The effects of continuous theta burst stimulation (cTBS) to the left dorsolateral prefrontal cortex

on executive control resources, subjective food cravings, and the consumption of appetitive

snack foods.

by

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Authors Declaration

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners. I understand that my thesis may be made electronically available to the public.

Abstract

Prior research has demonstrated that stronger executive control resources (ECR) are positively associated with healthy dietary habits. Given that ECRs are understood to involve the operation of the prefrontal cortex, specifically the dorsolateral prefrontal cortex (DLPFC), the differential operation of the DLPFC may explain individual differences in dietary self-control. The present study was designed to examine the causal status of the relationship between DLPFC function and two parameters of dietary self-control: subjective food cravings and the consumption of appetitive snack foods. Using a within subjects design, 21 female participants received both active and sham continuous theta burst stimulation (cTBS) to the left dorsolateral prefrontal cortex. Subjective food cravings were assessed before and after each stimulation session, and the amount of food consumed during a bogus taste test was objectively measured following each stimulation session. In addition, following each stimulation session participants completed three standardized ECR measures. Results indicated that participants consumed significantly more snack foods following active as compared to sham stimulation, but this finding was specific to the consumption of appetitive foods (i.e., milk chocolate and potato chips). In addition, as compared with sham stimulation, performance on the Stroop task was significantly impaired following active stimulation. Finally, stronger food cravings were reported following active relative to sham stimulation, but these were highly selective the reinforcement-anticipation aspect of cravings. Together, these results support the contention that the ECRs, as modulated through DLPFC activity, regulates food cravings and the consumption of palatable energy dense foods.

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Table of Contents

List of Figures

List of Tables

Chapter 1

1.0 Obesity Epidemic

Obesity is a major public health problem in most parts of the world today. Obesity is associated with various physical disabilities, psychological problems, and is a risk factor for numerous detrimental health conditions (e.g., hypertension, cardiovascular disease, diabetes, and cancer; WHO, 2011). In fact, obesity is the fifth leading risk factor for premature death worldwide, and it is estimated that more than 2.8 million people die each year as a result of being overweight, or obese (WHO, 2011). Additionally, it is estimated that 44 % of diabetes, 23 % of heart disease, and up 41 % of certain cancer cases can be attributed to being overweight, or obese (WHO, 2011). Given that the worldwide prevalence of obesity has doubled since 1980 (WHO, 2011), the medical costs associated with treating these health conditions could potentially overwhelm the health care system in many countries (Anis et al., 2010; Flegal, 2005; Peters, Wyatt, Donahoo, & Hill, 2002). For example, in 2001 it was estimated that the health care costs associated with the treatment of obesity related health conditions in Canada were $ 4.3 billion (2.2 % of the total health care expenditures; Katzmarzyk & Janssen, 2004). In the year 2006, the estimated health care costs increased to $ 6.0 billion (4.1 % of total health care expenditures; Anis et al., 2010). It is evident that obesity is a serious public health issue, but in order to stop and ultimately reverse the obesity epidemic, one must determine the causal and maintaining factors of obesity.

Prior studies have suggested that common genetic factors may explain individual differences in body mass index (Baessler et al., 2005; Schousboe et al., 2003; Silventoinen, Rokholm, Kaprio, & Sørensen, 2009). However, it is highly unlikely that the rate of change in common genetic factors can explain the rapid increase in the prevalence of obesity in such a

short time span (Hill & Peters, 1998; Peters et al., 2002; Poston & Foreyt, 1999). In addition, a recent genome-wide association study (GWAS) identified 32 genetic loci that increase the susceptibility to obesity, but it is estimated that these loci only explain 1.5% of the genetic variation in BMI (Speliotes et al., 2010). Moreover, Speliotes et al. (2010) estimated that there are 250 undiscovered genetic loci that increase the susceptibility to obesity, but even after accounting for the influence of these undiscovered loci, it was estimated that common genetic factors can only explain between 6 % and 11% of the inter-individual variance in BMI. Therefore, although genetic factors may play a role in adiposity, the obesity epidemic *per se* is more likely related to non-genetic influences, or at minimum, a complex interplay of genetic predispositions and dynamic environmental factors.

1.1 Etiological Factors and Obesity

Humans have a strong and well-demonstrated preference for foods that are high in fat and sugar (Drewnowski & Greenwood, 1983; Drewnowski, 1997); a preference that is thought to be evolutionary in origin. The majority of human evolution took place under conditions of food scarcity, in which the food supply was inconsistent and a high level of energy expenditure was required to procure food. As such, it is largely thought that humans evolved with a preference for foods high in fat and sugar, because such preferences would result in a favourable balance between the energy gained per energy expended on food procurement (Peters et al., 2002). However, the modern environment is no longer characterized by conditions of food scarcity. The food production system has become highly mechanized and commercialized (Popkin, Duffey, & Gordon-Larsen, 2005; Poston & Foreyt, 1999), resulting in an environment characterized by a seemingly infinite access to inexpensive and palatable energy dense foods (Hill & Peters, 1998; Jeffery & Utter, 2003; Popkin et al., 2005); therefore acting on our evolved preferences is

2

tantamount to the chronic consumption of high caloric foods. Nonetheless, environmental factors only increase the likelihood an individual will become obese, and despite this mismatch between the modern environment and our evolved biology the majority of the population has managed to maintain a healthy weight. Given that not all are equally subject to the pull of the environment with respect to eating behavior, modern thinking about obesity has turned to internal modulators of environmental influence. Cognitive factors have been recently offered as one such internal modulator. I will discuss the rationale and supporting research in the next section.

Chapter 2

2.0 Executive Control Resources and Dietary Behaviours

It is evident that healthy dietary patterns are not fully supported externally (i.e., by the modern living environment), and therefore depend on internal factors. As such, one important class of modulators of dietary behaviour could be cognitively-based self-control abilities. Humans have a highly evolved prefrontal cortex that enables a number of higher order cognitive functions (Miller, 2000; Miller & Cohen, 2001). Executive functions (EF), or executive control resources (ECR), are a collection of distinguishable, but interconnected, cognitive functions that enable "top-down" control of behaviour (Miyake & Friedman, 2012; Miyake et al., 2000). As such, humans have the capacity for self-control, and therefore are able to override habitual responses, and act in accordance to behavioural intentions or other internally generated goals/aspirations (i.e., limit the consumption of energy dense foods to maintain a healthy diet). Therefore, the extent to which individuals differ in their ability to exercise self-control (i.e., ECRs), and therefore control how they eat, could modulate their risk for overeating and obesity in the modern environment.

An accumulating body of literature suggests that integrity of the executive control system is indeed correlated with obesogenic behavior tendencies in a theoretically meaningful way. For example, it has been demonstrated that individuals with weak inhibitory control, relative to individuals with strong inhibitory control, consume more high caloric foods during a bogus taste test (Guerrieri, Nederkoorn, & Jansen, 2007), gain the more weight, over the course of a year (Nederkoorn, Houben, Hofmann, Roefs, & Jansen, 2010), and are less successful in maintaining a weight loss diet (Guerrieri, Nederkoorn, & Jansen, 2008). Across a large age span, stronger ECRs have been selectively associated with the avoidance (i.e., decreased consumption)

of fatty foods (but not non-fatty foods), and this effect was largely invariant across the lifespan (Hall, Lowe, Vincent, Mourtzakis, & Roy, 2013; Hall, 2012). Moreover, other studies show that ECR strength also moderates the intention-behavior link for such behaviors. For example, in Allan and colleagues (Allan, Johnston & Campbell, 2010), individuals with impaired inhibitory control consumed more chocolate during a bogus taste test than those with effective inhibitory control, despite intentions to avoid high calorie snacks. Similar results were reported by Allan, Johnston and Campbell (2011): Individuals with effective ECRs were more likely to achieve or improve on their dietary intentions to consume more fruit and vegetables and avoid snack foods, whereas individuals with impaired inhibitory control were more likely to deviate from their dietary intentions, and consume more snack foods. Likewise, Hall, Fong, Epp and Elias (2008) reported that individual differences in ECRs moderated the association between behavioural intention and actual behavioural performance. Individuals with stronger ECRs were more likely to maintain their dietary intentions (i.e., fruit and vegetable intake) and turn their intended intentions into actions (i.e., consume the intended amount of fruit and vegetables). These results suggest that effective ECRs predict intention-behavior consistency in the dietary domain.

Several recent studies have suggested that environmental cues moderate the expression of ECRs in dietary behavior. For example, Hall, Lowe and Vincent (2013) found that in the presence of facilitating environmental cues (i.e., being told to consume as much food as they would like), individuals with weaker ECRs consumed significantly more food during a bogus taste test than those with high ECRs. A second study, involving older adults, replicated these effects (Hall et al., 2013). Together these suggest that the potency of ECRs in determining consumptive behavior of high calorie foods is amplified when environmental cues are facilitating in nature. Given that most food advertising for snacks encourages consumption, there is some

possibility that our modern living environment is especially encouraging of consumption among those with lower executive control.

Taken together, the current body of literature suggests that ECRs are associated with dietary behaviours. Given that ECRs are understood to centrally involve the operation of the prefrontal cortex (PFC) and associated neural systems (Miller & Cohen, 2001), it is possible that the differential operation of the PFC can explain individual differences in inhibitory control and subsequently dietary behaviours.

Chapter 3

3.0 The Prefrontal Cortex

The PFC is a set of interconnected cortical structures that has projections to and from various cortical and subcortical regions, such as the motor cortex, and the cortical regions associated with emotions and reward processing (Miller, 2000; Miller & Cohen, 2001; Ridderinkhof, van den Wildenberg, Segalowitz, & Carter, 2004). These widespread projections are thought to allow the PFC to exert "top-down" control over other cortical regions, and otherwise control various aspects of human behaviour (Miller, 2000; Miller & Cohen, 2001). Specifically, the PFC is implicated in cognitive control, such that the operation of the PFC allows humans to override habitual responses to external stimuli and act in accordance to our behavioural intentions (Miller, 2000). Additionally, the discrete sub regions of the PFC are implicated in differential facets of executive control (Ridderinkhof et al., 2004). For instance, the operation of the ventrolateral prefrontal cortex (vlPFC) is often implicated in task switching (Braver, Reynolds, & Donaldson, 2003), whereas the operation of the orbitofrontal cortex (OFC) is often associated with reward monitoring and encoding the reward value of various stimuli (Kringelbach & Rolls, 2004). The extent in which different sub regions of the PFC are functionally differentiated is well documented in the literature; however, an understanding of the functional anatomy and neuronal connectivity of the PFC is required to dissociate which aspects of ECRs are supported by the differential sub regions of the PFC.

3.1 Anatomy of the Prefrontal Cortex

The PFC resides in the anterior part of the frontal lobes, and is comprised of three main divisions: the lateral PFC, orbitofrontal cortex (OFC) and the medial frontal cortex (MFC; Ridderinkhof et al., 2004). The lateral PFC can be further divided into the dorsolateral prefrontal cortex (DLPFC) and the ventrolateral prefrontal cortex (vlPFC). The anterior cingulate cortex (ACC) resides within the MFC. The OFC can be divided into the medial, ventral, lateral and frontopolar subdivisions (Ridderinkhof et al., 2004).

3.2 Frontal-subcortical pathways

There are five differential, but parallel, frontal-subcortical pathways that link discrete regions of the frontal cortex with various subcortical regions (Cummings, 1995; Tekin & Cummings, 2002); the pathways are named according to the cortical structure in which they originate. Each pathway shares a common anatomical structure (see Figure 1), such that they originate in the frontal cortex and project to the basal ganglia (the basal ganglia consists of the caudate, putamen, and striatum; Middleton & Strick, 2000), the globus pallidus and substania nigra, and from there to the thalamus (Cummings, 1995; Tekin & Cummings, 2002). There are two pathways within each circuit: (1) a direct pathway that connects the striatum and the globus pallidus; (2) an indirect pathway connecting the striatum to the globus pallidus externa, then to the subthalamic nucleus, and back to the globus pallidus (Cummings, 1995; Tekin & Cummings, 2002).

The motor pathway originates in the supplementary motor area, and is thought to be involved in regulating motor functions. The oculomotor pathway originates in the frontal eye fields, and like the motor pathway is thought to be linked to motor functions. The DLPFC, OFC, and ACC pathway originate in their corresponding cortical region, and are thought to be linked

to ECRs, social behaviour and motivation (Tekin & Cummings, 2002). For the purpose of this paper, only the DLPFC subcortical circuit will be described in detail.

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    │         Thalamus              │
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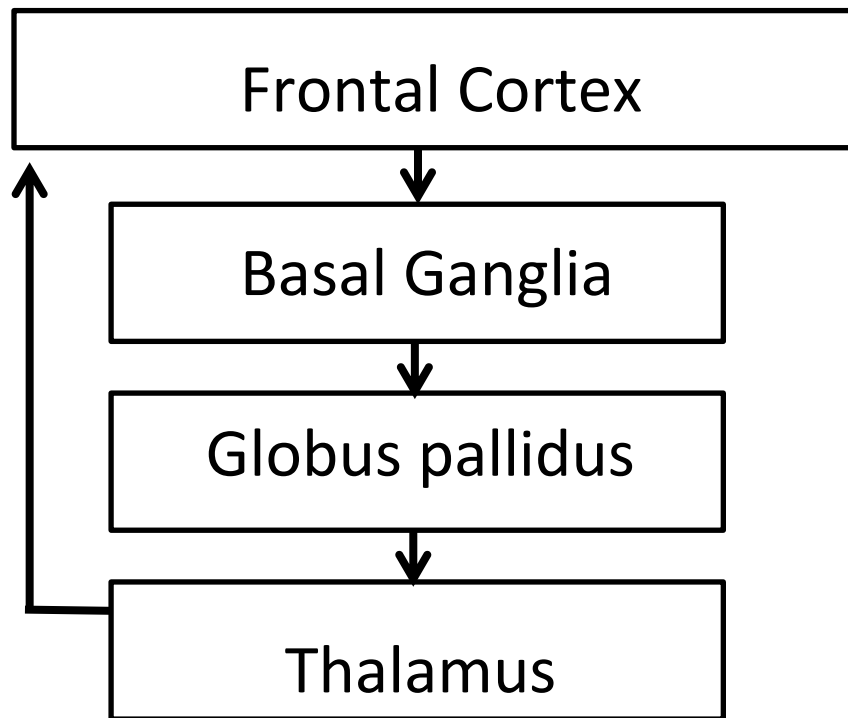
Figure 1: Schematic summary of the common anatomical structure of the frontal-subcortical pathways (adapted from Tekin & Cummings, 2002).

