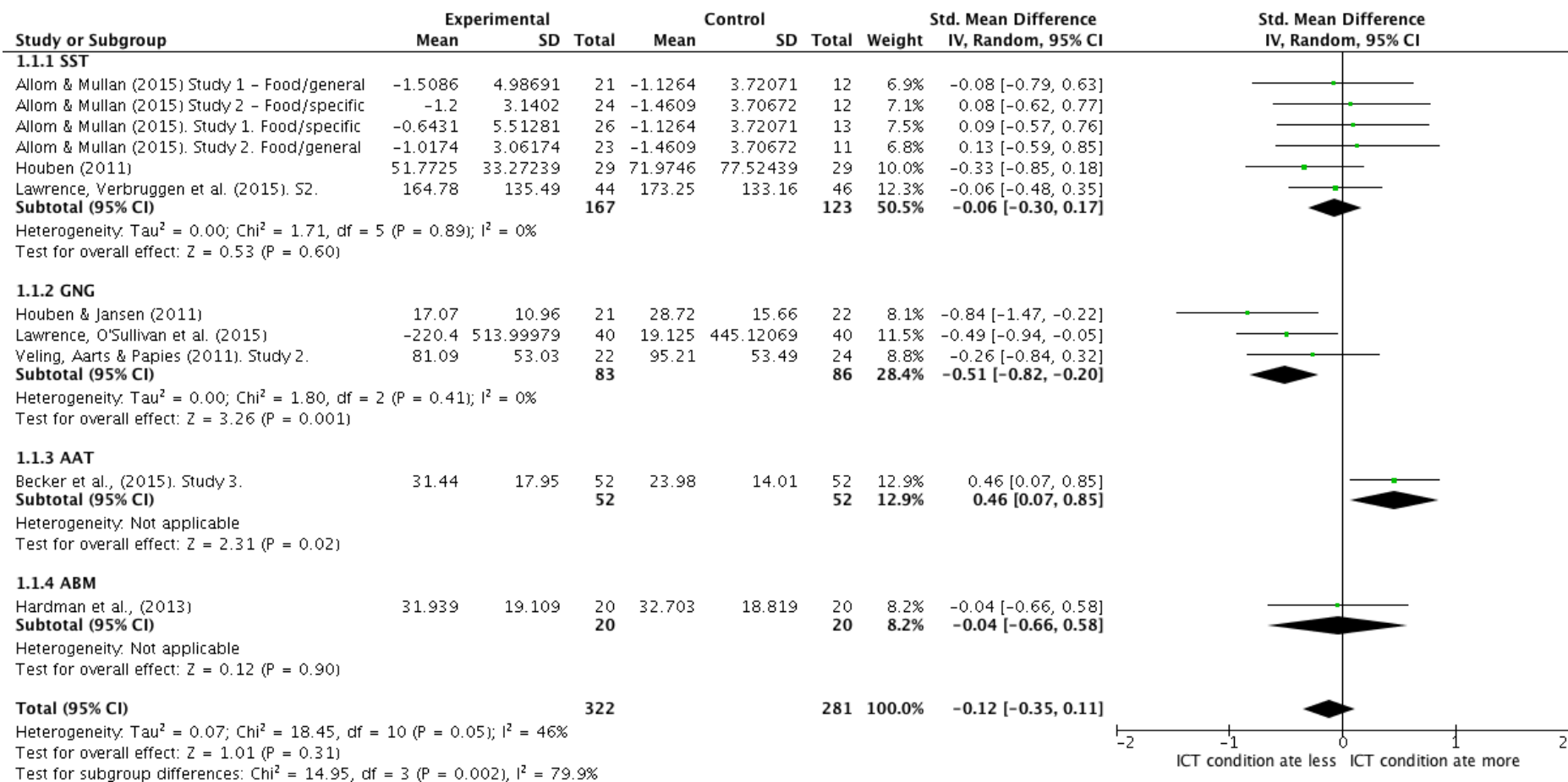
Stimuli type could only be investigated in the attend/approach comparison group meta-analysis, as all studies in the control group meta-analysis used food-specific inhibition training. Number of training sessions and when the outcome measure was assessed could only be investigated in the control group meta-analysis as all studies in the attend/approach comparison group meta-analysis utilised a single training session and

measured behaviour post-training only. There were not enough studies that looked at dietary restraint to allow this to be investigated as a moderator in any of the meta-analyses.

### Type of training

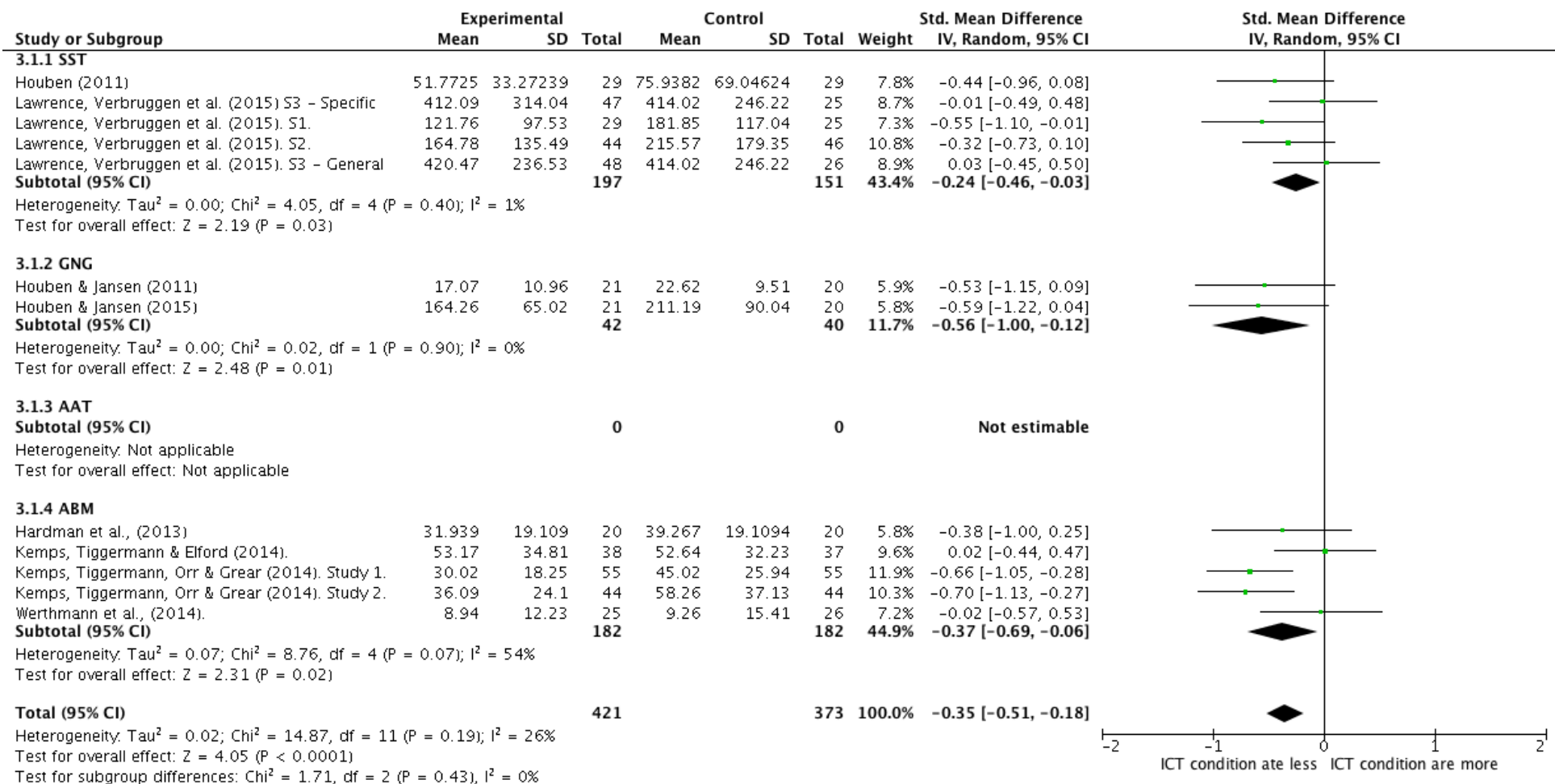
Six studies used stop-signals in the control group meta-analysis, 3 used no-go training, 1 used avoidance training and 1 used attention bias modification training. The test for subgroup differences was significant ( $X^2 = 14.95$ ,  $p = 0.002$ ). There was a non-significant effect of stop-signal training (SMD = -0.06, 95% CIs [-0.30, 0.17];  $Z = 0.53$ ,  $p = 0.60$ ;  $I^2 = 0\%$ ) and attention modification training on food intake (SMD = -0.04, 95% CIs [-0.66, 0.58];  $Z = 0.12$ ,  $p = 0.90$ ;  $I^2 = n/a$ ). No-go training did however have a significant effect on food intake (SMD = -0.51, 95% CIs [-0.82, -0.20];  $Z = 3.26$ ,  $p = 0.001$ ;  $I^2 = 0\%$ ), as did avoidance training (SMD = 0.46, 95% CIs [0.07, 0.85];  $Z = 2.31$ ,  $p = 0.02$ ;  $I^2 = n/a$ ). The direction of the SMDs suggests that no-go training reduced food intake, whereas avoidance training increased food intake. As only one study used attention modification ( $n = 40$ ) and avoidance training ( $n = 104$ ) tasks, the results of the subgroup analyses for these types of training may not be reliable. See Figure 3 for a forest plot of the effects of ICT compared to control groups split by type of training task.

In the attend/approach comparison group meta-analysis, 5 studies used stop-signals, 2 used no-go training, none used avoidance training, and 5 used attention bias modification training. There was a significant effect for all types of training: SST training (SMD = -0.24, 95% CIs [-0.46, -0.03];  $Z = 2.19$ ,  $p = 0.03$ ;  $I^2 = 1\%$ ); go/no-go training (SMD = -0.56, 95% CIs [-1.00, -0.12];  $Z = 2.48$ ,  $p = 0.01$ ;  $I^2 = 0\%$ ) and attention modification training (SMD = -0.37, 95% CIs [-0.69, -0.06];  $Z = 2.31$ ,  $p = 0.02$ ;  $I^2 = 54\%$ ). The test for subgroup differences was not significant ( $X^2 = 1.71$ ,  $p = 0.43$ ). See Figure 5 for a forest plot of the effects of ICT compared to attend/approach comparison groups split by type of training task.



**Figure 3.** Forest plot of comparison of the effect of ICT to control groups on food intake/consumption, separately for type of training used.

*Note.* SST = stop-signal training, GNG = go/no-go training, AAT = approach-avoidance training, ABM = attention bias modification.

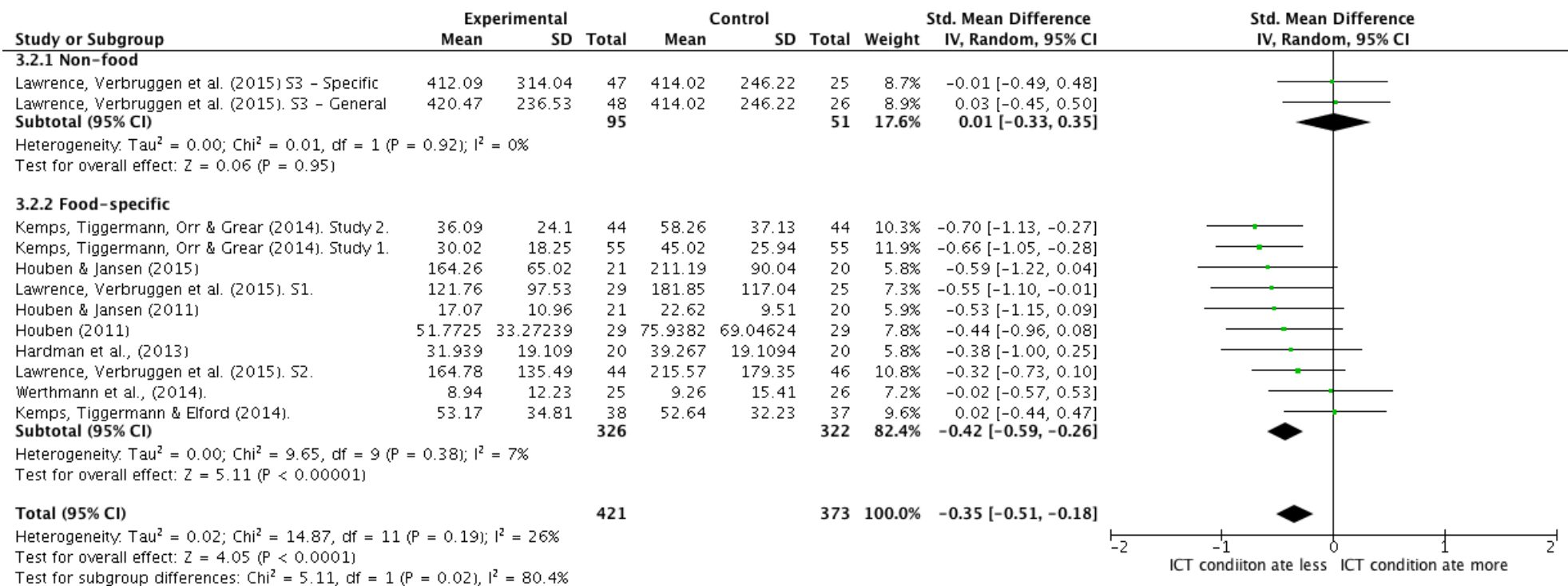


**Figure 5. Forest plot of comparison of the effect of ICT to attend/approach comparison groups on food intake/consumption, separately for type of training used.**

*Note.* SST = stop-signal training, GNG = go/no-go training, AAT = approach-avoidance training, ABM = attention bias modification.

## Type of stimuli

Two studies in the attend/approach comparison group meta-analysis used non-food ICT, and 10 used food-specific stimuli. The effect of non-food ICT was not significant (SMD = 0.01, 95% CIs [-0.33, 0.35];  $Z = 0.06$ ,  $p = 0.95$ ;  $I^2 = 0\%$ ), whereas food-specific ICT was significant (SMD = -0.42, 95% CIs [-0.59, -0.26];  $Z = 5.11$ ,  $p < 0.00001$ ;  $I^2 = 7\%$ ). The test for subgroup differences was also significant ( $X^2 = 5.11$ ,  $p = 0.02$ ). See Figure 6 for a forest plot of the effects of ICT compared to attend/approach comparison groups split by type of stimuli used.

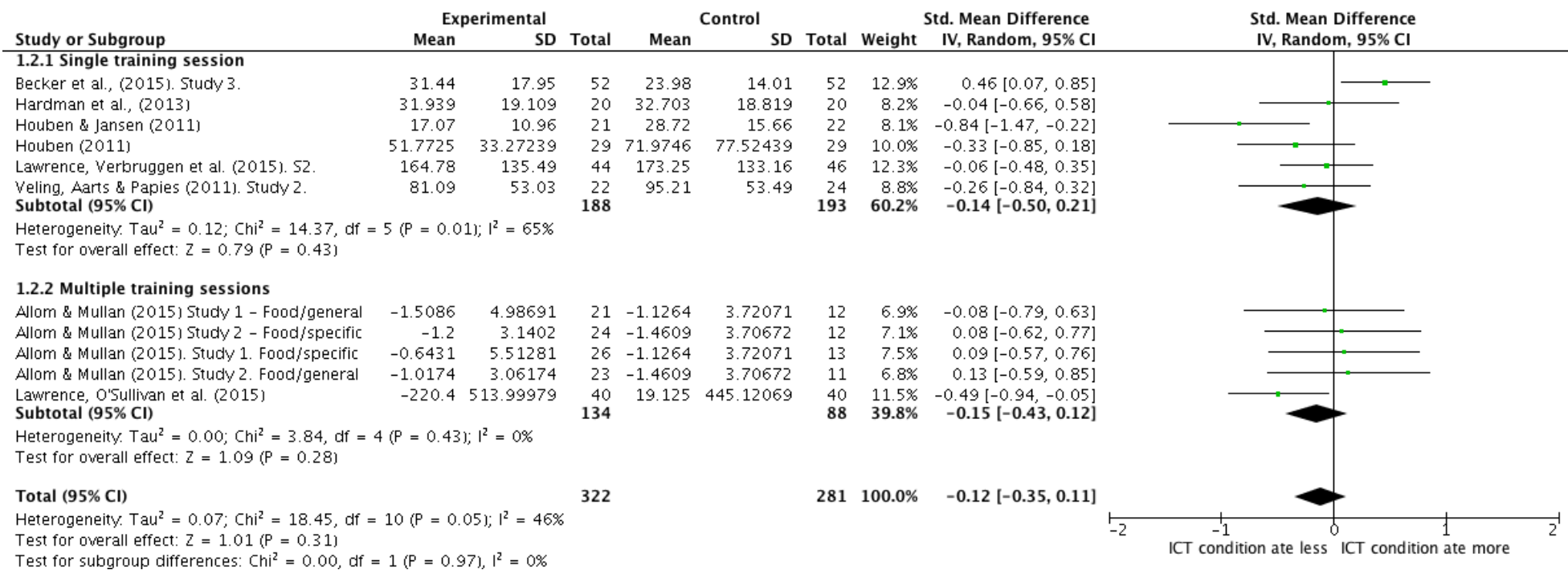


**Figure 6. Forest plot of the effects of ICT compared to attend/approach comparison groups split by type of stimuli used.**

## Number of training sessions

In the control group meta-analysis, 5 studies used multiple training sessions, and 6 used a single training session. Subgroup analyses indicated that neither a single training session (SMD = -0.14, 95% CIs [-0.50, 0.21];  $Z = 0.79$ ,  $p = 0.43$ ,  $I^2 = 65\%$ ) or multiple training sessions (SMD = -0.15, 95% CIs [-0.43, 0.12];  $Z = 1.09$ ,  $p = 0.28$ ;  $I^2 = 0\%$ ) were effective in changing behaviour. The test of subgroup differences was not significant ( $X^2 = 0.00$ ,  $p = 0.97$ ). Leave-one out analysis has already shown that omitting Becker et al. (2015 - S3) affects the overall effect of ICT compared to control groups, and it does so here too. The effect of a single training session becomes significant (SMD = -0.27, 95% CIs [-0.53, -0.01];  $Z = 2.02$ ,  $p = 0.04$ ), and heterogeneity is greatly reduced ( $I^2 = 16\%$ ). See Figure 7 for a forest plot of the effect of ICT compared to control groups on food intake/consumption, separately for number of training sessions used. It is also important to note here that the same studies that used a single training session and multiple training sessions also utilised only a post-training and a pre-post change score outcome measure, respectively. It is therefore not possible to distinguish any effects of the number of training sessions and when behaviour was assessed.

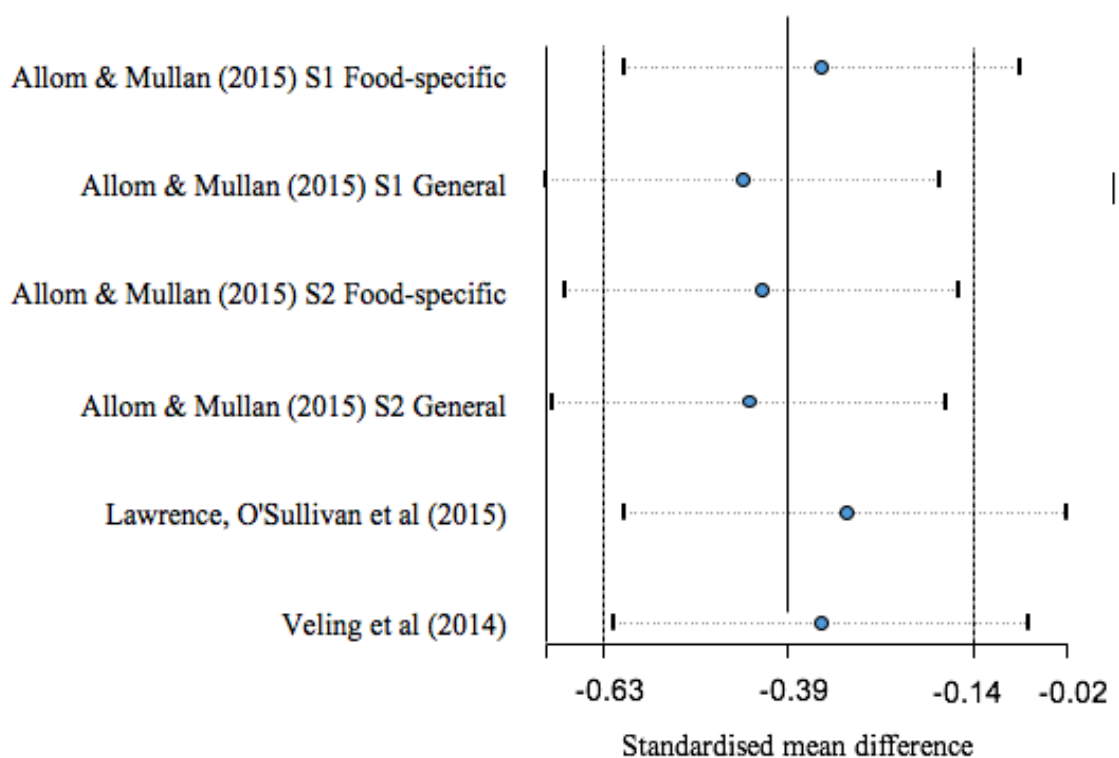




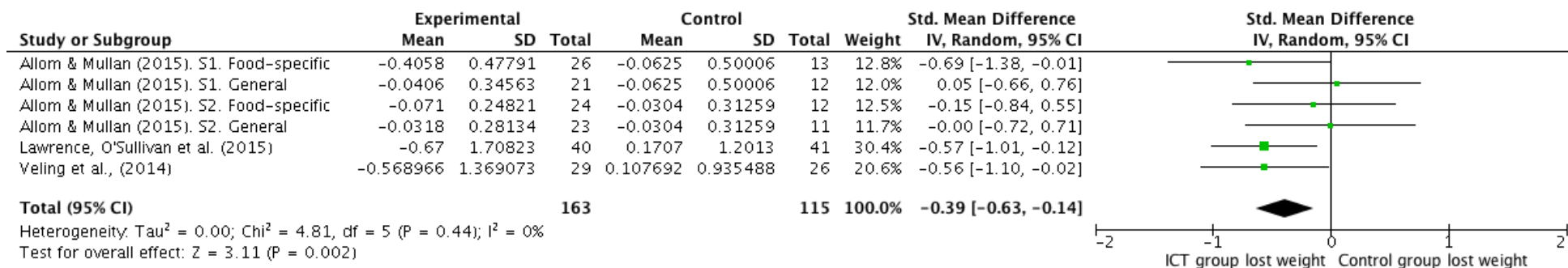
**Figure 7. Forest plot of the effect of ICT compared to control groups on food intake/consumption, separately for number of training sessions used.**

## Weight loss studies

Six comparisons were entered into the weight loss meta-analysis. The overall effect of ICT on weight loss was significant (SMD = -0.39, 95% CIs [-0.63, -0.14];  $Z = 3.11$ ,  $p = 0.002$ ,  $I^2 = 0\%$ ). There appears to be no heterogeneity in these comparisons. Leave-one-out analysis shows that omitting any one study does not affect the pooled estimate, demonstrating the robustness of the effect (Figure 8). While subgroup analyses are not possible here, it is interesting to note that all studies utilised multiple training sessions. Further, two studies used no-go training and four used stop-signals. See Figure 9 for a forest plot of the effects of ICT on weight loss compared to control groups.



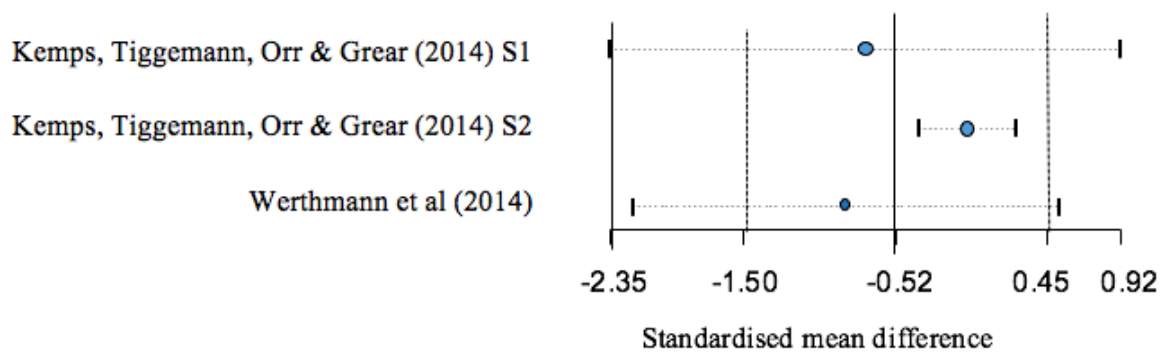
**Figure 8.** Leave-one-out sensitivity analysis for the effects of ICT on weight loss compared to a control group. The vertical axis shows the omitted study, and the horizontal axis depicts the pooled estimate (circle) when each study is removed, with 95% confidence intervals.



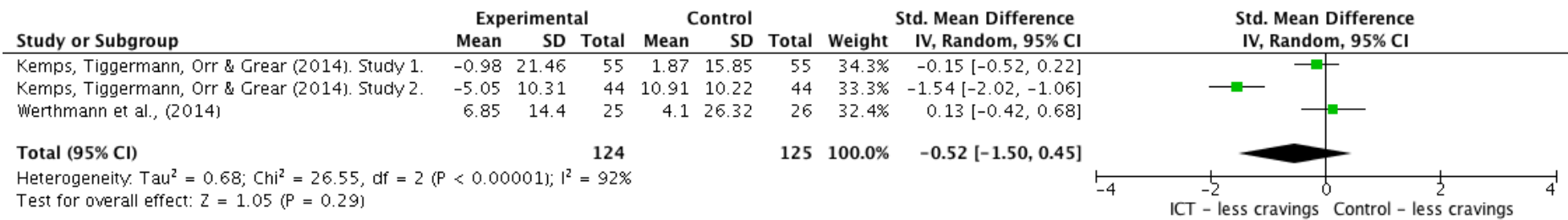
**Figure 9. Forest plot of the effect of ICT compared to control groups on weight loss. Note: Outcome measure for all Allom and Mullan (2015) comparisons are change in BMI (kg/m<sup>2</sup>), and the rest are weight loss (kg).**

## Craving studies

Three comparisons were entered into the food cravings meta-analysis. The overall effect of ICT on cravings was not significant (SMD = -0.52, 95% CIs [-1.50, 0.45];  $Z = 1.05$ ,  $p = 0.92$ ;  $I^2 = 92\%$ ). There was a large amount of heterogeneity in these results. Leave-one-out analysis showed that omitting any one study had no effect on the pooled estimate, however Kemps, Tiggemann, Orr, et al. (2014 - S2) was the most influential study and heterogeneity reduced to 0% when it was omitted (Figure 10). As this study found such a large increase in cravings after attend training ( $M = 10.91$ ), compared to the other comparisons (means = 1.87, 4.1), this could be causing the large amount of heterogeneity found. All studies assessing food cravings utilised one type of ICT, namely attention bias modification training. See Figure 11 for a forest plot of the effects of ICT on cravings compared to attend/approach training.



**Figure 10.** Leave-one-out sensitivity analysis for the effects of ICT on food cravings compared to a control group. The vertical axis shows the omitted study, and the horizontal axis depicts the pooled estimate (circle) when each study is removed, with 95% confidence intervals.



**Figure 11. Forest plot of the effect of ICT compared to attend/approach training on cravings.**

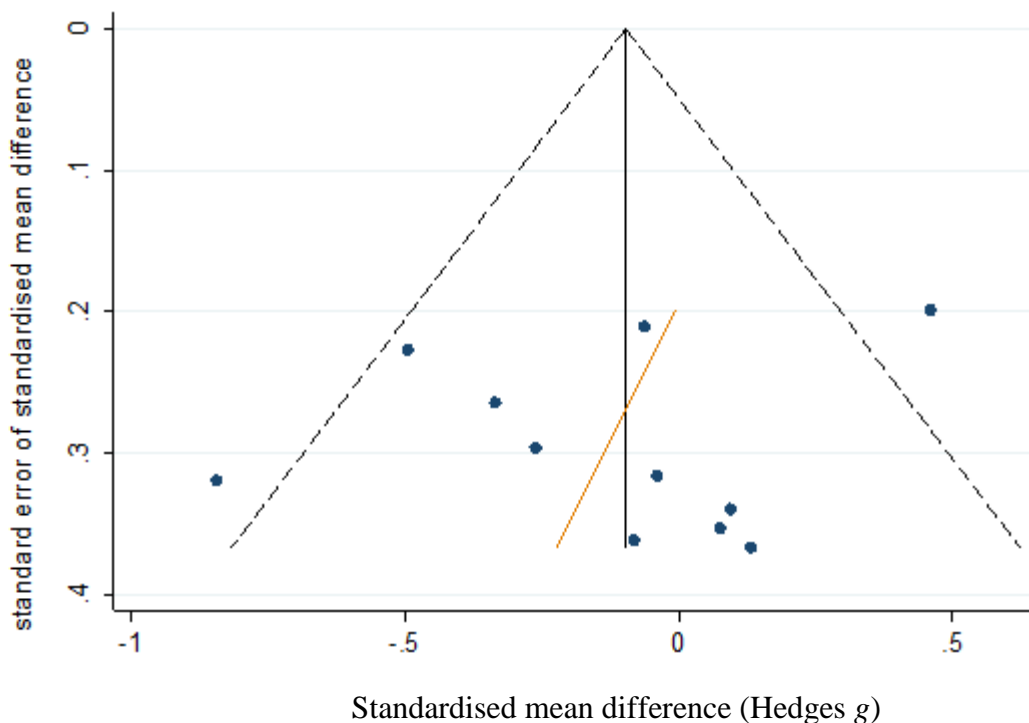
## Food selection/choice studies

Ten studies measured how inhibitory control training affects food choice/selection. Three used no-go training (van Koningsbruggen et al., 2013 - S1 & 2; Veling et al., 2013a), three used stop-signals (Schonberg et al., 2014; Veling et al., 2013b - S1 & 2), three used avoidance training (Becker et al., 2015 - S1 & 2; Fishbach & Shah, 2006 - S5) and one used attention modification training (Kakoschke et al., 2014). For the narrative review, these studies have been split into those looking at whether training increases food choices (typically for low energy dense healthy foods) and whether training reduces food choices (typically high energy dense unhealthy food). The last column in Table 2 summarises the results of each study.

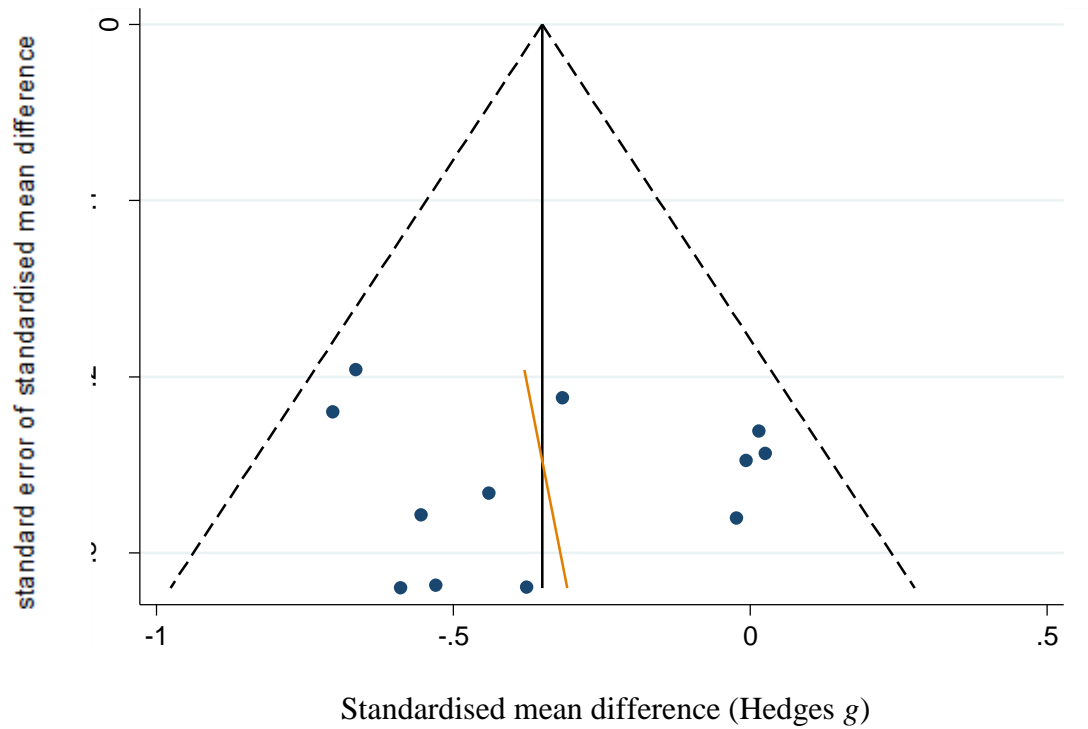
## Quality Analysis

### Publication Bias

Inspection of funnel plots and the Egger's tests showed no significant evidence of publication bias in food intake studies with a control group ( $p = 0.52$ ) and those with an attend/approach group ( $p = 0.80$ ) (Figures 12 & 13).

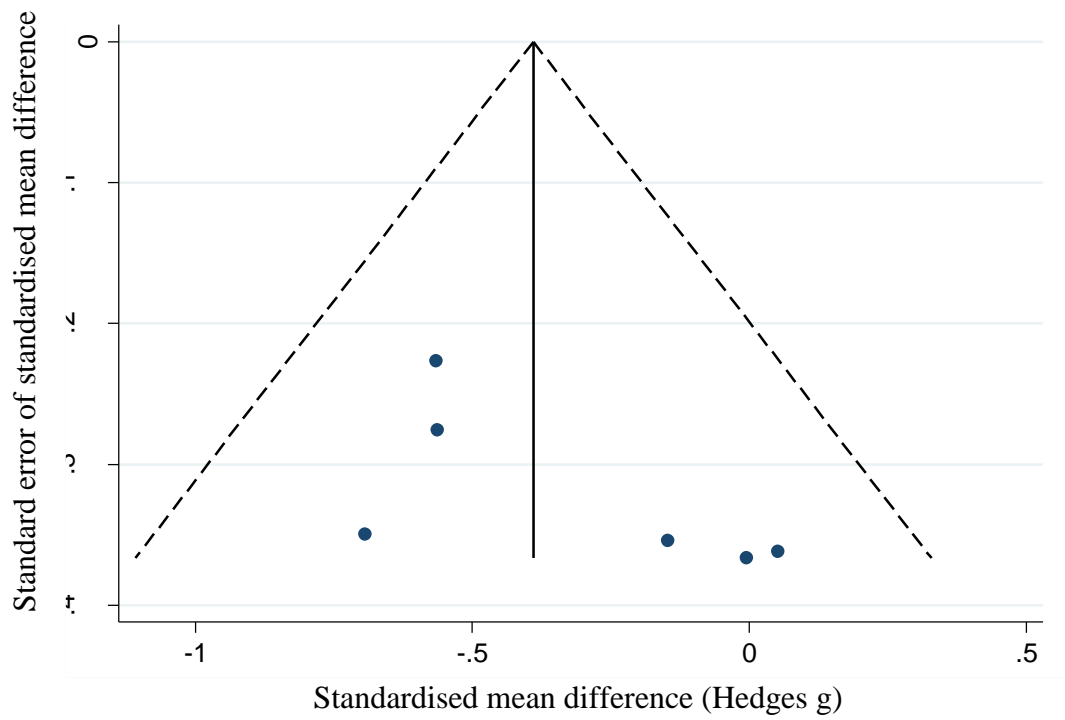


**Figure 12. Funnel plot for ICT effects on food intake compared to a control group, with 95% CI limits and Egger's weighted regression line.**



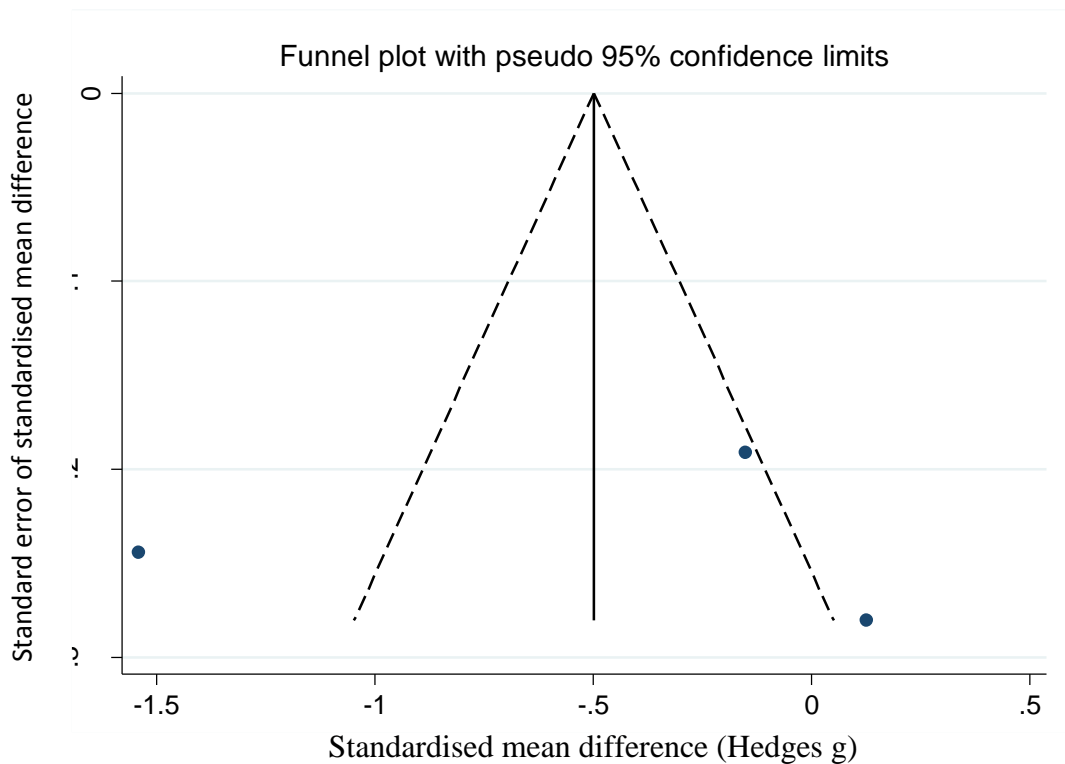
**Figure 13. Funnel plot for ICT effects on food intake compared to an attend/approach group, with 95% CI limits and Egger’s weighted regression line.**

Egger’s test is not recommended where fewer than 10 studies are used in the meta-analysis (section 10.4.3.1, Higgins & Green, 2011), so this was not conducted on the weight loss and food craving studies. Further, very little can be said about publication bias from the funnel plots for these studies (Figures 14 & 15).