3.21 DLPFC-subcortical pathway

The DLPFC-subcortical circuit originates in the DLPFC and projects to the dorsolateral head of the caudate nucleus, and from there projects to the lateral dorsomedial globus pallidus interna and ventral anterior and mediodorsal thalamus (see Figure 2; Tekin & Cummings, 2002). These projections are thought to allow the DLPFC to directly modulate the operation of the basal ganglia, and vice versa; (Groenewegen, Wright, & Uylings, 1997); however, indirect modulation can occur through other cortical pathways. At the level of the striatum, the DLPFC is believed to interact with the striatal output neurons, in which the information from various cortical regions is projected to the striatum (i.e., the caudate), projected through the DLPFC-subcortical pathway,

9

and then processed in the DLPFC, which in turn modulates the operation of the striatum (Alexander, DeLong, & Strick, 1986; Cummings, 1995; Groenewegen et al., 1997). As such, it has been argued that the DLPFC and striatum constitute an integrated neural circuit (Alexander et al., 1986; Groenewegen et al., 1997), and the existence this prefrontal-striatal loop in humans has been recently validated through the use of diffusion tensor imaging (Leh, Ptito, Chakravarty, & Strafella, 2007). Therefore, given that the DLPFC circuit is thought to be involved in executive functions (Cummings, 1995; Tekin & Cummings, 2002), the differential operation of the DLPFC may explain individual differences in inhibitory control.
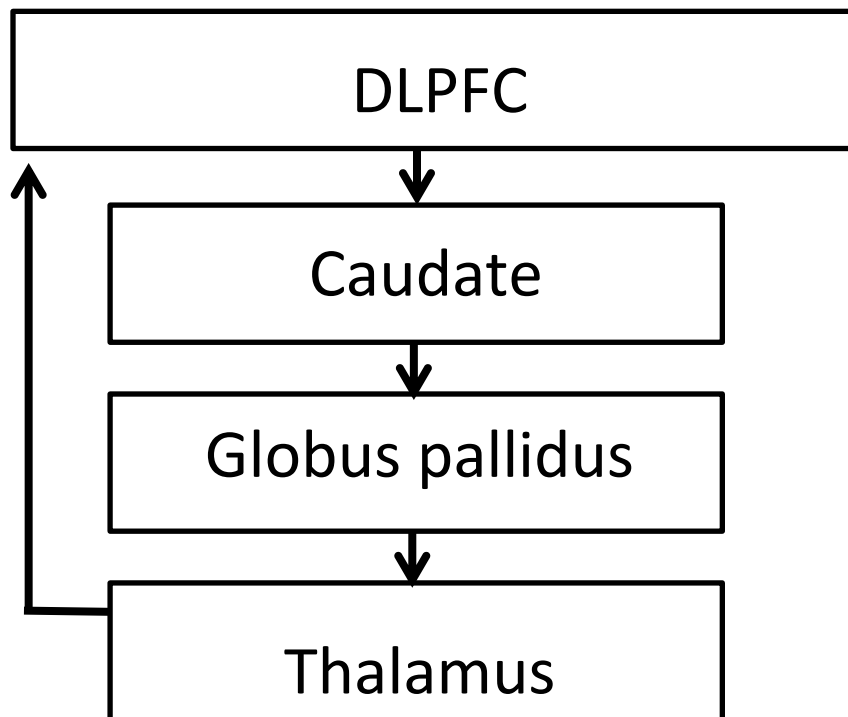
Figure 2: The anatomy of the DLPFC-subcortical circuit. The circuit originates in the DLPFC, and projects to the dorsolateral caudate, lateral dorsomedial globus pallidus, and ventral anterior and mediodorsal thalamus (adapted from Tekin & Cummings, 2002).

3.3 DLPFC and Behavioural Inhibition

Indeed, there is strong evidence that suggests that the operation of the DLPFC is involved in behavioral inhibition. For instance, evidence from animal studies, human lesion studies,

conditions characterized by defective inhibitory control (e.g., attention deficit disorder; ADHD) and fMRI studies have consistently implicated that the DLPFC is the pivotal cortical region associated with inhibitory control, particularly when behaviour is guided by internal c (Alvarez & Emory, 2006; Chambers, Garavan, & Bellgrove, 2009; Garavan et al., 2006; Hoshi, 2013; Mega & Cummings, 1994; Ridderinkhof et al., 2004; Rubia et al., 2001 Toplak, Jain, & Tannock, 2005; Zheng, Oka, Bokura, & Yamaguchi, 2008). In addition, among adolescents, Go No/Go task performance is associated with the maturation of the DLPFC-striatal circuit (Stevens, Kiehl, Pearlson, & Calhoun, 2007). As such, it is plausible that the differential operation of the DLPFC may explain individual differences in inhibitory control, and subsequently dietary behaviours.

3.4 DLPFC and Dietary Self Control

An increasing body of evidence suggests that dietary self-control is modulated by the operation of the DLPFC. Obesity is often associated with heightened or abnormal responses to food cues, and this association may be attributed to the differential operation of the DLPFC among the obese population. Visual food cues activate the brain regions crucial for reward processing (e.g., OFC, dorsal and ventral striatum; (Dimitropoulos, Tkach, Ho, & Kennedy, 2012), and high calorie food cues elicit a greater response in these areas relative to low calorie food cues (Killgore et al., 2003). Obese individuals as compared to their normal weight counterparts show greater response in these cortical regions to high calorie food cues, suggesting that obese individuals are more susceptible to the rewarding properties of high caloric foods. For example, in a recent study by (Rothemund et al. (2007b), the authors reported that obese women had greater activation in the dorsal striatum while viewing high caloric food images. Similar results were reported by Schienle et al. (2009). When exposed to high calorie foods, obese

women had greater activation in the lateral OFC, ventral striatum and the insula relative to normal weight women. In addition, food cravings are elevated in the obese population, and this association may be attributed to enhanced reward reactivity to food cues. Pelchat et al. (2004) reported an increased food craving specific activity in the caudate, a cortical region associated with reward processing; therefore, it is possible that increased activity in the neural regions associated with reward processing may increase food cravings. Given that food cravings are thought to influence snacking behaviours (Scharmuller, Ubel, Ebner, & Schienle, 2012), enhanced reward reactivity to high caloric food cues may increase food cravings and subsequently influence snacking behaviours (i.e., increase the likelihood an individual will consume high caloric food).

However, humans have the capacity to exert control over their dietary behaviours, and therefore the operation of the neural regions associated with cognitive control (i.e., DLPFC), may potentially allow humans to exert control over food cravings and influence dietary choices. In fact, previous research has demonstrated that the activation of the DLPFC is necessary to decrease the subjective value of high caloric food cues. Scharmuller et al. (2012) showed participants a series of images of either high caloric foods, or neutral non-food items (e.g., geometric figures). In the watch condition, participants passively viewed the images. However in the decrease condition participants were instructed to decrease the value of the food images (i.e., they were instructed to imagine the food was not real), and in the increase condition participants were instructed to increase the value of the food images (i.e., they were instructed to imagine they were allowed to eat the food). When shown the images of the high caloric foods, obese women showed greater activation in the insula and lateral and medial OFC. In both the increase and the decrease condition, obese individuals, as compared to healthy weight controls, had

greater activation in the insula, striatum, and dorsomedial prefrontal cortex (dmPFC). However, compared to the increase condition, obese individuals had greater activation in DLPFC during the decrease condition, indicating that obese individuals recruited the DLPFC when attempting to decrease the value of the food; however, there was no change in DLPFC activity when attempting to increase the value of the food. Given that the insula and dorsal striatum are associated with reward processing and food cravings, the recruitment of the DLPFC during the decrease condition may be related to the attempts to attenuate the value of the food and otherwise exert dietary self-control. Therefore the DLPFC may play a pivotal role in controlling habitual responses to food cues; as such the differential operation of the DLPFC may explain individual differences in dietary behaviours.

Consistent with this perspective, data from neuroimaging studies have demonstrated that the operation of the DLPFC is associated with dietary behaviours. For example, Hare, Camerer and Rangeli (2009), reported that individuals with effective self-control made decisions about which foods they would like to eat on the basis of health and tastes, whereas, individuals with impaired inhibitory control made decisions on the basis of taste alone. Participants with effective self-control choose not to eat the tasty, but unhealthy foods, more often than those with impaired self-control. Regardless of the degree of self-control, regions of the ventral medial prefrontal cortex (vmPFC) were activated when making decisions about which foods to eat, whereas, an increase in the left DLFPC was only observed only in participants with high self-control, suggesting that the DLPFC may be important for regulating food intake and inhibitory control. The authors concluded that self-control problems occur in situations where health and taste factors must be integrated in the vmPFC , to compute goal values. The vmPFC is typically associated with the short term value of a given stimuli whereas the DLPFC is required for higher

order cognitive functions, such that the operation of the DLPFC is required to incorporate healthy values into the vmPFC value signal. Therefore individual differences in self-control, and subsequently dietary behaviours, may be associated to the extent in which the DLPFC can modulate the vmPFC (Hare, Camerer, & Rangel, 2009).

Together, these results suggest that the differential operation of the DLPFC may explain individual differences in dietary self-control. However, these studies have been observational in nature, and statements about causality must be made very tentatively. Therefore, in order to make firm causal statements about the role of ECRs (i.e., inhibitory control) in dietary behaviour, one must manipulate the brain regions underlying inhibitory control (i.e., DLPFC) and observe subsequent effects on dietary behaviours.

Chapter 4

4.0 Transcranial Magnetic Stimulation

Transcranial magnetic stimulation (TMS) can be used to manipulate cortical activity, and observe the subsequent effects on dietary self-control. TMS is a non-invasive tool that provides researchers the unique opportunity to interfere with neural activity in specific brain regions with high temporal (i.e., time-course) and regional (i.e., brain region) specificity; thus, allowing researchers to increase or decrease cortical excitability in a specific brain region and measure the subsequent behavioral outcomes (Allen, Pasley, Duong, & Freeman, 2007; Sandrini, Umiltà, & Rusconi, 2011; Wassermann & Zimmermann, 2011). The basic TMS apparatus consists of a wire coil that is placed directly on the scalp. To permit focal stimulation, two circular coils are combined to form a figure eight (Sandrini et al., 2011; Wassermann & Zimmermann, 2011). The coil emits electromagnetic pulses—of varying length, form and intensity—that induce changes in cortical excitability (upwards or downwards); this modulation of excitability can increase or decrease activity in the cortical region below the area of application.

Unlike other methodologies, TMS allows researchers to map brain function in a cognitively intact human population, rather than relying on animal models, neurosurgical procedures or patients with focal brain lesions (Pascual-Leone, Bartres-Faz, & Keenan, 1999). Using TMS on healthy populations allows researchers to map brain functions while avoiding the confounds associated with uncontrollable brain lesions or the reorganization of brain function, which may occur in the event of a brain lesion (Pascual-Leone et al., 1999). In addition, TMS studies can be conducted across multiple participants, and can be repeated on the same participant, allowing for controlled experimental designs; thus researchers are able to infer a

causal relationship between focal brain activity and subsequent behavior (Pascual-Leone et al., 1999).

4.1 Types of TMS

TMS can be applied as a single pulse (spTMS) or a repetitive train of pulses (rTMS; (Sandrini et al., 2011). The duration of spTMS is less than 1 ms, whereas the duration of rTMS can typically span between 10 and 25 minutes (Anand & Hotson, 2002; Sandrini et al., 2011). The type of TMS paradigm used depends on the brain behavior relation being investigated. Single pulses TMS is effective for producing short responses, and are usually used to measure muscle movements; spTMS-induced neuronal changes only last for approximately 40-60ms (Sandrini et al., 2011), which is sufficient for studying motor movements (Wassermann & Zimmermann, 2011). Stimulation and task performance must occur concurrently when using spTMS paradigm (Sandrini et al., 2011). For example, a single pulse of TMS to the primary motor cortex (M1) evokes immediate muscle activity (motor evoked potential; MEP), which can be measured using electromyogram (EMG; Wassermann & Zimmermann, 2011). Given that, single pulse TMS is effective at producing short term responses, it is ideal for measuring immediate behavioural effects; however, spTMS is not as effective as rTMS at investigating how cortical stimulation can affect higher order cognitive processing (e.g., language or memory; Anand & Hotson, 2002; Ridding & Rothwell, 2007; Sandrini et al., 2011). In rTMS, a train of pulses is delivered at a frequency up to 50 Hz, which can evoke sustained neural activity (after effects), thus allowing researchers to examine cognitive functions that are not affected by spTMS (Anand & Hotson, 2002; Wassermann, 1998). The duration of rTMS after effects can range between 30 and 60 minutes, depending on the number of pulses applied, the rate of application and the stimulus intensity (Ridding & Rothwell, 2007). Generally speaking, stimulation

frequencies higher than 1 Hz tend to cause facilliatory after effects by increasing cortical excitability (Ridding & Rothwell, 2007; Sandrini et al., 2011). Conversely, stimulation frequencies lower than 1 Hz tends to produce an inhibitory after effect by decreasing cortical excitability (Ridding & Rothwell, 2007; Sandrini et al., 2011). When using an rTMS paradigm, stimulation and task performance do not have to occur concurrently (Sandrini et al., 2011).

Theta burst stimulation (TBS) is a variant of rTMS which consists of three short pulses (between 50-100 Hz) that are repeated every 200 ms (5Hz; Grossheinrich et al., 2009; Huang, Edwards, Rounis, Bhatia, & Rothwell, 2005; Oberman, Edwards, Eldaief, & Pascual-Leone, 2011). The parameters for TBS were designed to mimic theta rhythms, which are associated with a phenomenon known as "long-term potentiation," or enhancement in signal transmission between nerve cells (Oberman et al., 2011). There are two types of TBS, continuous TBS (cTBS) and intermittent TBS (iTBS; Grossheinrich et al., 2009; Huang et al., 2005; Oberman et al., 2011). In cTBS, the pulses are applied at a rate of 5 Hz for either 20 seconds (100 bursts) or 40 seconds (200) bursts, resulting in an inhibitory effect (Huang et al., 2005; Oberman et al., 2011). Conversely, in iTBS the pulses are applied at a rate of 0.1 Hz in 2s intervals, resulting in a facilitating effect (Huang et al., 2005; Oberman et al., 2011). Because TBS can be administered in a shorter time interval, and is considered to be more efficient than other forms of rTMS, TBS is becoming the preferred method of administering rTMS from an experimental standpoint (Oberman et al., 2011).

Another non-invasive tool used to stimulate cortical regions is transcranial direct current stimulation (tDCS). In tDCS, electrodes of different polarities (anodal and cathodal) are placed in different positions on the skin of the scalp, in order to apply a direct current over the cortex (Utz, Dimova, Oppenlander, & Kerkhoff, 2010). The positioning of the electrodes depends on

the brain region and function being investigated (Utz et al., 2010). In addition, the effectiveness of tDCS depends on the positioning of the electrodes; the positioning of the electrodes determines the direction and distribution of the electrical current (Utz et al., 2010). An anodal electrode increases cortical excitability, whereas a cathodal electrode decreases cortical excitability (Utz et al., 2010). In comparison with TMS, tDCS produces similar after effects and is easier to use, however tDCS is less focal than TMS (Utz et al., 2010). For the purposes of the current document, TMS will be the focus of interest.

4.2 How TMS Works

TMS utilizes the principles of electromagnetic induction to selectively activate or inhibit regions of the cortex (Wassermann & Zimmermann, 2011). The basic TMS apparatus consists of a wire coil that is placed directly on the scalp. To permit focal stimulation, two circular coils are combined to form a figure eight (Sandrini et al., 2011; Wassermann & Zimmermann, 2011). A single coil can be used to stimulate a specific brain region or two coils can be used to stimulate different brain regions simultaneously (e.g., right and left dorsolateral prefrontal cortex (Anand & Hotson, 2002). A standard TMS coil can be used to stimulate cortical regions located 1.5-2 cm beneath the surface of the skull, thus limiting the brain regions that can be stimulated; therefore, TMS cannot be used to directly stimulate deep brain regions, such as the hippocampus (Wassermann, 1998).

The coil produces a small magnetic field (between 1.5-2 tesla; T), that lasts for approximately a millisecond (Sandrini et al., 2011; Wassermann, 1998; Wassermann & Zimmermann, 2011). The magnetic field penetrates the skull and induces an intracranial electrical current, resulting in neuronal depolarization and subsequently an action potential (Oberman et al., 2011; Ridding & Rothwell, 2007; Sandrini et al., 2011; Sandrini et al., 2011;

Wagner, Valero-Cabre & Pascual-Leone, 2007). Although the mechanisms responsible for TMS after effects are still unclear, the induced intracranial electrical current is thought to stimulate the axons of the neurons in the cortex and subcortical white matter, as opposed to the neuronal cell bodies (Allen et al., 2007; Ridding & Rothwell, 2007; Sandrini et al., 2011). Short term after effects (a few seconds to a couple minutes) can be attributed to changes in neural excitability (e.g., shifts in ionic balance) and disappear almost immediately after TMS cessation (Ridding & Rothwell, 2007). However, longer lasting after effects (30 to 60 minutes) are likened to changes in synaptic efficiency in the forms of long term depression (LTD) or long term potentiation (LTP) between neurons (Huang, Chen, Rothwell, & Wen, 2007; Ridding & Rothwell, 2007).

LTP is the process by which synaptic strength between neurons is increased (Clapp, Hamm, Kirk, & Teyler, 2012). Conversely, LTD is the process by which synaptic strength is decreased. High frequency TMS activates postsynaptic glutamate neurons leading to increased excitability of the dendritic spine (Clapp et al., 2012). This in turn activates postsynaptic N-methyl-d-aspartate (NMDA) receptors increasing the influx of calcium ions, which triggers a variety of reactions leading to long-term changes in synaptic strength (Clapp et al., 2012; Huang et al., 2007). Depending on the frequency of stimulation, cortical excitability increases (LTP) or decreases (LTD; (Huang et al., 2007; Wagner et al., 2007). In addition, the number of neurons affected by TMS stimulation is dependent upon stimulation intensity; lower stimulation intensities activate a smaller number of neurons compared to higher intensities (Ridding & Rothwell, 2007).

However, direct evidence is difficult to obtain from human studies, resulting in researchers having to depend on animal models to explain the mechanisms responsible for TMS induced effects (Huang et al., 2007; Ridding & Rothwell, 2007). TMS studies that use

pharmacological interventions to interfere with NMDA receptors have provided indirect

evidence that suggests that TMS after effects are likened to changes in synaptic efficiency

(Huang et al., 2007; Ridding & Rothwell, 2007). NMDA receptor antagonists (such as

memantine or dextromethorphan) can suppress TMS after effects (Huang et al., 2007; Ridding &

Rothwell, 2007). Conversely, NMDA agonists (such as D-cycloserine) can prolong the after

effects of TMS. Taken together, these data suggest that TMS after effects can be attributed to

LTP/LTD; however, the precise mechanisms underlying TMS after effects are still unclear

(Huang et al., 2007).

4.3 Methodological issues/safety concerns

TMS is a widely used for both experimental and clinical purposes. In fact, the number of

laboratories using TMS techniques has dramatically increased over the last decade (Sandrini et

al., 2011). However, there are certain safety risks and methodological issues that need to be

considered when using TMS. Single pulse TMS is relatively safe and non-invasive tool,

however, rTMS is more powerful and potentially more dangerous than spTMS (Wassermann,

1998). A number of adverse side effects and risks are associated with rTMS, however, these side

effects and risks are generally trivial (Machii, Cohen, Ramos-Estebanez, & Pascual-Leone, 2006;

Wassermann, 1998). The most common side effects (approximately 40 % of participants are

affected) of rTMS are mild headaches and neck pain. These side effects are typically mild, but

can vary depending on the site of stimulation, stimulation frequency and duration (Machii et al.,

2006; Wassermann, 1998). The need for participants to hold their head in a forced immobilized

position for the duration of the TMS stimulation combined with contact of the coil on the scalp

are thought to be the primary factors relating to TMS induced headaches and neck pains (Machii

et al., 2006). In addition, the TMS coil activates muscles and nerves near the stimulation site,

which can be quite uncomfortable depending on the site of stimulation (Wassermann, 1998). However, the pain and discomfort can be minimized by varying the stimulation intensity and frequency (Wassermann, 1998).

Other potential (but rare) side effects of rTMS include nausea, tinnitus, mood alterations and transient cognitive complaints (Machii et al., 2006). When the current passes through the TMS coil, a loud clicking noise is produced, which can result in tinnitus (i.e., "ringing" in the ears) and transient decreases in hearing; however, foam earplugs can effectively prevent the risk of hearing disturbances (Wassermann, 1998). In addition to the side effects listed above, studies have reported that rTMS can induce more serious side effects (i.e., seizures, pseudoseizures, loss of consciousness, and induction of psychotic symptoms; Machii et al., 2005). However, there have only been 11 reported cases of TMS induced seizures, all of which occurred in patients with pre-existing brain damage or neuropsychiatric conditions (Rossi, Hallett, Rossini, Pascual-Leone, & Safety of TMS Consensus Group, 2009; Wassermann, 1998). Overall, the risks for serious adverse effects are minimal.

TMS is used extensively in both the healthy and patient populations without adverse side effects. By following the current safety guidelines (see Wasserman et al., 2008 and Rossi et al., 2009) the risks associated with rTMS can be minimized. For example, the current safety guidelines stipulate the methodology used to determine the stimulation intensity of rTMS or TBS. The stimulation intensity used in rTMS and TBS paradigms is set at a percentage of the resting motor threshold (RMT) stimulus intensity (e.g., 110%). Given that TMS thresholds vary widely across the population, possibly due to variations in cortical depth of M1, it is of the utmost importance to determine individual rMT in order to minimize the risks and discomforts associated with TMS (Wasserman, 1998; Sandrini et al., 2011). Despite the fact that there is no

evidence suggesting that TMS is harmful (if appropriate guidelines are followed), the risk factors associated with TMS may be an issue for researchers. Ethical and legal requirements stipulate that researchers must disclose all potential risks to potential participants (Wassermann, 1998). The potential risks associated with TMS may discourage potential participants, thus limiting the number of participants researchers are able to recruit.

Another issue researchers need to consider when using TMS paradigms is that the effects of TMS vary both between and within individuals, presumably from biological differences (Ridding & Rothwell, 2007; Sandrini et al., 2011). Individual differences in brain anatomy can shift the location of a particular brain region (e.g., M1) by a centimeter or more (Ridding & Rothwell, 2007). However, MRI scans can be used to guide individual placement of the TMS coil over brain regions of interest, essentially correcting for anatomical differences (Ridding & Rothwell, 2007). Nonetheless, there are other unavoidable factors that can interact with TMS effects (Ridding & Rothwell, 2007). Changes in hormonal levels, diurnal rhythms and genetic differences are all sources of variation in the observed effects of TMS (Ridding & Rothwell, 2007). As such, the effects of TMS can be influenced by pre-existing biological differences; however, this is an innate characteristic of all studies using human participants.

Chapter 5

TMS can be used to examine the causal impact of DLPFC function on dietary behaviors, however, to date, there are only a few studies that have used cortical stimulation methodologies to examine this relationship, and these are summarized below (see also Table 1). The studies summarized below all used cortical stimulation methodologies to enhance DLPFC activity.

5.0 Review of TMS and Dietary Behaviours Literature

Uher et al. (2005) reported that high-frequency (10 Hz) rTMS to the left DLPFC decreased food cravings in women when compared to sham rTMS. Participants were preselected based upon self-reported frequent, "very strong" or "strong" urges to eat at least one of the unhealthy snack foods and assigned to receive either active, or sham rTMS. Before and after the TMS session, participants underwent a food exposure session, in which they were required to rate the food on taste, smell, appearance and their current urge to eat. Food cravings in the active rTMS group remained constant across pre- and post-food exposure sessions, whereas post-food exposure cravings significantly increased in the sham rTMS group. Because participants were given the opportunity to taste, smell and inspect the foods before and after rTMS, it was posited that the increase in food cravings during sham rTMS treatment can be attributed to a cue-reactivity effect. Therefore, active rTMS stimulation to the left DLPFC was able to decrease food cravings, thereby down regulating the usual craving response. However, the authors reported that there was no significant difference in food consumption between active and sham rTMS groups, indicating that active rTMS had no effect on regulating food consumption in this case per se.

Consistent with the results of Uher and colleagues, Fregni et al. (2008) found that tDCS to the left DLFPC significantly reduced food cravings among participants with frequent food

cravings. In this study, participants received three different types of tDCS to the DLPFC: (1) active anode left/cathode right; (2) active anode right/cathode left; (3) sham tDCS. Using a methodology similar to Uher et al. (2005), participants underwent food exposure before and after tDCS, in which they were required to rate the food on taste, smell, appearance and their current urge to eat. In addition, participants were shown a 5 minute movie that was designed to elicit food cravings. As a secondary measure of food cravings, participants were required to look at slides of different foods. Each slide contained four different pictures, with only one of the pictures being a food picture. Using an eye tracker device, the authors also measured the fixation time and number of fixations on pictures of foods associated with cravings.

After active anode right/cathode left tDCS there was a significant decrease in the fixation time on the food picture, whereas there was a significant increase in fixation time after sham tDCS. Active anode right/cathode left stimulation of the DLPFC significantly decreased food cravings, whereas there was no change in food cravings after active anode left/cathode right tDCS. There was a significant increase in food cravings after sham tDCS. These findings suggest that the left and right DLPFC may play different roles in regulating food cravings; the right DLPFC might suppress desire to eat altogether, thus decreasing food cravings, whereas the left DLPFC might regulate cravings or function as the neural mechanism needed to suppress food cravings (Fregni et al., 2008b). In contrast to the results reported by Uher et al. (2005), Fregni et al. (2008b) reported a decrease in the caloric content of food consumed after active tDCS (both conditions) compared to sham tDCS, which may be due to hemispheric laterality differences. However, in a subsequent study by Goldman et al. (2011), there was no significant difference in the amount of food consumed between active right DLPFC stimulation and sham tDCS sessions,

indicating that hemispheric laterality may not account for differences observed in the amount of food consumed between Fregni et al. (2008b) and Uher et al (2005) studies.

Goldman et al. (2011) showed participants pictures of foods that typically elicit cravings before and after tDCS treatment. Similar to the studies described above, participants were preselected based upon frequent food cravings. While viewing the images participants rated how much they would like to eat the food (cravings), liked the food, and if they would be able to resist tasting the food. The authors found that the self-reported ability to resist food cravings, among individuals who had frequent food cravings, was significantly higher after active anodal right tDCS to the DLPFC compared to sham tDCS. Overall, the data summarized above support the conclusion that the selective stimulation of the DLPFC has an effect on food cravings

Similar results are also observed in clinical populations. Van de Eynde et al. (2010) reported that high frequency rTMS to the left DLPFC significantly decreased the urge to eat in participants with bulimia nervosa. However, Van den Eynde et al. (2013) reported that there was no significant stimulation effect on the urge to eat in patients with anorexia nervosa. These differences may be attributed to population differences, as the core symptoms of anorexia nervosa are severe food restriction, whereas the bingeing and strong food cravings are core symptoms of bulimia nervosa. Food consumption was not measured in either of the studies described above.

Contrary to prior research, Barth el al. (2011) reported that food cravings were significantly decreased following both active and sham rTMS. The authors propose that because the sham condition produced a similar amount of pain as the real rTMS, the emotional reaction to the painful procedure may have caused the inhibition of food cravings.