**Figure 14. Funnel plot for ICT effects on weight loss compared to control groups, with 95% CI limits.**

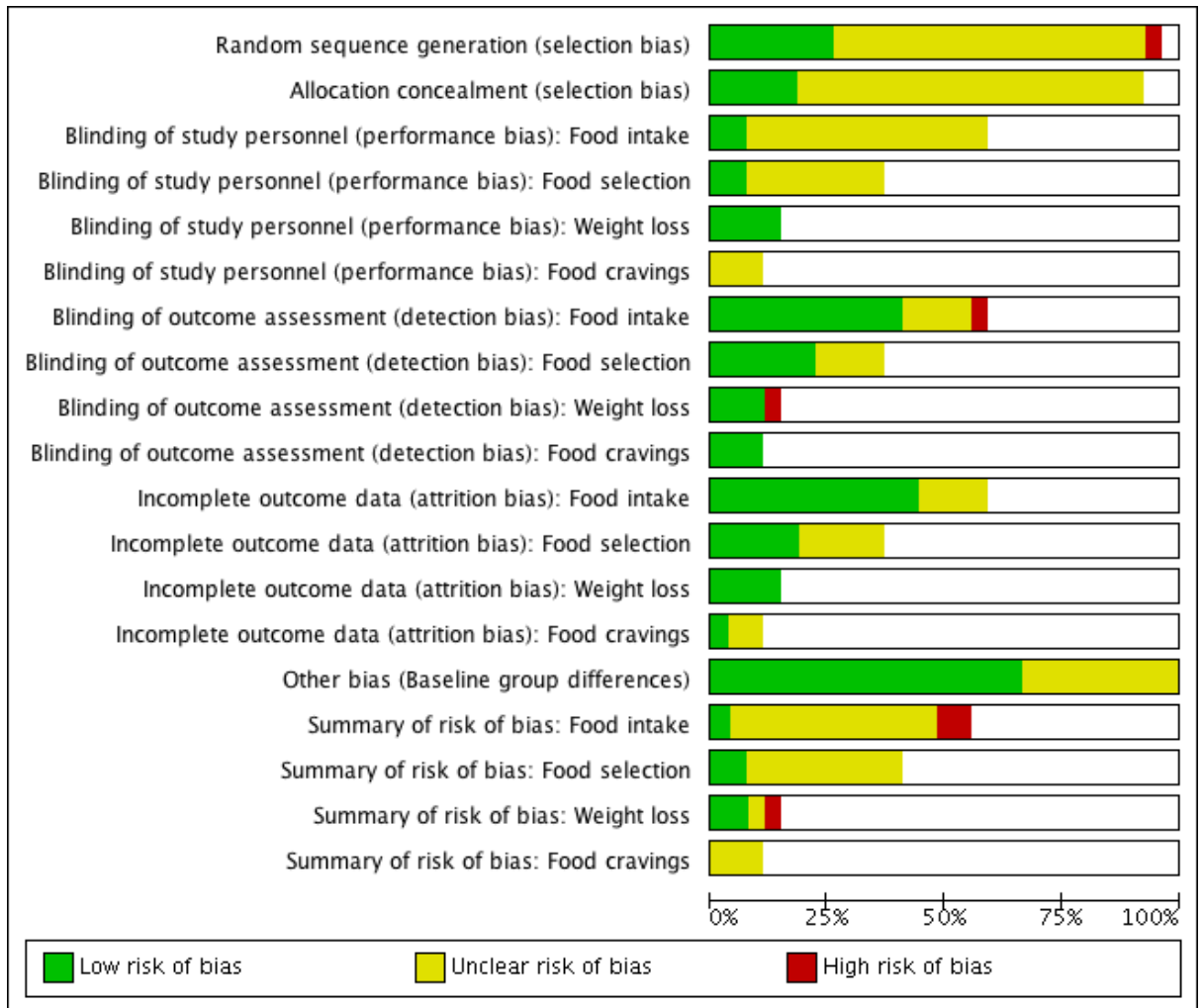




**Figure 15. Funnel plot for ICT effects on food cravings compared to control groups, with 95% CI limits.**

#### Risk of bias

Risk of bias was assessed at the study level for some criteria (random sequence generation, allocation concealment and other bias – baseline group differences), and at the outcome level (food intake, food selection, weight loss, food cravings) for the remaining risk of bias criteria. If studies used both a control and an attend/approach/go comparison group, the quality analysis was applied to the use of the author defined control group. Published protocols were not found for any studies, therefore selective reporting could not be assessed, and is not discussed further. See Figure 16 for a risk of bias graph. Overall, of the 16 studies that measured food intake, 2 were considered to have a high risk of bias, one was low risk, and 13 had unclear risk of bias. Out of the 10 studies with a food selection outcome 2 had a low risk and 8 had unclear risk of bias. One study out of the 4 that measured weight loss had a high risk, 2 had a low risk and 1 had an unclear risk of bias. All 3 studies that measured food cravings had an unclear risk of bias.



**Figure 16. Risk of bias graph for food intake/consumption studies.**

**Note.** White space in the figure indicates that the criteria were not applicable.

#### Random sequence generation and allocation concealment

Only seven studies reported enough information on methods used to randomly allocate participants to conditions in order to allow a low risk of bias judgement. Five also clearly reported that researchers could not foresee which condition participants would be allocated to. In the majority of studies, method of random allocation and allocation concealment were unclear (19 and 22 studies respectively). One study used alternate allocation, and hence was judged as high risk of bias for random sequence generation, and allocation concealment was therefore not applicable. One study had a within-subjects design, and hence neither selection bias judgements were applicable. Overall, the majority of studies described that participants were randomly allocated, but did not report

information on exactly how, and hence received an unclear risk of bias judgement. This suggests that perhaps publication word limits were a factor in this.

#### Blinding of study personnel and outcome assessment

Out of the 16 studies that measured food intake, researchers appeared to be blind to condition after allocation in only 2 studies, whereas insufficient information was provided in 14 studies. In the 10 food selection outcome studies, researchers were blind to condition in 2 studies, and insufficient information was reported in 8 studies. In all 4 weight loss outcome studies, researchers were blind to condition, whereas insufficient information was provided in all 3 food craving outcome studies.

Blinding of outcome assessment typically relates to blinding of participants in self-report outcome measures, whereas the likelihood of lack of blinding affecting researcher measured weight was considered in weight loss studies where this was more appropriate. Blinding of outcome assessment was judged as low risk in 11 food intake studies, 6 food selection studies, 3 weight loss studies and 3 food craving studies. Participants were deemed unlikely to be blind to condition (and hence a high risk of bias judgement was made) in one food intake study (no evidence of cover story or awareness probe) and one weight loss study (self-reported weight). Evidence of participant blinding was unclear in 4 food intake and 4 food selection studies. Overall, efforts were made by researchers to ensure blinding of study participants, however, minimal effort was made to ensure studies were double-blind (except in weight loss studies).

#### Attrition bias

Incomplete outcome data was either minimal and therefore unlikely to be related to the intervention of interest, or reasons for exclusions were adequate in 12 food intake, 5 food selection, all 4 weight loss and 1 food craving studies (low risk of bias judgement given). Insufficient information was provided in the remaining studies for each outcome, and hence no study was judged as at high risk of bias. Bias due to attrition was therefore not a major factor for ICT studies.

#### Other bias

Across the 27 studies included in this review 18 sufficiently identified no baseline group differences, or adequately controlled for these in the analyses. Nine studies reported

insufficient information to allow judgement other than as unclear risk of bias. Baseline group differences were therefore fairly well addressed in ICT studies.

### Control groups

Sixteen studies out of the included 27 used a “control” or “sham” comparison group. In five studies signals to withhold a response were removed, and hence participants consistently responded to all stimuli (Van Koningsbruggen et al., 2013 - S1 & 2; Veling, Aarts, & Papies, 2011 - S2; Veling et al., 2013b - S1 & 2). This was also the case in another study that asked participants to ignore stop-signals entirely (Lawrence, Verbruggen, et al., 2015 - S2). These control conditions could therefore be training behaviour towards food and the conclusions that can be drawn about the effect of ICT on unhealthy food intake/choice may therefore be limited. In two studies, non-food stimuli were paired with stop-signals as the control group (Lawrence, O’Sullivan, et al., 2015; Veling et al., 2014). Since the contingencies in these control groups is similar to ICT, these groups could have trained general inhibition, and underestimated the effects of the food-specific training groups. In other studies, participants had to make an equal number of go and no-go responses to food stimuli (Houben, 2011; Houben & Jansen, 2011); approach and avoid healthy and unhealthy food stimuli equally (Becker et al., 2015 - S1-3); attend to food and non-food pictures equally (Hardman, Rogers, Etchells, Houstoun, & Munafò, 2013) or make all go responses, but there were an equal amount of go responses to both healthy and unhealthy food stimuli (Allom & Mullan, 2015 - S1 & 2). It has not yet been assessed whether making an equal number of go and no-go responses, or an equal number of go responses towards healthy and unhealthy stimuli, are truly neutral control groups that do not train behaviour in either direction. One way to test this would be to compare performance before and after training.

Three of the studies discussed above have so far utilised a pre-post design, and none found significant changes in food intake or weight after training in the control groups (Allom & Mullan, 2015 - S1 & 2; Lawrence, O’Sullivan, et al., 2015). These studies provide some initial evidence to suggest that these types of control groups may not be having an effect on behaviour, but more studies are needed to clarify if this is the case.

## 2.4 Discussion

This systematic review and meta-analysis investigated the effects of inhibitory control training using four types of task (no-go training, stop-signal training, approach-avoidance

training and attentional bias modification) to change responses towards food. Four meta-analyses were conducted to identify the effect of ICT on 1) food intake when compared to a control group; 2) food intake when compared to an attend/approach training group, 3) weight loss and 4) food cravings. Subgroup analyses were used to investigate a number of moderators, including; the type of training task used, type of stimuli, number of training sessions and when behaviour was assessed. A narrative review was conducted on food choice/selection studies due to the large amount of heterogeneity found in the outcome measures used.

### Main effects

The effect of ICT on food intake behaviour was significant when ICT was compared to an attend/approach comparison group but not when compared to a control group. This suggests that the effectiveness of ICT to reduce food intake may be inflated when compared to an attend/approach training condition. There are, however, several caveats to this conclusion. First, leave-one-out analysis indicated that omitting one study (Becker et al., 2015 - S3), made the main effect of ICT compared to control groups significant. Heterogeneity also dropped from 46% to 0% when this study was excluded. This is the only study in this analysis that found ICT to increase food intake, therefore explaining the high heterogeneity when it is included, and the change in effect when it is omitted. This suggests that the results of this meta-analysis may not be robust. However, the effect when Becker et al. is excluded ( $p = 0.02$ ) is still much weaker than the effect of ICT compared to attend/approach training groups ( $p < 0.0001$ ), suggesting there are still inflation effects of comparison to attend/approach training. Second, as discussed in the quality analyses, it is questionable whether the author-defined control groups were in fact neutral groups not training inhibition or behaviour towards stimuli. It is possible that these types of training fall on a continuum from training behaviour away from stimuli at one end (ICT groups), and training behaviour towards stimuli at the other end (attend/go/approach groups). A truly neutral control group that does not train behaviour in either direction would fall in the middle of this continuum. The author-defined control groups may fall somewhere between a truly neutral control group and attend/go/approach training. Hence go/approach/attend training groups and author-defined control groups may be exaggerating the effect of ICT, and only comparison to a truly neutral control group will show their true effects.

There was a main effect of no-go/stop-signal training compared to comparison groups on weight loss, but no effect of attention bias modification training on food cravings. This is the first meta-analysis to consider the effect of ICT on weight loss and food cravings. Only 3 comparisons contributed to the cravings meta-analysis, and hence conclusions from these results should be cautious. Further, four out of the six comparisons entered into the weight loss meta-analysis had a comparison group that may have been training behaviour towards stimuli (Allom & Mullan, 2015). It is therefore possible that the effects of ICT on weight loss found in this review were inflated by the type of comparison group used. The weight loss studies were unlikely to be affected by the use of self-reported weight loss in one of the studies (Allom & Mullan, 2015). The information available for craving studies meant risk of bias could not be ascertained for most of the criteria, and again the type of comparison group (all attend training groups) is a concern. Whether no-go/stop-signals can reduce food cravings and attention bias modification training can induce weight loss remains to be tested.

#### Moderators

Subgroup differences for the type of training used were only found for the control group meta-analysis. Specifically, stop-signals and attention modification training did not result in significant changes in food intake, whereas both no-go and avoidance training did. No-go training reduced food intake, whereas avoidance training increased it. The effect of attention modification training was based on only one comparison, so these effects may not be reliable. These results suggest that training inhibition of initiating a motor response (as in no-go training) is more effective at reducing food intake than training inhibition of an already initiated motor response (stop-signals), oculomotor inhibition (attentional bias modification), and pushing something away from you (approach-avoidance task). These findings are consistent with two previous meta-analyses which also found stop-signals to be much less effective than no-go training in reducing health-damaging behaviours (Allom et al., 2015; Jones et al., 2016). Jones et al. (2016) also found attention modification to not significantly change behaviour. The finding that food-specific training effectively reduced food intake but non-food training did not (attend/approach comparison group meta-analysis) is in line with the Allom et al. (2015) review which also found food-specific training to be more successful than neutral training.

In the control group meta-analyses, there were no subgroup effects of the number of training sessions (single or multiple) and when the outcome measured was assessed (post-

training only or pre and post-training). Omitting the comparison by Becker et al. (2015 - S3) changed these results, suggesting that a single training session was more effective than multiple, and that post-training measurement of behaviour showed greater effects than pre-post training changes in behaviour. However, the exact same studies used a single training session as assessed behaviour post-training only, and the same studies that used multiple training sessions also assessed behaviour both pre and post-training, making it difficult to distinguish any effects here. Other reviews have also shown no effect of the amount of training received on behavioural outcomes. The number of training trials did not significantly affect behaviour (Allom et al., 2015) nor did the number of critical training pairs or the training contingency used (Jones et al., 2016). What does seem to be important is participant's performance on the training. Jones et al. found that the amount of successful inhibition on critical trials predicted training success. That is, ICT was more effective in those who successfully inhibited behaviour during the training. Perhaps future research should therefore change focus from "the more training the better" to improving performance during the training. For example, emphasising accuracy over speed to participants reduced food intake in non-dieters (Guerrieri et al., 2009). Asking participants to focus on correctly inhibiting their responses rather than responding as quickly as possible may have the desired effect of improving task performance. Fewer but more successful training sessions might make the training more acceptable to clinical populations in the future.

#### Food choices/selection narrative review

The narrative review of food choice outcome studies suggests that ICT to reduce choices for palatable foods may be effective under limited conditions, such as when participants are hungry, or when the trained foods are frequently consumed by participants (Veling et al., 2013b). However, many of these studies compared ICT to a control group that may have been more akin to an attend/approach/go training group than a neutral control group, limiting the conclusions that can be made. Further, the findings of one study may be limited, as the same stimuli were used to assess food choices as were used to train behaviour (Veling et al., 2013a). It is therefore not clear how well these findings generalise to food not used in the training. Evidence for the effect of ICT to increase choices for healthy foods is limited, and again the types of comparison groups used is a concern.

## Underlying mechanisms

The underlying mechanisms of the four types of training included in this review are by no means simple. It is clear to see that on a surface level these tasks appear to train inhibitory control, in the sense that participants are practising inhibiting their behaviour (particularly in the no-go, stop-signal and attention bias modification tasks). Behavioural evidence also supports this as a mechanism of action in these tasks, such as improvements in Stroop task performance, a measure of inhibitory control, after stop-signal training (Allom & Mullan, 2015). Neuroimaging evidence of the mediating role of the lateral prefrontal cortex in attention bias modification training is also strong support for this (Browning et al., 2010), as is recruitment of event-related potentials indicative of improved top-down attentional control in participants immediately after attention bias modification training (Eldar & Bar-Haim, 2010).

Evidence is, however, accumulating to suggest that these tasks aid the development of automatic stopping associations with trained stimuli and that inhibition can become a prepared or learned reflex (Verbruggen, Best, et al., 2014). Studies have supported this underlying mechanism primarily for the no-go and stop-signal tasks. For example, devaluation of stimuli occurred after stop-signal training (Wessel et al., 2015) and others found increased implicit associations between stopping and chocolate after no-go training (Houben & Jansen, 2015). However, there is also evidence of changes in automatic behaviours underlying attention bias modification and avoidance training too. For example, reduced automatic action tendencies towards alcohol have been found to mediate avoidance training effects on alcohol consumption (Sharbanee et al., 2014), and reduced attentional bias for chocolate was found following attention bias modification training (Kemps et al., 2015).

Dual-process theories are frequently used to describe these tasks as training top-down inhibition (by engaging the reflective process; Strack & Deutsch, 2004). However, a key element of dual-process theories often omitted is that reflective and impulsive processes are not entirely independent and can in fact interact and influence each other (Strack & Deutsch, 2004). It therefore makes theoretical sense that training inhibitory control via engaging reflective processes interacts with impulsive processes to develop automatic inhibition. This also makes behavioural sense, as behavioural inhibition requires effort, and self-control is typically considered a limited resource (Baumeister & Vohs, 2004; Muraven & Baumeister, 2000). Successful behaviour change is therefore likely to occur



only when the required behaviour becomes automatic and no longer requires effortful inhibition. The evidence that supports changes in top-down mechanisms of action may therefore reflect temporary early changes that occur during and immediately after training. It may be changes in automatic behaviours, such as automatic inhibition that facilitate longer lasting behaviour change. Further research is needed to clarify the time-frame of changes in both top-down and bottom-up processes as the mechanisms underlying these tasks.

#### Future research

There are a number of limitations to the current research that when addressed will provide a better understanding of whether inhibitory control training is effective in changing eating behaviour and other related outcomes. First, the majority of studies in this review sampled university students that were predominantly female, limiting the generalisability of this work to other populations, such as men, non-students and overweight/obese participants. Some work has shown greater effectiveness in those with a higher BMI (Veling et al., 2014), but this sample was still composed of mostly students with an average BMI in the lean range. Only one study in this review had an average BMI in the overweight range (Lawrence, O'Sullivan, et al., 2015). During the literature searches for this meta-analysis a handful of studies using ICT in overweight/obese children were identified, a meta-analysis of these studies that use a more clinically relevant sample may aid understanding of ICT effects (e.g. Boutelle et al., 2014; Verbeken et al., 2013). The durability of inhibitory control training effects are also relatively unknown as so few studies have utilised follow-up assessment sessions. For an intervention to be clinically useful, it must have lasting effects on behaviour. Three meta-analyses have now found that the number of training sessions/trials/critical pairs does not predict training effectiveness (Allom et al., 2015; Jones et al., 2016). Future research should therefore consider identifying ways to improve training performance, considering the finding that successful inhibition predicts training outcomes (Jones et al., 2016).

Two key suggestions can be made based on the quality analyses conducted in this review. Firstly, researchers should ensure that studies are double-blind, as this is a gold standard method for randomised controlled trials. The use of appropriate control groups should also be addressed. It is not entirely clear what type of control group would provide the perfect combination of controlling for demand characteristics while not training inhibitory control or behaviour towards stimuli, but an appropriate control group may be general inhibition

training that uses the same contingencies as typical ICT, but uses non-food stimuli throughout (Jones et al., 2016). However, a better solution to this problem may be increased use of a pre-post design in future research. This would, 1) allow researchers to identify whether ICT results in changes in behaviour from before training to after training, and 2) demonstrate whether control groups result in changes in behaviour from before training to after training, allowing identification of control groups that do not affect behaviour.

## **Conclusions**

This meta-analysis found ICT to significantly reduce food intake/consumption behaviour only when compared to attend/approach comparison groups, but not when compared to control groups. No-go training was most effective in reducing food intake, as was food-specific training. There was also a significant effect of ICT on weight loss but not food cravings. Future research should carefully consider the type of control groups used, and should use pre-post designs to ensure control groups are not training behaviour either away from or towards food. Future work should also consider techniques to improve participants' performance on training tasks, identify the longevity of training effects, and test the effectiveness of ICT in clinical populations.

## **Chapter 3. The role of working memory sub-components in food intake and dieting behaviours.**

### **3.1 Introduction**

Factors affecting food intake decisions are far-reaching and include both internal and external influences (Herman & Polivy, 2008). Important internal influences include cognitive functions, such as memory, learning and executive functions (Higgs, Robinson, et al., 2012). Executive functions are a set of higher order cognitive abilities that are recruited when behaviour is effortful and deliberate, and not automatic (Diamond, 2013). Executive functions may be a key determinant of the strength of reflective processes in the dual-process theories of behaviour control (Hofmann et al., 2012; Strack & Deutsch, 2004). The current consensus is that there are three core executive functions: inhibition, working memory and cognitive flexibility/set-shifting (Diamond, 2013; Miyake et al., 2000). The importance of executive functions in controlling eating behaviour has been shown repeatedly, with findings suggesting that better executive functions are associated with more healthful eating habits (Allom & Mullan, 2014; Hall, Fong, Epp, & Elias, 2008; Hall, 2012). Evidence for the importance of (behavioural) inhibition is particularly strong, with studies showing that training inhibitory control can improve eating behaviour and aid weight loss (Lawrence, O'Sullivan, et al., 2015; Veling et al., 2014).

The second of these core executive functions, working memory (WM), and its role in eating behaviour has been relatively less well studied. Nonetheless, WM is now considered an important executive function, alongside inhibitory control ability, that may play a role in the reflective processes that influence eating behaviour (Hofmann, Friese, et al., 2008). Important components of WM relevant to self-regulation of behaviour include not only the amount of information that can be held active at any given time, but also the ability to hold in mind information stored in long-term memory and to maintain focused attention on currently active information while preventing the interference of other potentially distracting information (Hofmann, Gschwendner, et al., 2008). Applied to eating behaviour, WM capacity may be important in retrieving long-term memories and holding these active in WM (e.g. dieting goals); resisting attending to eye-catching stimuli in the environment (e.g. tempting foods); protecting active goals from distracting stimuli by maintaining focused attention on the active goals; and down-regulating emotions (e.g. cravings) (Hofmann et al., 2012).

Working memory capacity has been reported to moderate the role of impulsive processes in predicting health behaviours. For example, in people with low WM capacity, impulsive processes were better predictors of high energy dense (HED) food consumption than in people with higher WM capacity (Hofmann, Friese, & Roefs, 2009; Hofmann, Gschwendner, et al., 2008). Few studies have examined the direct relationship between WM and food intake, and the findings are contradictory. Two studies found that WM negatively correlated with snack food intake (Riggs, Chou, et al., 2010; Riggs, Spruijt-Metz, et al., 2010), and two studies did not (Allom & Mullan, 2014; Limbers & Young, 2015). The former two studies assessed self-reported executive functioning using the Behavioural Rating Inventory of Executive Functioning (using the subscales “emotional control”, “inhibitory control”, “working memory” - e.g. “I forget what I’m doing in the middle of things” and “organisation of materials”) (Guy et al., 2004). The final analysis in both studies combined scores on all subscales to form a composite executive function score (Riggs, Chou, et al., 2010; Riggs, Spruijt-Metz, et al., 2010). Therefore, little can be said about the role of WM in food intake, because an overall composite score leaves the contribution of the WM subscale unclear. Limbers and Young (2015) found that the relationship between WM and snack food intake disappeared when controlling for demographic factors, BMI and eating styles. While this study also used the BRIEF measure of executive functioning, the relationship between food intake and performance on the individual subscales was assessed, increasing confidence that these findings relate to WM specifically. Allom and Mullan (2014) used the N-back and operation span tasks to assess WM (updating ability specifically), which are validated measures of WM that do not rely on self-reports of behaviour (Diamond, 2013; Miyake et al., 2000). Overall, the strength of evidence suggests that perhaps WM is not important for intake of high energy dense foods.

Research on the relationship between WM and fruit and vegetable intake also appears to be contradictory but may be explained by the differing methods used to assess WM across studies. Allom and Mullan (2014) and Sabia et al. (2009) used computerised assessment of WM and found a positive correlation between WM and fruit/vegetable intake. Limbers and Young (2015) did not find a relationship between WM and fruit/vegetable intake, but these authors assessed WM via self-report. On the other hand Riggs, Chou, et al., (2010) who also used a self-report measure of WM ability did report a positive relationship between WM ability and fruit/vegetable intake. Theoretically, WM may play a more important role in intake of low energy dense foods than high energy dense foods. Allom and Mullan (2014) argued that inhibitory control is not important for health improving

behaviours, but rather updating, or working memory is important as it directly supports activation and maintenance of long-term goals (such as weight loss) that encourages LED food consumption.

Several factors limit the research conducted to date on the relationship between WM and food intake. While the self-report measures of WM may provide greater ecological validity due to assessment of WM performance in everyday situations, these measures are subject to self-report bias. A further limiting factor is the lack of consideration of the role of WM sub-components. There are three core components of WM: the central executive is an attentional control system that allocates, divides and switches attention across two slave sub-systems. The two slave sub-systems (the phonological loop and the visuo-spatial sketchpad) deal with different information, namely verbal and acoustic information and visual and spatial information, respectively (Baddeley, 2007). The three core components of WM have very different functions that could differentially relate to food intake. For example, the slave sub-systems could be important in the processing of visual aspects of food (e.g. what looks appetizing and food cravings) and the auditory aspects (e.g. the sound of food cooking or unwrapping food), whereas the central executive could be important for the allocation of attention to these sub-components and retrieving long-term memories about health goals. A final limitation of previous studies is that food frequency questionnaires have been used to measure food intake, which is subject to self-report biases and error. More reliable measures of food intake are needed, such as a laboratory-based taste-test that measures actual food consumption.

It is also important to consider potential moderators of the relationship between WM and food intake, such as psychological eating styles that are associated with differences in WM. Dieting in individuals high in cognitive restraint is related to WM deficits such as deficits in sustained attention (Rogers & Green, 1993), poorer immediate recall and slower reaction times compared with non-dieters (Green & Rogers, 1995; Green, Rogers, Elliman, & Gatenby, 1994). Specific deficits have also been shown in sub-components of WM (Green & Rogers, 1998; Green, Elliman, & Rogers, 1997), including the central executive (Green et al., 2003; Kemps & Tiggemann, 2005; Kemps, Tiggemann, & Marshall, 2005) and phonological loop (Green & Elliman, 2013; Shaw & Tiggemann, 2004; Vreugdenburg, Bryan, & Kemps, 2003), but not the visuospatial sketchpad (Green & Rogers, 1998; Kemps, Tiggemann, & Marshall, 2005; Kemps & Tiggemann, 2005; Shaw & Tiggemann, 2004; Vreugdenburg et al., 2003). However, evidence for deficits in phonological loop functions is somewhat contradictory (see Green et al., 2003; Kemps &

Tiggemann, 2005; Shaw & Tiggemann, 2004; Vreugdenburg et al., 2003). Overall, these data suggest a negative impact of dieting behaviour on some aspects of WM, which could moderate the relationship between WM and food intake.

A further consideration is that studies investigating the effects of dieting on WM have compared current dieters with non-dieters and have not usually distinguished between successful and unsuccessful dieters (Kemps & Tiggemann, 2005; Kemps, Tiggemann, & Marshall, 2005). Individuals who score high on cognitive restraint but low on the tendency towards disinhibition (successful dieters) respond differently to individuals scoring high in restraint and high in the tendency towards disinhibition (unsuccessful dieters) in a task assessing WM guidance of attention to food cues (Higgs, Dolmans, Humphreys, & Rutters, 2015). Successful and unsuccessful dieters have also been shown to differ in their experiences of food cravings: unsuccessful dieters reported more food cravings relating to difficulties in self-control over food intake and intentions to consume food than did successful dieters (Meule, Lutz, et al., 2012). Cravings are believed to be visual in nature (May et al., 2008, 2004; Tiggemann & Kemps, 2005) and to consume visuo-spatial WM resources, impairing performance on other visuo-spatial WM tasks (Green et al., 2000; Kemps, Tiggemann, & Grigg, 2008; Meule, Skirde, et al., 2012; Tiggemann et al., 2010). It is therefore possible that successful dieters have greater visuo-spatial WM capacity, allowing them to deal with demands on visuospatial WM more appropriately, such as food cravings.

In summary, there has been little investigation of the role of specific WM processes in eating behaviour to date. The aim of the present study was to investigate the role of WM sub-components in food intake using computerised measures of WM and a measure of actual food intake (food taste-test paradigm). In addition, the moderating effect of dietary restraint and the tendency towards disinhibition on the relationship between WM and food intake and the role of WM more generally in dieting success were assessed. The first hypothesis was that low energy dense food intake would be associated with better WM performance and that this relationship may be moderated by restraint and disinhibition. There is currently little evidence to suggest that any one sub-component of WM may play a more important role in food intake over other WM sub-components, and therefore predictions regarding specific WM sub-components were not made. Considering the effects of dieting on WM sub-components, there may be an interaction effect between restraint and disinhibition and central executive and/or phonological loop functioning on food intake. That is, poorer central executive and/or phonological loop (but not

visuospatial) functioning in highly restrained individuals may be associated with lower intake of low energy dense food. The second hypothesis was that restraint would be associated with impairments in central executive and phonological loop WM functioning irrespective of tendency towards disinhibition, but that there would also be an interaction between restraint and disinhibition on WM, such that successful dieters (high restraint, low disinhibition) would show better visuo-spatial WM than unsuccessful dieters (higher restraint, high disinhibition).

### **3.2 Methods**

#### **Participants**

Female undergraduate students at the University of Birmingham received course credit for taking part in this study (N=117). Only females were included because eating habits are known to differ between men and women, and dieting to control weight is more common in women (Kiefer, Rathmanner, & Kunze, 2005; Wardle et al., 2004). Participants were required to have normal or corrected-to-normal vision, but there were no restrictions based on age or BMI. To disguise the aims, the study was advertised as investigating the relationship between cognitive functioning and food taste perceptions. The sample size was decided a priori via a power calculation using G Power (Faul, Erdfelder, Lang, & Buchner, 2007). With power set at 0.8 and alpha 0.05, to identify a medium effect size (0.15) a sample size of 92 participants would be needed. As it would not be possible to predict which group participants would fall into prior to testing them (allocation to groups was based on levels of restraint and disinhibition using questionnaire responses), more than 92 participants were recruited to ensure there were sufficient numbers in each group. However, further targeted recruitment was required towards the end of the study to obtain more balanced groups. This study was approved by the Middlesex University Psychology Ethics Sub-committee and the University of Birmingham Research Ethics Committee.

#### **Measures**

##### Demographic information

Participants were asked to report their age, ethnicity, when they last ate, whether and how often they drink alcohol and smoke, whether they have any food allergies, or have past or current psychological issues. These were used to characterise the sample, and anyone with food allergies were excluded (none were excluded on this basis).

## Working memory assessments

### *Central executive*

The central executive component of WM was assessed using the validated Spatial Working Memory test of the Cambridge Cognition Neuropsychological Test Automated Battery (CANTAB, Cambridge Cognition, Cambridge, UK). This task required use of visuo-spatial WM as well as the central executive because manipulation of remembered items in WM was required. Participants had to search for blue tokens hidden inside coloured boxes. Once a token was found inside a box, a token would not be hidden inside that box again. Therefore, participants had to remember where they had already found tokens and update the information held in WM so as not to return to the same box twice. Updating ability is considered an important component of WM for self-regulation of behaviour (Hofmann et al., 2012). The task started with 4 boxes and 4 tokens to find, and increased to 6, 8 and finally 10 boxes and 10 tokens. Outcome measures were total number of extra inspections made that were unnecessary (i.e. errors) and the degree to which participants used a strategy to perform the task. The best strategy for this task was to search the boxes in the same order every time a new search commenced. The number of times a participant started the search from a different box was counted, and a higher score therefore indicated poorer use of this strategy. Strategy use was the key outcome measure for central executive ability, whereas errors were a measure of short-term visuo-spatial memory (Goghari et al., 2014; Owen, Downes, Sahakian, Polkey, & Robbins, 1990).

### *Phonological loop*

The phonological loop component of WM was assessed using the backwards digit span task. Participants were shown a sequence of numbers on screen and had to recall the sequence in reverse order, using the on-screen number pad. The first sequence contained 3 items and increased by one after two consecutive correct answers. The task finished when two consecutive incorrect answers were given. The longest sequence of numbers remembered correctly was taken as a measure of the participant's phonological loop capacity. The digit span task is a validated measure of short-term memory, specifically phonological loop capacity (Baddeley, Gathercole, & Papagno, 1998) and has previously been used to identify poorer phonological loop capacity in unsuccessful dieters compared to non-dieters (Kemps, Tiggemann, & Marshall, 2005).



### *Visuospatial sketchpad*

The visuospatial sketchpad component of WM was assessed using the Spatial Span Task from the Cambridge Cognition Neuropsychological Test Automated Battery (CANTAB, Cambridge Cognition, Cambridge, UK), which is a computerised version of the Corsi blocks task (a validated measure of visuospatial sketchpad capacity; Hanley, Young & Pearson, 1991). White squares were shown on screen, and several of these briefly changed colour. Participants had to touch the squares in the correct order in which they changed colour (on a touch screen monitor). The first sequence contained 2 square colour changes, and increased by one after every correctly recalled sequence. The task finished when three consecutive sequences were recalled incorrectly. Visuospatial WM capacity was taken as the highest level of this task successfully completed.

### Taste test

Eating behaviour was assessed in the laboratory using a bogus taste-test paradigm (Houben, 2011). Participants were presented with a snack buffet box containing 4 high energy dense (HED) foods (chocolate chip cookies ~65g, ~323 kcal; cheese and onion rolls ~65g, ~201 kcal; M&M's, ~165g, 799 kcal; and ready salted crisps, ~25g, ~133 kcal) and 4 low energy dense (LED) foods (carrot sticks ~110g, ~44 kcal; plum tomatoes ~139g, ~28 kcal; grapes, ~153g, ~101 kcal; and salt and vinegar rice cakes, ~10.5g, ~40 kcal). All food was manufactured by Sainsbury's UK, except for the M&Ms (Mars, France) and rice cakes (Snack a Jacks, UK). These foods were chosen to provide a range of high and low energy dense foods from both sweet and savoury categories to account for different preferences. To bolster the cover story, participants were given 10 minutes to taste each of the foods and rate them on three 100mm visual analogue scales, with the questions above "How pleasant was the taste of the...?"; "how bitter was the taste of the...?" and "how sweet was the taste of the...?", with anchors "not at all" and "extremely". Participants were told they could eat as much or as little of the foods as they wished, as any remaining food would be thrown away afterwards. The amount consumed by each participant was calculated by subtracting the post taste-test weight from the pre taste-test weight for each of the food items. This was totalled separately for the HED and LED foods. Total LED intake (grams) was divided by the total amount eaten (HED grams + LED grams), and multiplied by 100 to give the proportion of intake that was LED food. Previous research has found cognitive function to relate differentially to high and low

energy dense foods, so it is important to look at both food types (Riggs, Chou, et al., 2010; Riggs, Spruijt-Metz, et al., 2010).