In summary, prior studies have demonstrated that manipulating DLPFC activity (via various cortical stimulation methodologies) affects subjective cravings for appetitive (but unhealthy) foods among those who report frequent experience of such cravings. However, the relationship between DLPFC activity and consumptive behaviors is still unclear, with one study reporting that up-regulation of the DLPFC resulted in the decreased consumption of appetitive snack foods (Fregni et al., 2008b), and two other studies reporting null effects (Goldman et al., 2011; R. Uher et al., 2005). One plausible explanation for the different findings may be sample differences. Both Uher et al. (2005) and Goldman et al. (2011) noted that a large number of overweight and obese participants enrolled their respective studies; participant BMI was not reported in Fregni et al. (2008b). Additionally, Uher et al. (2005) noted that the non-significant stimulation effect on food consumption may be attributed to a ceiling effect, as participants consumed a substantial amount of food in a short time period. As such, the sizable amount of overweight and obese participants may have limited the sensitivity to detect a stimulation effect on food consumption. Alternatively, these differences may be due to an expectancy or a social desirability bias; i.e., participants may be reluctant to over consume high caloric snack foods in a laboratory setting. In addition, whether participants were able to distinguish between active and sham stimulation may influence subsequent eating patterns. In fact, Goldman et al. (2011) reported that 79 % of participants were able to distinguish between active and sham stimulation, which may explain the null findings with respect to food consumption; participant blinding descriptive were emote reported in Fregni et al. (2008b) or Uher et al. (2005). Therefore, these biases may have precluded the stimulation effects on consumptive behaviours.

Table 1

Summary of the TMS and Dietary Behaviours Literature

Citation	Design	N	Participants	DLPFC	DLPFC Localization	Stimulation Parameters	No of Sessions	Cue	Craving Measure	Consumption Measure	Results
Fregni et al., 2008	W	21	Women with frequent and strong urges to eat at least one experimental food No food 3h prior to start of study session	Left and Right	F3(left) and F4(right)	tDCS	3	Seated at table with experimental foods and shown 5 min video	VAS Eye tracking: time spent gazing at food pictures	Calories consumed	Right DLPFC: cravings reduced, not seen in left DLPFC stimulation Consumed significantly less food following active left and right stimulation
Uher et al., 2005	B	28	Women with frequent and Strong Urges to Eat at least one of the experimental foods (cookies, chocolate, potato chips and nuts)	Left	5cm anterior to M1	rTMS: 10Hz (1000 pulses (20 trains of 5sec with intertrain interval of 55 sec) 110% RMT	1	Seated at table with experimental foods	VAS	Calories consumed	Active stimulation significantly decreased cravings No stimulation effect was observed on food consumption

27

			No food, smoking or caffeine 3 hours before								
Goldman et al., 2011	W	19	Strong and Frequent food cravings for experimental foods No food 4 hours prior	Right	F4	tDCS	2	IAPS food pictures 20 images	VAS	Weight food consumed	Active stimulation significantly decreased cravings on the self-reported ability to resist foods VAS. No stimulation effect was observed on food consumption
Van den Eynde et al., 2013	W	10	Clinical diagnosis of AN	Left	5 cm anterior to M1	rTMS: 10 Hz(1000 pulses-20 trains of 5 seconds with 55-second inter-train interval) 110% RMT	1	Short film clip of people eating high calorie foods	VAS	Not measured /reported	No stimulation effect was observed on food cravings (i.e., urge to eat)

28

Van den Eynde, et al., 2010	B	38	Clinical diagnosis of BN No eating or drinking 2 hours prior to start of the study	Left	5cm anterior to M1	rTMS: 10 Hz(1000 pulses-20 trains of 5 seconds with 55-second inter-train interval) 110% RMT	1	2 min video of people eating palatable foods then presented a buffet with the same foods- asked to rate taste and smell and appearance	VAS and FCQS	Not measured /reported	Active stimulation significantly decreased food cravings (i.e., urge to eat) as measured on the VAS. There was no significant stimulation effect on food cravings measured using the FCQ-S.
Barth et al., 2011	W	11	Strong and frequent cravings for a least one of the following foods: sweet, fast food fats, high fats, and/or carbohydrates No food 3 hours prior	Left	5cm anterior to M1	rTMS: 10 Hz(3000 pulses-10 seconds on, 20 seconds off for 15 minutes) 100% RMT	2	IAPS food images	VAS	Not measured	No significant stimulation effect on food cravings

5.1 Summary of the TMS and Cravings for Appetitive Substances Literature

There is an accumulating body of evidence that suggests food and drug cravings (e.g., alcohol, cigarettes, cocaine) share the same neurobiological foundation (Styn, Bovbjerg, Lipsky, & Erblich, 2013; Tang, Fellows, Small, & Dagher, 2012). As such, it would be expected that similar stimulation effects would be observed when examining cravings for other appetitive substances. In fact, numerous studies that reported that increasing cortical activity in the DLPFC resulted in the subsequent decrease in cravings for other appetitive substances, such as tobacco (Amiaz, Levy, Vainiger, Grunhaus, & Zangen, 2009; Eichhammer et al., 2003; Fregni et al., 2008a; Johann et al., 2003), alcohol (Boggio et al., 2008b), and cocaine (Camprodon, Martinez-Raga, Alonso-Alonso, Shih, & Pascual-Leone, 2007). Additionally, a recent meta-analysis (Jansen et al., 2013) documented modest and reliable effects (Hedge's $g= 0.476$) of DLPFC modulation (via various cortical stimulation methodologies) on subjective cravings to appetitive substances (i.e., drugs and foods). No significant differences were observed across stimulation modalities (i.e., tDCS versus rTMS), between the various substances, or between left and right DLPFC stimulation. These findings provide further support to the contention that food cravings are regulated by DLPFC activity, and therefore suggest that modulating DLPFC activity results in subsequent changes in the cravings for appetitive substances.

Given that the differential operation of the DLPFC is associated with individual differences in ECR strength, and ECR strength is positively associated with the adherence to numerous health behaviours (refs), it is plausible that the stimulation effects on subjective cravings were related to changes in ECR strength. However, there are currently no studies that directly measure changes in ECR strength as a result of cortical stimulation, and therefore it cannot be ascertained whether the stimulation effect was associated with changes in ECR

strength or some other factor (e.g., discomfort from the procedure itself, or other unknown physiological consequences). Nonetheless, previous research has demonstrated that cortical stimulation of the DLPFC modulates various facets of executive control, indicating that TMS modulation of the DLPFC activity is associated with subsequent changes in ECR strength. These studies are summarized in the section below.

5.2 Summary of the TMS and ECR Literature

Prior research has shown that cortical stimulation of DLPFC modulates performance on various ECR measures in both healthy and clinical populations. For instance, anodal tDCS to the left DLPFC improved performance accuracy on a n-back task in healthy participants (Fregni et al., 2005; Mull & Seyal, 2001; Zaehle, Sandmann, Thorne, Jäncke, & Herrmann, 2011), and patients with Parkinson's disease (Boggio et al., 2006; Fregni et al., 2006). Additionally, Ko et al. (2008) reported that cTBS to the left DLPFC impaired performance on the Montreal Card Sorting Task (MCST). Moreover, Preston et al. (2010) reported that performance on the Sternberg working memory task was significantly improved following 10 Hz rTMS to the right and left DLPFC.

With respect to measures of inhibition, there is some evidence that stimulation of the DLPFC affects task performance; however, these findings are mixed. For example, Nyffeler et al. (2007) reported that spTMS to the DLPFC decreased performance accuracy on an antisaccade task. In addition, Boggio et al. (2007) reported that a single session of anodal tDCS to the left DLPFC improved the performance (i.e., accuracy) in an affective go no/go (GNG) task in depressed patients. Conversely, other studies have reported that there was no significant stimulation effect on performance on the Stroop (Vanderhasselt, De Raedt, Baeken, Leyman, & D'haenen, 2006; M. Wagner et al., 2006) or GNG task (Huang et al., 2004).

In sum, there is reasonable (but not universally consistent) evidence that suggests that modulating activity in the DLPFC results in subsequent changes in ECRs. As such, these findings suggest that the stimulation effects on food cravings and food consumption may be attributed to changes in ECR strength.

Chapter 6

6.0 Study Rationale

The current body of evidence suggests that ECRs may be implicated in the maintenance

of healthy dietary patterns,. Given that inhibitory control involves the operation of the DLPFC, it

is plausible that the operation of the DLPFC drives successful self-initiated self-regulatory

processes in eating behavior. Therefore, differences in DLPFC activity may explain individual

differences in dietary choices, vis-à-vis the connection between the DLPFC and executive

control. However, the directionality and causal status of this relationship is unclear. For example,

it is plausible that the overconsumption of energy dense foods may impair cognition

(Brinkworth, Buckley, Noakes, Clifton, & Wilson, 2009; Cheatham et al., 2009; Collison et al.,

2010; Dangour et al., 2009; Edwards et al., 2011; McNeilly, Williamson, Sutherland, Balfour, &

Stewart, 2011; Messier, Whately, Liang, Du, & Puissant, 2007; Sabia et al., 2009; Winocur &

Greenwood, 2005). In addition, given that the relationship between ECRs and behaviors are

hypothesized to operate by positive and negative feedback loops (Marteau & Hall, 2013),

demonstration of causal link between ECRs and dietary behaviours is essential.

Some studies have demonstrated that experimentally manipulating proxy states for

inhibitory control results in subsequent changes in food intake (Guerrieri et al., 2009; Guerrieri,

Nederkoorn, & Jansen, 2012; Houben, 2011; Houben & Jansen, 2011; Rotenberg et al., 2009).

For instance, one such study demonstrated that participants consumed more food during a bogus

taste after being primed with lack of control thoughts and thoughts about impulsivity (Guerrieri

et al., 2009; Rotenberg et al., 2005). In addition, prior studies have demonstrated that training

inhibition towards specific food items (i.e., pairing of a food item with a no-go signal during a

modified stop signal task) significantly decreases the consumption of these foods, relative to

control foods (Guerrieri, Nederkoorn, & Jansen, 2012; Houben & Jansen, 2011; Houben, 2011). These findings suggest that inhibitory control may be causally related to dietary behaviours. However, the validity of the manipulations themselves could be questioned, as they do not directly alter the neurophysiology implicated in inhibitory control. Use of cortical stimulation techniques, such as TMS, represents a more valid alternative for testing the causal significance of inhibitory abilities for self-regulation of dietary behaviors.

TMS is a way of directly modulating activity in the cortical regions underlying ECRs (i.e., the DLPFC). Several cortical stimulation studies have demonstrated that modulation of the DLPFC is causally linked to craving regulation, and (less consistently) to actual consumptive behaviours. However, the current studies (though promising) do not actually measure the hypothesized mediating variable (i.e., ECR) for the stimulation effects on cravings and consumptive behaviours. The primary contribution of the current study is to replicate prior cortical stimulation effects on food cravings and food consumption, but using cTBS to down-regulate DLPFC function. In addition, the current study actually measures the hypothesized mediator (i.e., ECR) for such stimulation effects. Prior studies have not utilized cTBS, nor have they included measures of ECRs to examine the effects of stimulation on this purported cognitive mediator.

It is expected that:

1. Participants will consume significantly more food following active as compared to sham stimulation

2. Stronger food cravings will be reported following active as compared to sham stimulation

3. The stimulation effects on food consumption and food cravings will be mediated by the

   effects of cTBS on ECRs.

Chapter 7

7.0 Methods

7.1 Participants

Healthy female participants were recruited from undergraduate psychology courses, using the University of Waterloo's SONA system. The sample was limited to female participants because an accumulating body of evidence suggests that women are more susceptible to food cues (Cornier, Salzberg, Endly, Bessesen, & Tregellas, 2010; W. D. Killgore & Yurgelun-Todd, 2010; R. Uher, Treasure, Heining, Brammer, & Campbell, 2006). Additionally, Cornier et al. (2010) reported that women had greater activation in the DLPFC in response to food cues, and DLPFC activity was negatively correlated with food consumption. As such, the authors concluded that the increased DLPFC activity in women may be attributed to increased inhibitory control, which in turn regulated food intake (i.e., men were more likely to overeat during the "ad libtum" eating session than women).

To disguise the true purpose of the study, participants were recruited to participate in a study examining the effects of cortical stimulation on taste perception. In exchange for their participation, participants either received $40, or were entered into a draw for a 16 GB iPad. Written and informed consent was obtained from all participants. Each participant was debriefed at the end of the second study session. This study was reviewed by and received approval from the University of Waterloo Research Ethics Board.

Similar to the inclusion criteria reported in Uher et al. (2005) (see also Fregni et al., 2008b and Goldman et al., 2011), participants were preselected based on strong and frequent food cravings for the experimental foods (i.e., chocolate and potato chips). Participants were excluded if they were left handed, had any neurological or psychiatric disorders, a history of

head trauma, were taking any psychiatric medications, had any allergies or intolerances to the experimental foods or nuts, or were pregnant (see Appendix B for screening questionnaire). All participants were naïve to TMS.

A total of 29 participants enrolled in the study, but only 21 completed both study sessions; four participants failed to return for the second study session, two individuals withdrew from the study because of physical discomfort, and, for safety reasons, two individuals were unable to participate because their motor thresholds exceeded 60% stimulator output (i.e., the stimulation intensity needed exceeded the recommended safety guidelines). See Table 2 for participant demographics.

Table 2
Participant Demographics

	Mean (SD)	% (n)
Age(years)	21.1 (1.86)	
BMI	23.355 (4.698)	
< 18		4.76 (1)
18.5-24.9		71.42 (15)
25-29.9		19.05 (4)
> 30		4.76 (1)
Waist Circumference (inches)	31.786 (5.993)	
< 35 inches		85.7 (18)
> 35 inches		14.3 (3)
Resting Motor Threshold	53.4 (4.50)	
cTBS Intensity	42.7 (3.53)	
Ethnicity		
Caucasian/white		61.9 (13)
Asian		9.5 (2)
Hispanic		9.5 (2)
South Asian		4.8 (1)
Middle Eastern		14.3 (3)

Note: Average RMT and cTBS intensity is the average across stimulation conditions.

7.2 Measures

7.21 Screening Measures

Several weeks prior to study participation, potential participants completed a pre-screening questionnaire package, which included the Food Craving Scale adapted to include the experimental foods (Hill, Weaver, & Blundell, 1991; Appendix C). The following items were used to identify participants with strong and frequent cravings for both chocolate and potato chips: (1) "how often do you experience cravings to eat potato chips/chocolate?" (response scale: 1= "never"; 10 = "all the time"); (2) "how strong are these cravings you experience to eat potato chips/chocolate (response scale: 1 = "extremely weak"; 10 = "extremely strong"); individuals who scored 7 or above on the response scale for both items and both experimental foods were deemed eligible to participate in the study.