### Dieting behaviour

The cognitive restraint and disinhibition sub-scales of the Three Factor Eating Questionnaire (TFEQ) were used to identify successful and unsuccessful dieters (Stunkard & Messick, 1985). The restraint sub-scale consisted of 21 questions, with the possible range of scores being 0 – 21. The disinhibitions sub-scale consisted of 16 questions, with the possible range of scores being 0 – 16. Those who scored  $\geq 9$  on the restraint sub-scale and  $\geq 7$  on the disinhibition sub-scale were classified as unsuccessful dieters (Higgs et al., 2015). Those scoring  $\geq 9$  and  $< 7$  on these subscales (respectively) were classified as successful dieters. Classification of dieting status took place after participants had taken part in the study, therefore reducing any experimenter-induced expectancy effects as the researcher was blind to dieting status during the testing sessions. Appended to the end of the TFEQ was the question “are you currently dieting to lose weight?” to characterize the sample.

### Procedure

Testing sessions took place between 9:30am-12pm and 1:30pm-5pm, and participants were tested individually in a cubicle. Upon arrival participants provided informed consent, completed the medical history and food allergies screening questionnaire, and rated their baseline hunger on a 100mm VAS scale asking “how hungry do you feel right now?” with the anchors “not at all hungry” and “extremely hungry”. As a further distraction to the aims of the study, participants completed a number of 100mm VAS scales asking about their mood. These consisted of the question “How .... do you feel right now?”, with various emotions inserted, for example, happy, sad, nervous and irritable. Anchors were “not at all” and “extremely”. The participant then completed the WM tests and repeated the hunger and mood questions. Then the participant completed the snack food taste-test and another set of hunger and mood questions. The questionnaire pack that contained questions on demographics and the TFEQ was then completed. To probe awareness of the study aims, participants were asked the following open ended question: 1) “what do you think was the purpose of the study?” and 2) “in the snack buffet, what do you think the researchers were interested in?” Height and weight were measured using a stadiometer and body weight scales (heavy clothing and shoes removed) in order to calculate BMI ( $\text{kg}/\text{m}^2$ ).

Participants were then debriefed. The first participant did not eat until 10am, and the last participant ate at 4:30pm, as these are considered normal snacking times.

### **Data analysis**

Group differences on baseline characteristics were checked with a multivariate ANOVA with restraint (high, low) and disinhibition (high, low) as factors and BMI, age and baseline hunger as outcomes. Correlations were also conducted to identify if food intake correlated with baseline characteristics (e.g. age, BMI, hunger, when last ate, and liking of each food).

To test the relationship between food intake and WM, and the moderating role of restraint and disinhibition (hypothesis 1) model 2 of the PROCESS macro in SPSS was used (Hayes, 2013), entering WM performance measures as the independent variable, disinhibition and restraint as moderators, and food intake as the dependent variable. To investigate the relationship between dieting status and WM performance, regressions with restraint and disinhibition as independent variables and WM performance as the dependent variables were conducted. Regressions were computed to confirm that successful dieters ate a higher proportion of LED foods than unsuccessful dieters. Bias-corrected and accelerated bootstrapping (based on 1000 bootstrap samples) was applied to overcome any issues with bias. In all cases, results are generally not reported where not significant. Because two outcome measures were used for central executive functioning, a Bonferroni correction was applied to the interpretation of results relating to the central executive tasks ( $\alpha$  level  $0.05/2 = \text{new } \alpha$  level 0.025).

One participant was excluded from the analyses as she was an outlier on a number of measures, and reported that she was sad during the experiment (final  $N = 116$ ). There were no outliers on any of the WM outcome measures. However, one participant failed twice on the lowest level of the backwards digit task, which was most likely because they did not understand the instruction to reverse the sequence, and therefore this participant was excluded on this task.

## **3.3 Results**

### **Participant characteristics**

Mean age of the sample was 18.9 years ( $SD = 1.0$ , range = 18-24 years) with a mean BMI of  $21.6 \text{ kg/m}^2$  ( $SD = 2.6$ , range = 16.9-30.6). Seventy-nine participants self-reported as

being white, 21 Asian/Asian British, 8 Black/African/Caribbean/Black British; 7 mixed/multiple ethnic group, and 1 as “other”. Twenty-three participants reported that they were currently dieting to lose weight. A small number of participants (5.2%) were self-reported light smokers or had past or current psychological health problems (11.2%), and 92.2% said that they drink the government guideline of 14 units of alcohol per week or less (Department of Health UK, 2016). Participants last ate on average 364 minutes prior to participating in the study (range = 80-1440 minutes), indicating that in general they had complied with the instruction to not eat for at least 2 hours before taking part. However, one person ate 80 minutes and two ate 90 minutes prior to the study. Excluding these from the analyses did not alter the results, and therefore their data were included in the analyses. Mean hunger and fullness ratings at the beginning of the study were 48.4 ( $SD = 20.2$ ) and 29.9 ( $SD = 20.3$ ), respectively. Mean restraint, disinhibition and hunger on the TFEQ were 8.7 ( $SD = 6.0$ ), 7.0 ( $SD = 3.4$ ) and 6.8 ( $SD = 3.3$ ), respectively. Participant’s characteristics grouped by restraint and disinhibition scores are in Table 1.

### **Baseline group differences**

BMI differed according to restraint scores, and there was a marginally significant effect on age, but no effect of group on baseline hunger (see Table 1). High restraint participants tended to be older and have a higher BMI. There were significant correlations between baseline hunger and food intake and between rated liking and intake of the foods, therefore baseline hunger and average liking of LED and HED food were included as covariates in the analyses.

**Table 1. Participant characteristics grouped by restraint and disinhibition scores.**

	LRLD	LRHD	HRLD	HRHD	Restraint <i>p</i> value	Disinhibition <i>p</i> value	Restraint x disinhibition interaction <i>p</i> value
N	30	26	24	36			
Age (years)	18.73	18.77	19.33	18.89	0.05	0.27	0.19
BMI (kg/m <sup>2</sup> )	20.71	21.34	22.14	22.32	0.02*	0.40	0.64
Hunger VAS (mm)	44.80	52.73	48.58	48.22	0.92	0.32	0.28

**Note.** LRLD = low restraint, low disinhibition; LRHD = low restraint high disinhibition; HRLD = high restraint low disinhibition; HRHD = high restraint high disinhibition; \* *p* < 0.05.

### Awareness of study aims

None of the participants guessed the exact purpose of the study, although 18% guessed the broad purpose (e.g. “the relationship between cognitive functioning and food intake”).

### Food intake and working memory

Moderation analyses showed a significant positive relationship between visuospatial WM span and the proportion of food intake that was LED food (see Table 2). There was no significant relationship between any other WM measure (central executive strategy use, total extra inspections and phonological loop span) and LED proportion. Dietary restraint and disinhibition did not moderate the relationship between any measures of food intake and WM.

**Table 2. Linear model of predictors of LED proportion, with 95% bias corrected and accelerated confidence intervals reported in parentheses. Confidence intervals and errors based on 1000 bootstrap samples.**

	<i>B</i>	<i>SE B</i>	<i>t</i>	<i>p</i>
Constant	43.49 (27.07, 59.92)	8.28	5.25	< 0.001
Restraint	-0.08 (-0.61, 0.45)	0.27	-0.29	= 0.77
SSP span	3.76 (0.36, 7.16)	1.72	2.19	= 0.03
SSP span x restraint	-0.16 (-0.71, 0.39)	0.28	-0.58	= 0.56
Disinhibition	-0.50 (-1.46, 0.42)	0.47	-1.07	= 0.29
SSP span x disinhibition	-0.10 (-1.12, 0.91)	0.51	-0.20	= 0.84
Baseline hunger	-0.06 (-0.19, 0.07)	0.07	-0.94	= 0.35
Average LED food liking	.29 (0.05, 0.54)	0.12	2.35	= 0.02

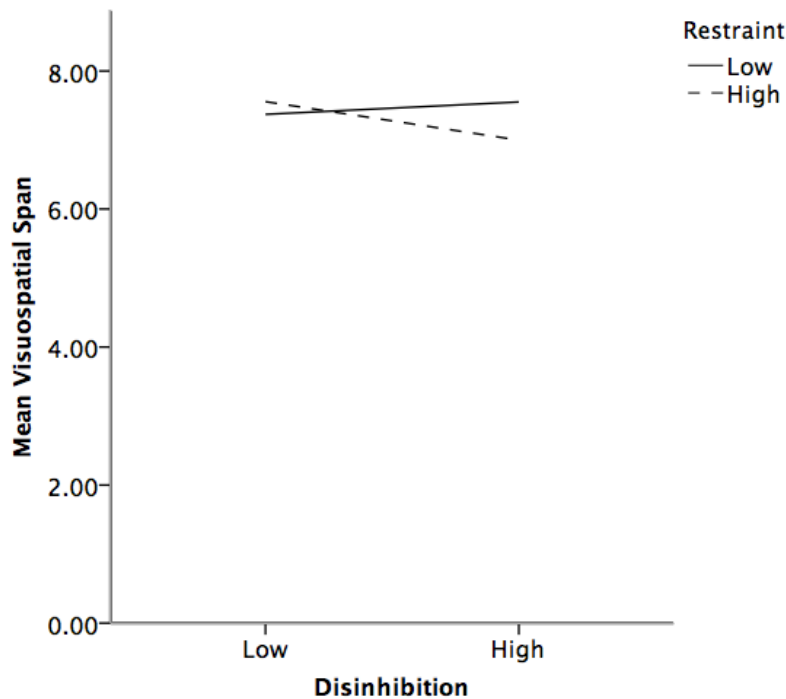
Note. SSP = spatial span task;  $R^2 = .14$

### Working memory as a function of restraint and disinhibition

Regressions revealed a significant interaction between restraint and disinhibition on visuospatial WM span (see Table 3). As plotted in Figure 1, simple slopes analysis showed that at high levels of restraint, visuospatial WM span decreased as disinhibition increased ( $b = -.08$ ,  $t(112) = -2.47$ ,  $p = 0.01$ ).

**Table 3. Linear model of predictors of visuospatial working memory span (95% bias corrected and accelerated confidence intervals). Confidence intervals and errors based on 1000 bootstrap samples.**

	<i>B</i>	SE <i>B</i>	<i>t</i>	<i>p</i>
Constant	7.37 (7.19, 7.55)	0.09	83.02	< 0.001
Restraint	-0.02 (-0.04, 0.01)	0.01	-1.09	= 0.28
Disinhibition	-0.03 (-0.08, 0.02)	0.03	-1.05	= 0.30
Restraint x disinhibition	-0.01 (-0.02, -0.0003)	0.004	-2.05	= 0.04



**Figure 1. Mean spatial span as a function of restraint and disinhibition.**

There was also a significant positive relationship between restraint and central executive strategy use score. A high score means poorer use of the strategy, suggesting that those high in restraint use the strategy less than those low in restraint (see Table 4). There were no other effects of restraint, disinhibition or the interaction between the two, on any other WM outcomes.

**Table 4. Linear model of predictors of central executive strategy use, with 95% bias corrected and accelerated confidence intervals reported in parentheses. Confidence intervals and errors based on 1000 bootstrap samples.**

	<i>B</i>	<i>SE B</i>	<i>t</i>	<i>p</i>
Constant	24.59 (23.50, 25.67)	0.55	44.77	< 0.001
Restraint	0.23 (0.04, 0.43)	0.10	2.38	= 0.02
Disinhibition	0.03 (-0.33, 0.39)	0.18	0.17	= 0.87
Restraint x disinhibition	-0.02 (-0.08, 0.05)	0.03	-0.49	= 0.63



Regressions showed that the proportion of food intake that was LED food was significantly predicted by the interaction between restraint and disinhibition ( $b = -.19$ ,  $t(105) = -2.24$ ,  $p = 0.03$ ). Simple slopes analyses showed that those high in restraint, and low in disinhibition (successful dieters) ate a higher proportion of LED foods than those high in disinhibition (unsuccessful dieters) ( $b = -1.70$ ,  $t(105) = -2.49$ ,  $p = 0.01$ ).

### **3.4 Discussion**

The aim of this study was to investigate the relationship between WM sub-components and food intake, using computerised non self-report measures of WM and a measure of actual food intake (food taste-test paradigm). Whether restraint and tendency towards disinhibition moderated this relationship were also investigated. A secondary aim of this study was to investigate the relationship between WM sub-components and dieting success. Hypotheses 1, that LED food intake would be associated with better WM performance and that this may be moderated by restraint and disinhibition, was partially supported. Greater visuospatial WM span was associated with a higher proportion of food intake that was LED food. This supports studies showing that WM is related to consumption of fruits and vegetables (Allom & Mullan, 2014; Riggs, Chou, et al., 2010; Sabia et al., 2009), and extends this to suggest that visuospatial WM in particular is important. Better visuospatial WM may enable people to deal with demands on visuospatial WM such as cravings (Green, Rogers, & Elliman, 2000; Kemps, Tiggemann, & Grigg, 2008; Meule, Skirde, Freund, Vögele, & Kübler, 2012; Tiggemann, Kemps, & Parnell, 2010), ultimately changing food preferences in favour of more LED food and less HED food if these can be dealt with appropriately. There were no moderating effects of restraint or disinhibition on the relationship between WM and food intake. While dieting has been associated with poorer central executive and phonological loop functioning (Green & Elliman, 2013; Kemps, Tiggemann, & Marshall, 2005; Kemps & Tiggemann, 2005; Shaw & Tiggemann, 2004; Vreugdenburg et al., 2003) these effects appear not to influence the relationship between WM and food intake.

Future work should extend the current findings by breaking down the WM components further and considering other functions of WM. For example, while there was no relationship between the phonological loop and food intake, the two sub-components of the phonological loop, articulatory control processes and the phonological store, may be differentially associated with food intake. The phonological store is responsible for holding verbal and acoustic information (for approximately 2.5 seconds before it fades).

The articulatory control process is responsible for rehearsal and hence maintenance of information held in the phonological store, and for converting visual information into verbal information so it can access the phonological store (Baddeley, 1992). Research on task-switching costs during articulatory suppression (i.e. when the phonological store is engaged) shows that participants are quicker to switch between two different tasks when external cues about the goals of the two tasks are available (Emerson & Miyake, 2003). This suggests that goal activation relies on the phonological loop only when external goal cues are not available, and hence articulatory control processes may be important for retrieving long-term health goals when environmental cues for healthy eating are not available. Similarly, updating is one function of the central executive believed to be important in eating habits (Hofmann et al., 2012). The central executive, however, is responsible for a number of other abilities and any one of these could be a key factor in food intake. For example, random generation (defined as the ability to inhibit stereotyped responses, Baddeley, 1996) is similar to the idea of inhibitory control which has been implicated in the control of eating behaviour and could play a key role in food intake (Guerrieri et al., 2009).

This study also investigated the role of WM in dieting success. Hypothesis 2, that restraint would be associated with impairments in central executive and phonological loop WM functioning irrespective of tendency towards disinhibition, and that there would be an effect of the interaction between restraint and disinhibition on WM, was partially supported. Specifically, it was predicted that successful dieters (high restraint, low disinhibition) would show better visuo-spatial WM than unsuccessful dieters (higher restraint, high disinhibition). As predicted, there was a significant difference between successful and unsuccessful dieters on visuospatial WM span. Those high in restraint and low in disinhibition (successful dieters) showed better visuo-spatial WM span than those high in restraint and high in disinhibition (unsuccessful dieters). It was also confirmed that successful dieters ate a higher proportion of LED food than the unsuccessful dieters. This suggests that poorer visuospatial WM may undermine dieting success, and is in line with my earlier finding that better visuo-spatial WM is associated with a greater proportion of LED food intake. Considering the evidence that food cravings are associated with visuospatial WM deficits (Kemps, Tiggemann, & Hart, 2005; Tiggemann et al., 2010), and differences between successful and unsuccessful dieters in their experiences of cravings (Meule, Lutz, et al., 2012), successful dieters may possess better visuo-spatial WM functioning to begin with, better enabling them to deal with demands on visuo-spatial WM, such as food cravings and advertising. Alternatively, it is possible that successful

dieters experience fewer food cravings, leaving them with greater capacity to deal with other visuo-spatial WM demands. To better understand the mechanism underlying this finding, future research should compare experiences of cravings between successful and unsuccessful dieters, how successful dieters deal with induced food cravings, and examine whether visuo-spatial WM mediates the relationship between food cravings and food intake/dieting success. Further, evidence suggests that visual and spatial information are dealt with separately in the visuospatial sketchpad (Darling et al., 2007). Investigating which of these are important for dieting success would inform methods to manipulate visuospatial WM in order to improve dieting performance.

We also found that irrespective of levels of disinhibition, high levels of restraint were associated with poorer central executive functioning (specifically poorer strategy use). This suggests that the negative effect of dieting on central executive functioning that has previously been found, is independent of tendency towards disinhibition (Green et al., 1997; Shaw & Tiggemann, 2004). There was no effect of restraint on phonological loop functioning. This is line with some research (Green et al., 2003; Kemps & Tiggemann, 2005), but not others (Green & Elliman, 2013; Shaw & Tiggemann, 2004; Vreugdenburg et al., 2003). It could be that assessing overall phonological loop functioning masked the effects of the two components of the phonological loop, since previous studies have found a relationship between dieting and articulatory control processes and not the phonological store (Shaw & Tiggemann, 2004) or vice versa (Vreugdenburg et al., 2003).

The size of effects found in the present study have clinical relevance. Specifically, the effect of the interaction between restraint and disinhibition on visuospatial span represented a decrease of 0.08 items recalled for every 1 point increase in disinhibition (at high levels of restraint). Therefore, visuospatial span in a person (high in dietary restraint) scoring 16 on tendency towards disinhibition (the maximum score) would be 1.28 items less than someone scoring 0 on the disinhibition sub-scale. Considering the relatively small range of visuospatial WM span found in the present study (6-9 items), we argue that this is not a small effect and could have clinical relevance. Similarly, the association between restraint and central executive strategy use reflected an increase in strategy use score (and hence poorer strategy use) of 0.23 for every 1 point increase in restraint. Strategy use score in someone scoring 21 on restraint (the highest possible score) would be 4.83 times higher than someone scoring 0 on restraint. To put this into context, highly restrained individuals started new searches for tokens from a new box 4.83 times more

often than those low in restraint (starting a new search from the same box each time is a better strategy to complete the task).

The relationships between dieting success and WM and proportion of food intake that was LED were also strong effects. The relationship between visuospatial span and LED proportion was such that for every 1 item increase in visuospatial span, there was a 3.76% increase in the proportion of LED food consumption. In those with the highest visuospatial span score in the current study (9 items), the proportion of LED intake would be 11.28% greater than those with the lowest score (6 items). Finally, the association between dieting success and LED intake reflects a 1.7% decrease in proportion of LED intake for every 1 point increase in disinhibition (in those high in dietary restraint). This means that in someone with a score of 16 on tendency towards disinhibition, proportion of LED food intake would be 27.2% less than someone scoring 0 on this sub-scale.

A number of outcome measures were used in this study to assess the different components of working memory. The results supporting relationships between restraint/disinhibition, food intake and certain components of WM and not others therefore support the specificity of these effects. However, future research could use Bayesian statistics to identify the strength of evidence for null results (Dienes, 2014, 2016). This would provide stronger support for the specificity of these effects than relying on non-significant *p*-values, which has been the traditional approach in this area of research to date.

The current study assessed associations between WM and food intake, and so no claims can be made about the causality. Indeed, there is evidence to support the suggestion that food intake influences WM as well as vice versa (Crichton, Murphy, Howe, Buckley, & Bryan, 2012). It will be important in future studies to investigate the effectiveness of WM training to improve food intake and measures of dieting success, such as weight loss and maintenance of weight loss. Initial evidence suggests that WM training in overweight/obese adults reduces food intake in individuals scoring high on a measure of dietary restraint (Houben, Dassen & Jansen, 2016). WM training to change eating behaviour and diabetes control in a sample of adults with type 2 diabetes is assessed in Study 2 (Chapters 4 & 5). The current sample was a group of undergraduate women with a low BMI (although BMI was still within the normal range). It would be interesting to see if the effects reported here would be replicated in higher BMI men and women, who may also have greater experience of dieting success and failure.

The conclusions that can be drawn from the current findings may be limited to the specific tasks used. For example, the backwards digit span task used in this study requires memorizing a sequence of verbal information and manipulating this sequence in order to recall it in the reverse order, therefore using both the phonological loop and the central executive. Similarly, the Spatial Working Memory Task used to assess the central executive requires remembering visuo-spatial information as well as updating of this information, and so engages both the visuospatial sketchpad and central executive sub-components of WM. The present findings may therefore be limited to phonological loop functioning that also involves manipulation, and central executive functioning that also involves the visuospatial sketchpad. The use of tasks that assess WM sub-components both independently and in conjunction, such as simple span and complex span tasks (Daneman & Carpenter, 1980) is recommended in future research.

In summary, the present results provide new insights into the specific components of WM that play an important role in the control of food intake. Specifically, it appears that visuospatial WM span is associated with LED food intake, and may play a role in a person's ability to choose LED food over HED food when both options are available. The finding that unsuccessful dieters have poorer visuospatial span suggests that poorer visuospatial WM may undermine dieting attempts. Previous findings that dietary restraint is associated with deficits in central executive functioning were also clarified, by supporting that this effect is independent of tendency towards disinhibition.

## **Chapter 4. Does neurocognitive training have the potential to improve dietary self-care in type 2 diabetes? Study protocol of a double blind randomised controlled trial.**

This chapter is published in BMC Nutrition, and is in this chapter exactly as it is in published form (see Appendix B for the published paper): Whitelock, V., Nouwen, A., Houben, K., Akker, O. Van Den, Neira Miller, I., Narendan, P., ... Higgs, S. (2015). Does neurocognitive training have the potential to improve dietary self-care in type 2 diabetes? Study protocol of a double-blind randomised controlled trial. *BMC Nutrition*, 1(11), 1–8. <http://doi.org/10.1186/s40795-015-0006-x>

### **4.1 Background**

Dietary self-care is a key element of self-management in people with type 2 diabetes. To reduce the risk of developing both short- and long-term physical complications, patients are encouraged to reduce their energy intake and to adopt a well-balanced diet that is low in fat and sugar and high in fibre. However, many have difficulty following this advice (Ary, Toobert, Wilson, & Glasgow, 1986). Moreover, those who do adhere to their dietary recommendations often report feeling deprived and experiencing cravings for foods (Hall, Joseph, & Schwartz-Barcott, 2003; Yannakoulia, 2006). The difficulties with following this diet and the burden reported by many patients together with treatment dissatisfaction have a direct effect on patient's self-reported quality of life (Bradley & Speight, 2002; Rubin & Peyrot, 2001). The modern food environment makes adherence to this diet especially difficult, with increases in availability, accessibility and convenience of high energy-dense palatable foods (Hill & Peters, 1998). Advertising for such foods is also omnipresent and highly persuasive (Swinburn et al., 2011). This presents a major challenge for anyone attempting to maintain a healthy diet, as exposure to food cues can lead to both cravings and overconsumption of these foods (Fedoroff et al., 1997; Sobik, Hutchison, & Craighead, 2005). In order to maintain a healthy diet it is therefore essential to resist immediate temptation and focus on more distal goals. While dietary changes can be effective in improving glycaemic control (Lindström et al., 2006), dietary self-care is generally poorly performed (Peyrot et al., 2005), and simple advice and motivation based interventions have had limited effects in improving this (England, Andrews, Jago, & Thompson, 2014). Novel and effective strategies to help people with type 2 diabetes adhere to dietary recommendations are therefore needed.

Being able to resist tempting food requires adhering to long-term health goals, and not giving in to short-term immediate desires. Dual-process theories of behaviour posit that

the ability to do this depends on the balance between two different cognitive systems that control behaviour (Strack & Deutsch, 2004): the reflective system, which promotes controlled, reflective behaviour, and the impulsive system which promotes impulsive, automatic behaviour. The reflective system can exert inhibitory control over the impulsive system, and is able to suppress its effects on behaviour (although not fully). When this occurs, self-control and resisting tempting foods is more likely to follow. Inhibitory control is therefore an important executive function implicated in the control of eating behaviour. Indeed, inhibitory control has been related to overeating and obesity. People with high impulsivity/weak inhibitory control are more likely to overeat (Guerrieri et al., 2007, 2009) and be overweight/obese (Nederkoorn et al., 2007; Sutin et al., 2011). Other work has specifically demonstrated that when inhibitory control is low, eating behaviour is more strongly guided by impulsivity (Hofmann & Friese, 2008; Hofmann et al., 2007; Nederkoorn et al., 2010). Suppression of automatic, motivational, impulsive responses to food however improves the ability to resist consumption of desirable food items (Guerrieri et al., 2009; Houben & Jansen, 2011).

Neuroimaging evidence has found that people with type 2 diabetes (compared to body weight matched healthy controls) show greater neural activity in subcortical areas of the brain in response to food cues (Chechlacz et al., 2009). These subcortical areas are part of the brain's impulsive system (Bechara, 2005). There was also greater activity in response to food pictures in cortical areas including the orbitofrontal cortex and insula (Chechlacz et al., 2009). These regions are part of the reflective system and as such are important for inhibitory control and restraining immediate desires in favour of long term outcomes (Bechara, 2005). This neuroimaging study further showed that increased activity in cortical areas was associated with better self-reported dietary self-care, whereas activity in subcortical areas was associated with poorer dietary self-care (Chechlacz et al., 2009). These findings suggest that interventions aimed at maximising inhibitory control may improve dietary self-care in type 2 diabetes.

WM capacity is an important executive control ability that has been shown to moderate the role of impulsive processes in predicting health behaviours. In people with low WM capacity (compared to those with high WM capacity) impulsive processes are better predictors of alcohol consumption (Grenard et al., 2008; Thush et al., 2008), cigarette use (Grenard et al., 2008) and unhealthy food consumption (Hofmann, Friese, & Roefs, 2009; Hofmann, Gschwendner, et al., 2008). Diabetes is associated with a range of cognitive impairments (McCrimmon et al., 2012) and deficits in executive functioning in particular

(including WM) could be contributing to difficulties in controlling food intake (Knopman et al., 2001). Evidence from studies of top-down inhibitory control demonstrate that training WM can improve inhibitory control and change behaviour in a variety of clinical contexts, including in children with attention-deficit hyperactivity disorder (Beck, Hanson, Puffenberger, Benninger, & Benninger, 2010; Holmes, Gathercole, Place et al., 2010), in older people (Borella, Carretti, Riboldi, & De Beni, 2010), problem drinkers (Houben, Wiers, & Jansen, 2011) and stimulant drug abusers (Bickel, Yi, Landes, Hill, & Baxter, 2011). For example, WM capacity increased and alcohol consumption decreased for more than one month afterwards in problem drinkers who underwent 25 sessions of online WM training (Houben et al., 2011). WM training is believed to work by increasing activity in the prefrontal cortex, another part of the reflective system (Olesen, Westerberg, & Klingberg, 2004). Given that common mechanisms are known to underlie responses to palatable foods and addictive substances like alcohol (Kenny, 2011), these data suggest that cognitive training could be effective in strengthening the ability to resist tempting foods and hence improve dietary control in people with type 2 diabetes.

### **Aims and Hypotheses**

The aim of this study therefore is to investigate whether 25 sessions of neurocognitive WM training can improve dietary self-care in people with type 2 diabetes (compared to passive control training).

#### Primary outcome measures

It is expected that WM training will enhance WM capacity and reduce high energy dense food intake. It is important to demonstrate that the WM training effects transfer to other measures of WM (to help rule out simple practice effects); therefore both the trained and novel non-trained tasks will be used to assess WM and executive functioning. Changes in food intake will be measured at a lunch buffet in the laboratory and via a 24-hour food recall task to obtain a measure of usual food intake outside of the laboratory.

#### Secondary outcome measures

It is expected that WM training will reduce lipid and glycated haemoglobin (HbA1c) blood levels. HbA1c is considered a long-term measure of diabetes control, and hence this will test the longer term effects of the training. Lipid blood levels will act as a biological measure of food intake; if less high energy dense food is consumed, lipid blood levels



should be lower. Participants' experiences of the training will be assessed qualitatively with semi-structured interviews post-training.

## **4.2 Methods/Design**

### **Ethics**

This study has been approved by the Middlesex University Ethics Committee and by an NHS Research Ethics Committee. Prior to this, the study was reviewed by the Research Committee of Diabetes-UK.

### **Design and Participants**

This is a randomised, double blind 2 (condition: active training, passive control training) x 3 (time-point: pre, post, follow-up) factorial design study. This multisite project will run in London and Birmingham, UK. Participants will be a total of 48 NHS patients with type 2 diabetes recruited from diabetes clinics at local hospitals. Patients will be informed about the research by their health care professional initially, and the researcher will be present in clinics to provide further information and answer questions. Upon acceptance to participate, the first pre-training assessment session will be arranged. Assessments will occur at baseline, immediately after and 3 months after completion of the training.

Inclusion criteria are: (1) have had type 2 diabetes for 2 years or more; (2) poor diabetes control (HbA1c >64mmol/l); (3) self-reported difficulty following a healthy diet; (4) general good health; (5) overweight with a BMI  $\geq 25$ ; (7) treatment of diabetes can include diet only, tablets or insulin (for at least the last 6 months). Exclusion criteria are: (1) neurological or psychiatric disorders, including eating disorders and clinical depression; (2) recent (within the last 6 months) changes in diabetes treatment (e.g. transfer to insulin); (3) alcohol and/or substance abuse; (4) treatment by GLP-1 or DPP-4 inhibitors. Participants will be reimbursed £10 for travel expenses for each of the three assessment sessions.

### **Power Calculation**

The power calculation for this study was based on Houben et al's WM training study in problem drinkers (Houben et al., 2011). In this study, WM training resulted in a large effect size of 0.27 for the interaction between time and condition. We anticipate a similar large effect size in our sample. Thus, using a 2 (condition: active, passive control) x 3 (time point: pre, post, follow-up) within-between design and assuming correlations among

measures of 0.4 and a non-sphericity correction of 0.6, the estimated sample size should be at least 20 participants per group when power is set at 0.80 and  $p < 0.05$ . Based on previous experience with longitudinal studies, we expect an attrition rate of 15-20%. Therefore, we will recruit a minimum of 24 participants per group to account for possible attrition (total sample size  $N= 48$ ).

### **Randomisation and Blinding**

Participants will be randomly allocated to either the active or passive control training conditions using an online program-generated block randomisation list (blocks of 10, (Sealed Envelope Ltd, 2015). Condition allocation will take place during the pre-training assessment session when the participant signs up to the online training program. Both participants and the researchers conducting the assessment sessions will be blind to participant condition.

### **Training Program**

The working memory training will be the same program of tasks as used by Houben et al., (2011). This was designed based on the work of Klingberg (Klingberg, Forssberg, & Westerberg, 2002). The training consists of repeatedly practicing three WM tasks; letter span task, backwards digit task, visuo-spatial task. In the backwards digit task, several numbers are presented on the screen one at a time, which participants have to remember and reproduce in reverse order (using the mouse and on-screen number pad). In the visuo-spatial task, a sequence of boxes light up one at a time in a 4x4 grid. The task here is to remember the location and order in which the boxes lit up, and to reproduce this using the mouse to click on the squares in the grid in the right order. In the letter span task, a sequence of letters is presented one at a time in a circle. Once the sequence has finished, one of the positions in the circle is cued and participants have to enter the letter that appeared in this location using the keyboard. In each training session, there are 30 trials of each task.

There will be two training conditions; active and passive control training. In the active training condition, the difficulty level closely follows the WM capacity of the participant. Following two correct answers, the number of items to remember increases by 1. Following two incorrect answers, the number of items to remember decreases by 1. In the passive control condition, participants complete the same set of three tasks, but the difficulty level remains low so as to not train WM. The active rather than passive control

group allows us to control for expectancy effects, as well as any effects that may occur due to repeated use of computers and adhering to a training schedule.

### **Primary Outcome Measures**

Working memory capacity (trained tasks)

The three tasks used in the training program will also be used in an assessment version. In the assessment version the number of items to remember for each task begins low (three items) and increases by one following two consecutive correct answers. When two incorrect answers are given the task is terminated. The longest sequence of items correctly recalled for each of the three tasks is summed and averaged to provide a measure of WM capacity across the three WM tasks.

Working memory capacity (non-trained tasks).

These will consist of the Cambridge Neuropsychological Test Automated Battery (CANTAB, Cambridge Cognition, Cambridge, UK) Attention Switching Task, Paired Associates Learning, Spatial Span and Spatial Working Memory tasks. The Spatial Span and Spatial Working Memory tasks measure WM ability/capacity. The Paired Associates Learning task measures visual memory and new learning. The Attention Switching Task measures interference of irrelevant information, and hence top-down cognitive control processes. Outcome measures for these tasks will include reaction times, error scores, span length and memory scores.

Lab-based food intake (lunch buffet).

Participants will be provided with a staple lunch food item (egg sandwiches or cheese sandwiches) along with six different snack foods. The weight (in grams) of the snack foods has been calculated so that a similar visual amount of each food is provided. Three of the snack foods are low energy dense (carrot sticks ~110g, ~44 kcal; plum tomatoes ~139g, ~28 kcal; salt and vinegar rice cakes ~10.5g, ~40 kcal) and three are high energy dense (ready salted crisps ~25g, ~133 kcal; chocolate chip cookies ~64g, ~323 kcal and cheese and onion rolls ~93g, ~283 kcal). The cookies, rice cakes, cheese and onion rolls and the sandwiches will be broken up into smaller pieces to prevent participants counting the number of items they eat and this influencing their intake. The food will be weighed before and after the lunch buffet (out of sight of the participant) and used to calculate how

much was eaten by subtracting the post-buffet weight from the pre-buffet weight of each food.

Non lab-based food intake (24-hour guided recall).

Participants will be asked to write down everything they ate and drank on the previous day. This is a guided recall procedure which asks participants about the time, location, and eating companions of the meal (Robinson, Blissett, & Higgs, 2011). While this approach covers only a limited sample of an individual's food intake, research has shown that this method provides an accurate and representative picture of usual food intake (Armstrong & MacDonald, 2000). The number of low and high energy dense food and drink items reported will be totalled as a measure of food/drink intake. Participants will also be asked how many junk food items and portions of fruits and vegetables they usually eat per day.

### **Secondary Outcome Measures**

HbA1c and lipids

HbA1c and lipid levels will be assessed by taking blood samples which will be sent for analysis at the hospital laboratories.

Semi-structured interviews

The semi-structured interviews will take place at the end of the post-training assessment session. The purpose of this is to understand people's experiences of the training.

Participants will be asked about what they had hoped to gain from the training, their experiences of it, how they managed to include it into their life and how the training affected their eating habits and the control of their diabetes.

### **Other Measures**

To characterise the study sample and to control for potential baseline differences we will also assess a number of other measures, including; BMI (height and weight will be measured without shoes and heavy outdoor clothing and used to calculate BMI kg/m<sup>2</sup>), eating styles (General Food Cravings Questionnaire, Nijs, Franken, & Muris, 2007; Three Factor Eating Questionnaire-18, Karlsson, Persson, Sjöström, & Sullivan, 2000; Dutch Eating Behaviour Questionnaire, van Strien et al., 1986), diabetes-related behaviours (Diabetes Specific Quality of Life Questionnaire, Bott, Mühlhauser, Overmann, & Berger, 1998; Summary of Diabetes Self-Care Activities Scale, Toobert et al., 2000, Dietary Self-

Efficacy Scale Senecal, Nouwen, & White, 2000, depressive symptoms (Patient Health Questionnaire-9, Spitzer, Kroenke, & Williams, 1999), physical activity (International Physical Activity Questionnaire, Booth, 2000), physiological data (blood pressure, blood glucose levels) and demographic information (gender, age, ethnicity, education level, length of diabetes diagnosis, how the diabetes is controlled, existence of co-morbid conditions). Illness-related information will be collected at each of the three assessment sessions to track any changes in co-morbid conditions and diabetes treatment. Mood and hunger will be measured both before and after the blood tests, computer tasks and lunch buffet, as these could influence task performance (Herman & Polivy, 1984, 2005; Macht & Simons, 2000). Food-specific inhibition will be assessed using a food go/no-go task. This task consists of 200 trials split across 4 blocks. In blocks 1 and 2, participants are instructed to respond (press the space bar on the keyboard) when they see a picture of toiletries and to withhold a response when they see sports-related pictures. In blocks 3 and 4, participants are instructed to respond to pictures of stationary, and withhold responses to food-related pictures. Fewer commission errors (responding to no-go trials) on no-go food picture trials compared to no-go sports objects trials will indicate greater baseline food-specific inhibitory control ability.