7.22 Craving Measure

Food cravings were evaluated using the Food Craving Questionnaire-State (FCQ-S; Cepeda-Benito et al., 2000). The FCQ-S is a 15-item self-report questionnaire (Appendix D) designed to measure current subjective food cravings on the following five dimensions: (1) An intense desire to eat; (2) anticipation of positive reinforcement that may result from eating (positive reinforcement); (3) anticipation of relief from negative states and feelings as a result of eating (negative reinforcement); (4) lack of control over eating; (5) craving as a physiological state (i.e., hunger). Cronbach's alpha for the FCQ-S ranges from .83 (Moreno, Rodriguez, Fernandez, Tamez, & Cepeda-Benito, 2008) to 0.93 (Nijs, Franken, & Muris, 2007) and 0.94 (Cepeda-Benito et al., 2000). Cravings on the different dimensions were calculated as the sum of their corresponding items. Higher scores were indicative of stronger subjective food cravings.

7.23 Food Consumption

The experimental foods were covertly weighed before and after the taste test, and the amount of each food consumed (grams) was recorded. The experimental foods were divided into the following two categories: (1) appetitive foods (milk chocolate, and both types of Pringles); (2) control foods (dark chocolate and crackers). The variables in each category were summed together, with higher scores indicating a greater quantity of food consumed. The following item from the taste rating questionnaire (Appendix F) was used to confirm that participants perceived the appetitive foods as more appealing than the control foods "Overall, how would you rate this food?"(response scale:1="not at all good"; 10="very good").

7.3 ECR Measures

All ECR tasks were presented on a Dell desktop computer with a 17 inch CRT monitor (60 Hz refresh rate) using E-Prime software (Psychology Software Tools, Inc). All responses were made via manual button press on the keys of a response box. For each ECR task, participants were instructed to respond as quickly as possible while still being accurate.

7.31 Stroop Task

The Stroop task (Stroop, 1992) is one of the most widely used measures of executive function and response inhibition. In the traditional Stroop task, participants are required to name the colour font of a colour word (e.g., blue) presented visually, while inhibiting the prepotent response to read the word. The colour word is either presented in the same colour ink as the word (e.g., the word blue in blue ink; congruent condition) or a different colour ink (e.g., the word blue in green ink; incongruent condition). Compared to congruent colour word trials, naming the colour ink takes longer and is more subject to errors in incongruent colour word trials. This difference in speed and accuracy is referred to as the Stroop interference effect. The test-retest

reliability correlation ranges from .79 to .87 (Friedman et al., 2008; Vainik, Dagher, Dube, & Fellows, 2013). Cronbach's alpha for the Stoop task ranges from .87-.88 (Vainik et al., 2013) to .91-.93 (Friedman et al., 2008; Wostmann et al., 2013), and the intra class coefficient (ICC) for the Stroop task is .82 (Wostmann et al., 2013).

The Stroop task used in this study was modelled after the variant in Miyake et al. (2000). The task consisted of a mixed block of 144 trials, in which the stimulus was either a string of asterisks (72 trials), a congruent colour word (12 trials) or an incongruent colour word (60 trials).The stimuli were presented individually in one of six colours (blue, green, orange, red, purple or yellow) on a black background. Participants were instructed to name the colour ink each stimulus was written in. On each trial, the stimulus remained on the computer screen until the participant responded, followed by a response to stimulus interval of 1000 ms minus the response time. The dependent variables of interest were the overall accuracy and the Stroop interference effect. Consistent with Miyake et al. (2000), the Stroop inference effect was calculated as the difference between the RTs on correct incongruent trials (ms) and the RTs on correct asterisk trials (ms). Shorter RTs and higher accuracy were taken to reflect stronger ECRs.

7.32 Stop Signal Task

The stop signal task (SST; (Logan, Cowan, & Davis, 1984) is a widely used behavioural task designed to measure insufficient response inhibition. The SST engages the demand for inhibitory control by presenting participants with two concurrent tasks. The first task (go task), is a simple choice reaction time task, in which participants have to classify a set of stimuli (e.g., classify a word as an animal or non-animal word). The go trials are used to build up a prepotent categorization response. The second task (stop task) involves the random presentation of a stop signal. When presented, participants are required to withhold their response (i.e., inhibit the

prepotent categorization response). Cronbach's alpha for the SST ranges from .75-.79 (Vainik et al., 2013), and the ICC is .72 (Vainik et al., 2013). The test-retest reliability correlation is .86 (Congdon et al., 2012)

The SST task used in this study was modelled after the variant in Miyake et al. (2000), and consisted of two blocks of trials. During the first block of 48 trials (go trials), a series of words were presented individually on the computer screen. The words were displayed in black ink on a white background. Participants were instructed to categorize the word as either an animal (e.g., dog) or non-animal word (e.g., chair). Each trial began with a fixation cross (500 ms), and then participants were given up to 1500 ms to categorize the word. During the second block of 96 trials, participants completed the same categorization task, but were instructed to withhold their response when the stop signal was presented (i.e., stop trials). The stop signal consisted of a 220 Hz computer emitted tone, with a duration of 100 ms. The stop signal appeared randomly on 25 % of the trials (24 trials). The stop signal delay (the interval between the onset of trial and the onset of the stop signal) was adjusted for each participant by subtracting 225 ms minus from the average RT on go trials. The dependent variable of interest was the proportion of incorrect categorization responses on stop trials; higher accuracy was taken to reflect stronger ECRs.

7.33 Go/No-Go Task

Like the other ECR measures, the Go No-Go (GNG) paradigm is a widely used measure of inhibitory control. The typical GNG consists of a series of stimuli presented one after another. Participants are required to respond to a particular stimulus (e.g., white letter; Go trial), while withholding their response when presented with a different stimulus (e.g., black letter; No-Go trial). The Go stimulus is more common than the No-Go stimulus, and therefore a prepotent

response is built up over the recurring go trials. The GNG measures an individual's ability to inhibit this prepotent response. The test-retest reliability correlations for the GNG range from. 78 (Wostmann et al., 2013) to .87 (Huang et al., 2005), and the Cronbach's alpha for the GNG task is .92 (Wostmann et al., 2013). The ICC for the GNG paradigm is .78 (Wostmann et al., 2013).

This particular version of the GNG task consisted of eight blocks of 60 trials (total of 480 trials). Each trial began with a fixation cross (500 ms), followed by a series of upper case and lower case letters (1000 ms). The letters were presented individually in white ink on a grey background. Participants were instructed to respond whenever a lower case letter was presented, and withhold their response whenever an upper case letter was presented. In half the experimental blocks, upper case letters were predominate (5:1 ratio) and in the other half of experimental blocks lower case letters were predominate (5:1 ratio). The primary dependent variable was the RT (ms) on correct trials. Shorter RTs were taken to reflect stronger ECRs.

7.4 Theta Burst Stimulation Procedure

A 75 mm outer diameter figure-8 coil (MCF-B65) connected to a MagPro (model X100) stimulation unit (Medtronic, Minneapolis, MN, USA) was used to administer cTBS. Continous TBS was applied according the protocol outlined in Huang et al (2005); a 40 second continuous train consisting of 600 pulses applied in the theta burst pattern (bursts of three stimuli at 50 HZ repeated at 5 Hz frequency). For active stimulation, the coil was placed over F3 in accordance with the International 10-20 System for locating the left DLPFC (Bolton & Staines, 2011; Grossheinrich et al., 2009). The coil was positioned at a 90˚angle from the mid-sagittal line with its center over F3. Stimulation intensity was set at 80 % of the resting motor threshold (RMT) for the right abductor pollicus brevis (APB) muscle. RMT was defined as the lowest stimulator output required to produce a motor-evoked potential (MEP) with a peak-to-peak amplitude

exceeding 50 µV in at least 5 out 10 consecutive trials. For sham stimulation, the coil was again positioned over F3, but rotated 90˚, such that the coil was perpendicular to the surface of the head with both the wings in contact with the scalp.

7.5 Procedure

A double-blind, sham-controlled, within-subjects crossover design was used, in which participants received both active and sham stimulation. Participants and the researchers, except for the researcher who applied the cTBS, were blinded to the treatment condition. The order of stimulation was counterbalanced across participants. A one week intersession interval was used to avoid any potential carryover effects, and each study session was identical and carried out at the same time of day. All participants were instructed not to consume any food or caffeinated beverages three hours prior to the start of each study session, with compliance checked upon arrival. Informed consent was obtained prior to the start of the first study session.

In order to stimulate food cravings, participants were seated in front of a desktop computer and shown two-dimensional images of the experimental foods (milk chocolate, original pringles, sour cream and onion pringles, and dark chocolate); the use of the food images to elicit food cravings is a widely used methodology in craving studies (Fletcher, Pine, Woodbridge, & Nash, 2007; Goldman et al., 2011; Killgore et al., 2003; Pelchat et al., 2004). The images were presented on PowerPoint slides, each slide and remained on the computer screen for five seconds. After viewing the images, participants completed the FCQ-S. Following this, participants completed the Positive Affect and Negative Affect Schedule (PANAS; Watson, Clark, & Tellegen, 1988; Appendix G). The PANAS is a 20 item self-report questionnaire designed to assess state affect, and consists of a list of 10 negative affect items and 10 positive affect items. Using a five point rating scale (response scale: 1= "very slightly or not at all"; 5 =

"extremely"), participants were instructed to report the degree they felt each item "right now at this very moment". State positive and negative affect were calculated as the sum of each of their respective items.

Following the completion of the PANAS, participants were taken to a different room where they received either active or sham cTBS. Following a 5 minute post cTBS interval, participants were again shown the food images and completed the FCQ-S and PANAS. Then, participants completed three computerized ECR tasks. To avoid any potential order effects, the order of the ECR tasks were counterbalanced across participants. Following this, participants completed a bogus taste test. For the taste test, participants were instructed to taste and rate the subjective properties (e.g., texture, sweetness, saltiness) of each experimental food. Participants were instructed to consume as much food as they would like, and were given five minutes per food item to eat "ad-libtum". During the "ad-libtum" eating period, the researcher left the room until the five minute interval concluded, at which point the previous food item was removed and the participant was presented with the next food item. The experimental foods were presented in the following order: (1) Lindt milk chocolate (one bar; 100 grams); (2) Lindt dark chocolate (one bar; 100 grams); (3) original Pringles (2 snack size containers; 42 grams); (4) sour cream and onion Pringles (2 snack size containers; 42 grams); (5) soda crackers (12 grams). Participants were not provided with any macronutrient information for any of the experimental foods.

Following the taste test (second study session only), participants completed a series of questionnaires pertaining to demographics, food habits and attitudes, and self-control (Appendix H). At this time weight (lbs), height (inches) and waist circumference (inches) was measured. At the end of the study, participants were asked to indicate whether they; (1) knew the true purpose of the study; (2) could tell the difference between active and sham stimulation (Appendix I).

Chapter 8

8.0 Results

8.1 Effects of TMS on Food Consumption

Separate one way analyses of variance (ANOVA) were conducted to determine whether there was a stimulation effect on the differential consumption of appetitive and control foods (quantified by grams consumed and by calories consumed). Using grams consumed as the outcome, a significant treatment effect on the total amount of appetitive food consumed ($F(1,20)=5.072$, $p=.036$) was observed, such that participants consumed significantly more appetitive foods *g* following active (*M*=68.05; *SD*=26.41) relative to sham (*M*=60.68;*SD*=21.17) stimulation. There was no significant effect of stimulation condition on grams of control food consumed ($F(1,20)=1.66$, $p=.212$; Figure 3). Similar results were observed when examining the treatment effect on calories consumed. Specifically, there was a marginally significant effect of stimulation on calories consumed from appetitive foods ($F(1,20)=4.140$, $p=.055$), such that more calories from appetitive foods were consumed following active (*M*=353.59;*SD*=138.82) as compared to sham (*M*=316.03;*SD*=110.66) stimulation. Again, there was no significant effect of stimulation on calories consumed from control foods ($F(1,20)=1.813$, $p=.193$).