## **Procedure**

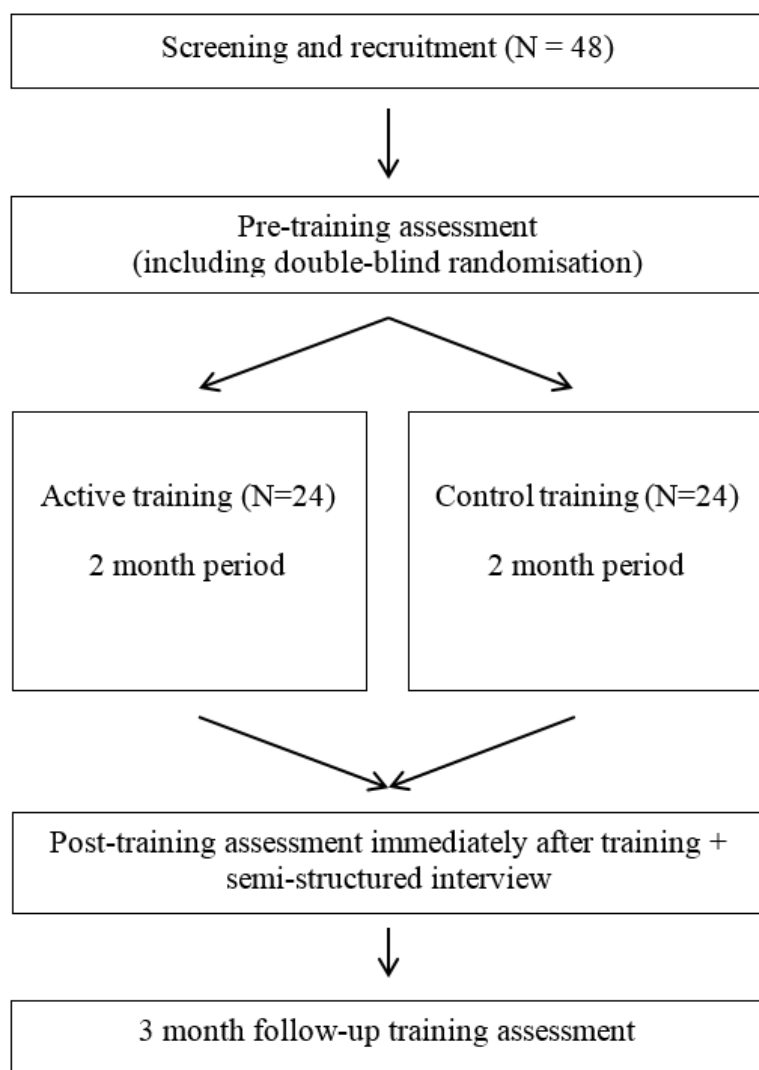
### Assessment sessions

Assessment sessions will last approximately 2.5 hours. Participants will provide informed consent at the beginning of the pre-training assessment session. See Table 1 for the order of completion of the tasks. For the lunch buffet, participants will be given 15 minutes to eat (alone) and will be told to eat as much or as little as they wish. Questionnaires regarding eating habits will be completed last, to avoid any influence on other responses. The post-training and follow-up assessment sessions will be the same as the pre-training assessment session, except that consent will not need to be re-taken, and in addition the semi-structured interview will be conducted (post-training assessment) and participants will be probed about their awareness of the purpose of the lunch buffet (follow-up assessment). See Figure 1 for a flowchart of how participants will progress through the trial.

**Table 1. Measures used at each time-point and the order in which they are used.**

Pre-training assessment	Immediate post-training assessment	3 month follow-up assessment
Informed Consent		
Hunger & Mood Questions	Hunger & Mood Questions	Hunger & Mood Questions
Blood Pressure	Blood Pressure	Blood Pressure
Blood Tests	Blood Tests	Blood Tests
Height & weight	Height & weight	Height & weight
Hunger & Mood Questions	Hunger & Mood Questions	Hunger & Mood Questions
Computer Tasks (go/no-go, CANTAB, WM assessment and sign-up to training)	Computer Tasks (go/no-go, CANTAB, WM assessment)	Computer Tasks (go/no-go, CANTAB, WM assessment)
Hunger & Mood Questions	Hunger & Mood Questions	Hunger & Mood Questions
Buffet Lunch + Food Liking Questions	Buffet Lunch + Food Liking Questions	Buffet Lunch + Food Liking Questions
Hunger & Mood Questions	Hunger & Mood Questions	Hunger & Mood Questions
24hr Guided Recall Task	24hr Guided Recall Task	24hr Guided Recall Task
Questionnaires (Demographics, DSQOL, SDSCA, DSES, IPAQ, PHQ-9, DEBQ, TFEQ-18, GFCQ)	Questionnaires (Demographics, DSQOL, SDSCA, DSES, IPAQ, PHQ-9, DEBQ, TFEQ-18, GFCQ)	Questionnaires (Demographics, DSQOL, SDSCA, DSES, IPAQ, PHQ-9, DEBQ, TFEQ-18, GFCQ)
	Semi-structured Interview	Awareness probe

**Note.** WM = working memory; DSQOL = Diabetes Specific Quality of Life Questionnaire; SDSCA = Summary of Diabetes Self-Care Activities Scale; DSES = Dietary Self- Efficacy Scale; IPAQ = International Physical Activity Questionnaire; PHQ-9 = Patient Health Questionnaire-9; DEBQ = Dutch Eating Behaviour Questionnaire; TFEQ-18 = Three Factor Eating Questionnaire-18; GFCQ = General Food Cravings Questionnaire



**Figure 1. Flowchart of participant's through the trial.**

### Training

The training starts the day after the pre-training assessment session and is completed online in the comfort of participants' own homes. Participants will complete 25 online training sessions over a minimum of 25 days and a maximum of 50 days. Only one session can be completed per day, and participants have 2 days to complete each session. Up to 5 sessions can be missed before they are excluded from the study.

### Interviews

Sixteen interviews will be conducted (lasting a maximum of 30 minutes each), 8 with participants from the Birmingham site, and 8 from the London site. Those interviewed will be targeted to represent the range of genders, age and ethnicities taking part in the study.

At the beginning of the interviews, participants will be reminded that their responses will be kept confidential and encouraged to be as honest as possible in their answers.

## **Analyses**

Baseline group differences on demographic and biographic data will be assessed using ANOVAs. Any found to be significant will be included as co-variables on subsequent analyses. The primary and secondary outcome measures of interest will be assessed using a 2 (condition: active, control) x 3 (time point: pre, post, follow-up) between-within ANOVA, with post-hoc tests as necessary. These analyses will be done twice, once taking an Intention to Treat approach and once taking a Per-Protocol approach (Gupta, 2011). In an Intention to Treat approach, all participants are included in the analysis, regardless of training adherence and withdrawal. This provides a more conservative estimate of the effect of the training, compared to a Per Protocol approach to analysis which only includes participants who completed the study.

The qualitative data obtained from the semi-structured interviews will be recorded, transcribed verbatim and imported into NVivo for analysis. A thematic analysis will be conducted to inductively identify initial codes, and ultimately broader themes important to participants' experiences of the training (Braun & Clarke, 2006).

## **4.3 Discussion**

This is the first trial to investigate whether WM training can change the eating behaviour of people with type 2 diabetes. This is a highly relevant population for testing the clinical effectiveness of such training. If successful, online WM training could prove to be a cost-effective intervention that can be used long-term without side effects, improving the quality of life of people with type 2 diabetes. It could also prevent or delay the need for drugs or insulin to control glycaemic levels. The possible applications would also extend beyond those who have type 2 diabetes. For example, it could be used by people who are overweight/obese or have "pre-diabetes" (impaired glucose regulation) to help prevent/delay the development of type 2 diabetes.

The ideal intervention for any medical condition is one that improves the condition, is easy for patients to do, and has no unpleasant short or long-term side effects. Therefore, the secondary aim of this study is to gain an understanding of patient's experiences with the training. An online intervention is ultimately only going to be successful if patients are able to incorporate it into their life. The semi-structured interviews will allow us to assess



how patients experienced the training, such as how they managed to integrate it into their lifestyle and the effects they think it had on their diet and diabetes control. This will provide future direction for research, such as investigating the effects of fewer or shorter training sessions.

As participants will not need to attend the clinic for each training session, but rather can do it at home, we hope this will improve adherence rates. Participants can do each training session at any time and in any place suitable to them. This will allow us to assess the effectiveness of a training program that would likely be impossible if participants had to attend the clinic for every training session. There are shortcomings to an online intervention however. Without a researcher present to ensure participants do each training session, patients may be more likely to not complete all sessions. Adherence to the intervention is therefore encouraged with an email reminder each day that they are now able to complete the next training session, with a URL link that participants can click on, taking them directly to the training session. Therefore, participants (1) receive a reminder every day to complete that day's training session, and (2) don't have to remember a username and password in order to do the training. This should ensure good rates of adherence to the training program. Another limitation to online training programs is that it requires participants to have a computer and internet access. Not all people will have this, especially older people, who we anticipate will form a large proportion of our sample. However, according to the Office of National Statistics, 84% of households in Great Britain have access to the internet in 2014, so we do not anticipate this being a barrier to recruitment (Office for National Statistics, 2014).

## **Chapter 5. Does neurocognitive training have the potential to improve dietary self-care in type 2 diabetes? Results of a double blind randomised controlled trial.**

### **5.1 Introduction**

The previous chapter introduced the design and methods of a double-blind RCT in people with type 2 diabetes that aimed to train WM and improve eating habits and diabetes control (Whitelock et al., 2015). The current chapter reports the results and discussion for this study. Before describing the results, more detail is provided on some of the measures and outcomes utilised since the full details could not be reported in the published protocol (reported in Chapter 4).

### **5.2 Methods**

#### **Measures**

##### Transfer effects

As mentioned in the published protocol, it is important to assess whether WM training effects transfer to other measures of WM (near transfer effects), as well as other aspects of cognition and behaviour (far transfer effects). The Attention Switching Task, Paired Associates Learning, Spatial Span and Spatial Working Memory tasks from the Cambridge Neuropsychological Test Automated Battery (CANTAB, Cambridge Cognition, Cambridge, UK) were used to assess transfer effects to different tests of WM and other aspects of cognition. A food-specific go/no-go task was also used to assess food specific inhibitory control.

##### Near transfer effects

Near transfer effects of WM training would include improvement on the tasks used to train WM (visuospatial task, letter span and backwards digit task). These tasks are described in detail in the previous chapter. The next level of near transfer effects would be improvements on non-trained measures of WM and these were assessed using the Spatial Span and Spatial Working Memory tasks from the CANTAB testing battery.

##### *Spatial span task*

The spatial span task used was identical to that used to assess visuospatial WM in Study 1 (Chapter 3) and was a computerised version of the Corsi blocks task, which is a validated

measure of visuospatial sketchpad capacity (Hanley, Young, & Pearson, 1991). Important outcome measures were span length (the longest sequence correctly recalled) and the total number of errors made.

#### *Spatial working memory task*

The spatial working memory task was identical to that used to assess central executive functioning in Study 1 (Chapter 3). The same outcome measures were used in the present study – the total number of unnecessary extra inspections made (total errors) and the degree to which participants used a strategy to perform the task. The best strategy for this task was to search the boxes in the same order every time a new search commences. The number of times a participant started the search from a different box was counted, and a higher score therefore indicated poorer use of this strategy. Strategy use is a measure of central executive ability, whereas errors are a measure of short-term visuo-spatial memory (Goghari et al., 2014; Owen et al., 1990).

#### Far transfer effects

Far transfer effects of WM training would include improved performance on other measures of cognition as well as behaviour. Behavioural far transfer effects in the present study were assessed via measures of food intake (lunch buffet taste-tests and 24-hour recalls), and physiological measures of dietary adherence (HbA1c and lipid levels). HbA1c was a measure of how well patients control their diabetes: the higher the value, the more poorly controlled the diabetes. Blood lipid level was a measure of fat consumption. Cognitive far transfer effects were assessed with the remaining two tasks from the CANTAB testing battery; the attention switching task was used as a measure of inhibitory control and the paired associates learning task was used as a measure of new learning and memory. Food-specific inhibitory control was assessed using a go/no-go task that included food stimuli.

#### *Attention switching task*

The attention switching task measured top-down inhibitory control processes by assessing a person's ability to ignore task-irrelevant and distracting information (Di Virgilio et al., 2016; Van Der Wardt et al., 2015). WM training effects may transfer to other executive functions and hence performance on this task may be expected to improve. In this task participants saw an arrow pointing either to the left or right, and was either on the left or right side of the screen. Participants were instructed to press the left and right press pad

buttons either in accordance with the direction the arrow was pointing or the location of the arrow on the screen. In some trials the instruction remained the same (e.g. always press the button according to the direction the arrow is pointing), and on some it switched randomly between asking participants to respond to the direction and location of the arrow (termed switching trials). In other blocks, the direction and location of the arrow was congruent (the arrow pointed left and was on the left side of the screen), and in others they were incongruent (the arrow pointed left but was on the right side of the screen). In switching trials participants had to quickly switch the rule they were following without warning (i.e. between responding to the direction and location of the arrow). On incongruent trials, participants had to prevent interference from distracting information (i.e. ignoring that the arrow was pointing left when it was on the right side of the screen). Important outcome measures were switching cost and congruency cost. Switching cost was the difference between response latencies on switching and non-switching trials. Congruency cost was the difference between response latencies on congruent versus incongruent trials. Positive scores on both reflect a preference (i.e. faster responding) to non-switching and congruent trials. Scores closer to zero indicate little preference between switching versus non-switching and congruent versus non-congruent trials.

#### *Food-specific inhibitory control*

A food go/no-go task was used to assess changes in food specific inhibition. Details of this task are provided in the published protocol. Key outcomes were commission and omission errors. This task has been used to measure food-specific inhibition in other work (Price, Lee, & Higgs, 2016).

#### *Paired associates learning task*

The paired associates task assesses visual memory and new learning (specifically episodic memory), and has been shown to be reliable and is able to discriminate mild cognitive impairment (Juncos-Rabadán, Pereiro, Facal, Reboredo, & Lojo-Seoane, 2014; Lowe & Rabbitt, 1998). A number of boxes appeared on the screen, and several of them contained a pattern (e.g. 2). The boxes opened one-by-one in a random order to reveal the location of the patterns. Participants had to remember the location of patterns. The number of patterns inside boxes increased if the previous locations were remembered correctly. If the pattern locations were not remembered correctly, the boxes opened up again to remind the participant of the location of the patterns. Up to 6 attempts were allowed on each level of the task. Key outcome measures were total errors and first trial memory score. First trial

memory score was the number of patterns correctly located after the first time they were shown, with a higher score indicating better new learning.

#### Behavioural far transfer effects

This included two measures of food intake, (1) laboratory based taste-test and (2) 24-hour recall, a measure of non-laboratory based food intake. These were two of the primary outcome measures for this study and the methods used for these are described in detail in the previous chapter. Since the protocol was published, however, the method of scoring the 24-hour recall was changed to provide more detailed food intake outcomes. Total consumption of kilocalories and macronutrients were calculated from recalls using the McCance and Widdowson's composition of foods database (McCance & Widdowson, 2002). Total kilocalories and saturated fat were used as outcomes from this. Biological measures of behaviour change (HbA1c and cholesterol levels) remained as secondary outcomes.

#### **Qualitative interviews**

The published protocol for this study stated that semi-structured interviews would be conducted on a total of 16 participants, 8 from the London site and 8 from the Birmingham site (Whitelock et al., 2015). However, as the research sites changed after the protocol was published, interviews were conducted on all participants that completed the active training to ensure sufficient data was obtained.

#### **Approach to analysis**

##### Data handling

As recommended by the CONSORT guidelines for randomised controlled trials and as stated in the published protocol for this trial, a modified intention to treat analysis approach was taken (mITT: Moher, Schulz, & Altman, 2001; Whitelock et al., 2015). In a full ITT approach, all patients randomised to a trial arm are included in the analyses, irrespective of compliance, withdrawal and false inclusion (participants found after randomisation to not meet the study criteria, Gupta, 2011). Modified ITT allows exclusion of some patients when there is suitable justification e.g. a patient did not start the treatment (Gupta, 2011). The (m)ITT approach provides a more conservative estimate of the intervention effects, as a number of patients will not have received the full intervention. Further, ITT analysis is only possible where complete outcome data is

available, and therefore missing data must be dealt with in some way. In the current trial, a last observation carried forward (LOCF) approach was applied, whereby the last measurement available for each participant prior to withdrawal was maintained in the analysis and carried forward to the post-training measurements. This is a relatively conservative approach that is likely to underestimate intervention effects. It is, however, less conservative than others approaches, such as allocating a poor outcome to patients in the group that fared better, which has been argued to prevent conclusive answers as to the intervention's efficacy (Hollis & Campbell, 1999). Some measures were unavailable at baseline and could not be imputed for post-training outcomes (e.g. unable to draw blood for blood tests); hence there is still some missing data in these analyses. Analyses were repeated taking a Per Protocol approach to identify the effect of the carry forward method on the results. This approach included only patients who complied with the protocol and exclusion of participants who were found to not meet the study criteria post randomisation (Hollis & Campbell, 1999).

A total of 26 semi-structured interviews with patients in the active training group were conducted. This is less than the number of people maintained in the mITT analysis on the quantitative data as 13 participants did not complete the interviews at T2. Interviews were recorded, transcribed verbatim and imported into NVivo for analysis. A thematic analysis was conducted to inductively identify initial codes, and ultimately broader themes important to participants' experiences of the training (Braun & Clarke, 2006). Following the 6 phases of thematic analysis described by Braun and Clarke, after transcribing and reading the data (phase 1), the data were systematically coded across the entire data set (phase 2) and then collated into themes (phase 3). The themes were then checked for internal homogeneity and external heterogeneity, and reviewed to make sure they represented the data extracts coded at each theme (phases 4 & 5). Phase 6 (producing the report) is presented below as a detailed summary of both the overarching and sub-themes identified from the thematic analysis.

#### Group differences and main analyses

Baseline group differences on demographic and biographic information were checked with ANOVAs for continuous data and Pearson's chi square test for categorical variables (Fisher's Exact Test when groups were small e.g. ethnicity). Primary and secondary outcomes measures of interest were assessed using 2 (condition: active, control) x 2 (time-

point: pre, post) mixed ANOVAs. Three-month follow-up data is not yet available and therefore these results are not reported here.

### **5.3 Results**

#### **Exclusions**

Three patients were excluded from the mITT analysis, meaning 71 patients were retained (active training = 39, control training = 32). One patient was excluded because of a technical error in the training program that switched the patient from the control training to the active training half-way through. One patient was excluded because they did not complete any training sessions or the baseline WM assessments. Therefore, there were no observations to carry forward for the WM training. One patient was excluded because the data suggested they had type 1 diabetes and not type 2 (they self-reported only taking insulin treatment and did not answer the question “how long have you been diagnosed with type 2 diabetes for?”). See Table 1 for participant characteristics. In the per protocol analyses, 55 patients were maintained (active training = 28, control training = 27). Thirteen were excluded due to missing T2 data, two were excluded for not completing enough training sessions (2 and 8 sessions only), and one was excluded due to the introduction of rapid insulin during the training, which could have affected their diabetes control. There were no differences on baseline measures between those who did not complete the active and control training (smallest  $p = 0.12$ ). The per protocol analyses made no difference to the pattern of the results, and hence individual results are not reported. Excluding two participants with a BMI just under overweight and excluding one participant whose glucose level during the testing session was under 4 mmol/l also made no difference to the results and so these participants were maintained in the analyses.

#### **Sample characteristics**

Participants were recruited from tertiary NHS care services across three geographical areas: London ( $n = 44$ ), Southampton ( $n = 26$ ) and Birmingham ( $n = 1$ ). All participants self-reported difficulty controlling food intake (for example, problems resisting high fat/sugar foods or experiencing food cravings). Both groups had a mean HbA1c that was above UK guidelines (48 mmol/mol; NICE guideline, 2015), and a mean BMI within the obese range. One exclusion criterion was changed after publication of the study protocol. Specifically, people on GLP1-agonists and DPP-4 inhibitors were allowed to take part if they had been on these medications for more than 6 months. This was because any effects

of the drugs on appetite would likely have stabilised by this point and should not obscure any effects of the intervention. Those who had had any major changes in medication within the last 6 months were still excluded (this resulted in one exclusion for the per protocol analyses). See Table 1 for a summary of the characteristics of the sample. Participants completed on average 20.68 training sessions (out of 25;  $SD = 6.67$ ).

### **Group differences**

The randomisation procedure was relatively successful, with significant baseline differences between groups found only for diastolic blood pressure, and trending effects for emotional eating and dietary self-efficacy (DSES) mean score. The control group had higher diastolic blood pressure and emotional eating score, but lower DSES score (see Table 1 for means and SD).



**Table 1. Participant characteristics and baseline differences.**

Characteristic	Active training Mean (SD) <i>n</i> = 39	Control training Mean (SD) <i>n</i> = 32	Range	<i>F</i> / $\chi^2$	<i>p</i> value
Age (years)	60.10 (8.40)	61.50 (10.20)	33.00 – 80.00	0.38	0.54
BMI (kg/m <sup>2</sup> )	33.10 (6.20)	33.00 (6.00)	22.57 - 48.98	0.001	0.98
Blood glucose (mmol/l)	7.92 (2.29)	8.94 (3.45)	2.90 - 17.20	1.68	0.20
HbA1c (mmol/mol)	53.99 (15.34)	58.41 (12.42)	30.00 - 90.20	1.52	0.22
Systolic blood pressure (mmHg)	135.97 (14.09)	141.75 (20.22)	109 – 191	2.00	0.16
Diastolic blood pressure (mmHg)	84.97 (10.00)	91.13 (12.04)	63 – 118	5.53	0.02
Duration of diabetes (years)	6.67 (5.73)	8.35 (7.66)	0.8 – 30.0	1.11	0.30
Physical activity (total MET minutes per week)	4062.49 (4073.21)	3530.28 (5599.15)	0.00 - 26037.00	0.21	0.65
Gender (male)	25	16		1.43	0.23

Ethnicity			2.43	0.52
White	31	23		
Asian/Asian British	6	6		
Black/African/Caribbean/Black British	1	0		
Other	1	3		
Employment* (working)	23	18	0.01	0.93
Highest level of education			3.56	0.32
Secondary school	6	10		
College	4	5		
Higher education	24	14		
Other	5	2		
Diabetes treatment ( <i>n</i> )				
Diet	22	17		

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Exercise	20	17
Tablets	32	27
Insulin	5	3
GLP-1 agonist	2	3
DPP4 inhibitors	2	4
Co-morbid condition ( <i>n</i> )		
Neuropathy	8	3
Retinopathy	7	5
Kidney disease	0	0
Vascular disease	2	2
Heart disease	2	4
Stroke	2	0
Ulcers	0	0

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DSQOL (burden scale)	77.84 (16.35)	70.69 (21.88)	19.30 – 99.30	2.48	0.12
SDSCA					
General diet	3.97 (2.31)	4.39 (1.87)	0 – 7	0.67	0.42
Specific diet	3.73 (1.74)	4.03 (1.61)	0 - 7	0.56	0.46
DSES	57.87 (20.28)	49.43 (21.21)	5.33 – 97.33	2.92	0.09
PHQ-9	5.21 (4.18)	7.03 (5.36)	0 – 20	2.60	0.11
DEBQ					
Restrained eating	2.90 (0.81)	2.78 (0.70)	1.20 - 4.40	0.45	0.51
Emotional eating	2.11 (0.90)	2.45 (0.74)	0.77 – 4.23	3.02	0.09
External eating	2.78 (0.69)	3.01 (0.56)	1.20 – 4.10	2.36	0.13
TFEQ (uncontrolled eating)	33.81 (19.82)	39.47 (21.03)	0 – 96.30	1.36	0.25
GFCQ					
State	22.97 (10.35)	27.13 (12.85)	15 – 69	2.27	0.14

Trait	52.23 (22.86)	59.22 (21.81)	21 - 119	1.71	0.20
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\*Missing information for 2 patients

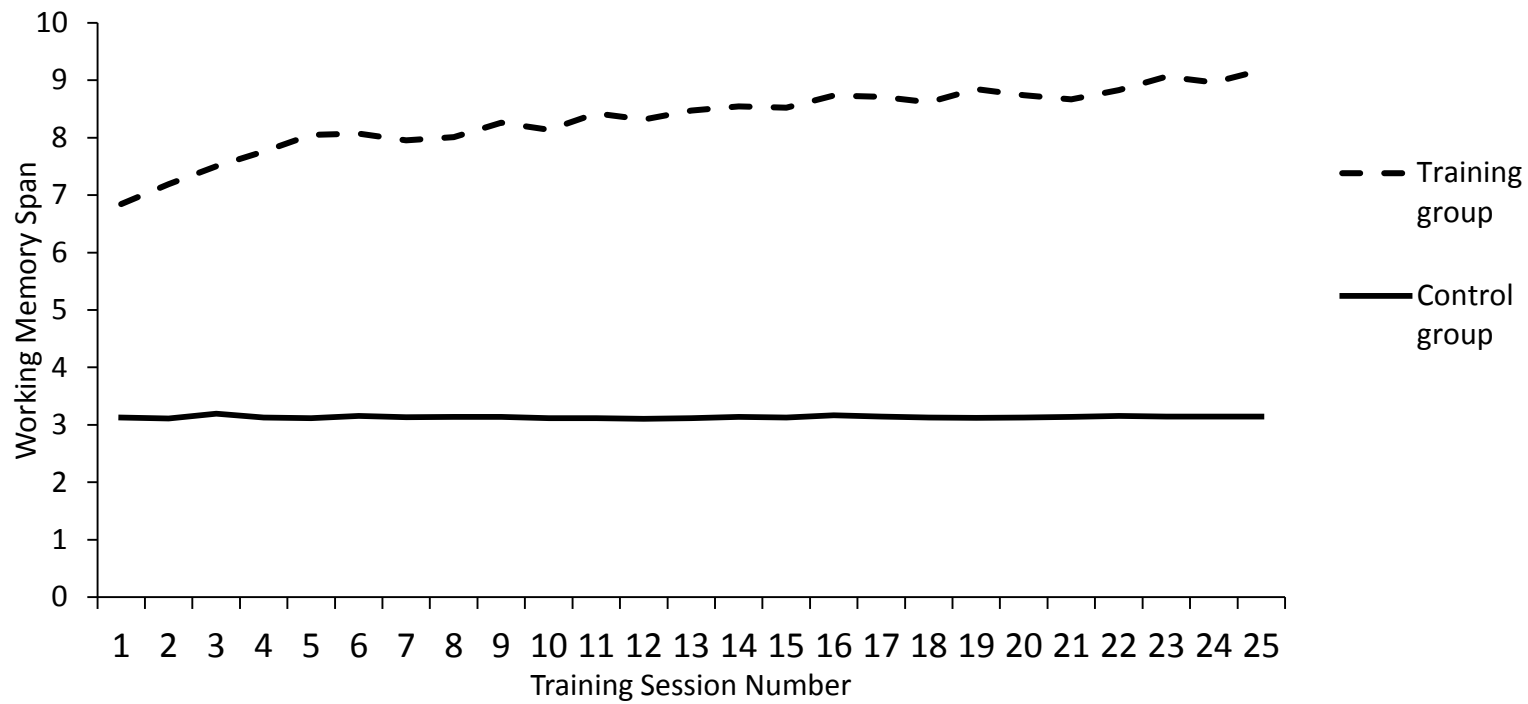
**Note.** HbA1c = glycated haemoglobin; DSQOL = diabetes-specific quality of life; SDSCA = summary of diabetes self-care activities; DSES = dietary self-efficacy scale; PHQ-9 = patient health questionnaire; DEBQ = Dutch eating behaviour questionnaire; TFEQ = three factor eating questionnaire; GFCQ = general food cravings questionnaire.

## **Primary outcome measures**

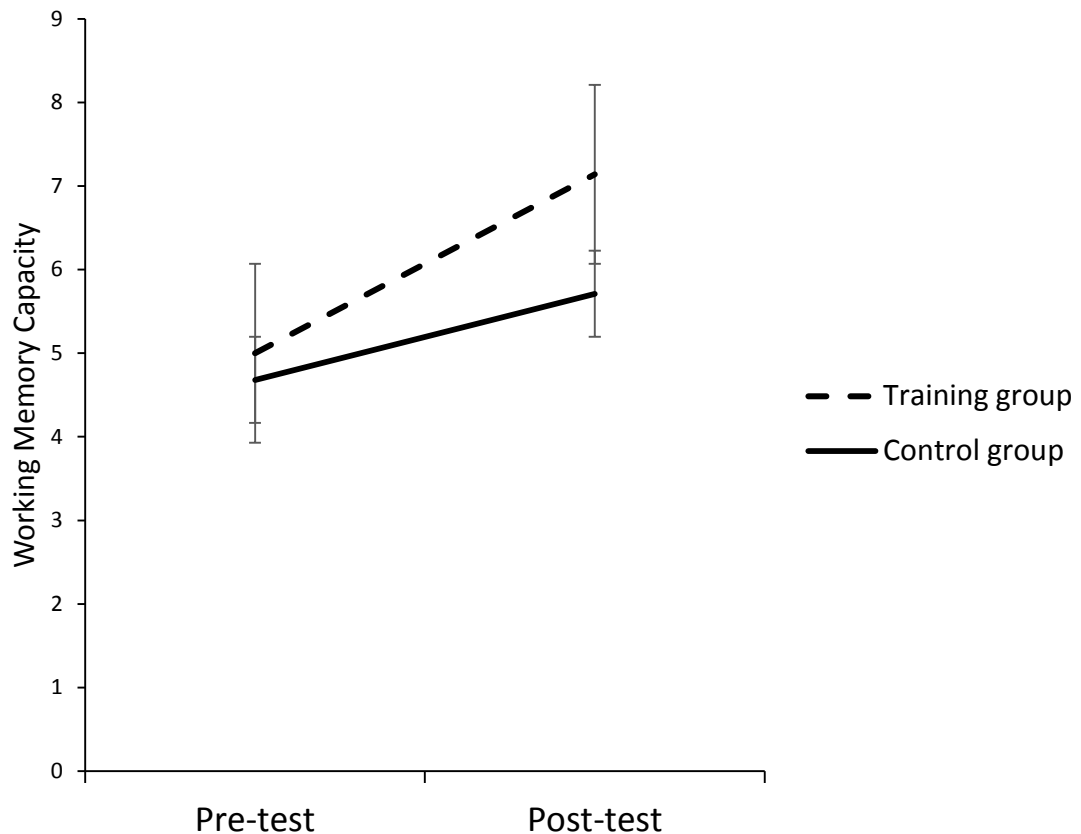
The means and standard deviations for the primary outcomes measures at pre-test and post-test as a function of condition are shown in Table 2. *F* values and effect sizes are also reported in Table 2.

### Working memory (trained tasks)

Figure 1 shows performance in each training session averaged across the three tasks. Working memory span gradually increased in the active training group. The control group always received the easiest level of the tasks (i.e. 3 items to remember), and hence performance of the control group remained at 3 across the training sessions. A mixed ANOVA revealed significant main effects of time, condition and a significant interaction between time and condition for WM span. Performance on the trained WM tasks over time increased significantly in the active training group but not in the control group (see Figure 2.). See Table 2 for means and standard deviations of each group across time, along with *F* values and effect sizes.



**Figure 1. Working memory span performance in each training session, averaged across the three training tasks, separately for the two training conditions.**



**Figure 2. Means and standard errors for working memory capacity at pre-test and post-test for the training and control group.**

Working memory (non-trained tasks)

#### *Spatial span test*

For spatial span maximum digits remembered and total errors, there were no significant main effects of time, condition nor any interactions between time and condition (all  $p$ 's > 0.05).

#### *Spatial working memory*

A mixed ANOVA on spatial WM strategy use showed non-significant main effects for time and condition (all  $p$ 's > 0.05). However, there was a significant interaction between time and condition, such that strategy use improved (shown by a decrease in score) from pre-test ( $M = 34.00$ ,  $SE = 1.07$ ) to post-test ( $M = 31.13$ ,  $SE = 1.12$ ) in the active training condition. Strategy use did not change from pre-test ( $M = 32.58$ ,  $SE = 1.20$ ) to post-test ( $M = 33.48$ ,  $SE = 1.24$ ) in the control group. For total errors, there was a significant main effect of time, and a marginal effect of condition, but a non-significant interaction. Over



time, the mean total number of errors decreased (pre-test:  $M = 51.04$ ,  $SE = 2.35$ ; post-test:  $M = 44.69$ ,  $SE = 2.35$ ). Overall, the active training condition made fewer errors ( $M = 43.90$ ,  $SE = 2.79$ ) than the control group ( $M = 51.84$ ,  $SE = 3.13$ ). For mean time to last response (level 10), there was a trending effect of time ( $p = 0.08$ ), but no effect of condition nor any interaction between time and condition. Mean time to last response was slightly less at post-test ( $M = 76561.96$ ,  $SE = 1917.98$ ) than pre-test ( $M = 79552.99$ ,  $SE = 2051.57$ ).

#### Attention switching task

For congruency cost, there was no main effect of condition, time, nor any interaction between time and condition (all  $p$ 's  $> 0.05$ ). For switching cost, there was a significant effect of time, but a non-significant effect of condition and no interaction between time and condition. A close to zero score indicates no difference in response latencies between blocks where the rule switched and did not switch. The main effect of time shows that the switching cost score was closer to zero at post-test than pre-test (pre-test:  $M = 356.37$ ,  $SE = 20.13$ ; post-test:  $M = 324.86$ ,  $SE = 23.12$ ), and therefore there was less variation in response latencies between switching and non-switching blocks (i.e. less preference for non-switching blocks).

#### Food-specific inhibitory control

There were no effects of time, condition nor an interaction between time and condition on commission errors (all  $p$ 's  $> 0.05$ ).

#### Paired associates learning task

For total number of errors (adjusted for the number of levels reached), the main effect of time was approaching significance ( $p = 0.07$ ), but there was no effect of condition nor any interaction between time and condition. There were no effects of time, condition nor the interaction on first trial memory score (all  $p$ 's  $> 0.05$ ).

#### Food intake

##### *Buffet taste-test and 24 HR recall*

There were no differences between groups prior to the lunch buffet taste-test for: hunger, (condition:  $F(1,69) = 0.84$ ,  $p = 0.36$ ,  $\eta^2 = 0.01$ ; time:  $F(1,69) = 0.36$ ,  $p = 0.55$ ,  $\eta^2 = 0.01$ ; condition x time:  $F(1,69) = 0.03$ ,  $p = 0.87$ ,  $\eta^2 < 0.001$ ); liking of the LED foods, (time:

$F(1,67) = 0.83, p = 0.37, \eta^2 = 0.01$ ; condition:  $F(1,67) = 0.92, p = 0.34, \eta^2 = 0.01$ ;  
condition x time:  $F(1,67) = 2.22, p = 0.14, \eta^2 = 0.03$ ); or liking of the HED foods (time:  
 $F(1,62) = 0.92, p = 0.34, \eta^2 = 0.02$ ; condition:  $F(1,62) = 0.35, p = 0.56, \eta^2 = 0.01$ ;  
condition x time:  $F(1,62) = 0.06, p = 0.80, \eta^2 = 0.001$ ). Mixed ANOVAs found no effects  
of time, condition, nor any interaction between time and condition for sandwich intake,  
HED intake, LED intake, kilocalories or grams of saturated fat consumed (all  $p$ 's  $> 0.05$ ;  
see Table 2.).