Table 3

Descriptive statistics for study variables by stimulation condition

	Active	Sham
	Mean (*SD*)	Mean (*SD*)
Stroop Interference (ms)	71.560 (115.398)	20.155 (61.062)
GNG RT (ms)	400.72 (44.92)	412.39 (39.76)
SST Accuracy (proportion of incorrect categorization responses)	.170 (.241)	.117 (.160)
Appetitive Food Consumed(grams)	68.050 (26.409)	60.667 (21.167)
Control Food Consumed (grams)	15.290 (8.082)	18.095 (10.963)
Appetitive Food Consumed(calories)	353.592 (138.824)	316.032 (110.665)
Control Food Consumed (calories)	73.004 (40.350)	88.225 (55.622)
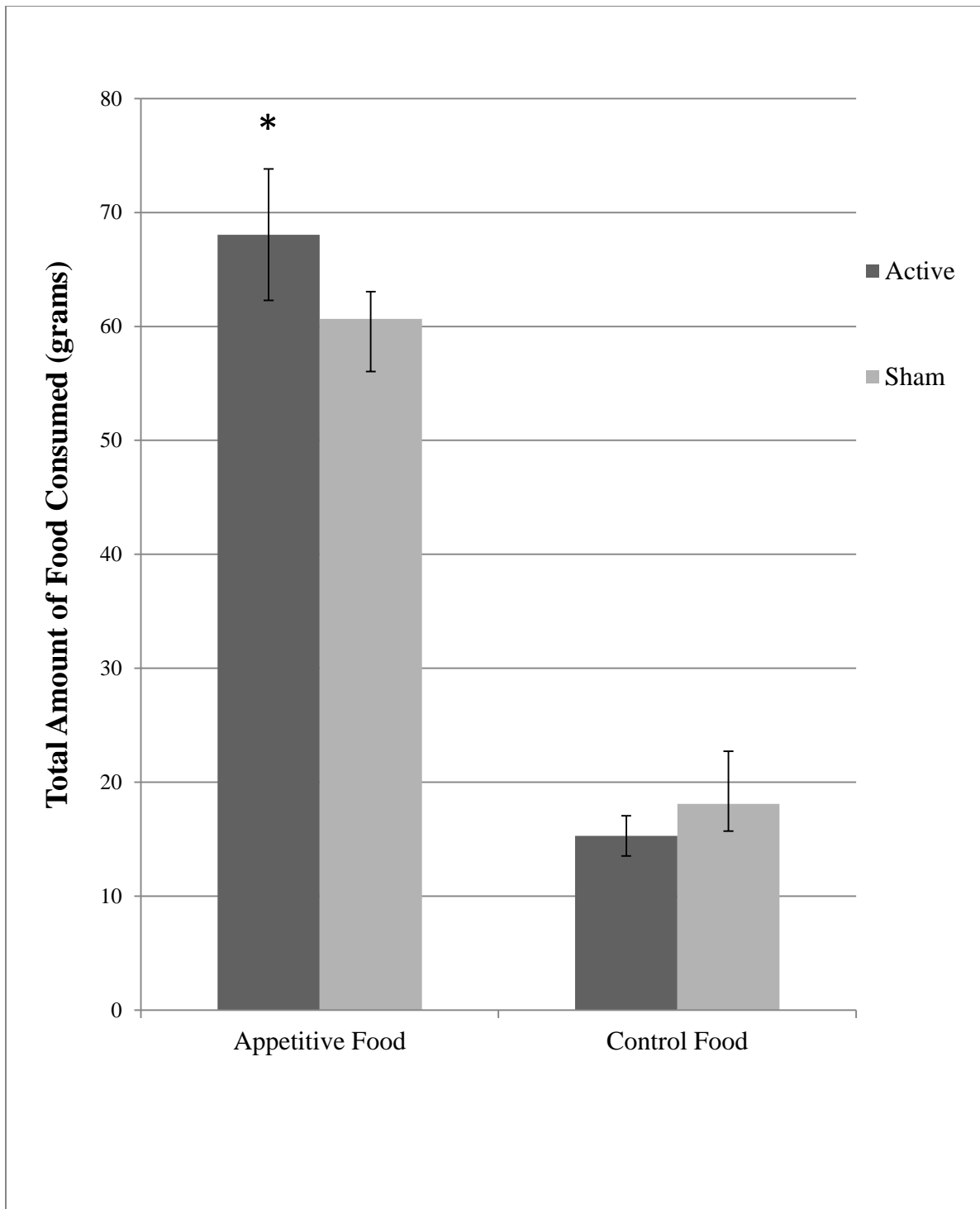
Figure 3: Mean (± SE) stimulation effects on the consumption of appetitive and control foods *g*. *

Significantly different from sham stimulation at the p<.05 level.

8.2 Effects of TMS on Food Cravings

A one-way repeated measures MANOVA was performed to determine whether there was a differential stimulation effect on the pre-to-post percent change in the five craving dimensions of the FCQ-S. The mean % change for each FCQ-S dimension by stimulation condition is presented in Table 4. A significant treatment effect was observed on the positive reinforcement dimension of the FCQ-S ($F(1,20)=7.706$, $p=.012$); this effect was highly selective in that it did not generalize to desire to eat ($F(1,20)=1.175$, $p=.292$), negative reinforcement ($F(1,20)=.001$, $p=.976$), lack of control ($F(1,20)=.166$, $p=.689$), or physiological ($F(1,20)=.402$, $p=.534$) dimensions of the FCQ-S (Figure 4).

Table 4
Pre-to-post percent change in food craving scores across all five dimensions of the FCQ-S by stimulation condition.

	Active	Sham
	Mean (*SD*)	Mean (*SD*)
Desire to Eat	-2.90 (30.04)	-14.53 (33.51)
Positive Reinforcement	9.98 (20.69)	-3.46 (17.62)
Negative Reinforcement	-6.72 (36.64)	-6.77 (17.87)
Lack of Control	-2.02 (33.23)	-6.65 (28.87)
Physiological State	-5.25 (21.54)	-2.08 (17.36)
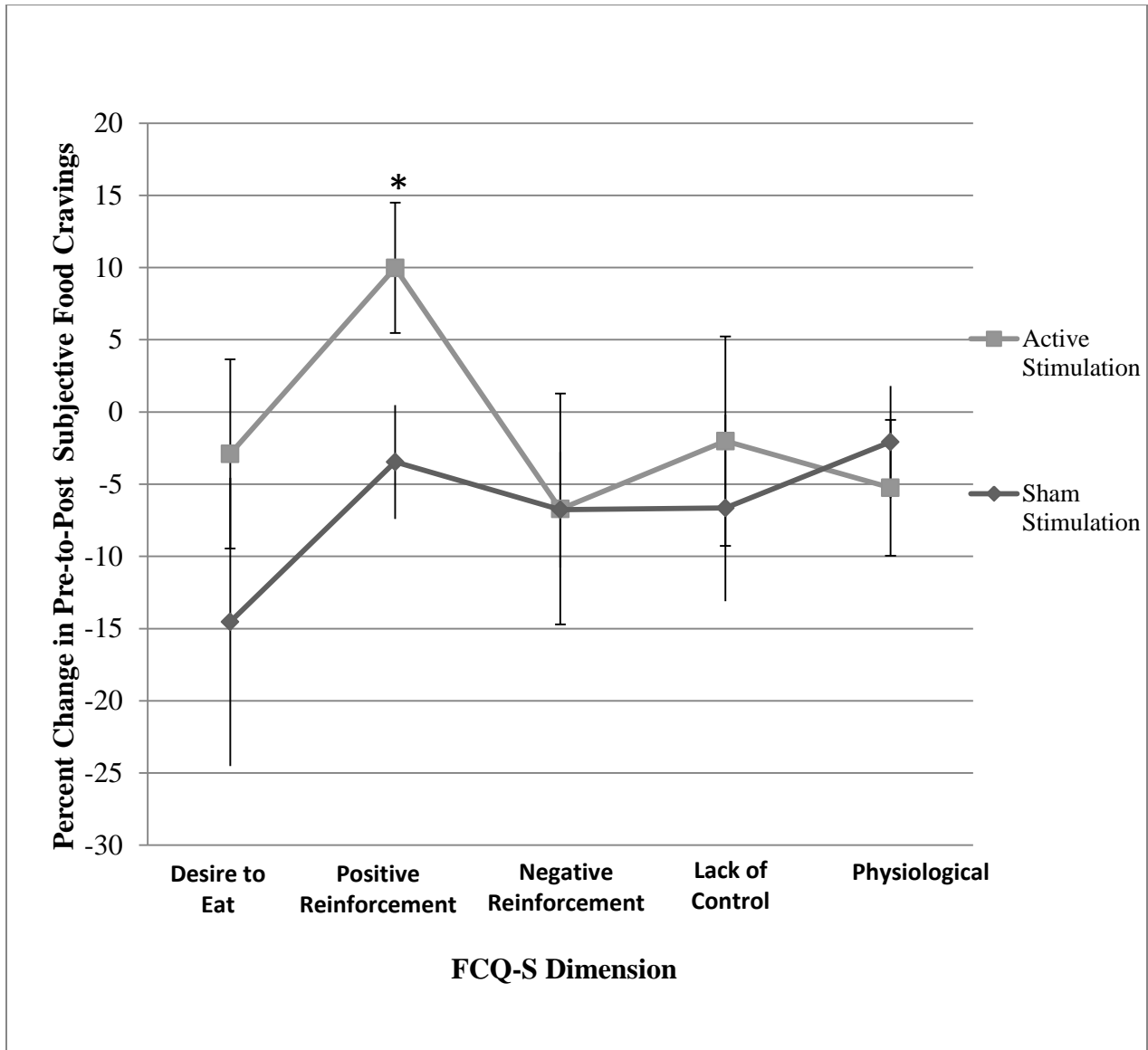
Figure 4: Mean (± SE) percent change in pre-to-post subjective food cravings across all five dimensions

of the FCQ-S by stimulation condition. * Significantly different from sham stimulation at the p<.05 level.

8.3 Effects of TMS on ECR

Separate one-way repeated measures ANOVAs were conducted to determine if there was an effect of stimulation on Stroop, GNG, and SST task performance. There was a significant effect of stimulation condition on performance on the Stroop task ($F(1,20)=5.261$, $p=.033$), such that there was a larger Stroop interference *ms* effect following active ($M=71.56$;SD$=115.39$) compared to sham stimulation ($M=20.16$;SD$=61.06$; Figure 5). However, there was no effect of stimulation condition on performance on the GNG ($F(1,20)=.000$, $p=1.00$) or SST ($F(1,20)=1.040$, $p=.320$) tasks.
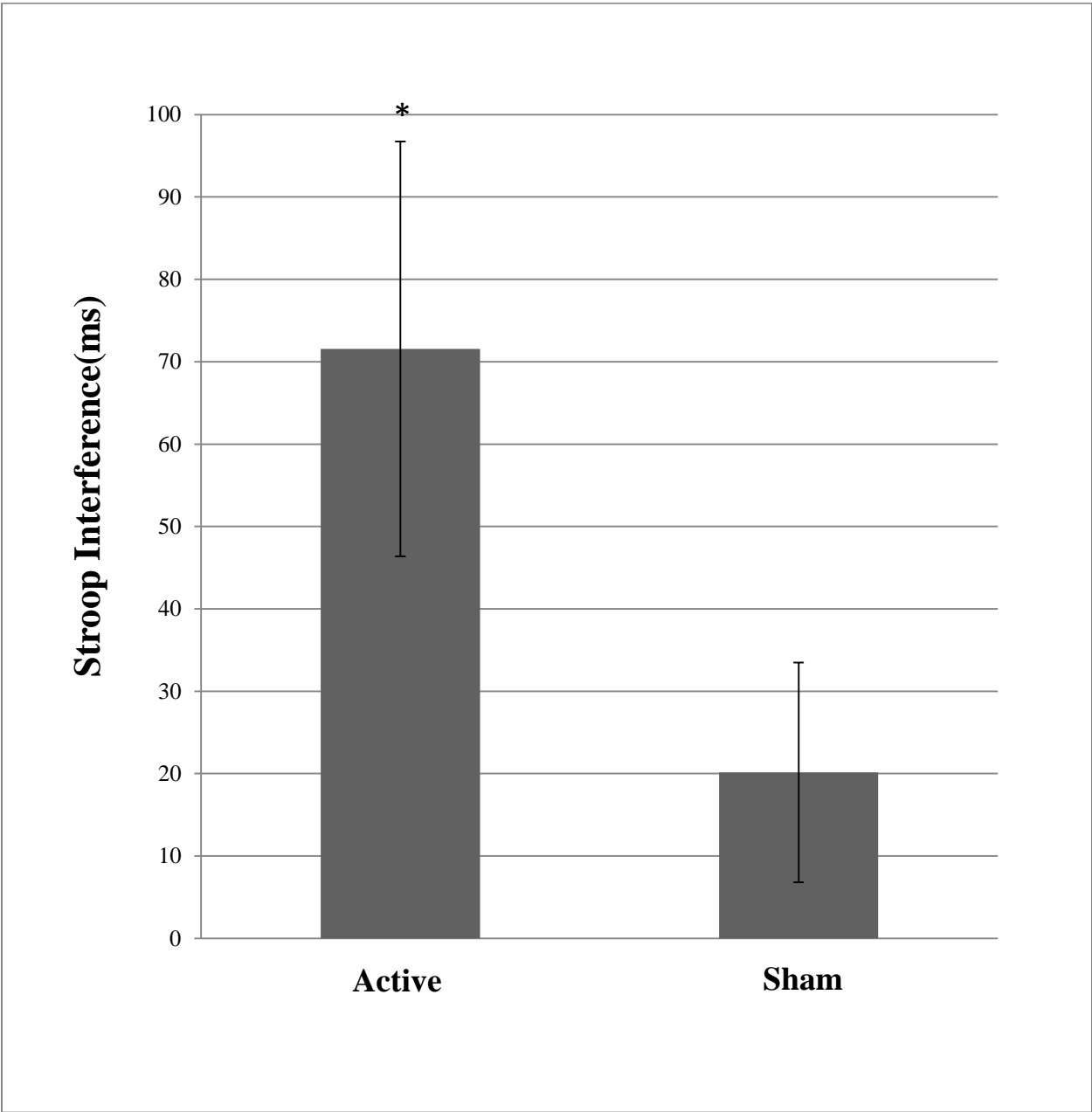
Figure 5: Mean (± SE) Stroop interference effect (ms; asterisk trial RT-congruent RT) as a function of

stimulation condition. * Significantly different from sham stimulation at the p<.05 level.

Chapter 9

9.0 Discussion

The present study was designed to examine the effects of cTBS to the left DLPFC on self-reported food cravings and food consumption. As expected, participants consumed significantly more appetitive food following active stimulation as compared to sham stimulation. This effect was highly selective to appetitive food, and did not generalize to less appetitive foods. In addition, participants reported significantly stronger food craving following active stimulation; this effect was also highly specific, in that only the anticipated positive reinforcement dimension of craving was influenced. Finally, there was a significant stimulation effect on the Stroop, confirming that TMS application did indeed influence at least one aspect of executive function. Together these findings suggest that the DLPFC modulates both subjective hedonic responses to appetitive foods as well as subsequent consumptive behavior, and that the effect may occur via down-regulated ECR strength.

The current finding of a significant stimulation effect on appetitive food cravings is consistent with several other studies using cortical stimulation techniques on healthy adults (Fregni et al., 2008b; Goldman et al., 2011; R. Uher et al., 2005). The additional finding here of an effect on selective consumption of high calorie foods provides additional evidence that actual eating behavior can also be influenced, a finding that has been demonstrated only in one prior study (Fregni et al., 2008b). Additionally, this study was the first to demonstrate that the stimulation effect on food cravings was specific to the reward anticipation. Finally, the stimulation effect on Stroop performance provides support for the contention that decreasing DLPFC activity resulted in craving and consumption effects through reduced ECR strength, a mediational pathway often assumed, but not previously measured.