**Table 2. Means and standard deviations for primary outcome measures at pre-test and post-test as a function of condition.**

	Active training		Control training		Time	Condition	Interaction
	Pre-test	Post-test	Pre-test	Post-test	$F (\eta^2)$	$F (\eta^2)$	$F (\eta^2)$
Trained working memory	5.00	7.14	4.68	5.71	129.17**	26.96**	15.73**
	(1.00)	(1.49)	(1.00)	(1.13)	(= 0.65)	(= 0.16)	(= 0.19)
SSP maximum digits	5.82	5.73	5.56	5.78	0.29	0.88	0.24
	(1.05)	(1.08)	(0.95)	(0.70)	(= 0.004)	(= 0.01)	(= 0.003)
SSP total errors	14.46	12.53	14.19	13.30	2.55	0.01	0.24
	(5.49)	(3.53)	(5.77)	(4.28)	(= 0.04)	(< 0.001)	(= 0.003)
SWM strategy use	34.00	30.37	32.13	33.07	2.14	0.10	7.85*
	(5.63)	(7.78)	(8.08)	(6.43)	(= 0.03)	(= 0.001)	(= 0.10)
SWM extra inspections	46.41	39.67	54.28	47.41	9.12*	3.60	0.40
	(19.71)	(21.28)	(20.64)	(17.43)	(= 0.12)	(= 0.05)	(= 0.01)

SWM mean time to last response	78345.53 (18264.97)	75221.28 (16911.21)	79959.42 (15793.32)	76944.63 (15251.59)	3.19 (= 0.05)	0.50 (= 0.01)	0.01 ( $< 0.001$ )
AST congruency cost	63.24 (57.83)	54.99 (43.51)	81.02 (45.49)	77.29 (53.29)	0.71 (= 0.01)	2.04 (= 0.03)	0.04 (= 0.001)
AST switching cost	329.68 (146.06)	297.66 (183.27)	391.70 (151.70)	351.29 (161.22)	4.37* (= 0.06)	1.71 (= 0.02)	1.42 (= 0.02)
Food-specific commission errors	1.62 (1.52)	1.54 (1.57)	1.40 (1.77)	1.10 (1.27)	0.53 (= 0.01)	1.08 (= 0.02)	0.53 (= 0.01)
PAL errors adjusted	29.00 (15.55)	20.13 (18.84)	25.00 (16.68)	24.68 (20.86)	3.50 (= 0.05)	0.34 (= 0.01)	0.91 (= 0.01)
PAL first trial memory score	10.28 (2.53)	11.43 (3.52)	10.78 (2.83)	10.21 (3.78)	0.26 (= 0.004)	0.01 ( $< 0.001$ )	1.57 (= 0.02)
Sandwich intake	123.38	118.59	128.65	129.39	0.12	0.25	0.16

	(66.02)	(65.99)	(70.32)	(81.65)	(= 0.002)	(= 0.004)	(= 0.002)
HED food intake (grams)	46.34	51.90	50.87	48.23	0.16	0.001	1.86
	(31.12)	(39.57)	(33.83)	(31.59)	(= 0.002)	(< 0.001)	(= 0.03)
LED food intake (grams)	104.25	104.09	96.40	96.74	0.05	0.24	0.06
	(62.98)	(73.48)	(40.58)	(47.94)	(= 0.001)	(= 0.004)	(= 0.001)
Total calories (kcal, 24-hour recall)	1828.06	1818.09	1806.41	1920.42	0.54	0.05	0.77
	(663.32)	(654.16)	(896.38)	(1024.60)	(= 0.01)	(= 0.001)	(= 0.01)
Total saturated fat (grams, 24-hour recall)	29.69	29.04	27.50	27.86	< 0.001	0.01	0.08
	(16.88)	(17.27)	(17.36)	(21.44)	(< 0.001)	(< 0.001)	(= 0.001)

**Note.** SSP = spatial span task; SWM = spatial working memory task; AST: attention switching task; PAL = paired associates learning task; HED = high energy dense; LED = low energy dense; \*  $p < .05$

## Secondary outcomes

The means and standard deviations for the secondary outcome measures at pre-test and post-test as a function of condition are shown in Table 3. *F* values and effect sizes are also reported in Table 3.

### HbA1c

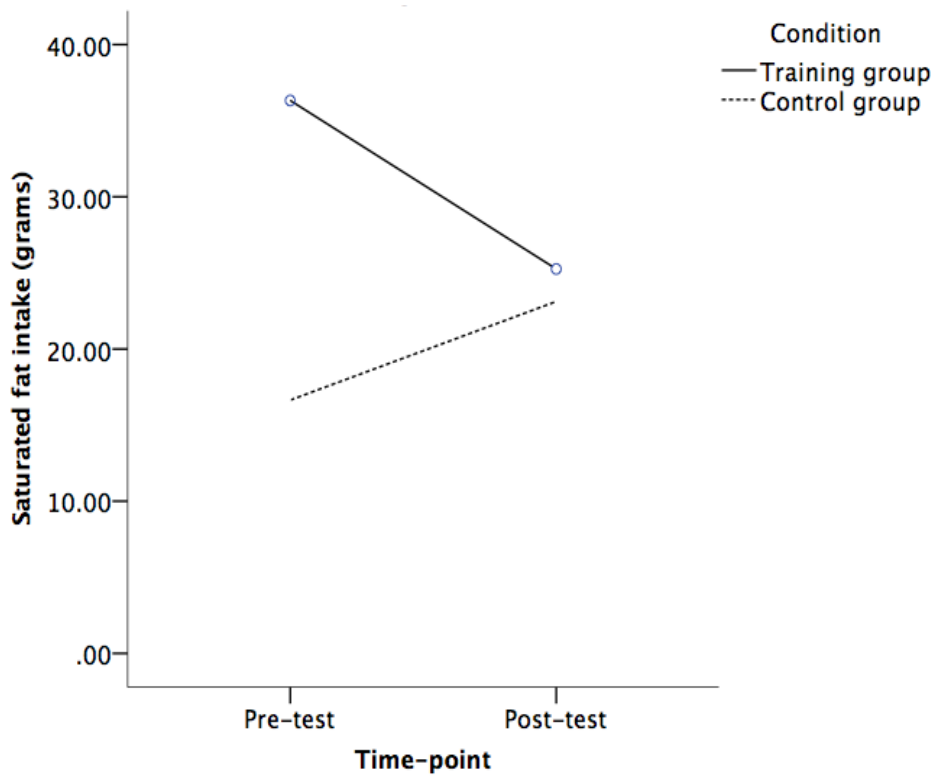
For HbA1c, there was a marginally significant main effect of time, such that over time HbA1c levels increased (pre-test:  $M = 56.51$ ,  $SE = 1.75$ ; post-test:  $M = 57.81$ ,  $SE = 1.82$ ). There was no significant main effect of condition nor an interaction between time and condition.

### Lipids

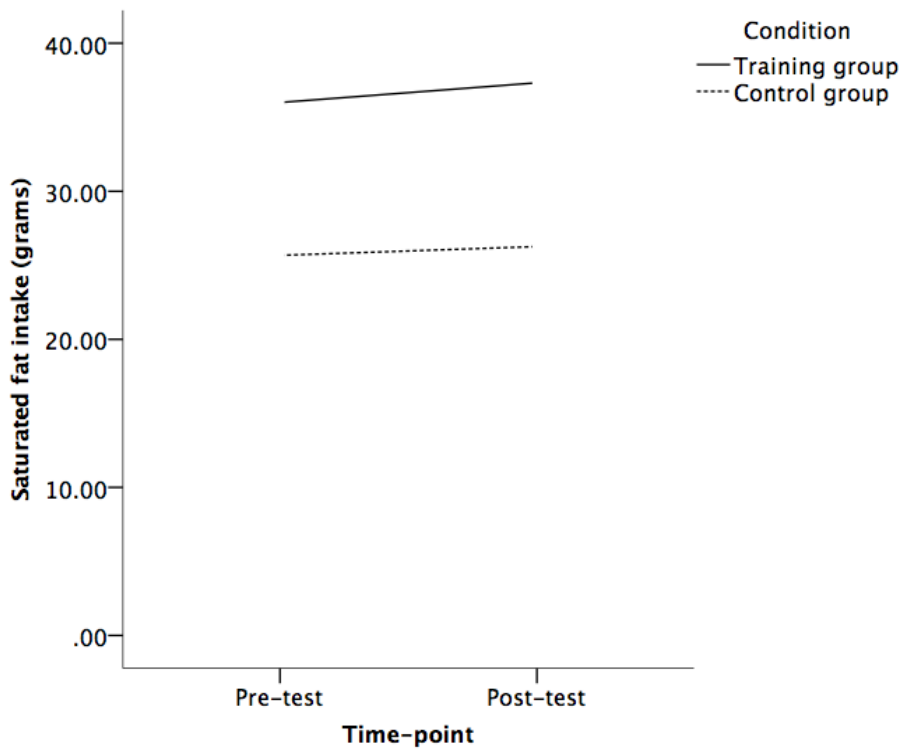
For total cholesterol, there was no main effect of time or condition and no significant interaction between time and condition.

## Post hoc analyses

Since the protocol for this study was published, it was reported that WM training in overweight/obese adults reduced food intake only in participants scoring high on a measure of dietary restraint (Houben, Dassen, & Jansen, 2016). To assess whether this was also the case in the current study, post hoc analyses using model 1 in the PROCESS macro for SPSS were run (Hayes, 2013). Change in food consumption from pre-post test was entered as the dependent variable (sandwich, HED, LED grams, total kcal and saturated fat), condition (active training vs control group) was entered as the independent variable and baseline dietary restraint (DEBQ) was entered as the moderator. There were no main effects of restraint or condition on any outcomes. There was, however, a significant interaction between restraint and condition on change in saturated fat intake ( $b = -9.66$ ,  $t(67) = -2.27$ ,  $p = 0.03$ ). In those high in dietary restraint (+ 1 SD) there was a marginally significant greater reduction in saturated fat intake in the training group than in the control group ( $b = -8.32$ ,  $t(67) = -1.92$ ,  $p = 0.06$ ). This effect did not exist at low levels of restraint ( $b = 6.38$ ,  $t(67) = 1.20$ ,  $p = 0.24$ ). Figures 3 and 4 show the effect of condition on saturated fat intake in those with high and low levels of restraint, respectively. The interaction between restraint and condition was not significant for any other primary or secondary outcomes (all  $p$ 's > 0.05).



**Figure 3. The effect of condition on saturated fat intake (grams) over time in those with high levels of restraint (+ 1 SD).**



**Figure 4. The effect of condition on saturated fat intake (grams) over time in those with low levels of restraint (- 1 SD).**

### **Dietary adherence and self-efficacy post hoc analyses**

Houben et al. (2016) also found changes in self-reported eating behaviour and eating styles. This was tested in the current study using ANOVAs on GFCQ state craving scores, SDSCA general and specific dietary adherence scores, and DSES mean score for dietary self-efficacy. The only effect found was a significant effect of time on state cravings (such that scores decreased over time; pre-test  $M = 25.05$ , post-test  $M = 22.45$ ), but no effect of condition or of the interaction between the two.



**Table 3. Means and standard deviations for secondary outcomes measures at pre-test and post-test as a function of condition. <sup>2</sup>**

	Active training		Control training		Time	Condition	Time x Condition
	Pre-test	Post-test	Pre-test	Post-test	<i>F</i> ( $\eta^2$ )	<i>F</i> ( $\eta^2$ )	<i>F</i> ( $\eta^2$ )
HbA1c (mmol/mol)	53.99 (15.34)	54.86 (14.92)	58.40 (12.19)	59.97 (13.58)	4.01* (= 0.06)	1.56 (= 0.02)	0.80 (= 0.01)
Total cholesterol (mmol/L)	4.48 (1.04)	4.49 (1.04)	4.33 (0.90)	4.36 (1.05)	0.04 (= 0.001)	0.21 (= 0.003)	0.26 (= 0.004)
DEBQ dietary restraint	2.90 (0.81)	2.89 (0.76)	2.781 (0.70)	2.77 (0.67)	0.09 (= 0.001)	0.47 (= 0.01)	0.01 (< 0.001)
DEBQ emotional eating	2.11 (0.90)	1.94 (0.94)	2.453 (0.56)	2.28 (0.86)	9.58* (= 0.12)	2.99 (= 0.04)	< 0.001 (< 0.001)
DEBQ external eating	2.78	2.74	3.01	2.87	5.16*	1.66	1.40

	(0.69)	(0.57)	(0.56)	(0.65)	(= 0.07)	(= 0.02)	(= 0.02)
TFEQ uncontrolled eating	33.81	32.67	39.47	36.57	2.08	1.08	0.39
	(19.82)	(19.50)	(21.03)	(20.37)	(= 0.03)	(= 0.02)	(= 0.01)
GFCQ state cravings	22.97	21.28	27.13	23.63	5.92*	1.76	0.72
	(10.35)	(10.96)	(12.85)	(10.73)	(= 0.08)	(= 0.03)	(= 0.01)
DSES	57.88	55.85	49.44	51.61	0.002	1.94	1.37
	(20.29)	(21.79)	(21.21)	(18.48)	(< 0.001)	(= 0.03)	(= 0.02)
SDSCA general diet	3.73	4.35	4.03	4.24	0.48	0.07	1.16
	(1.74)	(2.04)	(1.61)	(2.02)	(= 0.01)	(= 0.001)	(= 0.02)
SDSCA specific diet	3.97	3.82	4.39	4.27	1.01	1.12	0.20
	(2.31)	(1.52)	(1.87)	(1.63)	(= 0.01)	(= 0.02)	(= 0.003)

**Note: HbA1c = glycated haemoglobin; DEBQ = Dutch Eating Behaviour Questionnaire; TFEQ = Three Factor Eating Questionnaire; GFCQ = General Food Cravings Questionnaire; DSES = Dietary Self-Efficacy Scale; SDSCA = Summary of Diabetes Self-Care Activities; \*  $p < .05$**

## **Findings from qualitative interviews**

Two over-arching themes were identified in relation to participants' experiences of the training: acceptability and performance. Under acceptability there are 6 sub-themes and under performance there are 2 sub-themes. These themes will be discussed in turn with supporting evidence from appropriate extracts from the interviews (participant number is indicated for each). See Figure 3 for a model of the main themes and sub-themes.

### Acceptability

Acceptability of the training was a key theme in participant's interviews. The 6 sub-themes demonstrate that there were many factors that affected the acceptability of the training to participants.

#### *Sub-theme 1: Enthusiasm for the training*

Enthusiasm for many participants declined as they progressed through the training program. For example, "it soon became more of a chore... than something you wanted to do." (PP021) and "tedious because you knew you were gonna have this experience every day... uhm and it it became... laborious in the end... and not particularly enjoyable... you did it because you thought you should because you've committed to this and its best to finish it..." (PP014). This decline in enthusiasm for the training clearly affected acceptability of the training as participants often described struggling to reach the end of the training, as demonstrated in the previous quotes. A minority of participants found the training enjoyable and demonstrated maintained enthusiasm throughout the training program. For example, "I really enjoyed the online training..." (PP028). For these participants, their maintained enthusiasm for the training boosted its acceptability. A clear demonstration of how enthusiasm affected acceptability of the training is also clear from one participant's description of the balance between tedium and the desire to improve "cos i think there are two factors at least in play here... there's the one where... you know you're trying to improve something... so you want to improve... so there's a challenge to it... and you want to do it... but on the other side balancing that... there's the tedium factor... especially when your sort of set 30 at a time... and there's that sort of period where you think... the tedium is outweighing the... the sort of desire to get better..." (PP021). Participants suggested one potential solution to the common decline in enthusiasm for the training would be to include a greater variety of tasks that perhaps changed during the training, for example, "more variation to keep people's interest" (PP208).

### *Sub-theme 2: Intrusive*

Participants reported that the training was intrusive to both family and leisure life, and to a lesser extent, working life. Participants described having to ask family members and colleagues to leave them alone to get on with the training, for example, “I had to tell my wife to go upstairs... watch TV in the room whilst I was on my laptop at the dining table” (PP038). On occasion family members got offended and upset, for example, “my grandson came up and wasn’t very happy when I was doing it and I lost concentration completely when he came up and actually he was a bit upset as he thought he had upset me...” (PP208). The intrusive nature of the training is clearly shown by one participant who said “I see it in my dreams you know... when I’m sleeping it’s there you know...” (PP034). The intrusive nature of the training wasn’t always negative, however, as for some participant’s their family enjoyed getting involved, for example, “and of course sometimes I had my wife and my daughter looking over me while I was doing it... and they was sort of concentrating on their own... not saying anything... but they was sort of doing it themselves” (PP033). The intrusive nature of the training appeared to have a strong influence on the acceptability of the training.

### *Sub-theme 3: Fitting the training into one’s life*

How participants managed to include the training program into their life varied greatly across participants. For some, fitting the programme in was relatively easy due to them being retired or currently not working, for example, “well I’m retired now so I’m at home... a lot... so it’s just a case of when I looked at me emails picking up on it and clicking on it...” (PP014). For most participants, it was a case of trying to find time either at work, for example, “it was... it was just finding half an hour... uh it was mainly at work... so once my normal work had finished... and... before uh catching the commute back... uhm just managed to fit it in then” (PP025); or late at night, for example, “by doing it later at night after I’ve finished things that I needed to do” (PP015). Some participants fitted the training into their daily routine, while others fitted it in around what they were doing that day, for example, “I do early morning one day... I do middle of the night... whenever I wanted to do it... because of the different uhm hospitals appointments I couldn’t do it at 10 o’clock...” (PP027). Many participants tried doing the training at different times of the day to see if it affected their performance, for example, “I started playing on the time of day... I found I could do better in the evening than in the morning”

(PP011). There seemed to be greater acceptability of the training in those who found it easier to fit the training into their life.

#### *Sub-theme 4: Link between training and study aims*

Participants reported finding it difficult to understand how WM training may change eating habits and diabetes control. One participant stated “you know it's hard to find the correlation... between like the tests on the screen and what I'm eating and my blood sugar...” (PP017). This lack of understanding of the link between the training and eating habits/diabetes control was mentioned by the majority of participants, even after the researcher had explained the rationale in the first assessment session. It seems that this lack of understanding by many participants affected their enthusiasm for and acceptability of the training. As one participant mentions “if I had of understood more or less what... you're trying to achieve I possibly would have tried even harder... to improve my... my short-term memory” (PP017).

#### *Sub-theme 5: Usability of the training program*

Usability of the program emerged as an important experience of participants. Participants commented on the many ways in which the program could have been more user-friendly, for example, “a couple of times what happened was... you were sent the email and you couldn't correlate whether you've done it or whether you still had to do it... you have the email and then you go ‘have I done this one now or do I still have to?’” (PP017). Similarly, participants found it very difficult to use the scoring system that was displayed as they completed the training tasks, “I hardly had time to look at it... I was so busy concentrating on the task itself I mean... to sort of glance up at the score... would have taken a few seconds that I felt I didn't have...” A number of participants pointed out that the training would have been easier to do if it was compatible with tablet devices, “I could have just shut myself in the bedroom whereas the... the laptop was either in my daughter's room... or my son's room... or the office...”. There were clearly a number of technical and usability issues that if rectified or improved would likely increase acceptability of the training.

#### *Sub-theme 6: Commitment*

Participants felt that the training was a big commitment for them, but also showed some understanding that you need to do a certain amount of training in order to see some benefits for example, “I should imagine that has been calculated to have some effect on

the brain... so I wasn't sort of annoyed about that" and "6 would have been useless you know" (PP009). The time each training session took also didn't seem to be a problem, for example, "the time is yeah I think it's alright" (PP034). However, importantly, this may have been related to the fact that participants felt this was for research and felt that "if I was to do it for a longer period of time... without getting any benefit out of it I would maybe not do it". Feeling that they were getting something out of the training seemed to be an important factor to acceptability in relation to the amount of time and commitment required to do the training.

Overall, the acceptability theme demonstrates that key issues for participants were maintaining their enthusiasm for the training, managing to include it into their life, and the often too intrusive nature of the training. The usability of the training program, along with a lack of understanding of how WM training may improve dietary habits and diabetes control, also limited the extent to which participants found the training acceptable. The training also required a large amount of commitment from participants, which this group of participants, that completed the training, generally found acceptable.

## Performance

The performance theme encompasses two sub-themes: expectations versus reality, and tactics.

### *Sub-theme 1: Expectations versus reality*

Most participants had expectations that the training may improve their WM, willpower, eating habits or diabetes control. For example, "well I thought it was brain training to enable you to make more decisions about... choosing foods in diabetes..." (PP009). Others took part simply to help diabetes research progress or to help the author complete her PhD. For example, "it started actually... you are doing a lot of work... hard work... but you need some... patients... to help... if we don't help you... you can't find out what's going on with these people diabetic people..." (PP027). What participants actually experienced however, was in fact very little, if any, change in their eating habits and diabetes control. For example, "I don't think my blood sugar came down at all... in this period..." (PP017), and "all I would say is as of today... it doesn't appear... to have made me think "ah my higher brain is now taking control... wake up lazy brain"... you know..." (PP021).

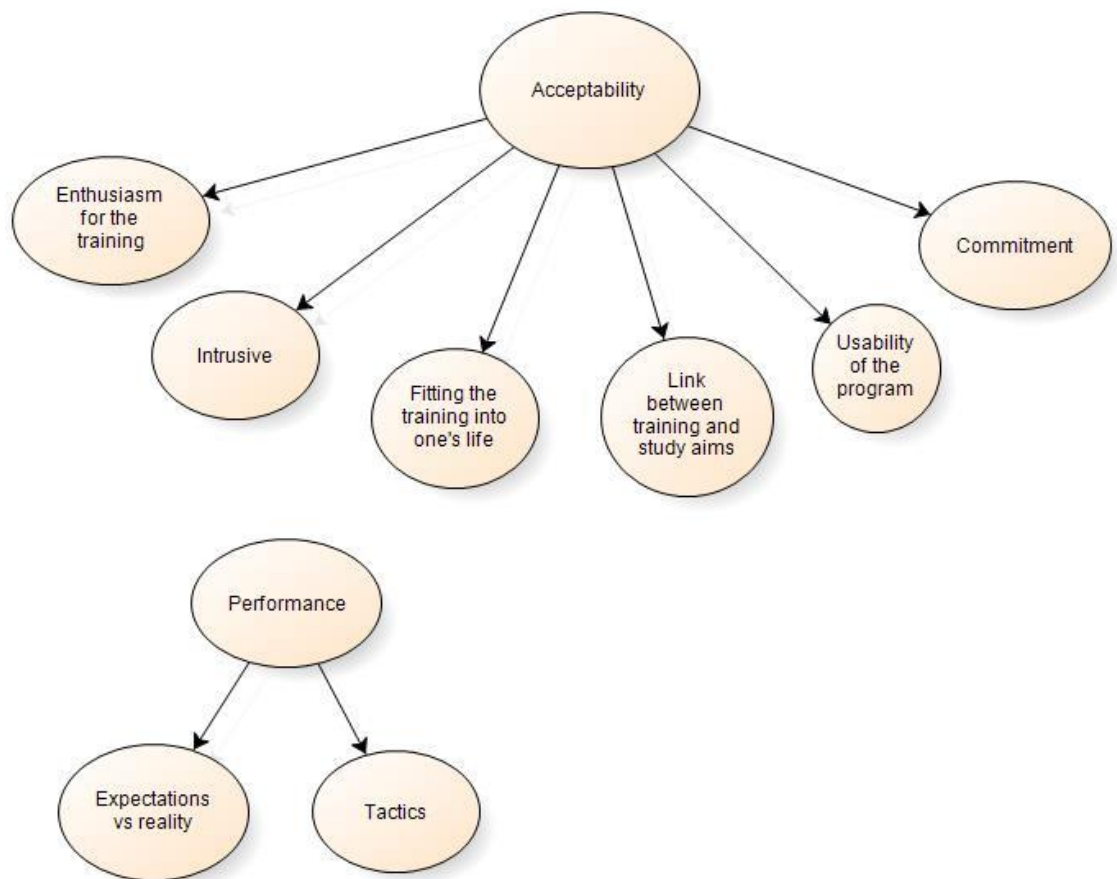
The majority of participants reported seeing improvements in their WM. For example, "but I did notice that on some of the exercises I improved... so like the numbers I think I

got started off with 6 numbers that I could remember and towards the end I think I was remembering up to 8 9 numbers you know...” (PP017). However, participants also reported feeling like they had reached the most they were going to be able to remember before the end of the training, for example “I’d say it was about two thirds of the way through... because I was getting the same number of tasks coming up... and I knew I was stretching myself” (PP033).

### *Sub-theme 2: Tactics*

The majority of participants developed tactics to help them do the training, such as “... I would chant the letters out loud” (PP220), “saying the letters in threes” (PP009), and “I tried to draw patterns... I had certain patterns on the grid and I was trying to sort of see if it was equally spaced and work out a little pattern thing” (PP015). For most people these tactics were employed to help them do better on the tasks, whereas others used them to reduce the effort needed to do the training, for example “I used them thinking how can I get the same scores without getting so many numbers to remember...” (PP208).

The performance theme shows that there were clearly discrepancies between what participants expected to achieve from doing the WM training and what they felt they actually achieved from doing it. The use of tactics is also interesting and is discussed further in the discussion section.



**Figure 3. Thematic map of patient's experiences of the working memory training.**

## 5.4 Discussion

The current study assessed whether WM training can reduce food intake and improve diabetes control in adults with type 2 diabetes. Previous research has found WM training to reduce other health-harming behaviours. For example, Houben and colleagues (Houben et al., 2011) found WM training to reduce alcohol consumption in problem drinkers for one month after training. The current study applied this novel type of executive function training to eating behaviour. Further, the training was tested in people with type 2 diabetes, a population for whom changes in food intake could have a significant impact on health.

### Working memory training performance

The significant time by condition interaction on performance in the training tasks showed that WM training successful improved WM, and that improvements were greater in the active training condition than in the control training condition. These findings are in line with a recently published study investigating the effects of WM training in overweight/obese adults (Houben et al., 2016). Houben and colleagues also found



performance on the trained tasks to improve in both groups (active and control), but significantly greater in the active training group. Both this study and Houben et al's (2016) found that participants in the active training group could remember an average of 2 more items at post-training compared to pre-training. Both controls groups could remember an average of 1 more item. These data justify the inclusion of inactive training conditions as control groups in future research.

#### Near transfer effects

There was some evidence of near transfer effects, whereby performance in the active training group improved on non-trained measures of WM. More specifically, strategy use on the visuospatial WM task significantly improved over time in the active training group. Ability to use a strategy to perform the task reflects central executive capabilities (Goghari et al., 2014; Owen et al., 1990). The backwards digit span task in the WM training required use of the central executive to reverse the number sequences. This effect therefore demonstrates that training the central executive in one task (backwards digit span) transferred to another non-trained task that uses the central executive in a different modality (i.e. visuospatial). There was no evidence of transfer effects to other measures of WM (spatial span task) or to other executive functions (general inhibitory control as measured by the attention switching task and food-specific inhibitory control) or new learning/episodic memory (as measured by the paired associates learning task). The two previous studies testing WM training in health-related behaviour did not assess near transfer effects to other measures of cognition or non-trained WM tasks (Houben et al., 2016, 2011). Research testing WM training in children with learning difficulties/ADHD, as well as healthy young and old adults, have demonstrated near transfer effects. For example, studies have shown improvements in non-trained aspects of WM (Holmes, Gathercole, Place, Dunning, et al., 2010; Loosli, Buschkuehl, Perrig, & Jaeggi, 2012; Schmiedek, Lovden, & Lindenberger, 2010) and general cognition including vocabulary and spelling (Alloway, Bibile, & Lau, 2013), fluid intelligence (Jaeggi, Buschkuehl, Jonides, & Perrig, 2008; Klingberg et al., 2005), and sustained attention (Brehmer, Westerberg, & Bäckman, 2012). However, not all studies have found such improvements. For example, Holmes et al. (2009) found no improvements in intelligence despite using the same training and type of sample as Klingberg et al. (2005). Further, Jaeggi et al. (2008) found that N-back training improved reasoning abilities but not verbal WM abilities. Reviews of the transfer effects of WM training have found short-term improvements only in near or intermediate transfer effects (such as other aspects of WM),

and little evidence of reliable far transfer effects (Klingberg, 2010; Melby-Lervåg & Hulme, 2013; Melby-Lervåg, Redick, & Hulme, 2016). The results of the current study are in line with previous reports of transfer effects to a WM ability closely related to the training (central executive strategy use), but no transfer effects to other closely related (spatial span) or more distant cognitive abilities (inhibition, new learning and memory). The former finding is promising as it suggests that WM training does not need to train all WM sub-components for improvement in non-trained components to be observed. This is likely to make future WM training less time-intensive and taxing, and hence more acceptable to patients. The latter finding suggests that WM training effects do not extend to more distantly related aspects of cognition. However, for some tasks, there may have been little room for improvement. For example, both groups made only 1-2 commission errors on the food-specific no-go task at baseline.

#### Far transfer effects

There were no overall effects of WM training on either laboratory-based (lunch taste-test) or non-laboratory based (24-hour recall) food intake. There was an effect of active, but not control training to reduce reported saturated fat intake, but only in participants scoring high on restraint. This finding is consistent with the results from other studies on WM and response inhibition training on food intake (Houben et al., 2016; Houben & Jansen, 2011; Lawrence, Verbruggen, et al., 2015). Dietary restraint is an indicator of conscious effort and motivation to control food intake, and hence these findings suggest that WM training brings actual food intake more in line with dietary goals. Other findings suggest that in individuals with higher WM capacity, explicit attitudes and self-regulatory goals are a better predictor of food intake than in those with lower WM capacity (Hofmann, Gschwendner, et al., 2008). It is perhaps not that surprising, that improved WM abilities are unlikely to be beneficial without the motivation to control food intake. However, it is a concern that WM training may be unlikely to be effective in people who do not already have some motivation to control their eating habits because such individuals are in most need of cognitive intervention to help them achieve dietary change.

There were no other significant effects found for any measures of food intake, or total cholesterol levels (a biological measure of fat consumption). It may be that there were no changes in the lunch buffet taste-test because of the unusual context of eating in the laboratory, in which participants may have felt inhibited. However, on average, the participants consumed an expected amount for a lunch time meal (almost a whole

sandwich and a number of the snacks), and hence this explanation is unlikely. Most participants believed that I was assessing what they ate in some way when probed at the end of the study (data not reported here). Therefore, while participants ate a normal total amount of food for a lunch time meal, their choices of different foods (e.g. HED vs LED snacks) may not have been their usual choice. If participants were eating as they thought they should be in the taste-test, there would likely have been little scope for changing these choices via the training. It is promising that changes in non-laboratory based food intake were found (24-hour recall saturated fat intake), as changes in behaviour in daily life are the most important as they are more likely to continue after training than changes found in the laboratory. It may be surprising that 24-hour recall saturated fat intake was reduced in restrained eaters but cholesterol levels in the blood was not. However, cholesterol levels are influenced by consumption of other types of fat and not just saturated fat (e.g. trans fat), and hence the changes in saturated fat may not have been sufficient to reduce total cholesterol. The average baseline cholesterol level was 4.4 mmol/L, whereas current NHS guidelines (NHS Choices, 2015b) suggest this should be below 4 mmol/L in those at high risk of high cholesterol levels (which includes those with diabetes). Therefore, floor effects are unlikely to have been a problem here.

There was also no change in HbA1c levels following WM training in the present study. This is not surprising considering that the only effect on food intake was on saturated fat, whereas HbA1c is a measure of average plasma glucose concentration. There was, however, a marginal main effect of time on HbA1c levels, where levels increased from pre-test to post-test. Diabetes is a progressive disease whereby the body's ability to deal with blood glucose declines over time (Fonseca, 2009). This main effect of time suggests that WM training did not slow the normal progressive nature of diabetes. Average HbA1c level of the sample was 55.89 mmol/mol. This is above UK guidelines (48 mmol/mol; NICE guideline, 2015), and hence there should have been no floor effects for improving HbA1c levels.

Post-hoc analyses looked at the effect of training on self-reported measures of dietary adherence, self-efficacy and food cravings. The only effect found was a main effect of time on state food cravings, whereby these decreased over time in both groups. It is unlikely that there were ceiling effects preventing improvements on these tasks. For example, participants reported that in a single week, they followed both their general and specific dietary plans approximately 4 days a week. Dietary self-efficacy was also not very high. The highest possible score on this questionnaire is 100, which would suggest that a

person felt they could adhere to their dietary regime 100% of the time in an array of different situations (such as negative emotions or while watching TV). In both groups participants felt they could stick to their dietary regime only about 50% of the time in any given situation. Participants also did not report particularly high levels of dietary restraint.

#### Findings from the interviews

Thematic analysis of the interviews suggests that key themes in participants' experiences of the training were acceptability and performance. These findings suggest that, in its current format, WM training was not acceptable to participants. A number of changes would need to be made to the training to make it acceptable, such as fewer and shorter training sessions and a clearer relevance to eating behaviour and diabetes control. Introducing novel tasks during the training may also help maintain enthusiasm and motivation for the training.

#### Study strengths, limitations and suggestions for future research

The present study sample was highly educated, with about half the sample having completed higher education. Contact with some of the participants who decided to withdraw from the study suggested that for many people the training required too much time commitment, which is supported by the interview responses. Those who finished the training were therefore more motivated to continue with the training than those who withdrew. A number of people could not take part in this study because they could not use a computer or did not have access to one at home. These factors may have contributed to the selection of a sample that was well educated and of a higher socioeconomic status. The effects of the training found here may therefore not be generalizable beyond this well-educated and fairly motivated sample.

The current study implemented two different measures of food intake: a lunch buffet taste-test and a 24-hour recall test. These methods have both strengths and limitations. Self-reported measures of food intake (such as 24-hour recalls) are subject to underreporting bias (Hill & Davies, 2001; Schoeller et al., 2013). Attempts to reduce these effects were made by asking for contextual information about eating episodes in an attempt to aid accurate recall (Armstrong & MacDonald, 2000). Despite this limitation, 24-hour recalls are still the recommended method of assessing acute changes in food intake by the National Cancer Institute (National Cancer Institute, 2016). One strength of the 24-hour recall test is that the reported intake may reflect more usual food intake, whereas tasting

and rating food within the laboratory is an unusual situation, and there are arguments that contextual information that typically guides food intake is missing (De Castro, 2000). Taste-tests are also limited to a small range of foods that may not be representative of the foods that the participants find difficult to resist eating. Twenty-four hour recalls are more likely to capture such problematic foods. Taste-tests do however provide a measure of actual food consumption, and hence are not subject to underreporting.

Despite the large effect size of performance on the trained working memory tasks (partial  $\eta^2 = 0.19$ , Cohen's  $d = 0.97$ ), near transfer effects were very limited. Specifically, there was an improvement only on central executive strategy use in the training group (partial  $\eta^2 = 0.1$ , Cohen's  $d = 0.67$ ). This suggests that training working memory transferred to a more complex visuospatial working memory task (that required updating and hence utilised the central executive) and not a simple visuospatial span task. Considering that simple visuospatial span was one of the training tasks, it not clear why this pattern of transfer effects was found, and hence it cannot be excluded that this is a spurious finding. It may also be of concern that the training reduced saturated fat intake, but did not influence any of the other measures of food intake. However, as already mentioned, taste-test tasks and 24-hour recalls are very different tasks that have their respective strengths and weakness, which may have influenced the pattern of results. For example, demand characteristics in the taste-test task may have masked apparent effects of the training on food intake. Further, the reduction in saturated fat intake found may not have been sufficient to reduce total calorie intake, which was also an outcome measure from the 24-hour recall tasks. Nonetheless, the effect of the training on saturated fat intake (in those high in restraint), supports a clinically relevant effect, such that saturated fat consumption reduced by 8.32 grams in the active training condition.

Future research should investigate the efficacy of WM strategy training to change eating behaviour. According to Morrison and Chein (2011), there are two types of WM training: WM capacity training and WM strategy use training. WM capacity training aims to improve the basic capacities of WM, such as the number of items that can be held in mind at a given time. This is the approach taken in the present study and those by Houben and colleagues (Houben et al., 2016, 2011). Alternatively, WM strategy training aims to improve a person's ability to use their WM and better remember items. Such training has involved instructing participants to group information into chunks (St Clair-Thompson, Stevens, Hunt, & Bolder, 2010) and use chaining to create mental stories (McNamara & Scott, 2001). The transfer effects of WM strategy training to both related cognitive tasks

and every day behaviour (such as language comprehension) has been demonstrated (Carretti, Borella, Zavagnin, & De Beni, 2012). However, the effects of such training in health-related behaviour remains to be tested. Considering the theorised role of WM in eating behaviour, WM strategy training may have more potential for transfer effects to eating behaviour than WM capacity training. Important components of WM to self-regulation of behaviour include not only the amount of information that can be held active at any given time, but also the ability to hold in mind information stored in long-term memory (e.g. dieting goals) and to maintain focused attention on currently active information while preventing the interference of other potentially distracting information (Hofmann, Gschwendner, et al., 2008; Hofmann et al., 2012). It therefore follows that a person's ability to use their WM and maintain information held in WM is likely to be more influential on food intake behaviour than the amount of information that can be stored. It is interesting to note here that an important sub-theme identified from the interviews with participants in the present study was the use of tactics and recall strategies akin to that used in WM strategy training, such as reports of chunking information and verbal rehearsal. Teaching participants about these kinds of tactics before they start the training might be a part of future training programmes.

Individual differences in dietary restraint and BMI have been shown to be an important factor moderating the effectiveness of cognitive training interventions (Lawrence, Verbruggen, et al., 2015; Veling et al., 2014). Hence a "one-size fits all" training is unlikely to be effective. Future research should continue to assess the moderating role of individual differences and identify for whom these types of training are likely to be successful. Since little is known about the vast array of individual differences that could be involved, one potential solution is to combine different types of cognitive training. Evidence exists to support a wide range of types of cognitive training, such as stop-signal/no-go training (Lawrence, Verbruggen, et al., 2015; Veling et al., 2013b) and attentional bias modification training (Werthmann et al., 2014). Combining different types of training may have additive effects and be more effective for a wider range of people. Pilot testing of training that combines multiple types of food response training has shown greater reduction in percent body fat compared to a control group (Stice, Lawrence, Kemps, & Veling, 2016).

A further point to consider is that the greatest amount of WM improvement occurred by the 6<sup>th</sup>/7<sup>th</sup> training session in both the present study, and that of Houben and colleagues (2016). While performance continued to improve after the 7<sup>th</sup> session, it was more gradual,

possibly because initial improvements were relatively easy, but once participants reached the higher levels of the task, it was harder and slower to improve performance.

Alternatively, as suggested from the interviews conducted in the present study, motivation and enthusiasm for the training declined for most people, and hence perhaps people were not trying as hard to increase their WM after 6/7 training sessions. Future research should examine whether similar improvements in WM can be achieved with fewer sessions to maximise enthusiasm and effort on the tasks.

In conclusion, WM training in adults with type 2 diabetes improved trained WM tasks and showed some near transfer effects to another measure of WM (central executive strategy use in the visuospatial domain). There was also evidence that active training reduced fat intake in those with high levels of dietary restraint. However, there was no evidence of transfer effects to other aspects of cognitive function (inhibitory control, new learning and memory), behavioural and biological measures of food intake (HED food, LED food, total calories and blood cholesterol levels) or diabetes control (HbA1c levels). There were also no effects of training on measures of dietary self-efficacy and adherence. These findings suggest that WM training may change food consumption in people with type 2 diabetes who are motivated to control their food intake. Future research should continue to assess the effects of individual differences on training efficacy and whether combining different types of cognitive training enhances efficacy. There may also be some merit to training WM strategy rather than capacity.

## **Chapter 6. The importance of cognition to self-reported food intake in the general population and in adults with type 2 diabetes using the UK Biobank cohort.**

### **6.1 Introduction**

Experimental and longitudinal research has demonstrated the importance of a wide range of cognitive abilities to dietary behaviour. This includes learning and memory (Higgs, Robinson, et al., 2012), executive functions, such as inhibitory control and working memory (Allom & Mullan, 2014; Hall, Lowe, & Vincent, 2014), and intelligence (Batty, Deary, & Macintyre, 2007). Diabetes is associated with a range of cognitive deficits (McCrimmon et al., 2012; van den Berg et al., 2009), and avoiding high fat and/or sugary foods is a key aspect of self-management of type 2 diabetes. Considering the importance of cognition to the control of food intake, it is possible that the cognitive impairments found in diabetes contribute to the reported difficulties controlling food intake. To my knowledge, only two studies to date have investigated the relationship between cognition and dietary self-care in type 2 diabetes. Compeán-Ortiz et al. (2010) found that immediate and delayed visual memory recall predicted 7% and 8% of the variance in ability to follow the prescribed diet, respectively. Asimakopoulou and Hampson (2002) implemented a range of cognitive assessments designed to assess cognitive flexibility, psychomotor efficiency, short-term and working memory, learning and immediate recall, and general and diabetes-specific problem solving. After controlling for age, pre-morbid IQ and depression, dietary self-care was predicted by performance on a measure of set-shifting ability (Wisconsin Card Sorting Task) and diabetes-specific problem solving only. No studies have yet assessed how cognitive function in diabetes relates to food consumption, and the relatively small samples used may have limited power to detect effects of other aspects of cognition. The research so far has also failed to control for a range of confounding factors.

Factors that have been reported to influence, or at least be associated with food intake, include age (Mattes, 2002; Rolls & McDermott, 1991), gender (O'Doherty Jensen & Holm, 1999; Rolls, Fedoroff, & Guthrie, 1991), ethnicity (Leung & Stanner, 2011; Storey & Anderson, 2014), income (Roberts, Cavill, Hancock, & Rutter, 2013; Storey & Anderson, 2014) and education level (Foods Standards Agency, 2007). Physical health factors have also been implicated in dietary intake, including body mass (Shay et al., 2012), smoker status (Subar, Harlan, & Mattson, 1990), physical activity (Martins, Morgan, & Truby, 2008), alcohol (Yeomans, 2010), sleep (Brondel, Romer, Nougues,



Touyarou, & Davenne, 2010), cancer (Read, Choy, Beale, & Clarke, 2006), respiratory problems (Hallin, Koivisto-Hursti, Lindberg, & Janson, 2006), vascular problems (Ness & Powles, 1997) and indeed diabetes (Nothlings et al., 2011). Psychological factors related to food intake include depression (Paykel, 1977) and anxiety (Herman et al., 1987; Weinstein, Shide, & Rolls, 1997). When investigating the relationship between cognitive functioning and dietary intake in both the general population and in those with diabetes, it is important to also consider the influence of multiple factors to be able to determine more reliably the importance of cognition. Since only a sufficiently large sample size will allow for the inclusion of a large number of potentially confounding factors, a large database is necessary. The UK Biobank cohort is one such large database that contains information on the self-reported food intake and cognitive function of half a million people in the UK.

The food intake measures used by the UK Biobank are a food frequency questionnaire and multiple 24-hour recalls over the course of one year. Information is also available (via researcher assessment and self-report) on a wide range of demographic, lifestyle, physical and psychological health factors. The measures of cognitive function used by the UK Biobank include fluid intelligence, prospective memory, simple reaction time, visual learning and memory, and short-term/working memory. Both memory and learning have been suggested to be important processes underpinning the control of food intake. The learning processes implicated include simple learning in the form of habituation (reduction in the desire to eat foods as they are consumed; Epstein et al., 2009), incentive salience attribution (whereby food acquires the ability to trigger food intake due to learnt associations between cues and the pleasurable taste of foods; Robinson & Berridge, 1993), and learning about the post-ingestive consequences of food (e.g. creamy or sweet tastes signal high fat and sugar, and hence calories; Woods & Ramsay, 2000) (for a review of memory and learning processes in food intake see Higgs et al., 2012). Both memory for recent eating episodes and remembered liking of foods eaten affect subsequent food intake (Higgs, Robinson, et al., 2012). Short-term memory and working memory have also been linked to food intake, with studies showing better WM is associated with less snack intake (Riggs, Chou, et al., 2010; Riggs, Spruijt-Metz, et al., 2010) and greater fruit and vegetable intake (Allom & Mullan, 2014; Riggs, Chou, et al., 2010; Sabia et al., 2009). In Chapter 3 of this thesis, visuospatial WM was positively associated with intake of low energy dense foods, and in Chapter 5 WM training reduced saturated fat intake in restrained eaters. As far as I am aware, no studies have assessed the importance of prospective memory specifically to dietary behaviour. Prospective memory is described as the ability to remember to perform a planned action, and could be important for food

intake decisions when you need to remember to perform actions compatible with long-term health goals. For example, remembering to take fruit with you to work to snack on, reducing the need to buy other higher energy dense snacks. The importance of intelligence has been demonstrated, with longitudinal studies finding that childhood intelligence predicts adult dietary patterns and weight (Batty, Deary, & Macintyre, 2007; Chandola et al., 2006). Little research has looked at the importance of reaction time and processing speed in dietary behaviour.

The aim of the present study was to assess the importance of cognition to food intake behaviour in adults with type 2 diabetes (T2DM), while controlling for a large number of other potentially confounding factors. As a comparison, data from cohort participants who did not report a diagnosis of T2DM were also analysed. Considering the cognitive deficits frequently found in those with diabetes, it was predicted that cognition may be more important to food intake in those with T2DM than in those without diabetes.

## **6.2 Methods**

### **Participants**

The UK Biobank consists of data collected from 503,325 adults aged 40-69 years recruited via NHS registers across England, Scotland and Wales (Allen et al., 2012). Initial invitations were sent out to 9.2 million people living within 25 miles of one of the 22 assessment centres, aiming to be as inclusive as possible, and resulted in a response rate of 5.47%. Despite this low response rate, the sample size recruited consists of half a million people, which means that findings from the data should be generalizable to the rest of the UK population. Participants were invited to complete a single 2-3 hour testing session. The procedure for data collection included providing written consent, followed by touch screen questionnaires (and cognitive tasks), face-to-face interviews, and collection of physical measures and biological samples (for more detail on how the data was collected see Allen et al., 2012). Only baseline data were used in the current study.

### **Ethics**

The UK Biobank has obtained ethical approval from the North West Multi-centre Research Ethics Committee (covering the UK) and possesses Research Tissue Bank approval. The latter covers all research conducted using the data, thus researchers using the data do not need to seek NHS approval for their specific study. See the UK Biobank

website for more information (<http://www.ukbiobank.ac.uk/ethics/>). This study has also been approved by Middlesex University's psychology research ethics sub-committee.

## **Measures**

### Identification of type 2 diabetes

Participants self-reported diagnosis of diabetes. Participants were excluded if they reported being prescribed insulin within 1 year of diagnosis or were diagnosed before they were 35 years of age. This was done in an attempt to exclude those who likely had type 1 diabetes and maintain only those with type 2 diabetes. Participants who self-reported as having gestational diabetes only were also excluded. Participants who self-reported no diagnosis of diabetes were classed as not having diabetes.

### Cognition

Five tasks were used to assess a range of cognitive abilities.

#### *Fluid intelligence test*

This task was intended to assess a person's ability to solve problems that require logic and reasoning, but that is independent of acquired knowledge (Kane & Engle, 2002). Example questions include 'If Truda's mother's brother is Tim's sister's father, what relation is Truda to Tim?' and 'Age is to years as height is to?' Participants were given 2 minutes to answer as many questions as possible (out of 13), and the total number of correct answers was the outcome measure.

#### *Reaction time task*

This task required participants to press a button when two identical cards were shown on the screen, and hence assessed simple processing speed (Karia, Ghuntla, Mehta, Gokhale, & Shah, 2012). Mean time taken to press the button on trials where the cards matched was the outcome measure.

#### *Pairs memory test*

This was a paired associates task where participants were presented with an array of cards and were asked to remember as many matching pairs as possible. The cards were then turned over so that they were face down (on the screen) and the participant's task was to touch as many matching pairs as possible with the fewest attempts. Paired associate tasks

have been validated as, and are typically implemented as, a measure of new learning and memory (Tulsky & Price, 2003; Wechsler, 1987, 1997). However, validation attempts have found performance on visual paired associate tasks to correlate with WM, such as performance on a backwards visual memory span task (Torgersen, Flaatten, Engelsen, & Gramstad, 2012). Paired associate tasks may therefore also be tapping into WM abilities. The outcome variable for this task was the number of incorrect matches found on the highest level of the task (level 6). A greater number of incorrect matches suggests poorer visual memory as participants were less able to remember where the correct matching pair locations were. This task is referred to as a visual memory task from here on.

#### *Numeric memory test*

In this task participants were shown a sequence of numbers on a screen for a brief period of time (the number of digits x 500ms). After a 3000ms blank screen, participants had to enter the remembered sequence in the correct order using the keyboard. The sequence began with 2 digits, and increased by one (up to 12) each time the sequence was correctly recalled. The task ended after two consecutive incorrect answers. The maximum sequence length correctly recalled was the outcome measure for this task, with a longer sequence recalled indicating better WM. This task is essentially a forwards digit span task, which is a validated measure of phonological loop WM capacity (Baddeley, Gathercole, & Papagno, 1998).

#### *Prospective memory test*

At the beginning of the cognitive assessments participants were shown the following instruction on the screen “At the end of the games we will show you four coloured shapes and ask you to touch the Blue Square. However, to test your memory, we want you to actually touch the Orange Circle instead”. As the final cognition task participants were shown a number of shapes on the screen and they were asked to touch the blue square, as they were told they would be. The outcome measure for this task was the number of people that correctly touched the orange circle on the first attempt and on the second attempt. This task assessed an individual’s ability to remember an instruction and recall it at a later time following a cue (McDaniel & Scullin, 2010).

#### Dietary Intake

The UK Biobank utilised two measures of self-reported dietary intake: a food frequency questionnaire and 24-hour recalls (administered up to 5 times). The food frequency

questionnaire asked participants how much of a list of foods they eat per day on average (including fruits and vegetables). The first 24-hour dietary recall task was added to the assessment session towards the end of recruitment (for the remaining 70,000 participants). Up to four further 24-hour recalls were administered over the subsequent year via email. This was done to obtain an average measure for each participant and to account for changes in the diet across seasons. The email invitations were sent on specified days, allowing capture of dietary intake across both weekdays and weekends.

#### *Fruit and vegetable intake*

Vegetable (cooked, raw and salad) and fruit (fresh and dried) was reported as the number of heaped tablespoons eaten on average per day via the food frequency questionnaire. These data were recoded to reflect the number of portions of fruit and vegetables consumed, based on current UK guidelines that 3 heaped tablespoons of cooked vegetables and 1 heaped tablespoon of dried fruit constitute one portion (NHS Choices, 2015a). The amount of fresh fruit that constitutes a single portion varies between a half, 1 and 2 depending of the size of the fruit. The average of these was taken, and a single piece of fruit was counted as one portion. There are no current guidelines on raw vegetables and guidelines about salad are not easily quantifiable, and therefore the same was followed for these as for cooked vegetables (3 heaped tablespoons equates to 1 portion). These variables were summed to calculate the total number of portions of fruit and vegetables eaten per day as a continuous variable.

#### *Fat and saturated fat intake*

For each 24-hour recall participants were asked about their consumption of 200 foods and drinks. Responses were converted into estimated daily nutrient intake by multiplying the assigned portion size by the amount participants said they consumed; and then multiplying this by the nutrient composition of the food/beverage according to the UK food composition database McCance and Widdowson's *The Composition of Foods* (McCance & Widdowson, 2002). Daily intake of energy (kilojoules) and saturated fat (grams) averaged across the number of 24-hour recalls completed were used in the current analyses.

Potential confounds

#### *Demographic information*

Participants provided information on their ethnicity, sex and age. Townsend deprivation index score was used as a proxy measure of socioeconomic status (Townsend, Phillimore, & Beattie, 1988). The score reflects material deprivation, and is based on information about unemployment, housing, access to a car and social class. Higher scores indicate greater deprivation.

### *Physical Health*

Physical health assessments included the measurement of waist circumference, and self-reported smoking and alcohol consumption status (never, previous or current), which were recoded into dichotomous variables (never and previous/current). Vascular problems were identified if participants self-reported a diagnosis of angina, high blood pressure, blood clot, lung clot, deep vein thrombosis, or previous heart attack or stroke. Respiratory problems were identified if participants self-reported a diagnosis of emphysema/chronic bronchitis, asthma, hay fever/allergic rhinitis/eczema. Presence of cancer was identified based on a self-reported diagnosis of cancer. Possible sleep disturbances were identified if participants self-reported experiencing either insomnia “usually” or narcolepsy “often/all of the time”. Finally, physical activity was measured via the International Physical Activity Questionnaire (IPAQ; Craig et al., 2003). IPAQ data processing guidelines were followed to calculate total MET minutes across walking, moderate and vigorous physical activity (IPAQ, 2005).

### *Psychological Health*

Depressive symptoms were assessed using four questions from the Patient Health Questionnaire (PHQ-9, Spitzer et al., 1999). These asked “over the past two weeks, how often have you... felt down, depressed or hopeless/had little interest or pleasure in doing things/felt tense, fidgety or restless/felt tired or had little energy?” Answers were scored in line with PHQ-9 scoring guidelines to create a total depressive symptoms score (Spitzer et al., 1999). Five questions relevant to anxiety asked about nervous feelings, worry/anxiety, feeling tense or “highly strung”, worrying too long after embarrassment and suffering from “nerves”. Answers were summed to provide a total score on anxiety related symptoms. For both depressive and anxiety symptoms, a higher score indicates more symptoms.

## Analyses

To compare group differences on demographic and other characteristics, one-way MANOVAs and chi-square tests were run with diabetes status (no diabetes, T2DM) as the independent variable, and demographic and other factors as the dependent variables. More specifically, those with and without T2DM who also had data available on all of the cognition measures and at least one of the self-report food consumption outcomes were compared. In the main analyses, separate hierarchical regressions were conducted with fruit and vegetable portions and saturated fat intake as the dependent variables.

Categorical variables were dummy coded. Demographic variables (ethnicity – reference “white”, age when attended assessment centre, sex – reference = “male”, Townsend deprivation index) were entered in step one of the model, followed by physical health variables (step 2: total MET minutes, BMI/waist circumference, current/past smoking and alcohol consumption – references = “never”, presence of sleep disturbances, vascular problems or respiratory problems – reference = “absence”, cancer diagnosis – reference = “no”) and psychiatric variables (step 3: anxiety and depressive symptoms). Because greater fruit and vegetable or saturated fat intake could simply reflect greater total energy intake, total energy consumed was included as a predictor in step four of the models. Cognitive measures were entered into step 5. Each regression was conducted separately in those with T2DM and those without. Due to the large sample sizes in this study, many relationships were likely to be significant (i.e.  $p < 0.05$ ). Greater importance was therefore placed on the amount of variance accounted for in step 5 of the models when cognitive measures were included. Whether cognitive abilities account for any additional variance in fruit/vegetable and saturated fat intake above that of other potential confounds was therefore identified.

## 6.3 Results

Log transformation of skewed variables (incorrect matches on visual memory task) made no difference to the results and hence the data were left untransformed. Sample characteristics are reported for the total sample (those who completed all five cognition measures and either the food frequency or 24-hour dietary recall tasks) in Table 1.

## Group differences

### Demographics

There was a greater proportion of men in the T2DM group than in the non-diabetes group ( $X^2(1) = 306.98, p < 0.001$ ). Those without diabetes tended to be younger ( $F(1,47598) = 513.12, p < 0.001$ ) and have lower levels of deprivation (Townsend deprivation index score;  $F(1, 47479) = 127.41, p < 0.001$ ). Groups also significantly differed in proportions of different ethnic backgrounds ( $X^2(5) = 239.47, p < 0.001$ ); there was a higher proportion of White ethnic background in those without diabetes, whereas in those with T2DM there was a greater proportion of Asian/Asian British, Black/Black British and “other” ethnic backgrounds. Both those with and without T2DM had the same proportion of people with mixed and Chinese ethnic backgrounds.

### Physical health

The non-diabetes group did significantly more physical activity (total MET minutes;  $F(1,37539) = 20.41, p < 0.001$ ) and had a lower BMI ( $F(1,47444) = 1679.00, p < 0.001$ ) and waist circumference ( $F(1,47517) = 2257.67, p < 0.001$ ). Participants with T2DM had a higher proportion of previous/current smokers ( $X^2(1) = 113.85, p < 0.001$ ), sleep disturbances ( $X^2(1) = 72.13, p < 0.001$ ), self-reported diagnosis of cancer ( $X^2(1) = 6.27, p = 0.01$ ) and vascular problems ( $X^2(1) = 1543.25, p < 0.001$ ). However, T2DM participants had a lower proportion of previous/current alcohol drinkers ( $X^2(1) = 41.42, p < 0.001$ ). There was no significant difference between groups in presence of respiratory problems ( $X^2(1) = 2.41, p = 0.12$ ).

### Psychological health

Participants in the T2DM group had fewer anxiety symptoms ( $F(1,47584) = 21.12, p < 0.001$ ), but more depressive symptoms ( $F(1,47497) = 66.64, p < 0.001$ ) than participants in the non-diabetes group.

### Cognition

Compared to those with T2DM, participants without diabetes remembered more digits on the digit span task ( $F(1,47598) = 79.25, p < 0.001$ ), made fewer incorrect matches on the visual memory task ( $F(1,47598) = 16.44, p < 0.001$ ), had a higher intelligence score ( $F(1,47598) = 36.91, p < 0.001$ ), and faster simple reaction times ( $F(1,47598) = 92.91, p < 0.001$ ). Further, participants without diabetes were more likely to give the correct answer



on the prospective memory test on the first attempt ( $X^2(1) = 50.44, p < 0.001$ ), and less likely to give the correct answer on the second attempt ( $X^2(1) = 14.18, p < 0.001$ ) than participants with T2DM.

#### Self-reported food intake

Participants with T2DM consumed a greater number fruit and vegetable portions ( $F(1,47103) = 17.87, p < 0.001$ ) than participants without T2DM. When fruit and vegetable portions were separated, participants with T2DM consumed more fruit portions ( $F(1,47338) = 19.06, p < 0.001$ ) but not vegetable portions ( $F(1,47288) = 2.60, p = 0.12$ ) than participants without diabetes. There were no significant differences between groups for saturated fat intake ( $F(1,30967) = 0.26, p = 0.61$ ).

**Table 1. Characteristics of participants for total sample (mean and SD/percentage).**

Characteristic	Total sample	No diabetes	T2DM
N	47,600	45,772	1,828
Age (years)	47,600	56.27 (8.27)	60.71 (6.29)
Sex (Males)	47,600	20,351 (44.5%)	1,193 (65.3%)
Ethnicity	47,476		
White		44,134 (96.7%)	1,657 (90.9%)
Mixed		197 (0.4%)	13 (0.7%)
Asian/Asian British		716 (1.6%)	112 (6.1%)
Black/Black British		274 (0.6%)	23 (1.3%)
Chinese		88 (0.2%)	1 (0.1%)
Other		234 (0.5%)	17 (0.9%)
Townsend deprivation index	47,481	-1.61 (2.71)	-0.88 (2.94)
Physical health			
MET minutes per week	37,541	3,234.95 (3,584.03)	2,781.53 (3,294.52)
Waist circumference (cm)	47,519	88.84 (12.95)	103.59 (13.75)
Smoker	47,468		
Never		25,244 (55.3%)	777 (42.6%)
Previous/current		20,401 (44.7%)	1,046 (57.4%)
Alcohol consumer	47,569		
Never		1,616 (3.5%)	117 (6.4%)

Previous/current		44,128 (96.5%)	1,708 (93.6%)
Sleep disturbances (yes)	49,281	13,473 (29.5%)	706 (38.8%)
Cancer (yes)	47,497	3,517 (7.7%)	170 (9.3%)
Vascular problems (yes)	47,530	13,247 (29.0%)	1,319 (72.2%)
Respiratory problems (yes)	47,520	13,889 (30.4%)	523 (28.7%)
Psychological health			
Anxiety symptoms	47,586	1.59 (1.49)	1.43 (1.48)
Depressive symptoms	47,499	1.53 (2.00)	1.93 (2.33)
Total energy intake	30,969	8,873.44 (2,746.02)	8,780.68 (3,140.71)
Maximum digits remembered	47,600	6.74 (1.32)	6.46 (1.41)
Incorrect matches	47,600	3.97 (3.09)	4.27 (3.37)
Fluid intelligence score	47,600	6.10 (2.08)	5.79 (2.20)
Reaction time (ms)	47,600	562.46 (120.14)	590.14 (127.07)
Prospective memory	47,600		
Correct 1 <sup>st</sup> attempt		35,994 (78.6%)	1,310 (71.7%)
Correct 2 <sup>nd</sup> attempt		7906 (17.3%)	378 (20.7%)
Saturated fat (grams)	30,969	30.18 (13.76)	29.96 (14.80)
Fruit and vegetable portions	47,105	4.70 (3.00)	5.00 (2.95)

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**Note.** T2DM = type 2 diabetes mellitus

## **Main analyses**

### Confounding factors

Table 2 shows standardized beta values for all confounding factors in each regression analysis. Compared to White ethnicity, Asian, Black, and “other” ethnicities tended to consume more fruit and vegetables and less saturated fat (consistently in those without diabetes, less so in those with T2DM). Age was positively associated with greater fruit and vegetable intake, but was not significantly associated with saturated fat intake (in both the no diabetes and T2DM groups). Townsend deprivation index was negatively associated with fruit and vegetable portions and positively associated with saturated fat intake. Therefore, greater deprivation was associated with less fruits and vegetables and more saturated fat. This was the case only in those without diabetes, and these relationships were non-significant in those with T2DM. Greater physical activity (higher total MET minutes) was positively associated with fruit and vegetable intake and negatively associated with saturated fat intake (in both no diabetes and T2DM). Larger waist circumference was negatively associated with less fruit and vegetable intake (in those without diabetes only) and positively associated with saturated fat intake (in both groups). In participants without T2DM, current and previous smokers tended to consume less fruit and vegetable portions than non-smokers (the relationship was non-significant in those with T2DM). There was no significant relationship between smoking status and saturated fat intake in those with and without T2DM. Current and previous alcohol consumers tended to eat less saturated fat than non-drinkers (in those without diabetes only). There were no consistent significant relationships between alcohol consumption and fruit and vegetable intake. The presence of a sleep disorder, cancer and respiratory problems were not consistently associated with fruit and vegetable or saturated fat intake. The presence of vascular problems was associated with less saturated fat intake, only in those without diabetes. Both anxiety and depressive symptoms were negatively associated with fruit and vegetable intake (in those without diabetes only). Depressive symptoms were positively associated with saturated fat intake (in those without diabetes only), however, anxiety symptoms were not (both groups). Total energy consumption was positively associated with both fruit and vegetable intake (in those with diabetes only) and saturated fat intake (both groups).

**Table 2. Multiple linear regression standardised Beta values for confounding factors.**

Model	Fruit/vegetable portions		Saturated fat (grams)	
	No diabetes	T2DM	No diabetes	T2DM
Step 1				
(demographic factors)				
Mixed ethnicity	0.002	0.00	-0.003	0.02
Asian ethnicity	0.07***	0.12**	-0.02***	-0.03
Black ethnicity	0.02**	0.02	-0.02***	-0.05*
Chinese ethnicity	0.01		-0.002	
Other ethnicity	0.06***	0.07	-0.01**	0.01
Age	0.13***	0.08*	-0.01	-0.01
Sex	0.12***	0.08*	0.05***	0.07**
Deprivation	-0.03***	-0.06	0.01*	-0.01
Step 2				
(physical health)				
Total MET minutes	0.1***	0.12**	-0.01*	-0.05*
Waist circumference	-0.05*	0.02	0.03***	0.09***
Smoking status	-0.02***	-0.06	-0.003	0.01
Alcohol consumption	-0.01	-0.04	-0.01***	-0.02
Sleep disorder	0.00	0.05	-0.01	-0.01
Cancer	0.00	0.02	0.004	0.02

Vascular problems	0.002	-0.03	-0.02***	-0.002
Respiratory problems	0.01	0.06	-0.01	0.03
Step 3				
(psychological health)				
Anxiety symptoms	-0.03***	-0.03	-0.003	0.01
Depressive symptoms	-0.04***	0.01	0.02***	0.01
Step 4	0.05***	0.04	0.82***	0.82***
Total energy intake (kilojoules)				

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**Note.** \*\*\*  $p < 0.001$ ; \*\*  $p < 0.01$ ; \*  $p < 0.05$

#### Fruit and vegetable intake

In participants without diabetes, demographic factors accounted for 4.0% of the variance in fruit and vegetable intake, with physical health factors accounting for an additional 1.5%. Psychological factors and total energy consumption both accounted for an additional 0.2% each. Cognition accounted for an additional 0.1% of the variance. See Table 3.

In participants with T2DM, demographic and physical health factors accounted for the greatest amount of variance in fruit and vegetable intake (4.0% and 2.7% respectively). Both psychological factors and total energy intake accounted for an additional 0.1% each. Cognition accounted for a further 0.5%. See Table 3.

#### Saturated fat intake

In participants without diabetes, demographic factors accounted for 3.7% of the variance in saturated fat intake. Physical and psychological factors accounted for an additional 0.5% and 0.4% respectively. Total energy intake accounted for 61.0% of additional variance. Cognition variables did not account for any additional variance. See Table 3.

In participants with T2DM, demographic factors accounted for 1.7% of the variance in saturated fat intake. Physical and psychological factors accounted for a further 2.8% and

1% of the variance, respectively. Total energy consumption accounted for 63.0% of additional variance. Cognitive factors accounted for an additional 0.3% of the variance. See Table 3.

**Table 3. Hierarchical regression of variance accounted for in dietary intake (change in  $R^2$ ) as a function of diabetes status.**

Model	Fruit/vegetable portions		Saturated fat (grams)	
	No diabetes	T2DM	No diabetes	T2DM
Step 1 (demographic factors)	0.040***	0.040***	0.037***	0.017
Step 2 (physical health)	0.015***	0.027**	0.005***	0.028**
Step 3 (psychological health)	0.002***	0.001	0.004***	0.010*
Step 4 (total energy intake, kilojoules)	0.002***	0.001	0.610***	0.630***
Step 5 (cognition)	0.001	0.005	< 0.001*	0.003

Note. \*\*\*  $p < 0.001$ ; \*\*  $p < 0.01$ ; \*  $p < 0.05$

## 6.4 Discussion

The role of cognition in self-reported food intake in T2DM, in the context of a large number of other potentially confounding factors, had not been assessed to date. The importance of cognition to dietary behaviour in healthy populations has been extensively studied. For example, it has been reported that adults and children with better cognitive abilities demonstrate healthier dietary behaviour (Hall, 2012; Hofmann & Friese, 2008; Riggs, Spruijt-Metz, et al., 2010). Evidence from longitudinal studies also suggests that better childhood cognition predicts better adult dietary patterns (Batty, Deary, & Macintyre, 2007; Chandola et al., 2006). The research conducted in type 2 diabetes to date, however, has only investigated the importance of cognition to dietary behaviour in small sample sizes using dietary self-care measures based on a few questions about how well participants feel they adhere to their dietary regime (Asimakopoulou, 2001; Asimakopoulou & Hampson, 2002; Coker & Shumaker, 2003; Compeán-Ortiz et al., 2010). The UK Biobank provided an opportunity to assess the relationship between cognition and self-reported food intake, while at the same time controlling for



confounding factors. This was made possible by the large sample size of the UK Biobank and the breadth of demographic and health information collected about participants.

Participants with and without T2DM differed in a number of respects in line with published reports. There was a significantly greater proportion of non-white ethnicities in the T2DM group than the non-diabetes group, and no difference in proportion of Chinese and mixed ethnicity. This is in line with a wealth of previous research suggesting that the incidence of T2DM is higher in non-white ethnicities and in ethnic minorities living in developed countries than White ethnicities (for a review see Oldroyd, Banerjee, Heald, & Cruickshank, 2005). The prevalence of T2DM has also been found to be similar in individuals of Chinese origin and the general UK population (Oldroyd et al., 2005). In the present study, participants with T2DM reported greater material deprivation (indicated by a higher Townsend deprivation score) than participants without T2DM, which is in line with previous reports that T2DM is most prevalent in lower socioeconomic status groups both in the UK and elsewhere (Connolly, Unwin, Sherriff, Bilous, & Kelly, 2000; Hwang & Shon, 2014). The T2DM group also had a greater waist circumference and BMI than the non-diabetes group, which has also been reported elsewhere (Bays, Chapman, Grandy, & SHIELD Investigators' Group, 2007). Research has further suggested that BMI may be the intermediate factor between the relationship between poorer socioeconomic status and prevalence of T2DM (Krishnan, Cozier, Rosenberg, & Palmer, 2010). Participants with T2DM were more likely to have had cancer and to report sleep disturbances than participants without diabetes. Both cancer and sleep disturbances have been extensively linked to T2DM (for reviews see Cappuccio, D'Elia, Strazzullo, & Miller, 2010; Tsilidis, Kasimis, Lopez, Ntzani, & Ioannidis, 2015). Participants with T2DM had significantly more vascular health problems than those without diabetes. Given that micro- and macro-vascular health problems are a consequence of poorly controlled diabetes, this relationship is not surprising. Type 2 diabetes has been associated with greater levels of both depressive and anxiety symptoms (Demmer et al., 2015; Grigsby, Anderson, Freedland, Clouse, & Lustman, 2002; Smith et al., 2013), however, in the current analyses participants with T2DM had more depressive symptoms than those without diabetes only.

In the present analyses, people with T2DM performed significantly worse than those without diabetes on all measures of cognition. Participants with T2DM remembered significantly fewer digits on the numeric memory task, made more errors on the visual memory task, had a lower intelligence score, had slower simple reaction times and were less likely to give the correct answer on the prospective memory test first time (and more

likely to give the correct answer on their second attempt) than did participants without diabetes. In the most recent systematic review of the relationship between diabetes and cognition, the most consistent deficits in diabetes compared to controls were in memory, cognitive speed and mental flexibility (van den Berg et al., 2009). However, the differences between those with and without T2DM in the current analyses were small. The effect sizes were also small, suggesting that the differences between groups may not be meaningful. The difference between groups on simple reaction time, however, had a medium effect size. Poorer processing speed in T2DM was the most supported aspect of cognitive decline in the review by van den Berg et al. (2009), with 63% of studies finding a significant difference between T2DM and controls. Research on mild cognitive impairment (MCI; a transition phase between normal age-related cognitive decline and Alzheimer's disease) has found similar differences in simple reaction time between MCI and controls (Saunders & Summers, 2010), suggesting that slowing of simple reaction time in T2DM participants may be comparable to that found in mild cognitive impairment, a known precursor to Alzheimer's disease.

The T2DM participants in the present analyses reported consuming less total energy from food and more portions of fruits than did the non-diabetes group. This suggests that while those with T2DM may be consuming less overall energy, they appear to be consuming more fruits, and hence more sugar (although these differences are small, as are the effect sizes). There was no difference between groups in reported saturated fat intake.

Demographic factors typically accounted for the greatest amount of variance in fruit and vegetable, and saturated fat intake in both groups. Physical health factors typically accounted for a further small amount of the variance. Psychological health factors accounted for very little additional variance in self-reported food intake. Cognition measures accounted for a maximum of 0.5% of the variance on top of that already accounted for by these other factors. The pattern of results was similar across groups, except that physical health accounted for a greater amount of variance in both fruit and vegetable and saturated fat intake in the group with T2DM than in the group without diabetes. Overall, the amount of variance in self-reported food consumption these accounted for was low, but is not out of line with other reports. Limbers and Young (2015) reported that demographic variables (gender, age, ethnicity and parental education) accounted for 2% of the variance in fruit and vegetable intake, and 4% of the variance of intake of foods high in saturated fat. BMI and eating pathology scores accounted for an additional 4% of the variance in both. In another study, depressive symptoms accounted

for an additional 5.3% of the variance in food and drink energy density, above that accounted for by demographic factors (Grossniklaus et al., 2010).

Despite a wealth of research demonstrating the importance of cognition to food intake decisions (Allom & Mullan, 2014; Epstein et al., 2009; Higgs, Robinson, et al., 2012; Robinson & Berridge, 1993; Woods & Ramsay, 2000), the results in the current study suggest that cognition (as measured by the specific tasks available in the UK Biobank), contribute little to self-reported food intake in the context of other demographic, physical and psychological factors. Others have found similar results. Limbers and Young (2015) found that the relationship between WM and snack food intake disappeared when controlling for demographic factors, BMI and eating styles. Batty et al. (2007) found that the relationship between intelligence and food intake was attenuated when controlling for socioeconomic status. Overall, these findings are beginning to suggest that cognition contributes little to variance in food intake above other factors.

The pattern of results observed in the T2DM sample was very similar to that observed in the non-diabetes sample. Similar to the present findings, Compeán-Ortiz et al. (2010) found that immediate and delayed visual memory recall predicted only 7% and 8% of the variance in ability to follow a prescribed diet, respectively. Asimakopoulou and Hampson (2002) found that after controlling for age, pre-morbid IQ and depression, dietary self-care was predicted by performance on a measure of set-shifting ability (Wisconsin Card Sorting Task) and diabetes-specific problem solving only. However, as stated by the authors, the small sample size (N = 57) may have been a limiting factor in this study, as there may not have been sufficient power to detect effects of other aspects of cognition. The results of the current analyses are therefore generally in line with the very limited previous research in T2DM. However, there are a number of limitations to the current study that reduce the strength of any conclusions that cognition and specific cognitive domains have a null effect on food intake.