At the basic neurobiological level, these findings provide direct evidence that the DLPFC plays a role in modulating one specific facet of food cravings: reward anticipation. There is some evidence that suggests individual differences in reward sensitivity and valuation (i.e., preference for immediate versus delayed rewards) is associated with extent that the PFC can modulate activity in the brain regions associated with motivation and reward valuation (e.g., orbitofrontal cortex, striatum; (Peper et al., 2013; Peters & Buchel, 2011). For example, neuroimaging studies have demonstrated that activity in the DLPFC is enhanced when participants choose larger delayed rewards (McClure, Laibson, Loewenstein, & Cohen, 2004; McClure, Ericson, Laibson, Loewenstein, & Cohen, 2007). Additionally, using diffusion tensor imaging Peper et al. reported that individual differences in reward valuation was associated with the structural integrity of the white matter fiber bundles connecting the PFC with the striatum, such that enhanced integrity of these prefrontal-striatal tracts was associated with a preference for larger delayed rewards over smaller immediate rewards. Moreover, Scharmuller et al. (2012) reported that the activation of the DLPFC is necessary to decrease the subjective value of high caloric food cues, suggesting that the DLPFC may play a crucial role in controlling the rewarding properties of energy dense foods. As such, the degree in which the DLPFC can modulate activity in the striatum may explain individual differences in reward sensitivity.

This contention is further supported by evidence from cortical stimulation studies that support this notion. For instance, Knoch et al. (2006) reported that low frequency rTMS to the right DLPFC increased risk-taking behaviours on the IOWA Gambling Task, such that participants choose more often the option that had the highest reward but yielded the greatest penalty. In addition, Fecteau et al. (2007) reported that the upregulation of DLPFC activity resulted in decreased reward sensitivity, such that participants choose more often the low risk

low reward option over the high risk, but more rewarding option. Furthermore, a recent cortical stimulation study reported that transiently inhibiting the left lateral prefrontal cortex (LPFC) with low-frequency rTMS resulted in the increased preference for small immediate rewards over larger delayed rewards (Figner et al., 2010). Together, these results suggest that reward sensitivity is dependent on the differential operation of the PFC, such that reward sensitivity is negatively associated with the operation of the PFC.

As such, craving regulation may depend on the extent that the DLPFC can modulate activity in the striatum (i.e., decrease the rewarding properties of appetitive substances). For example, a recent neuroimaging study demonstrated that activity in the ventral striatum (VS) mediated the relationship between DLPFC activity and food and cigarette cravings, such that as cravings decreased, activity in the DLPFC increased and activity in the VS decreased (Kober et al., 2010). These findings suggest that effective craving regulation requires the brain regions associated with self-control (i.e., DLPFC) to modulate activity in the brain regions associated with reward and motivation (i.e, striatum). In addition, several studies have reported that the stimulation of the DLPFC results in the subsequent change in striatal dopamine levels (Ko et al., 2008; Strafella, Paus, Fraraccio, & Dagher, 2003; Strafella, Ko, Grant, Fraraccio, & Monchi, 2005), and these effects were specific to stimulation of left DLPFC. Therefore, the observed increase in reward anticipation following active as compared to sham stimulation may be attributed to the inability of the DLPFC to modulate activity in the striatum, resulting in increased reward sensitivity (i.e., participants were more sensitive to the rewarding properties of palatable high caloric foods).

The current findings also suggest that the relationship between reward sensitivity and obesity may be attributed to the differential operation of the DLPFC. There is sufficient evidence

that suggests that obese individuals are more susceptible to the rewarding properties of high caloric foods. For example, obese individuals as compared to their healthy weight counterparts show greater activation in the neural regions associated with reward valuation in response to visual food cues (Bruce et al., 2010; Dimitropoulos et al., 2012; Martin et al., 2010; Nummenmaa et al., 2012; Rothemund, Preuschhof, Bohner, Bauknecht, Klingebiel, Flor, & Klapp, 2007a; Schienle et al., 2009; Stice, Yokum, Bohon, Marti, & Smolen, 2010; Stoeckel et al., 2008), and to cues associated with the upcoming receipt of energy dense foods (Ng, Stice, Yokum, & Bohon, 2011; Stice, Spoor, Bohon, Veldhuizen, & Small, 2008). In addition, an increasing body of evidence suggests that obesity is associated with attenuated DLPFC activity (Le et al., 2006; Le et al., 2007; Le et al., 2009). Although the neural mechanisms associated with enhanced reward sensitivity in the obese population are unclear, the evidence from this study suggests that it may be attributed to relationship between obesity and attenuated DLPFC activity.

Applying these findings to health protective behaviors, the results from this study provide causal evidence that the differential operation of the DLPFC can explain individual differences in reward anticipation and consumptive behaviors for calorie dense foods As such, these findings provide a theoretical framework that can be used to shape effective public health interventions. Obese individuals are more sensitive to the rewarding properties of high caloric foods, and given the association between food cravings and food consumption (Scharmüller et al., 2012), population interventions aimed at enhancing DLPFC activity (through aerobic exercise or other means) in the obese individuals may subsequently enhance dietary self-control (i.e., reduce excessive food intake). Moreover, given that many of the health conditions associated with obesity can be managed through lifestyle interventions (e.g., hypertension), interventions aimed

at enhancing DLPFC activity in this population may result in subsequent improvements in disease management. Additionally, numerous cross-sectional studies (Ishizawa, Kumano, Sato, Sakura, & Iwamoto, 2010; Mehrabian et al., 2012; Yaffe et al., 2012), and longitudinal studies (Fontbonne, Berr, Ducimetiere, & Alperovitch, 2001; Kuo et al., 2005; Rouch et al., 2012) have reported that there is an association between type 2 diabetes mellitus (T2DM) and impaired ECRs. However, dietary self-control is particularly important for this population, as healthy dietary habits are essential for effective glucose management. Due to the cognitive deficits associated with T2DM, individuals with T2DM may lack the dietary self-control needed to maintain healthy dietary habits; i.e., they may be more sensitive to the rewarding properties of palatable high caloric foods, and more likely to over consume appetitive foods. Therefore, As such, interventions focused at, enhancing DLPFC activity, through aerobic exercise or other means, may result in increased dietary self-control, and subsequently improve disease management.

9.1 Strengths and Limitations

The key strengths of this study include the inclusion of the standardized measures of ECRs, which has not been done in previous research. By including the ECR measures, we were able to demonstrate that the stimulation effects on food cravings and food consumption may occur through the down-regulation of ECR strength. Additionally, the use of the FCQ-S provided a more comprehensive measure of food cravings, and thus we were able to demonstrate that the DLPFC modulates a highly specific aspect of food cravings (i.e., reward anticipation); again something that has not been done in previous research. Moreover, a blinding procedure (i.e., the bogus taste test) was implemented to minimize any social desirability and expectancy effects. Furthermore, the categorization of the experimental foods into appetitive and control foods is

something that has not been done in previous cortical stimulation studies. Although it can be argued that dark chocolate and soda crackers are appetitive snack foods, the categorization of the experimental foods was based on participant ratings, and the appetitive foods were rated as significantly more appealing than the control foods. It is also important to note that there was no stimulation effect on affect, and therefore mood would not have influenced the stimulation effect on food cravings and consumption.

There are a few limitations that warrant mention. First, stimulation effects were observed on the Stroop but not the GNG and SST, suggesting the possibility that the operation of the DLPFC may regulate different dimensions of inhibition; the GNG and SST are both measures of response or motor inhibition, whereas the Stroop task measures the inability to inhibit interfering information. Indeed, there is some evidence that suggests that the operation of the inferior frontal gyrus (IFG), ventrolateral prefrontal cortex and presupplementary motor areas (pre-SMA) are implicated in the inhibition of motor reponses during the GNG and SST paradigms (Aron, Robbins, & Poldrack, 2004; Aron, Fletcher, Bullmore, Sahakian, & Robbins, 2003; Aron, Monsell, Sahakian, & Robbins, 2004; Aron & Poldrack, 2006; Garavan, Hester, Murphy, Fassbender, & Kelly, 2006; Kenner et al., 2010; Konishi et al., 1999; Li, Huang, Constable, & Sinha, 2006). Additionally, a recent diffusion-weighted imaging tractography study reported that response inhibition was associated with the activation of the pre-SMA, right IFG, and subthalamic nucleus (STN; Aron, Behrens, Smith, Frank, & Poldrack, 2007). However, some studies have also implicated the operation of the DLPFC in successful response inhibition (Garavan et al., 2006; Rubia et al., 2001; Zheng,et al., 2008). Nonetheless, these findings may be attributed to task demands, such that the operation of the PFC is implicated in measures that also involve additional cognitive processes (i.e., task shifting, working memory). For instance, a

recent meta-analysis (Simmonds et al., 2008) reported that that both simple (i.e., No-go stimulus is always the same) and complex (i.e., No-Go stimulus varies) GNG paradigms recruited the operation of the pre-SMA and left fusiform gyrus. However, the operation of right DLPFC and inferior parietal circuits were recruited as the working memory demands increased in more complex GNG paradigms. Taken together, these results suggest that the operation of the pre-SMA and IFG are the primary cortical regions associated with response inhibition in simple GNG and SST paradigms, whereas the operation of the PFC is implicated in more complex tasks.

This notion is further supported by evidence from cortical stimulation studies. For instance, Upton et al. (2010) reported that there was no stimulation effect on SST performance, as indexed by the N2 or P3 stop trial event related potential (ERP) components, following 1Hz rTMS to the left and right DLPFC, indicating that the DLPFC is not directly involved in motor inhibition. Additionally, Huang et al. (2004) reported that there was no stimulation effect on RT, performance accuracy or choice reaction time on a GNG task following active 5Hz rTMS to the left DLPFC. Furthermore, Chambers et al. (2006) reported that there was no stimulation effect on SST performance following 1Hz rTMS to the middle frontal gyrus. However, a stimulation effect on SST performance was observed following low frequency rTMS to the right IFG, indicating that the IFG plays a crucial role in response inhibition. Moreover, Hsu et al. (2011) reported that anodal stimulation of the pre-SMA improved performance on a stop-signal task. Furthermore, Chen et al. (2009) reported that low frequency rTMS to the pre-SMA significantly impaired performance on a SST. Together, these results suggest that successful motor inhibition is associated with the differential operation of the IFG and pre-SMA as opposed the DLPFC; thus explaining why no stimulation effect on GNG and SST performance was observed.

These null findings could also be attributed to a potential ceiling effect. The study population consisted of healthy young adults, with relatively strong performance, rendering the measures only partially sensitive to manipulation. Therefore, it is plausible that different effects may have been observed in a community sample or older adult sample, where a larger range of EF scores would have been observed.

However, it is also possible that there was a stimulation effect on GNG and SST task performance, but the sample size was too small to detect an effect. In fact, based on the observed effect sizes for the stimulation effect on SST (Cohen's d = 0.261) and GNG (Cohen's d= -0.275) performance, a sample of 45 (d=.30) to 64 (d=.45) participants is necessary to achieve statistical power of 0.80 for both paradigms; sample size was determined using the sample size tables in Cohen (1988). Additionally, Upton et al. (2010) reported that a comparable sample size (n=50) would be required to notice a pre-to-post stimulation effect on SST performance (i.e., achieve statistical power of 0.80 with an effect size of 0.33). Consequently, it is plausible that differential results would have been observed with a larger sample size.

Additionally, the sample was limited to female participants, and therefore it is unknown whether the observed experimental effect would generalize to men. However, the study was designed to measure the experimental effects in a specific population (i.e., females), and therefore the results from this study were always intended to generalize to specific population as opposed to the general population (i.e., both males and females). As such, the fact that the experimental effects cannot be generalized to men may not be a threat to the internal validity of the study. In addition, evidence from cortical stimulation studies suggests that women are more susceptible to effects of cortical stimulation methodologies. For instance, Boggio et al. (2008a) reported that modulating activity in the temporal cortex had a differential effect on in females

compared to male participants, such that performance on a face recognition task improved in females and decreased in males. Additionally, Huber et al. (2003) reported that performance on a number-connection test was improved in female patients with schizophrenia following active rTMS, however, there was no significant difference in task performance among male patients. Therefore, it is plausible that differential results would have been observed in sample of male participants.

Finally, menstrual cycle was not controlled for, and therefore hormonal differences between and across participants may have been a source of variation in the observed experimental effect. However, there was no significant stimulation effect on the pre-to-post percent change in food cravings on the negative reinforcement/emotional eating dimension of the FCQ-S, suggesting that variations in menstrual cycle did not influence the stimulation effect on food cravings. Furthermore, stimulation order was randomized across participants, and therefore any confounding effect of menstrual cycle on the experimental effects was minimized. Nonetheless, menstrual cycle variations was not controlled for, and therefore it is currently unknown whether hormonal fluctuations across stimulation sessions and between participants influenced the experimental effect. As such, future research should consider examining whether the stimulation effect on ECR task performance and dietary behaviours is indeed influenced by variations in menstrual cycle.

9.2 Conclusion

In conclusion, the current findings demonstrate that cTBS to the left DLPFC increases food cravings and the selective consumption of highly appealing snack foods. Further, the pattern of findings suggests that the effects of DLPFC stimulation on cravings and behavior may occur via attenuation of executive control. These findings shed a light on the role of the DLPFC

60

in food cravings (specifically reward anticipation), the consumption of appealing high caloric

foods, and the relation between self-control and food consumption. Future research should

consider using ECR measures that tap into different facets of ECR (i.e., working memory and

mental flexibility) to determine if the stimulation effects on ECR are limited to the inhibition

facet. Additionally, by examining the effects of the up-regulation of the DLPFC on food cravings

and food consumption, future research can determine if the opposite effects are observed when

increasing DLPFC activity, thus providing a more comprehensive model regarding the

differential operation of the DLPFC and individual differences in dietary behaviors.

References

Alexander, G. E., DeLong, M. R., & Strick, P. L. (1986). Parallel organization of functionally
segregated circuits linking basal ganglia and cortex. *Annual Review of Neuroscience, 9*(1),
357-381.