### **Strengths and limitations**

A key strength of the present study is the large sample that allowed the many potentially confounding factors that have already been found to play an important role in food intake to be controlled for. The importance of cognition to the control of food intake in the context of these other factors could therefore be assessed. The UK Biobank collected a large amount of demographic, physical and psychological health information about participants, enabling the current analyses to control for a wider range of factors than has

been possible in previous research. The reliability of the current results is also supported, as findings of known predictors of food intake and differences between T2DM and controls on demographic, physical and psychological health were replicated.

The measures of dietary intake used by the UK Biobank all rely on self-reported consumption (24-hour recall and food frequency questionnaire). Self-reported food intake can be unreliable and the intakes reported are generally underestimated relative to the amounts suggested by more precise methods for examining energy metabolism, such as the doubly labelled water method (Hill & Davies, 2001; Schoeller et al., 2013). Further, the food frequency questionnaire completed by UK Biobank cohort has not been validated against other measures of consumption, and hence its validity is unknown. Nevertheless, the resources available to the UK Biobank meant they could administer up to five 24-hour recalls over the space of one year, covering all seasons and both weekdays and weekends. Multiple 24-hour recall administrations are believed to provide a more accurate measure of people's usual dietary intake than a single 24-hour recall (Ma et al., 2009). Twenty-four hour recalls are also a highly cost effective and practical method of assessing food intake in samples of this size. Nonetheless, reliance on self-reported food intake is a limitation of the current study.

Laboratory taste-test measures are more appropriate for detecting changes in actual food intake in controlled laboratory studies where the effect of a specific manipulation can be examined. In contrast to the present findings, visuospatial WM was found to be positively associated with LED food consumption when intake was assessed using a snack food taste-test (Chapter 3). It may be that the different food intake measures explain why the findings reported here differ from those reported in Chapter 3. It may also be important that both 24-hour recall and food frequency questionnaires rely on recall of previous eating because a potential relationship between WM and food intake could be obscured by memory-related variability in the outcome measure. However, research suggests that 24-hour recall tasks rely more on long-term memory process, such as episodic memory than working memory processes (Armstrong & MacDonald, 2000).

The five cognition measures included in the UK Biobank test battery assessed a range of cognitive domains (prospective memory, short-term/working memory, new learning and memory, intelligence and simple reaction time/processing speed). However, this was still a fairly limited cognition battery. As described already in this chapter, cognitive abilities not assessed by the UK Biobank tests may be related to food intake. For example, assessment

of WM was limited to one task, a forwards digit span task that is a validated measure of phonological loop WM capacity (Baddeley, Gathercole, & Papagno, 1998). Since there is no manipulation component to this task (such as in a backward digit span task), this can only be said to be measuring short-term storage capacity. True WM involves some form of manipulation or updating, and hence very little can be said about the importance of WM to food intake in the current analyses. The visual memory task may have been tapping into visuo-spatial WM: performance on paired associate tasks has previously been shown to correlate with measures of visual WM span (Torgersen et al., 2012). However, it is impossible to tease out these functions in an analysis. There is no direct measure of the central executive component of WM in the UK Biobank, which is an important limitation to the present analysis because the previous studies in this thesis have demonstrated the importance of the central executive in a number of ways. In Study 1 (Chapter 3), dietary restraint was associated with impaired central executive functioning (strategy use in particular), while in Study 2 (Chapters 4 and 5) WM training improved central executive functioning (again, strategy use in particular). It would be informative if future iterations of the UK Biobank test battery included a measure of central executive function. It is also recommended that other aspects of executive functioning such as inhibitory control are assessed in future (Allom & Mullan, 2014; Hall, Lowe, & Vincent, 2014; Hall, 2012; Limbers & Young, 2015; Riggs, Chou, et al., 2010; Riggs, Spruijt-Metz, et al., 2010). Allom and Mullan (2014) reported that Stroop test performance accounted for 3.73% of the variance in saturated fat intake, whilst stop-signal performance accounted for 4.88% of the variance. Limbers and Young (2015) also found that inhibition was associated with consumption of high fat foods, whereas initiation skills were associated with fruit and vegetable consumption. Cognitive flexibility was an important area of cognition found to be impaired in T2DM compared to controls in the review by van den Berg et al. (2009), and hence there is merit in future research assessing how this impairment may impact food intake.

Psychological eating styles were not assessed by the UK Biobank but these measures may account for some of the missing variance in food intake. Dietary restraint and emotional eating have been reported to account for 14.2% of the variance in saturated fat intake (Allom & Mullan, 2014). There are other reports that disordered eating is positively associated with fruit and vegetable consumption and negatively associated with high fat food consumption (Limbers & Young, 2015). Further, psychosocial factors such as self-efficacy, social support and knowledge have all been shown to predict fruit and vegetable consumption (Shaikh, Yaroch, Nebeling, Yeh, & Resnicow, 2008). While the current

study controlled for a greater number of potentially confounding factors than has been possible in other studies of food intake and cognition, there are still many other factors that need to be taken into account in future research.

Glycated haemoglobin (HbA1c) levels will be available from the UK Biobank in the future and may be used to identify pre-diabetes (indicated by impaired glucose tolerance and impaired fasting glucose) so that the relationship between cognition and food intake across a continuum of glucose levels may be examined (no diabetes, pre-diabetes and type 2 diabetes). It would also be interesting to investigate whether HbA1c status moderates any relationship given that cognitive control may be more important for individuals who experience difficulties controlling their sugar levels.

## **Conclusions**

Small-scale experimental studies and larger longitudinal studies have shown a relationship between cognition (including working memory) and food intake in the general population. Research on the relationship between cognition and eating behaviour in those with T2DM has been limited to self-report questionnaires about dietary self-care. This is the first large-scale study to assess the relationship between cognition and food intake in adults with T2DM while controlling for confounding factors. The results suggest that cognition accounts for very little variance in both saturated fat and fruit and vegetable consumption in addition to that accounted for by demographic, physical and psychological factors (in both those with and without T2DM). However, considering the limitations of both the cognition (working memory included) and food intake measures available in the UK Biobank, further experimental and longitudinal research is needed to implement a more comprehensive assessment of cognition and to identify causal relationships between cognition and food intake.

## **Chapter 7. General Discussion**

The primary aim of this thesis was to advance understanding of the role of cognition and in particular, working memory, in eating behaviour. Initial work was conducted to assess the effectiveness of inhibition training programs to change eating behaviour, aid weight loss and reduce food cravings. Based on the findings, attention was turned towards an alternative executive function, namely working memory. The WM sub-components important to food intake and dieting behaviour were investigated, followed by experimental work to examine whether training WM can change food intake and associated behaviours in people with type 2 diabetes. Further work examined the importance of cognition more generally, and WM specifically, to food intake in the context of other factors known to relate to food intake. This chapter presents a summary of the findings from each study, and discusses the findings in the context of published research. The theoretical implications of the work are discussed and potential future directions of this work are suggested. An evaluation of the methodological strengths and limitations of the studies presented in this thesis are then presented.

### **7.1 Summary of results**

As rates of overweight and obesity continue to rise, so will the health complications associated with obesity, including cancer, heart disease, stroke and diabetes (NCD Risk Factor Collaboration, 2016; Wang et al., 2011). An increase in the medical costs required to treat these preventable diseases will also follow (Wang et al., 2011). Overconsumption of cheap and widely available energy dense food in increasing portion sizes is likely to be one important contributing factor to fat accumulation (Ello-Martin, Ledikwe, & Rolls, 2005; McConahy, Smiciklas-Wright, Birch, Mitchell, & Picciano, 2002; Nielsen, 2003; Young & Nestle, 2002). Novel approaches are therefore needed to identify new ways to curtail poor eating habits and help people lose weight. However, in order to identify new intervention methods, we must first better understand the processes that underlie eating habits.

Both obesity and diabetes are associated with cognitive deficits (Prickett et al., 2015; van den Berg et al., 2009). A bidirectional relationship likely exists, whereby food intake influences cognition (Davidson et al., 2007; Gómez-Pinilla, 2008; Kanoski & Davidson, 2010, 2011; Valls-Pedret et al., 2015) and cognition influences decision making around food (Hall, 2012; Higgs, Robinson, et al., 2012; Hofmann, Gschwendner, et al., 2008; Hofmann et al., 2012). Executive functions appear to be an important aspect of cognition

that have been shown to play an important role in food intake (Hall, 2012; Higgs, Robinson, et al., 2012; Hofmann, Friese, et al., 2008; Hofmann et al., 2012). Executive functions play an integral role when behaviour becomes effortful and requires top-down control, and are therefore likely to be a core component of the hypothesized reflective system in dual-process theories of behavioural control (Hofmann, Friese, & Strack, 2009; Hofmann, Friese, et al., 2008; Strack & Deutsch, 2004).

A logical conclusion is that perhaps improving executive functions will improve the reflective system and hence enhance top-down control over eating behaviour. A number of studies have investigated this hypothesis by implementing inhibitory control training programmes (for example, Houben & Jansen, 2015; Lawrence, Verbruggen, et al., 2015; Veling et al., 2014). In these tasks participants practice directing their behaviour away from food stimuli. Chapter 2 of this thesis was a systematic review and meta-analysis of the results from these training studies. Two previous reviews suggested an overall small to medium effect of training on food intake and alcohol consumption (Allom et al., 2015; Jones et al., 2016). My review extended these previous reviews in a number of ways. I included approach-avoidance training in addition to stop-signal, no-go and attention bias modification training. There is evidence that these approaches train similar underlying mechanisms, and so the inclusion of approach-avoidance training was appropriate. Weight loss and food cravings had also not been previously considered, yet these are important outcomes that should be assessed. The type of control conditions to which inhibition training is compared is a widely debated topic in the current literature because comparison with certain control conditions could inflate the observed effects of the training (see Jones et al., 2016 for a discussion of this). In my meta-analysis I was able to systematically assess whether the type of control condition used is a factor that determines the size of training effects.

Four meta-analyses were conducted. These assessed the effect of inhibition training on 1) food intake compared to a control group; 2) food intake compared to an attend/approach/go group; and 3) weight loss and food cravings. A narrative review was conducted on studies reporting food choice/selection outcomes. ICT (inhibitory control training) had no overall effect on food intake, except when compared to attend/approach/go training that trains behaviour towards food rather than not training behaviour at all (as a classic control group would). No-go training and food-specific training were most effective at reducing food intake. ICT promoted weight loss (compared to a control condition), but did not reduce food cravings (compared to attend training).



ICT reduced unhealthy food choices, but evidence was limited for increases in healthy food choices. The quality analysis indicated concerns over the type of comparison/control groups used. The effectiveness of ICT to reduce food intake appears to be inflated by comparison to go/attend/approach training groups. These findings were generally in line with previous reviews (Allom et al., 2015; Jones et al., 2016). Future research in this area should use pre-post experimental designs in order to identify the effect of both training and control conditions on behaviour. Importantly, the effects of these types of training on clinical populations is relatively unknown, and future research should address this issue by recruiting participants with obesity or other conditions associated with difficulties controlling food intake.

Due to the apparent limited efficacy of inhibition training to change eating and other related behavioural outcomes, along with the fact that there are many researchers already investigating this topic, I decided to focus on a different executive function: working memory. WM capacity has more recently been considered an important executive function, alongside inhibitory control ability, that plays a role in the reflective processes that are believed to influence eating behaviour (Hofmann, Friese, & Strack, 2009; Hofmann, Friese, et al., 2008; Hofmann, Gschwendner, et al., 2008; Hofmann et al., 2012). WM is more than just holding items in mind (short-term memory), and crucially involves some sort of manipulation or processing of the information stored (Diamond, 2013). Important components of WM that are relevant to self-regulation of behaviour include the ability to hold in mind information stored in long-term memory and to maintain focused attention on currently active information while preventing the interference of other potentially distracting information (Hofmann, Gschwendner, et al., 2008). Applied to eating behaviour, WM capacity may therefore be important in retrieving long-term memories and holding these active in WM (e.g. dieting goals); resisting attending to eye-catching stimuli in the environment (e.g. tempting foods); protecting active goals from distracting stimuli by maintaining focused attention on the active goals; and down-regulating emotions (e.g. cravings) (Hofmann et al., 2012). Hence, WM may be an executive function that is important for the reflective processes that underpin eating behaviour.

However, few studies to date have examined the direct relationship between WM and food intake, and the findings are contradictory (Allom & Mullan, 2014; Limbers & Young, 2015; Riggs, Chou, et al., 2010; Riggs, Spruijt-Metz, et al., 2010). Therefore, Study 1 in this thesis assessed the relationship between WM and food intake and addressed some of

the limitations of previous studies. The methodological changes implemented included: (1) using computer-based assessment of WM, reducing self-report bias; (2) assessing WM sub-components to provide a more fine-grained analysis of how WM relates to food intake; and (3) measurement of actual food consumption via a bogus taste-test instead of using a food frequency questionnaire.

In addition, the relationship between WM sub-components and psychological eating styles, more specifically dieting success, was assessed. Previous research in this area has focused on dieters vs non-dieters (currently and never), with little attention paid to dieting success (Green et al., 2003; Green & Rogers, 1995, 1998; Green & Elliman, 2013; Green et al., 1997; Kemps & Tiggemann, 2005; Kemps, Tiggemann, & Marshall, 2005; Rogers & Green, 1993; Shaw & Tiggemann, 2004; Vreugdenburg et al., 2003). Dieting success was measured via the dietary restraint and disinhibition sub-scales of the Three Factor Eating Questionnaire (Stunkard & Messick, 1985). Participants scoring high in restraint and the tendency towards disinhibition were classed as unsuccessful dieters, whereas those high in restraint but low in the tendency towards disinhibition were classed as successful dieters.

Visuospatial WM span was positively associated with the proportion of low energy dense food intake, which is consistent with results from other studies (Allom & Mullan, 2014; Riggs, Chou, et al., 2010; Sabia et al., 2009), but also suggests more specifically that visuospatial WM is important. Further, unsuccessful dieters (high restraint, high disinhibition) had poorer visuospatial WM span than successful dieters (high restraint, low disinhibition), which suggests that poorer visuospatial WM may undermine dieting success.

We also found that restraint was associated with poorer central executive strategy use, irrespective of disinhibition. This suggests that the negative effect of dieting on central executive functioning that has previously been found, is independent of tendency towards disinhibition (Green et al., 1997; Shaw & Tiggemann, 2004). The findings from Study 1 suggest that better visuospatial WM is associated with a greater preference for low energy dense foods, and that deficits in visuospatial WM may undermine dieting attempts. They also suggest that restraint impairs central executive functioning, irrespective of dieting success (disinhibition levels). These results only provide information about the relationship between these variables; nothing can be said about any causal relationships.

One way to assess the causal relationship is to assess whether training WM can change eating behaviour. This was addressed in Study 2 (Chapters 4 and 5).

Study 2 investigated whether WM training can change eating behaviour and indicators of diabetes control in people with type 2 diabetes. WM on the trained tasks improved significantly in both the active and inactive training groups, however it did so significantly more in the active training group. These effects also extended to some non-trained measures of WM, specifically central executive strategy use. However, there was no evidence of transfer effects to other aspects of cognition (inhibitory control, new learning and memory). Effects on food intake were found only in those high in dietary restraint. Specifically, saturated fat intake was reduced as a result of active training in those high but not low in dietary restraint. There were no effects of training on other measures of food intake (both laboratory based and non-laboratory based measures), or biological indicators of food intake (lipids) and diabetes control (glycated haemoglobin). There were also no effects of training on measures of dietary self-efficacy and adherence. These findings are in line with a recently published study of the same WM training in overweight/obese adults (Houben et al., 2016). Houben and colleagues (2016) also found that both groups improved on trained WM tasks, but there was significantly more improvement in the active training group. They also only found an effect of training on food intake in those high in dietary restraint (a proxy measure of strong dietary goals) (Houben et al., 2016).

Based on interviews with participants in the training study, I identified two key themes to their experiences of the training: acceptability and performance. Under acceptability, participants often found the training quite invasive to their daily life, struggled to fit it into their lives, and struggled to maintain motivation throughout the training period.

Participants also struggled to understand how WM training could change eating habits, and sometimes found the program difficult to use. Under performance, while participants felt that their WM improved, they generally did not feel that their eating habits had changed, despite their expectations that it would. Participants also reported developing tactics to help them improve on the training, despite not being explicitly instructed to use any tactics or how they could use tactics. Some participants found ways to make the training less demanding while still giving the impression that they were doing the training and fulfilling the requirements of the study. Overall, the results of Study 2 suggest that WM training transfers to some related aspects of cognition (central executive strategy use) and reduces saturated fat intake only in those who already have some motivation to restrict

their food intake. In general, the training was not experienced particularly positively by participants.

It would be clinically useful to identify how many training sessions are typically needed to change eating habits, as reducing the number of training sessions without reducing the effects of the training may make it more acceptable to patients. The sharpest increase in WM in Study 2 (see results, section 5.3, in Chapter 5) and in Houben et al. (2016) was by the 6<sup>th</sup>/7<sup>th</sup> training session, and hence there may be reason to believe the greatest benefits of WM training are achieved by the 7<sup>th</sup> training session. WM capacity training may also be more effective if combined with WM strategy training (Morrison & Chein, 2011).

The results of Study 2 (Chapters 4 and 5) support the existence of a causal relationship between WM and food intake, a claim that could not be made based on the results of Study 1 (Chapter 3). The WM training used incorporated three different training tasks, one specifically training visuospatial WM. However, from the current results it is not possible to tell which training task was the most effective, or if all three were necessary for the found effects to occur. The results from Study 1 (Chapter 3) suggest that training visuospatial WM may be the most effective and important component to train, and this could be examined in future research.

In Study 3 (Chapter 6), I used the UK Biobank cohort to assess the role of cognition in food intake in people with and without type 2 diabetes, while controlling for the effect of potentially confounding factors. The UK Biobank's large sample of half a million adults aged 40-69 years provided a unique opportunity to assess this relationship, while maintaining enough power to detect effects when controlling for a multitude of confounding factors. The UK Biobank test battery includes five tests of cognition: prospective memory, numeric memory test (a forwards digit span task), visual pairs matching test, intelligence test and simple reaction time test. The results showed that while there were significant differences between those with type 2 diabetes and controls on all 5 of these measures, these were mostly very small differences with small effects sizes. One exception to this was simple reaction time, where those with type 2 diabetes had an average reaction time of 27.68 milliseconds slower than controls, with an effect size of 0.42. These results are surprising considering the wealth of research that suggests diabetes is associated with cognitive deficits (Crichton, Elias, Davey, & Alkerwi, 2014; van den Berg et al., 2009). The effect of simple reaction time is less surprising, as this was the most supported effect in the most recent review by van den Berg et al. (2009), where 63%

of included studies found that those with T2DM had significantly poorer processing speed than controls. In the same review, 44% of included studies found significant differences in memory between T2DM and controls. However, as discussed in the introduction chapter, only 10 of these studies assessed WM specifically (Atiea et al., 1995; Brands et al., 2007; Elias et al., 2005; Fuh et al., 2007; Hassing et al., 2004; Kilander et al., 1997; Lindeman et al., 2001; Reaven et al., 1990; Ryan & Geckle, 2000; Vanhanen et al., 1997), and only one found a significant difference between groups on a forwards digit span task (Fuh et al., 2007). The results in Study 3 are therefore in line with the results of other studies.

The main results in Study 3 suggest that cognition accounts for very little additional variance in fruit and vegetable intake and saturated fat intake above that accounted for by demographic, physical and psychological health factors. This was the case for people with and without type 2 diabetes. Others have found similar results. Limbers and Young (2015) found that the relationship between WM and snack food intake disappeared when controlling for demographic factors, BMI and eating styles. Batty et al. (2007) found that the relationship between intelligence and food intake was attenuated when controlling for socioeconomic status. Overall, these findings are beginning to suggest that cognition contributes little to variance in food intake above other factors.

The results of Study 3 (Chapter 6) contribute to understanding of the cognitive deficits in T2DM and the importance of cognition to food intake in the context of other factors. However, little can be said about the contribution of WM specifically, because only one task assessed WM (numeric memory test) and this task only measured the storage capacity of the phonological loop sub-component. In both Study 1 and 2 (Chapters 3 – 5), a backwards digit span task was used which taps into central executive functioning as well as the phonological loop. Taken together, the results of Study 1 and Study 3 suggest that simple phonological storage capacity is of little importance to food intake. This is a novel finding because research conducted to date into WM and food intake has not assessed WM sub-components (for example, Allom & Mullan, 2014; Limbers & Young, 2015).

To summarise, the studies in this thesis suggest that specific sub-components of WM are associated with food intake and dieting success (Study 1, Chapter 3) and that training WM can improve dietary habits in adults with type 2 diabetes, but only in those who already have some motivation to restrict their food intake (Study 2, Chapters 4 & 5). The results from Study 3 suggest that type 2 diabetes is associated with deficits in processing speed (as measured by simple reaction time), but not any other aspects of cognition that were

measured by the UK Biobank. This study also found that cognition, again as measured by the specific tasks implemented by the UK Biobank, accounts for little variance in self-reported fruit and vegetable intake and saturated fat intake in addition to that accounted for by other demographic, physical and psychological health factors. This was the case in both those with and without type 2 diabetes.

## **7.2 Theoretical implications and future research**

The results from this thesis are generally in line with dual-process theories of the cognitive controls of behaviour. These theories argue that overt behaviour is a result of the balance and interaction between an impulsive and reflective system (Hofmann, Friese, et al., 2008; Strack & Deutsch, 2004). WM is posited to contribute to these reflective processes (Hofmann, Gschwendner, et al., 2008; Hofmann et al., 2012) and the results from Studies 1 and 2 (Chapters 3 – 5) support the importance of WM to food intake decisions. However, dual-process theories provide little insight into the mechanisms underlying how WM may be important to food intake choices. The Elaborated Intrusion Theory suggests that intrusive thoughts such as preoccupation with food are driven by automatic processes, and elaboration of these is guided by controlled processes (Kavanagh, Andrade, & May, 2005; May et al., 2015). Most importantly, it is how intrusive thoughts are elaborated upon that determines overt behaviour. A key function of WM is elaboration and manipulation of information held in short-term memory stores (Diamond, 2013), and it may be these functions of WM that play a crucial role in food intake decisions (Higgs, 2015a; Hofmann, Gschwendner, et al., 2008; Hofmann et al., 2012).

Research has shown that simply holding information in mind biases attention towards related stimuli (Soto, Heinke, Humphreys, & Blanco, 2005; Soto, Humphreys, & Heinke, 2006). Holding a picture of food in mind also subsequently biases attention towards food pictures specifically (Higgs, Rutters, Thomas, Naish, & Humphreys, 2012). The contents of WM, therefore, readily guide attention. However, it is further elaboration of the contents of WM, such as imagining consuming the food and the pleasure associated with this, that may facilitate food seeking behaviour (May et al., 2015). Food cravings may constitute one such elaboration of thoughts about food, and these have been shown to consume WM resources and impair performance on WM tasks (Kemps, Tiggemann, & Grigg, 2008; Tiggemann et al., 2010). In support of this, asking participants to perform a task that utilises WM reduces food cravings (Harvey et al., 2005; Kemps & Tiggemann, 2013; Kemps, Tiggemann, & Hart, 2005; Kemps et al., 2004). In these studies, loading

WM may be preventing food cravings from accessing WM, ultimately preventing elaboration of food-related thoughts and cravings into food seeking behaviour.

The results of the studies in my thesis and from other research suggest that some people may have a greater ability to prevent elaboration of intrusive thoughts about food than others. Indeed, one key function of WM that may underlie this is the ability to maintain focused attention on currently active information and prevent interference from other potentially distracting information (Hofmann et al., 2012). When asked to hold a picture of food in mind, the subsequent attention of successful dieters is less biased towards other food pictures than unsuccessful dieters (Higgs et al., 2015). This suggests that successful dieters may be preventing this information from interfering with current goals and so elaborating on the contents of WM less. Less elaboration of WM contents may also be why successful dieters have been found to experience fewer food cravings (Meule, Lutz, et al., 2012). Greater visuospatial WM abilities, as found in Study 1 (Chapter 3) may be what underlies this ability, however further research is needed to identify whether visuospatial WM capacity is involved in elaboration of working memory contents. Research finding that food cravings are visual in nature support that this may be the case (May et al., 2008, 2004).

Better WM may also enable successful dieters to activate alternative thoughts when faced with food cues. Indeed, another key function of WM theorised to play an important role in food intake decisions is the ability to retrieve long-term memories and hold these active in WM (Allom & Mullan, 2014; Hofmann et al., 2012). Studies have shown that food cues elicit health goals in successful dieters and not in unsuccessful dieters (Papies, Stroebe, & Aarts, 2008a; Papies, Stroebe, & Aarts, 2008b). Just as elaboration of thoughts about food can elicit actions to obtain food, elaboration of thoughts about health goals can activate the associated means by which these goals can be obtained (Kruglanski et al., 2002; Miller & Cohen, 2001). Superior WM in successful dieters may therefore support elaboration of food thoughts to activate behavioural schemas in line with health goals, such as seeking fruits and vegetables instead of high fat/sugar foods. Studies have found that better WM is selectively associated with fruit and vegetable intake and not saturated fat intake (Allom & Mullan, 2014; Sabia et al., 2009). This is further supported by the finding in Study 1 (Chapter 3) that better visuospatial WM was associated with a greater proportion of LED food consumption and dieting success.

The results from the UK Biobank analysis (Chapter 6) are also in line with dual-process theories. Dual-process theories applied to eating behaviour do not posit that WM is the only factor influencing the reflective-impulsive balance. According to Friese et al. (2011) reflective processes incorporate personal standards, attitudes and expectancies, whereas impulsive processes incorporate automatic associations, attentional biases and approach-avoidance tendencies. WM capacity falls within the “boundary conditions”, along with mood, alcohol, cognitive load, motivation to self-control, self-control strength and inhibition (Friese et al., 2011; Hofmann, Friese, et al., 2008). Boundary conditions are situational and dispositional boundaries that can influence the balance between the two systems. At any given time one of these factors may be changing this balance, e.g. if something happens that puts someone in a negative mood, all other factors may become irrelevant and that person may reach for a high energy dense snack. In a tightly controlled laboratory experiment, such as Study 1 in this thesis, the influence of WM on food intake decisions may be clear and easily measured. However, in the real world where a multitude of factors can influence behaviour at any given point in time, the influence and importance of WM is likely to be much harder to measure. The findings from the UK Biobank analysis are therefore not surprising when so many other factors contribute to behavioural decisions.

Measuring the wider context surrounding food choices may aid understanding of how WM relates to food intake outside of the laboratory. Executive functions are recruited when behaviour is effortful and cannot rely on automatic responses (Diamond, 2013). Situational and personal demands can create a situation where executive functions are recruited to aid decision making. For example, when in a negative mood many people will reach for high energy snacks (Heatherton et al., 1998; Herman et al., 1987), and trigger recruitment of executive functions to help maintain behaviour in line with health goals. Ecological momentary assessment, discussed in the next section on strengths and limitations, is one method that could be used to record both food intake and other factors that coincide with or trigger food intake, such as emotions and food cravings. In brief, ecological momentary assessment involves recording behaviour as it happens, instead of relying on retrospective self-report. This would help further understanding of the situations in which WM may be an important predictor of food intake outside of the laboratory.

Research should further consider the importance of cognition to food intake decisions more broadly. Responses to food cues are influenced by expectations and goals, whereby



previous experience of the consequences of consuming food contributes to expectations about future consumption (Balleine & O'Doherty, 2010). Food can therefore acquire the ability to trigger food intake due to learnt associations (Robinson & Berridge, 1993). Consideration of long-term health goals and the consequences of consuming food reduces the likelihood of consumption (Collazos et al., 2007). Long-term memory, specifically episodic memories of eating experiences, also influence future expectations about consumption as well as actual consumption. For example, recalling an enjoyable episode of eating vegetables increased expected enjoyment and actual consumption of vegetables (Robinson et al., 2011). Manipulating memory for an eating episode also influenced food intake, whereby both enhancing and reducing attention paid to a meal decreased and increased (respectively) later snack intake (Higgs & Donohoe, 2011; Higgs & Woodward, 2009). Future research should consider how WM may interact with these other aspects of cognition to influence food intake. Those with better WM may be better able to retrieve memories for recent eating and incorporate these into subsequent food intake decisions. Similarly, loading WM, and so preventing use of WM, might prevent retrieval and incorporation of memories for recent eating into subsequent food intake decisions. This may also be the case for retrieval and utilisation of long-term health goals from memory.

Improving cognitive abilities may not have substantial effects on eating behaviour without changes to the environment as well. We live in an obesogenic environment where advertising for high energy dense foods is omnipresent, constantly drawing attention to these foods. Energy dense foods are also widely available and often cheaper than healthier alternatives (Monsivais & Drewnowski, 2007), and increasing portion sizes of commercial foods is a factor contributing to over-consumption (Nielsen, 2003; Young & Nestle, 2003). Well-controlled laboratory studies have shown that food served in larger portion sizes increases intended and actual food consumption in children and adults (Cowling et al., 2013; Robinson, te Raa, & Hardman, 2015; Rolls, Morris, & Roe, 2002). Other environmental factors that influence food intake include plate shape, lighting, layout, labelling, and colour (Benton, 2015; Wansink, 2004, 2010). Qualitative research suggests that people are already aware of the increases in portion sizes available, yet they describe difficulties regulating consumption of foods provided in large portion sizes (Vermeer, Steenhuis, & Seidell, 2010). Simply telling people about these effects of the environment on behaviour, therefore, seems unlikely to work. Changing the environment, such as reducing the packaging sizes available and advertising of foods, is an alternative option that is likely to be met with resistance from the public (Vermeer et al., 2010). There is also no incentive to the food industry to make these changes, as smaller packaging and

restricted advertising are likely to reduce profits. Changes in the law could enforce such changes (Benton, 2015).

Environmental factors can also interact with cognition to influence expectations and food consumption. For example, labelling can be used to bring long-term health goals to mind, and this has been shown to reduce food consumption (Papies, 2012). Perhaps drawing attention to health goals encourages incorporation of these into food-related decisions. However, food labelling can have the opposite effect on behaviour. Labelling a food as ‘healthy’ reduced expectations that the food would taste good and actual enjoyment when the food was consumed (Raghunathan, Naylor, & Hoyer, 2006). Similarly, labelling food as low-fat increased the amount eaten and what participants believed was an appropriate serving size of that food (Wansink & Chandon, 2006). It may be that when a food is labelled as low-fat, people think it is acceptable to eat more of that food. Other environmental manipulations have also been less successful than expected. For example, traffic light labelling on foods changed the perceived healthiness of foods, but did not change shopping purchases or food selection (Borgmeier & Westenhoefer, 2009; Sacks, Rayner, & Swinburn, 2009). Yet traffic light labelling has been shown to increase connectivity between sub-regions of the prefrontal cortex implicated in successful control of food intake (Enax, Hu, Trautner, & Weber, 2015; Hare, Camerer, & Rangel, 2009). Future research is needed to investigate how manipulating the environment interacts with cognition to influence behaviour. Imaging research suggests that traffic light systems result in the necessary changes in brain activation and connectivity, yet these are not translated into changes in overt behaviour. Perhaps increased perceptions of health as a result change expectations about taste, eliciting self-control over behaviour in a way that reduces consumption of those foods.

Mindfulness may be an alternative method to bring behaviour in line with health goals without directly training self-control. Mindfulness is described as awareness of current thoughts and feelings, without judgment, reflection or rumination on these (Brown, Ryan, & Creswell, 2007; Chambers, Gullone, & Allen, 2009). Instead, people are instructed to view these experiences as momentary and passing mental events (Bishop et al., 2004). Often responses to food cues occur without conscious awareness, and mindfulness may serve to “de-automatise” these reactions and behaviour more generally by directing attention towards them. Dispositional mindfulness has been negatively associated with trait impulsivity and tendency towards disinhibition (Brown & Ryan, 2003; Lattimore, Fisher, & Malinowski, 2011), while brief mindfulness training reduced automatic

approach actions towards food (measured by an approach-avoidance task, Papies, Barsalou, & Custers, 2011). Mindfulness training also increased fullness, and reduced food cravings and food consumption in the laboratory (Alberts, Mulken, Smeets, & Thewissen, 2010; Fisher, Lattimore, & Malinowski, 2016). In a field study, brief mindfulness training reduced snack food consumption and increased salad consumption (Papies, Keesman, Pronk, & Barsalou, 2014). Mindfulness has also been shown to change dietary self-efficacy, increase cognitive control and reduce disinhibition in adults with type 2 diabetes (Miller, Kristeller, Headings, & Nagaraja, 2014). Mindfulness may therefore encourage controlled processing without the time and effort required to complete WM training. Future research should investigate whether changes in self-control and WM abilities mediate the effects of mindfulness training on behaviour.

### **7.3 Strengths and limitations**

#### **7.3.1 Study samples**

The samples used in studies in this thesis varied extensively. The Study in Chapter 3 was conducted in female undergraduate students, whereas Studies 2 (Chapters 4 and 5) and 3 (Chapter 6) were in men and women typically aged 40 plus, and with type 2 diabetes. Female undergraduate students were an appropriate sample to test the basic principle that WM plays a role in food intake decisions. This was also especially important for assessing how WM relates to dieting success, as dieting to control weight is more common in females (Rolls et al., 1991; Wardle et al., 2004). Since other research on the role of WM in food intake has not reported any differences between genders, I would expect the same results to be found in men (Allom & Mullan, 2014; Limbers & Young, 2015; Riggs, Chou, et al., 2010; Riggs, Spruijt-Metz, et al., 2010). Despite this, the purely female undergraduate sample used in this study remains a limitation. Type 2 diabetes was a particularly relevant sample to test the effectiveness of WM training, since changes in food intake as a result could have tangible health benefits to these people. There was also other ongoing research testing WM training in overweight/obese adults at the time the study was designed, and hence WM training in type 2 diabetes was a novel extension (Houben et al., 2016). Type 2 diabetes was also a population that was likely to have poorer WM at baseline than a non-diabetes sample, due to the cognitive deficits typically associated with diabetes (van den Berg et al., 2009). This was likely to reduce ceiling effects and increase the chances of finding effects of WM training. Although, studies have shown that there do not need to be WM deficits for WM training work (Klingberg et al.,

2002). Due to the large sample size available in Study 3 (Chapter 6), I was able to look at both people with and without type 2 diabetes and was able to control for sex.

### **7.3.2 Measuring food consumption**

Food intake was assessed in two main ways in the studies in this thesis: 1) a bogus taste-test; and 2) 24-hour recalls. The bogus taste-test paradigm is commonly used in laboratory based studies that assess the effect of a specific manipulation on food intake, but because it is often difficult to hide from participants that the amount they eat is being measured, there is a risk that demand characteristics may affect the results. In addition, the laboratory is an unusual context in which to consume food and so behaviour may be very different from consumption outside of the laboratory (De Castro, 2000). Food intake measured by 24-hour recall is a more ecologically valid measure than the laboratory taste-test, as it reflects food intake outside of the laboratory. However, food recalls are subject to self-reporting bias and under reporting (Hill & Davies, 2001), and research has shown that multiple 24-hour recalls are required to provide a measure of usual food intake (Ma et al., 2009). Scoring 24-hour recalls can also be very time-consuming if they are not linked to a nutritional database that can calculate macronutrient intake automatically.

The outcome measures of taste tests and 24-hour recall methods are often not the same. In a bogus taste-test, intake of specific foods can be measured, such as low energy dense (LED) versus high energy dense (HED) foods. In a 24-hour recall, outcomes are typically total macronutrients, such as total calories, carbohydrates, protein, fat, saturated fat and fibre. In Study 1 (Chapter 3), it was important to assess whether WM relates to LED and/or HED food intake because previous research has suggested that WM may be more important for LED than HED food consumption (Allom & Mullan, 2014; Riggs, Chou, et al., 2010; Sabia et al., 2009). The bogus taste-test paradigm was therefore preferred over other methods. In Study 2 (Chapters 4 and 5), I implemented both a food taste-test and a 24-hour recall to examine whether WM training differentially affects laboratory based and non-laboratory based food intake. WM training reduced saturated fat intake (in those high in dietary restraint) as measured by the 24-hour recall task, and did not affect intake measured by the taste-test. In Chapter 6, I was limited by the measures implemented by the UK Biobank cohort, which were 24-hour recalls and food frequency questionnaires. As mentioned in the discussion section for Chapter 6, multiple 24-hour recalls were implemented, providing a measure of usual food intake over a period of one year. The food frequency questionnaire was a weaker measure of food intake, as it was not a

validated measure and did not assess consumption of typical HED foods such as HED snacks, desserts etc. However, between the 24-hour recalls and food frequency questionnaires, I was able to derive measures of consumption of fruits and vegetables (FFQ) and total saturated fat intake (24-hour recall).

One possible limitation of the use of 24-hour recalls used to measure food intake in this thesis is that recall of eating episodes relies on memory. Since the main aim of this thesis was to assess the relationship between working memory and food intake, a measure of food intake that relies on memory may constitute a confound. However, a number of measures were taken to reduce this risk. Research suggests that accuracy of recall of food intake declines as more time passes between the day of recall and the day being recalled (Armstrong & MacDonald, 2000). In Chapters 4 and 5, participants were therefore asked to recall food intake for the day immediately before, and the same method was implemented in the UK Biobank (Chapter 6). Recall of the context of eating episodes has been shown to improve accuracy of recall (Armstrong & MacDonald, 2000). Participants were therefore asked to recall the time, location and eating companions of each eating episode in the 24-hour recalls implemented in Study 2 (Chapter 3). Eating context was not recalled in the 24-hour recalls implemented by the UK Biobank (Chapter 6), however the implementation of up to five 24-hour recalls increases my confidence that this reflects usual intake. The focus of this thesis was working memory, and research shows that 24-hour recalls rely on long-term memory (Armstrong & MacDonald, 2000). Despite this, working memory may still be important for retrieval of information from long-term memory and holding these active in mind.

Ecological momentary assessment (EMA) is an alternative measure of food intake that does not rely on memory for eating that could have been used in this thesis. EMA encompasses a range of methods that aim to capture behaviour as it happens and as people live their daily lives (LaCaille et al., 2013). Food diaries are one method of EMA, and advancements in technology have enabled more sophisticated food diary data collection, for example estimating energy intake from photographs of food (Martin et al., 2012). Martin et al. (2012) found that estimated energy intake was comparable to the gold standard doubly labelled water method. While EMA methods may still be subject to self-report bias (Ann Yon, Johnson, Harvey-Berino, & Gold, 2006) they reduce recall bias and provide a more ecologically valid assessment of dietary behaviour. However, use of such methods may limit study samples to those competent in using smart phones. Reactivity may also be a problem whereby close self-monitoring of a behaviour changes that

behaviour (LaCaille et al., 2013). EMA would have been a particularly relevant method for assessing changes in food intake following WM training in Study 2 (Chapters 4 and 5). However, due to the high demands of the WM training itself, I decided not to place any further demands on participants, such as asking them to keep a food diary.

Laboratory based assessment of food intake can be improved by making the laboratory more naturalistic. For example, by making it more like a home environment, with a dining table and chairs, soft lighting and other furniture. Ultimately researchers must aim to achieve an acceptable balance between control and ecological validity. The use of virtual reality technologies can aid this balance by submerging participants in a virtual reality and assessing their behaviour. For example, virtual reality can be used to assess purchasing behaviour in a virtual supermarket (Waterlander, Jiang, Steenhuis, & Ni Mhurchu, 2015). In some ways this may overcome issues of measuring actual purchasing behaviour where food purchased may be consumed by others (e.g. other family members). Of course the major limitation of such measures is that food is not actually consumed.

### **7.3.3 Measuring and training working memory**

A number of validated tasks to assess WM sub-components are available (Diamond, 2013). WM training has typically taken these validated tasks and turned them into a training version. The WM training used in Study 2 (Chapters 4 and 5) was a result of collaboration with other researchers who have conducted WM training before (Houben et al., 2016, 2011). Houben and colleagues designed this training based on the original work by Klingberg and colleagues in children with ADHD (Klingberg et al., 2002), and these tasks are now part of a commercialised battery of WM training tasks (see <http://www.cogmed.com>). The training used in Study 2 consisted of three tasks: a backwards digit span task, a visuospatial task and a letter span task. The digit span task is a validated measure of phonological loop capacity (Baddeley, Gathercole, & Papagno, 1998). The WM training utilised a backwards digit span task, and therefore trained the phonological loop sub-component of WM. The requirement to reverse the sequence before it is entered implements an additional demand on participants, namely a manipulation demand that is a core function of the central executive sub-component of WM (Diamond, 2013). The visuospatial WM task used in the training required participants to remember both the location and order of boxes that changed colour. Visuospatial WM consists of both visual (what) and spatial (where) components, and research suggests that these are processed separately (Darling et al., 2007). The training task used in this thesis therefore

likely trained mostly spatial WM, since participants had to remember location. While the task required the use of visual memory, this may have been minimal as the items to be remembered did not change (i.e. it was always a blue box). The letter span task was somewhat similar to an N-back task, as participants had to recall the Nth item in each sequence. In a classic N-back task, participants must continually update their memory of the sequence to remember what the Nth item is. However, in the task used in the WM training, the item in the sequence to be recalled was random, and hence participants had to remember the entire sequence and then recall one item at random. This is different from trying to remember the Nth back item, and may have required simple recall and not updating the contents of short-term memory. Future research should consider developing a full N-back training task. The use of validated tasks to train all three sub-components of WM is a strength of this thesis.

#### **7.3.4 Demand characteristics**

Demand characteristics were minimised in the studies in this thesis in a number of ways. Cover stories are widely used in food-related experimental research, and are one way to disguise the true aims of the study and prevent demand characteristics. In Study 1 (Chapter 3) participants were told they were taking part in a study on cognitive functioning and food taste perceptions. I also further distracted participants from the study aims by including questionnaires about mood. The cover story and distraction were implemented successfully, shown by few people guessing the aims of the study. However, a cover story was less appropriate for Study 2 (Chapters 4 and 5), and irrelevant for Study 3 (Chapter 6). As an intervention study requiring a large commitment from participants, the WM training used in Study 2 had to appeal to patients in some way. Using a control group that completed a dummy version of the training therefore allowed me to control for any effects of awareness of the study aims, since both groups would have the same knowledge and expectations. The inactive version of the training completed by the control group also allowed me to control for any effects of using a computer regularly and engaging in basic memory tasks. This choice was justified by the significantly improved WM in the control group from pre to post-training. I attempted to make the lunch buffet taste-test seem incidental to the long testing sessions (these took 2.5 hours), however this was unsuccessful and most people reported that they thought I was looking at what they ate in some way. In Study 3 (Chapter 6), the UK Biobank data collection procedures had no specific research aims, and hence a cover story was not applicable. However, the 24-

hour recalls may still have been subject to self-report bias, where participants underreported what they ate.

Ensuring the researcher is blind to the condition participants are in can also reduce demand characteristics and study bias. In Study 1 (Chapter 3) participants were allocated to condition after taking part in the study, based on their responses to the dietary restraint and disinhibition subscales of the TFEQ (Stunkard & Messick, 1985). I was therefore blind to whether participants were successful or unsuccessful dieters during the testing sessions, and hence this should have reduced bias in how participants were treated during the study. However, the need for targeted recruitment to balance the groups prevented this towards the end of the study. I was also blind to condition allocation for Study 2 (Chapters 4 and 5), as the online WM program was designed to display “condition 1” and “condition 2” rather than the true names of the conditions (and so selection bias was reduced in this study). I also remained blind to condition during the pre- and post-training assessment sessions, and so both performance bias and detection bias were also reduced. Maintaining this was difficult, however, as participants tended to talk about their experiences of the training quite freely even before the interviews were conducted at the end of the post-training assessment session. Researcher blinding was not applicable for Study 3 (Chapter 6) using the UK Biobank cohort.

#### **7.4.5 Assumption of the need to remember to choose LED food and inhibit automatic processes to choose HED food.**

Throughout this thesis it was assumed that participants had to remember to eat LED food and inhibit their automatic processes to seek HED foods. However, food cues do not appear to elicit automatic tendencies towards food in everyone. For example, a recent review found consistent evidence of attentional bias towards food stimuli in overweight/obese compared to healthy weight controls (Hendrikse et al., 2015). Studies also support that overweight/obese participants show an approach bias towards food compared to controls (Brockmeyer, Hahn, Reetz, Schmidt, & Friederich, 2015; Kemps & Tiggemann, 2014). Further evidence comes from the limited literature on successful vs unsuccessful dieting which has found that the attention of successful dieters is less biased towards food than unsuccessful dieters (Higgs et al., 2015), that food cues elicit health goals in successful dieters and not in unsuccessful dieters (Papies, Stroebe, & Aarts, 2008a; Papies, Stroebe, & Aarts, 2008b). Future research may benefit from identifying samples who do and do not show automatic tendencies towards HED foods. This may help to clarify the role of cognitive functions, like working memory and inhibitory control, in



food intake decisions. For example, working memory may play less of a role in food intake decisions in people for whom food cues do not elicit automatic responses to seek food.

#### **7.4 Conclusions**

Overall, experimental studies in this thesis provided evidence that sub-components of working memory may play a role in food intake and dieting success only in a controlled laboratory environment. Outside of the laboratory, the importance of working memory is minimal in the context of other factors. This suggests that working memory may be a resource recruited to guide behavioural decisions only in specific situations and contexts. Future research should investigate whether this is the case, and aim to understand the specific situations in which working memory influences behaviour.

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## Appendices

### Appendix A

Medline search terms

S1	(MH "Inhibition (Psychology)+")	Search modes - Boolean/Phrase
S2	SU "response inhibition"	Search modes - Boolean/Phrase
S3	SU "stop signals" OR TI "stop signals" OR AB "stop signals"	Search modes - Boolean/Phrase
S4	SU "stop signal" OR TI "stop signal" OR AB "stop signal"	Search modes - Boolean/Phrase
S5	(MH "Cues")	Search modes - Boolean/Phrase
S6	(MH "Diet, Reducing/PX")	Search modes - Boolean/Phrase
S7	SU "attentional bias modification" OR TI "attentional bias modification" OR AB "attentional bias modification"	Search modes - Boolean/Phrase
S8	SU "attention bias modification" OR TI "attention bias modification" OR AB "attention bias modification"	Search modes - Boolean/Phrase
S9	TI "attentional retraining" OR AB "attentional retraining"	Search modes - Boolean/Phrase
S10	SU "approach avoidance training"	Search modes - Boolean/Phrase



S11	(MH "Food Preferences") OR (MH "Feeding Behavior/PX") OR (MH "Eating/PX")	Search modes - Boolean/Phrase
S12	SU "eating behaviour" OR SU "eating behavior"	Search modes - Boolean/Phrase
S13	(MH "Energy Intake")	Search modes - Boolean/Phrase
S14	(MH "Food")	Search modes - Boolean/Phrase
S15	SU "dietary restraint"	Search modes - Boolean/Phrase
S16	TI "eating domain" OR AB "eating domain"	Search modes - Boolean/Phrase
S17	SU "food cues" OR TI "food cues" OR AB "food cues"	Search modes - Boolean/Phrase
S18	SU "food evaluation"	Search modes - Boolean/Phrase
S19	SU temptation OR TI temptation OR AB temptation	Search modes - Boolean/Phrase
S20	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10	Search modes - Boolean/Phrase
S21	S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19	Search modes - Boolean/Phrase
S22	S20 AND S21	Search modes - Boolean/Phrase
S23	S20 AND S21	Limiters - English Language

PsychInfo search terms

S1	DE “response inhibition”	Search modes - Boolean/Phrase
S2	DE “self control”	Search modes - Boolean/Phrase
S3	SU “stop signal” OR TI “stop signal” OR AB “stop signal”	Search modes - Boolean/Phrase
S4	SU “stop signals” OR TI “stop signals” OR AB “stop signals”	Search modes - Boolean/Phrase
S5	DE cues TI cue* OR AB cue*	Search modes - Boolean/Phrase
S6	SU “approach avoidance training” OR TI “approach avoidance training” OR AB “approach avoidance training”	Search modes - Boolean/Phrase
S7	SU “attentional bias modification” OR TI “attentional bias modification” OR AB “attentional bias modification”	Search modes - Boolean/Phrase
S8	SU “attentional training” OR TI “attentional training” OR AB “attentional training”	Search modes - Boolean/Phrase
S9	SU “attention modification” OR TI “attention modification” OR AB “attention modification”	Search modes - Boolean/Phrase
S10	DE “food intake”	Search modes - Boolean/Phrase
S11	DE “food preferences”	Search modes - Boolean/Phrase
S12	DE “eating behavior”	Search modes - Boolean/Phrase

S13	TI “value of food” OR AB “value of food”	Search modes - Boolean/Phrase
S14	DE temptation OR TI temptation OR AB temptation	Search modes - Boolean/Phrase
S15	DE “dietary restraint”	Search modes - Boolean/Phrase
S16	DE food	Search modes - Boolean/Phrase
S17	SU “food cues” OR TI “food cues” OR AB “food cues”	Search modes - Boolean/Phrase
S18	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9	Search modes - Boolean/Phrase
S19	S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17	Search modes - Boolean/Phrase
S20	S18 AND S19	Search modes - Boolean/Phrase

#### Embase search terms

S1	"inhibition (psychology)"/
S2	"response inhibition".kw.
S3	"stop signal".mp.
S4	"stop signals".mp.
S5	cue*.mp.
S6	"self control".mp. or self control/
S7	"approach avoidance training".mp.

S8	*"attentional training"/
S9	*"attention modification training"/
S10	"attentional bias training".mp.
S11	"attention modification".mp
S12	"attentional bias modification".mp.
S13	food intake/
S14	food preference/
S15	feeding behavior/
S16	"eating behavior".mp
S17	"eating behaviour".mp
S18	"value of food".mp.
S19	temptation*.mp.
S20	food/
S21	diet restriction/ or "dietary restraint".mp.
S22	"food cues".mp.
S23	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12
S24	13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22
S25	23 and 24
S26	limit 25 to (human and english language)

## Appendix B

Does neurocognitive training have the potential to improve dietary self-care in type 2 diabetes? Study protocol of a double-blind randomised controlled trial

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### Abstract

**Background:** Dietary self-care is a key element of self-management in type 2 diabetes. It is also the most difficult aspect of diabetes self-management. Adhering to long-term dietary goals and resisting immediate food desires requires top-down inhibitory control over subcortical impulsive and emotional responses to food. Practising simple neurocognitive tasks can improve inhibitory control and health behaviours that depend on inhibitory control, such as resisting alcohol consumption. It is yet to be investigated, however, whether neurocognitive training can improve dietary self-care in people with type 2 diabetes. The aim of this randomised controlled trial is to investigate whether web-based neurocognitive training can improve the ability of people with type 2 diabetes to resist tempting foods and better adhere to a healthy dietary regime.

**Methods/design:** In a double-blind multicentre parallel-group randomised controlled trial, 48 patients (based on power analysis results) with type 2 diabetes recruited from secondary health care services in Birmingham and London, will be randomly allocated to

either 25 online sessions of active or control working memory training. Selection criteria include being overweight/obese, having poor diabetes control and reporting to have difficulty following a healthy diet, but having good general health otherwise. Before, immediately after and 3 months after the training, assessment sessions will be conducted. Primary outcome measures include changes in working memory capacity, lab-based food intake and a 24-h guided food recall. Secondary outcome measures include changes in glycaemic control (HbA1c) and lipids. Participants' experiences of the training will be assessed qualitatively with semi-structured interviews post-training.

Discussion: This is the first trial investigating whether working memory training can improve dietary self-care in people with type 2 diabetes. If effective, this could prove to be a low-cost, easy to do online training that can be used long-term without side effects.

Trial registration: Current Controlled Trials ISRCTN22806944

Keywords: Type 2 diabetes, Working memory, Inhibitory control, Dietary self-care, Food

## Background

Dietary self-care is a key element of self-management in people with type 2 diabetes. To reduce the risk of developing both short- and long-term physical complications, patients are encouraged to reduce their energy intake and to adopt a well-balanced diet that is low in fat and sugar and high in fibre. However, many have difficulty following this advice [1]. Moreover, those who do adhere to their dietary recommendations often report feeling deprived and experiencing cravings for foods [2, 3]. The difficulties with following this diet and the burden reported by many patients together with treatment dissatisfaction have a direct effect on patient's self-reported quality of life [4, 5]. The modern food environment makes adherence to this diet especially difficult, with increases in availability, accessibility and convenience of high energy-dense food [6]. Advertising for such foods is also omnipresent and highly persuasive [7]. This presents a major challenge for anyone attempting to maintain a healthy diet, as exposure to food cues can lead to both cravings and overconsumption of these foods [8, 9]. In order to maintain a healthy diet, it is therefore essential to resist immediate temptation and focus on more distal goals. While dietary changes can be effective in improving glycaemic control [10], dietary self-care is generally poorly performed [11], and simple advice- and motivation-based interventions have had limited effects in improving this [12]. Novel and effective strategies to help people with type 2 diabetes that adhere to dietary recommendations are therefore needed.

Being able to resist tempting food requires adhering to long-term health goals and not giving in to short-term immediate desires. Dual-process theories of behaviour posit that the ability to do this depends on the balance between two different cognitive systems that control behaviour [13]: the reflective system, which promotes controlled, reflective behaviour and the impulsive system which promotes impulsive, automatic behaviour. The reflective system can exert inhibitory control over the impulsive system and is able to suppress its effects on behaviour (although not fully). When this occurs, self-control and resisting tempting foods is more likely to follow. Inhibitory control is therefore an important executive function implicated in the control of eating behaviour. Indeed, inhibitory control has been related to overeating and obesity. People with high impulsivity/ weak inhibitory control are more likely to overeat [14, 15] and be overweight/obese [16, 17]. Other work has specifically demonstrated that when inhibitory control is low, eating behaviour is more strongly guided by impulsivity [18–20]. Suppression of automatic, motivational, impulsive responses to food however improves the ability to resist consumption of desirable food items [15, 21].

Neuroimaging evidence has found that people with type 2 diabetes (compared to body weight matched healthy controls) show greater neural activity in subcortical areas of the brain in response to food cues [22]. These subcortical areas are part of the brain's impulsive system [23]. There was also greater activity in response to food pictures in cortical areas including the orbitofrontal cortex and insula [22]. These regions are part of the reflective system and as such are important for inhibitory control and restraining immediate desires in favour of long-term outcomes [23]. This neuroimaging study further showed that increased activity in cortical areas was associated with better self-reported dietary self-care, whereas activity in subcortical areas was associated with poorer dietary self-care [22]. These findings suggest that interventions aimed at maximising inhibitory control may improve dietary self-care in type 2 diabetes.

Working memory capacity is an important executive control ability that has been shown to moderate the role of impulsive processes in predicting health behaviours. In people with low working memory capacity (compared to those with high working memory capacity), impulsive processes are better predictors of alcohol consumption [24, 25], cigarette use [25] and unhealthy food consumption [26, 27]. Diabetes is associated with a range of cognitive impairments [28], and deficits in executive functioning in particular (including working memory) could be contributing to difficulties in controlling food intake [29]. Evidence from studies of top-down inhibitory control demonstrate that training working

memory (WM) can improve inhibitory control and change behaviour in a variety of clinical contexts, including in children with attention-deficit hyperactivity disorder [30, 31], in older people [32], problem drinkers [33] and stimulant drug abusers [34]. For example, working memory capacity increased and alcohol consumption decreased for more than 1 month afterwards in problem drinkers who underwent 25 sessions of online WM training [33]. Working memory training is believed to work by increasing activity in the prefrontal cortex, another part of the reflective system [35]. Given that common mechanisms are known to underlie responses to palatable foods and addictive substances like alcohol [36], these data suggest that cognitive training could be effective in strengthening the ability to resist tempting foods and hence improve dietary control in people with type 2 diabetes.

#### Aims and hypotheses

The aim of this study therefore is to investigate whether 25 sessions of neurocognitive working memory training can improve dietary self-care in people with type 2 diabetes (compared to passive control training).

#### Primary outcome measures

It is expected that WM training will enhance working memory capacity and reduce high-energy-dense food intake. It is important to demonstrate that the WM training effects transfer to other measures of working memory (to help rule out simple practice effects); therefore, both the trained and novel non-trained tasks will be used to assess working memory and executive functioning. Changes in food intake will be measured at a lunch buffet in the laboratory and via a 24-h food recall task to obtain a measure of usual food intake outside of the laboratory.

#### Secondary outcome measures

It is expected that WM training will reduce lipid and glycated haemoglobin (HbA1c) blood levels. HbA1c is considered a long-term measure of diabetes control, and hence, this will test the longer term effects of the training. Lipid blood levels will act as a biological measure of food intake; if less high-energy-dense food is consumed, lipid blood levels should be lower. Participants' experiences of the training will be assessed qualitatively with semi-structured interviews post-training.

#### Methods/design



## Ethics

This study has been approved by the Middlesex University Ethics Committee and by an NHS Research Ethics Committee. Prior to this, the study was reviewed by the Research Committee of Diabetes UK.

## Design and participants

This is a randomised, double-blind 2 (condition: active training, passive control training) × 3 (time point: pre, post, follow-up) factorial design study. This multisite project will run in London and Birmingham, UK. Participants will be a total of 48 NHS patients with type 2 diabetes recruited from diabetes clinics at local hospitals. Patients will be informed about the research by their health care professional initially, and the researcher will be present in clinics to provide further information and answer questions. Upon acceptance to participate, the first pre-training assessment session will be arranged. Assessments will occur at baseline, immediately after and 3 months after completion of the training.

Inclusion criteria are (1) have had type 2 diabetes for 2 years or more, (2) poor diabetes control (HbA1c >64 mmol/l),

(3) self-reported difficulty following a healthy diet, (4) general good health, (5) overweight with a BMI  $\geq 25$  and

(7) treatment of diabetes can include diet only, tablets or insulin (for at least the last 6 months). Exclusion criteria are (1) neurological or psychiatric disorders, including eating disorders and clinical depression, (2) recent (within the last 6 months) changes in diabetes treatment (e.g., transfer to insulin), (3) alcohol and/or substance abuse and (4) treatment by GLP-1 or DPP-4 inhibitors. The participants will be reimbursed £10 for travel expenses for each of the three assessment sessions.

## Power calculation

The power calculation for this study was based on Houben et al.'s working memory training study in problem drinkers [33]. In this study, working memory training resulted in a large effect size of 0.27 for the interaction between time and condition. We anticipate a similar large effect size in our sample. Thus, using a 2 (condition: active, passive control) × 3 (time point: pre, post, follow-up) within-between design and assuming correlations among measures of 0.4 and a nonsphericity correction of 0.6, the estimated sample size should be at least 20 participants per group when power is set at 0.80 and  $p < 0.05$ . Based

on previous experience with longitudinal studies, we expect an attrition rate of 15–20 %. Therefore, we will recruit a minimum of 24 participants per group to account for possible attrition (total sample size  $N = 48$ ).

#### Randomisation and blinding

The participants will be randomly allocated to either the active or passive control training conditions using an on-line program-generated block randomisation list (blocks of ten, [37]). Condition allocation will take place during the pre-training assessment session when the participant signs up to the online training program. Both participants and the researchers conducting the assessment sessions will be blind to the training condition participants were allocated to.

#### Training program

The working memory training will be the same program of tasks as used by Houben et al. [33]. This was designed based on the work of Klingberg et al. [38]. The training consists of repeatedly practising three working memory tasks: letter span task, backwards digit task and visuo-spatial task. In the backwards digit task, several numbers are presented on the screen one at a time, which participants have to remember and reproduce in reverse order (using the mouse and on-screen number pad). In the visuo-spatial task, a sequence of boxes light up one at a time in a  $4 \times 4$  grid. The task here is to remember the location and order in which the boxes lit up and to reproduce this using the mouse to click on the squares in the grid in the right order. In the letter span task, a sequence of letters is presented one at a time in a circle. Once the sequence has finished, one of the positions in the circle is cued and the participants have to enter the letter that appeared in this location using the keyboard. In each training session, there are 30 trials of each task.

There will be two training conditions: active and passive control training. In the active training condition, the difficulty level closely follows the working memory capacity of the participant. Following two correct answers, the number of items to remember increases by 1. Following two incorrect answers, the number of items to remember decreases by 1. In the passive control condition, the participants complete the same set of three tasks, but the difficulty level remains low so as to not train WM. The active rather than passive control group allows us to control for expectancy effects, as well as any effects that may occur due to repeated use of computers and adhering to a training schedule.

#### Primary outcome measures

### Working memory capacity (trained tasks)

The three tasks used in the training program will also be used in an assessment version. In the assessment version, the number of items to remember for each task begins low (three items) and increases by one following two consecutive correct answers. When two incorrect answers are given, the task is terminated. The longest sequence of items correctly recalled for each of the three tasks is summed and averaged to provide a measure of WM capacity across the three WM tasks.

### Working memory capacity (non-trained tasks)

These will consist of the Cambridge Neuropsychological Test Automated Battery (CANTAB, Cambridge Cognition, Cambridge, UK) Attention Switching Task, Paired Associates Learning, Spatial Span and Spatial Working Memory tasks. The Spatial Span and Spatial Working Memory tasks measure working memory ability/capacity. The Paired Associates Learning task measures visual memory and new learning. The Attention Switching Task measures interference of irrelevant information and hence top-down cognitive control processes. Outcome measures for these tasks will include reaction times, error scores, span length and memory scores.

### Lab-based food intake (lunch buffet)

The participants will be provided with a staple lunch food item (egg sandwiches or cheese sandwiches) along with six different snack foods. The weight (in grams) of the snack foods has been calculated so that a similar visual amount of each food is provided. Three of the snack foods are low energy dense (carrot sticks ~110 g, ~44 kcal; plum tomatoes ~139 g, ~28 kcal; salt and vinegar rice cakes ~10.5 g, ~40 kcal) and three are high energy dense (ready salted crisps ~25 g, ~133 kcal; chocolate chip cookies ~64 g, ~323 kcal and cheese and onion rolls ~93 g, ~283 kcal). The cookies, rice cakes, cheese and onion rolls and the sandwiches will be broken up into smaller pieces to prevent the participants from counting the number of items they eat and this influencing their intake. The food will be weighed before and after the lunch buffet (out of sight of the participant) and used to calculate how much was eaten by subtracting the post-buffet weight from the pre-buffet weight of each food.

### Non-lab-based food intake (24-h guided recall)

The participants will be asked to write down everything they ate and drank on the previous day. This is a guided recall procedure which asks the participants about the time, location and eating companions of the meal [39]. While this approach covers only a limited sample of an individual's food intake, research has shown that this method provides an accurate and representative picture of usual food intake [40]. The number of low- and high-energy-dense food and drink items reported will be totalled as a measure of food/drink intake. The participants will also be asked how many junk food items and portions of fruits and vegetables they usually eat per day.

#### Secondary outcome measures

##### HbA1c and lipids

HbA1c and lipid levels will be assessed by taking blood samples which will be sent for analysis at the hospital laboratories.

##### Semi-structured interviews

The semi-structured interviews will take place at the end of the post-training assessment session. The purpose of this is to understand people's experiences of the training. The participants will be asked about what they had hoped to gain from the training, their experiences of it, how they managed to include it into their life and how the training affected their eating habits and the control of their diabetes.

##### Other measures

To characterise the study sample and to control for potential baseline differences, we will also assess a number of other measures, including BMI (height and weight will be measured without shoes and heavy outdoor clothing and used to calculate BMI kg/m<sup>2</sup>), eating style (General Food Cravings Questionnaire [41], Three Factor Eating Questionnaire-18 [42], Dutch Eating Behavior Questionnaire [43]), diabetes-related behaviours (Diabetes Specific Quality of Life Questionnaire [44], Summary of Diabetes Self-Care Activities Scale [45], Dietary Self-Efficacy Scale [46]), depressive symptoms (Patient Health Questionnaire-9 [47]), physical activity (International Physical Activity Questionnaire [48]), physiological data (blood pressure, blood glucose levels) and demographic information (gender, age, ethnicity, education level, length of diabetes diagnosis, how the diabetes is controlled, existence of co-morbid conditions). Illness-related information will be collected at each of the three assessment sessions to track any

changes in co-morbid conditions and diabetes treatment. Mood and hunger will be measured both before and after the blood tests, computer tasks and lunch buffet, as these could influence task performance [49–51]. Food-specific inhibition will be assessed using a food go/ no-go task. This task consists of 200 trials split across four blocks. In blocks one and two, the participants are instructed to respond (press the space bar on the keyboard) when they see a picture of toiletries and to withhold a response when they see sports-related pictures. In blocks three and four, the participants are instructed to respond to pictures of stationary and withhold responses to food-related pictures. Fewer commission errors (responding to no-go trials) on no-go food picture trials compared to no-go sports objects trials will indicate greater baseline food-specific inhibitory control ability.

## Procedure

### Assessment sessions

Assessment sessions will last approximately 2.5 h. The participants will provide informed consent at the beginning of the pre-training assessment session. See Table 1 for the order of completion of the tasks. For the lunch buffet, the participants will be given 15 min to eat (alone) and will be told to eat as much or as little as they wish. Questionnaires regarding eating habits will be completed last to avoid any influence on other responses. The post-training and follow-up assessment sessions will be the same as the pre-training assessment session, except that consent will not need to be retaken, and in addition, the semi-structured interview will be conducted (post-training assessment) and the participants will be probed about their awareness of the purpose of the lunch buffet (follow-up assessment). See Fig. 1. for a flowchart of how the participants will progress through the trial.

Table 1 Measures used at each time point and the order in which they are used

	Immediate post-training	3-month follow-up assessment
Pre-training assessment	assessment	
Informed consent		
Hunger and mood questions	Hunger and mood questions	Hunger and mood questions

Blood pressure	Blood pressure	Blood pressure
Blood tests	Blood tests	Blood tests
Height and weight	Height and weight	Height and weight
Hunger and mood questions	Hunger and mood questions	Hunger and mood questions
Computer tasks (go/no-go, CANTAB, WM assessment and sign-up to training)	Computer tasks (go/no-go, CANTAB, WM assessment)	Computer tasks (go/no-go, CANTAB, WM assessment)
Hunger and mood questions	Hunger and mood questions	Hunger and mood questions
Buffet lunch + food liking questions	Buffet lunch + food liking questions	Buffet lunch + food liking questions
Hunger and mood questions	Hunger and mood questions	Hunger and mood questions
24-h guided recall task	24-h guided recall task	24-h guided recall task
Questionnaires (demographics, DSQOL, SDSCA.	Questionnaires (demographics, DSQOL, SDSCA.	Questionnaires (demographics, DSQOL, SDSCA.
DSES, IPAQ, PHQ-9, DEBQ, TFEQ-18, GFCQ)	DSES, IPAQ, PHQ-9, DEBQ, TFEQ-18, GFCQ)	DSES, IPAQ, PHQ-9, DEBQ, TFEQ-18, GFCQ)
	Semi-structured interview	Awareness probe

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Note: WM, working memory; DSQOL, Diabetes Specific Quality of Life Questionnaire; SDSCA, Summary of Diabetes Self-Care Activities Scale; DSES, Dietary Self-Efficacy Scale; IPAQ, International Physical Activity Questionnaire; PHQ-9, Patient Health Questionnaire-9; DEBQ, Dutch Eating Behavior Questionnaire; TFEQ-18, Three Factor Eating Questionnaire-18; GFCQ, General Food Cravings Questionnaire

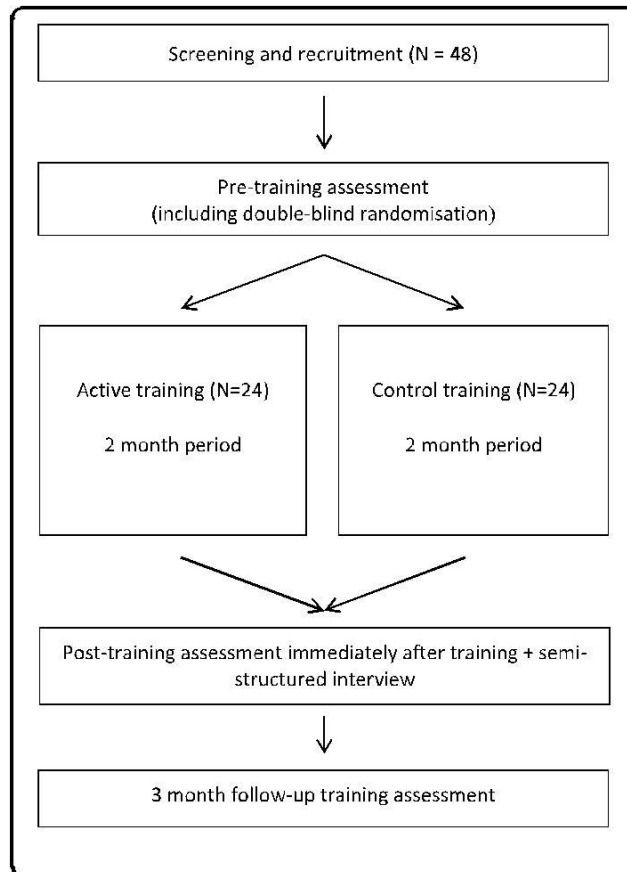


Fig. 1 Flowchart of the participants through trial

### Training

The training starts the day after the pre-training assessment session and is completed online in the comfort of the participants' own homes. The participants will complete 25 online training sessions over a minimum of 25 days and a maximum of 50 days. Only one session can be completed per day, and the participants have 2 days to complete each session. Up to five sessions can be missed before they are excluded from the study.

### Interviews

Sixteen interviews will be conducted (lasting a maximum of 30 min each), 8 with participants from the Birmingham site and 8 from the London site. Those interviewed will be targeted to represent the range of genders, age and ethnicities taking part in the study. At the beginning of the interviews, the participants will be reminded that their responses will be kept confidential and encouraged to be as honest as possible in their answers.

### Analyses

Baseline group differences on demographic and biographic data will be assessed using ANOVAs. Any found to be significant will be included as covariates on subsequent analyses. The primary and secondary outcome measures of interest will be assessed using a 2 (condition: active, control)  $\times$  3 (time point: pre, post, follow-up) between-within ANOVA, with post hoc tests as necessary. These analyses will be done twice, once taking an Intention to Treat approach and once taking a Per-Protocol approach [52]. In an Intention to Treat approach, all participants are included in the analysis, regardless of training adherence and withdrawal. This provides a more conservative estimate of the effect of the training, compared to a Per Protocol approach to analysis which only includes the participants who completed the study.

The qualitative data obtained from the semi-structured interviews will be recorded, transcribed verbatim and imported into NVivo for analysis. A thematic analysis will be conducted to inductively identify initial codes and ultimately broader themes important to the participants' experiences of the training [53].

## Discussion

This is the first trial to investigate whether working memory training can change the eating behaviour of people with type 2 diabetes. This is a highly relevant population for testing the clinical effectiveness of such training. If successful, online working memory training could prove to be a cost-effective intervention that can be used long-term without side effects, improving the quality of life of people with type 2 diabetes. It could also prevent or delay the need for drugs or insulin to control glycaemic levels. The possible applications would also extend beyond those who have type 2 diabetes. For example, it could be used by people who are overweight/ obese or have "pre-diabetes" (impaired glucose regulation) to help prevent/delay the development of type 2 diabetes.

The ideal intervention for any medical condition is one that improves the condition, is easy for patients to do and has no unpleasant short- or long-term side effects. Therefore, the secondary aim of this study is to gain an understanding of patient's experiences with the training. An online intervention is ultimately only going to be successful if patients are able to incorporate it into their life. The semi-structured interviews will allow us to assess how patients experienced the training, such as how they managed to integrate it into their lifestyle and the effects they think it had on their diet and diabetes control. This will provide future direction for research, such as investigating the effects of fewer or shorter training sessions.



As the participants will not need to attend the clinic for each training session, but rather can do it at home, we hope this will improve adherence rates. The participants can do each training session at any time and in any place suitable to them. This will allow us to assess the effectiveness of a training program that would likely be impossible if the participants had to attend the clinic for every training session. There are shortcomings to an online intervention however. Without a researcher present to ensure that the participants do each training session, patients may be more likely to not complete all sessions. Adherence to the intervention is therefore encouraged with an email reminder each day that they are now able to complete the next training session, with a URL link that the participants can click on, taking them directly to the training session. Therefore, the participants (1) receive a reminder every day to complete that day's training session and (2) do not have to remember a username and password in order to do the training. This should ensure good rates of adherence to the training program. Another limitation to online training programs is that it requires the participants to have a computer and internet access. Not all people will have this, especially older people, whom we anticipate will form a large proportion of our sample. However, according to the Office of National Statistics, 84 % of households in Great Britain have access to the internet in 2014, so we do not anticipate this being a barrier to recruitment [54].

#### Abbreviation

WM: working memory.

#### Competing interests

The authors declare that they have no competing interests.

#### Authors' contributions

AN, SH and KH conceptualised the study, and all authors contributed to the design of the study. VW and INM conducted data collection, along with PN and MR. VW drafted the manuscript with input from all authors. All authors have read and approved the final manuscript.

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