Allan, J. L., Johnston, M., & Campbell, N. (2010). Unintentional eating. what determines goal-
incongruent chocolate consumption? *Appetite, 54*(2), 422-425.
doi:10.1016/j.appet.2010.01.009

Allan, J. L., Johnston, M., & Campbell, N. (2011). Missed by an inch or a mile? predicting the
size of intention-behaviour gap from measures of executive control. *Psychology & Health,
26*(6), 635-650. doi:10.1080/08870441003681307

Allen, E. A., Pasley, B. N., Duong, T., & Freeman, R. D. (2007). Transcranial magnetic
stimulation elicits coupled neural and hemodynamic consequences. *Science (New York,
N.Y.), 317*(5846), 1918-1921. doi:10.1126/science.1146426

Alvarez, J. A., & Emory, E. (2006). Executive function and the frontal lobes: A meta-analytic
review. *Neuropsychology Review, 16*(1), 17-42. doi:10.1007/s11065-006-9002-x

Amiaz, R., Levy, D., Vainiger, D., Grunhaus, L., & Zangen, A. (2009). Repeated high-frequency
transcranial magnetic stimulation over the dorsolateral prefrontal cortex reduces cigarette
craving and consumption. *Addiction (Abingdon, England), 104*(4), 653-660.
doi:10.1111/j.1360-0443.2008.02448.x; 10.1111/j.1360-0443.2008.02448.x

Anand, S., & Hotson, J. (2002). Transcranial magnetic stimulation: Neurophysiological

　　applications and safety. *Brain and Cognition, 50*(3), 366-386.

Anis, A. H., Zhang, W., Bansback, N., Guh, D. P., Amarsi, Z., & Birmingham, C. L. (2010).

　　Obesity and overweight in canada: An updated cost-of-illness study. *Obesity Reviews : An*

　　Official Journal of the International Association for the Study of Obesity, 11(1), 31-40.

　　doi:10.1111/j.1467-789X.2009.00579.x

Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2004). Inhibition and the right inferior frontal

　　cortex. *Trends in Cognitive Sciences, 8*(4), 170-177.

Aron, A. R., Behrens, T. E., Smith, S., Frank, M. J., & Poldrack, R. A. (2007). Triangulating a

　　cognitive control network using diffusion-weighted magnetic resonance imaging (MRI) and

　　functional MRI. *The Journal of Neuroscience : The Official Journal of the Society for*

　　Neuroscience, 27(14), 3743-3752. doi:10.1523/JNEUROSCI.0519-07.2007

Aron, A. R., Fletcher, P. C., Bullmore, E. T., Sahakian, B. J., & Robbins, T. W. (2003). Stop-

　　signal inhibition disrupted by damage to right inferior frontal gyrus in humans. *Nature*

　　Neuroscience, 6(2), 115-116. doi:10.1038/nn1003

Aron, A. R., Monsell, S., Sahakian, B. J., & Robbins, T. W. (2004). A componential analysis of

　　task-switching deficits associated with lesions of left and right frontal cortex. *Brain : A*

　　Journal of Neurology, 127(Pt 7), 1561-1573. doi:10.1093/brain/awh169

Aron, A. R., & Poldrack, R. A. (2006). Cortical and subcortical contributions to stop signal

    response inhibition: Role of the subthalamic nucleus. *The Journal of Neuroscience 26*(9),

    2424-2433. doi:10.1523/JNEUROSCI.4682-05.2006

Baessler, A., Hasinoff, M. J., Fischer, M., Reinhard, W., Sonnenberg, G. E., Olivier, M., . . .

    Jacob, H. J. (2005). Genetic linkage and association of the growth hormone secretagogue

    receptor (ghrelin receptor) gene in human obesity. *Diabetes, 54*(1), 259-267.

Barth, K. S., Rydin-Gray, S., Kose, S., Borckardt, J. J., O'Neil, P. M., Shaw, D., . . . George, M.

    S. (2011). Food cravings and the effects of left prefrontal repetitive transcranial magnetic

    stimulation using an improved sham condition. *Frontiers in Psychiatry / Frontiers Research*

    Foundation, 2, 9. doi:10.3389/fpsyt.2011.00009

Boggio, P. S., Bermpohl, F., Vergara, A. O., Muniz, A. L., Nahas, F. H., Leme, P. B., . . . Fregni,

    F. (2007). Go-no-go task performance improvement after anodal transcranial DC

    stimulation of the left dorsolateral prefrontal cortex in major depression. *Journal of Affective*

    Disorders, 101(1), 91-98.

Boggio, P. S., Ferrucci, R., Rigonatti, S. P., Covre, P., Nitsche, M., Pascual-Leone, A., & Fregni,

    F. (2006). Effects of transcranial direct current stimulation on working memory in patients

    with parkinson's disease. *Journal of the Neurological Sciences, 249*(1), 31-38.

Boggio, P. S., Rocha, R. R., da Silva, M. T., & Fregni, F. (2008a). Differential modulatory

    effects of transcranial direct current stimulation on a facial expression go-no-go task in

    males and females. *Neuroscience Letters, 447*(2), 101-105

Boggio, P. S., Sultani, N., Fecteau, S., Merabet, L., Mecca, T., Pascual-Leone, A., . . . Fregni, F. (2008b). Prefrontal cortex modulation using transcranial DC stimulation reduces alcohol craving: A double-blind, sham-controlled study. *Drug and Alcohol Dependence, 92*(1-3), 55-60. doi:10.1016/j.drugalcdep.2007.06.011

Bolton, D. A., & Staines, W. R. (2011). Transient inhibition of the dorsolateral prefrontal cortex disrupts attention-based modulation of tactile stimuli at early stages of somatosensory processing. *Neuropsychologia, 49*(7), 1928-1937. doi:10.1016/j.neuropsychologia.2011.03.020; 10.1016/j.neuropsychologia.2011.03.020

Braver, T. S., Reynolds, J. R., & Donaldson, D. I. (2003). Neural mechanisms of transient and sustained cognitive control during task switching. *Neuron, 39*(4), 713-726.

Brinkworth, G. D., Buckley, J. D., Noakes, M., Clifton, P. M., & Wilson, C. J. (2009). Long-term effects of a very low-carbohydrate diet and a low-fat diet on mood and cognitive function. *Archives of Internal Medicine, 169*(20), 1873-1880. doi:10.1001/archinternmed.2009.329

Bruce, A. S., Holsen, L. M., Chambers, R. J., Martin, L. E., Brooks, W. M., Zarcone, J. R., . . . Savage, C. R. (2010). Obese children show hyperactivation to food pictures in brain networks linked to motivation, reward and cognitive control. *International Journal of Obesity (2005), 34*(10), 1494-1500. doi:10.1038/ijo.2010.84; 10.1038/ijo.2010.84

Camprodon, J. A., Martinez-Raga, J., Alonso-Alonso, M., Shih, M. C., & Pascual-Leone, A. (2007). One session of high frequency repetitive transcranial magnetic stimulation (rTMS) to the right prefrontal cortex transiently reduces cocaine craving. *Drug and Alcohol Dependence, 86*(1), 91-94. doi:10.1016/j.drugalcdep.2006.06.002

Cepeda-Benito, A., Gleaves, D. H., Fernandez, M. C., Vila, J., Williams, T. L., & Reynoso, J. (2000). The development and validation of spanish versions of the state and trait food cravings questionnaires. *Behaviour Research and Therapy, 38*(11), 1125-1138.

Chambers, C. D., Bellgrove, M. A., Stokes, M. G., Henderson, T. R., Garavan, H., Robertson, I. H., . . . Mattingley, J. B. (2006). Executive "brake failure" following deactivation of human frontal lobe. *Journal of Cognitive Neuroscience, 18*(3), 444-455. doi:10.1162/089892906775990606

Chambers, C. D., Garavan, H., & Bellgrove, M. A. (2009). Insights into the neural basis of response inhibition from cognitive and clinical neuroscience. *Neuroscience and Biobehavioral Reviews, 33*(5), 631-646. doi:10.1016/j.neubiorev.2008.08.016; 10.1016/j.neubiorev.2008.08.016

Cheatham, R. A., Roberts, S. B., Das, S. K., Gilhooly, C. H., Golden, J. K., Hyatt, R., . . . Lieberman, H. R. (2009). Long-term effects of provided low and high glycemic load low energy diets on mood and cognition. *Physiology & Behavior, 98*(3), 374-379. doi:10.1016/j.physbeh.2009.06.015

Chen, C., Muggleton, N. G., Tzeng, O. J., Hung, D. L., & Juan, C. (2009). Control of prepotent responses by the superior medial frontal cortex. *Neuroimage, 44*(2), 537-545.

Clapp, W. C., Hamm, J. P., Kirk, I. J., & Teyler, T. J. (2012). Translating long-term potentiation

from animals to humans: A novel method for noninvasive assessment of cortical plasticity.

Biological Psychiatry, 71(6), 496-502. doi:10.1016/j.biopsych.2011.08.021;

10.1016/j.biopsych.2011.08.021

Cohen, J. (1988). *Statistical power for the behavioral sciences* (2nd ed.). Hillsdale, New Jersey:

Lawrence Erlbaum Associates Publishers.

Collison, K. S., Makhoul, N. J., Inglis, A., Al-Johi, M., Zaidi, M. Z., Maqbool, Z., . . . Al-

Mohanna, F. A. (2010). Dietary trans-fat combined with monosodium glutamate induces

dyslipidemia and impairs spatial memory. *Physiology & Behavior, 99*(3), 334-342.

doi:10.1016/j.physbeh.2009.11.010

Congdon, E., Mumford, J. A., Cohen, J. R., Galvan, A., Canli, T., & Poldrack, R. A. (2012).

Measurement and reliability of response inhibition. *Frontiers in Psychology, 3*, 37.

doi:10.3389/fpsyg.2012.00037

Cornier, M. A., Salzberg, A. K., Endly, D. C., Bessesen, D. H., & Tregellas, J. R. (2010). Sex-

based differences in the behavioral and neuronal responses to food. *Physiology & Behavior,

99*(4), 538-543. doi:10.1016/j.physbeh.2010.01.008; 10.1016/j.physbeh.2010.01.008

Cummings, J. L. (1995). Anatomic and behavioral aspects of Frontal-Subcortical circuitsa.

Annals of the New York Academy of Sciences, 769(1), 1-14.

Dangour, A. D., Allen, E., Elbourne, D., Fletcher, A., Richards, M., & Uauy, R. (2009). Fish

    consumption and cognitive function among older people in the UK: Baseline data from the

    OPAL study. *The Journal of Nutrition, Health & Aging, 13*(3), 198-202.

Dimitropoulos, A., Tkach, J., Ho, A., & Kennedy, J. (2012). Greater corticolimbic activation to

    high-calorie food cues after eating in obese vs. normal-weight adults. *Appetite, 58*(1), 303-

    312.

Drewnowski, A. (1997). Why do we like fat? *Journal of the American Dietetic Association, 97*(7

    Suppl), S58-62.

Drewnowski, A., & Greenwood, M. R. (1983). Cream and sugar: Human preferences for high-fat

    foods. *Physiology & Behavior, 30*(4), 629-633.

Edwards, L. M., Murray, A. J., Holloway, C. J., Carter, E. E., Kemp, G. J., Codreanu, I., . . .

    Clarke, K. (2011). Short-term consumption of a high-fat diet impairs whole-body efficiency

    and cognitive function in sedentary men. *FASEB Journal : Official Publication of the*

    Federation of American Societies for Experimental Biology, 25(3), 1088-1096.

    doi:10.1096/fj.10-171983

Eichhammer, P., Johann, M., Kharraz, A., Binder, H., Pittrow, D., Wodarz, N., & Hajak, G.

    (2003). High-frequency repetitive transcranial magnetic stimulation decreases cigarette

    smoking. *The Journal of Clinical Psychiatry, 64*(8), 951-953.

Fecteau, S., Fregni, F., Boggio, P. S., Camprodon, J. A., & Pascual-Leone, A. (2010).
Neuromodulation of decision-making in the addictive brain. *Substance use & Misuse, 45*(11), 1766-1786. doi:10.3109/10826084.2010.482434; 10.3109/10826084.2010.482434

Figner, B., Knoch, D., Johnson, E. J., Krosch, A. R., Lisanby, S. H., Fehr, E., & Weber, E. U. (2010). Lateral prefrontal cortex and self-control in intertemporal choice. *Nature Neuroscience, 13*(5), 538-539.

Flegal, K. M. (2005). Epidemiologic aspects of overweight and obesity in the united states. *Physiology & Behavior, 86*(5), 599-602. doi:10.1016/j.physbeh.2005.08.050

Fletcher, B. C., Pine, K. J., Woodbridge, Z., & Nash, A. (2007). How visual images of chocolate affect the craving and guilt of female dieters. *Appetite, 48*(2), 211-217. doi:10.1016/j.appet.2006.09.002

Fontbonne, A., Berr, C., Ducimetiere, P., & Alperovitch, A. (2001). Changes in cognitive abilities over a 4-year period are unfavorably affected in elderly diabetic subjects: Results of the epidemiology of vascular aging study. *Diabetes Care, 24*(2), 366-370.

Fregni, F., Boggio, P. S., Santos, M. C., Lima, M., Vieira, A. L., Rigonatti, S. P., . . . Pascual-Leone, A. (2006). Noninvasive cortical stimulation with transcranial direct current stimulation in parkinson's disease. *Movement Disorders, 21*(10), 1693-1702.

Fregni, F., Boggio, P. S., Nitsche, M., Bermpohl, F., Antal, A., Feredoes, E., . . . Pascual-Leone, A. (2005). Anodal transcranial direct current stimulation of prefrontal cortex enhances

working memory. *Experimental Brain Research.Experimentelle Hirnforschung.Experimentation Cerebrale, 166*(1), 23-30. doi:10.1007/s00221-005-2334-6

Fregni, F., Liguori, P., Fecteau, S., Nitsche, M. A., Pascual-Leone, A., & Boggio, P. S. (2008a). Cortical stimulation of the prefrontal cortex with transcranial direct current stimulation reduces cue-provoked smoking craving: A randomized, sham-controlled study. *The Journal of Clinical Psychiatry, 69*(1), 32-40.

Fregni, F., Orsati, F., Pedrosa, W., Fecteau, S., Tome, F. A. M., Nitsche, M. A., . . . Boggio, P. S. (2008b). Transcranial direct current stimulation of the prefrontal cortex modulates the desire for specific foods. *Appetite, 51*(1), 34-41. doi:DOI: 10.1016/j.appet.2007.09.016

Friedman, N. P., Miyake, A., Young, S. E., Defries, J. C., Corley, R. P., & Hewitt, J. K. (2008). Individual differences in executive functions are almost entirely genetic in origin. *Journal of Experimental Psychology.General, 137*(2), 201-225. doi:10.1037/0096-3445.137.2.201

Garavan, H., Hester, R., Murphy, K., Fassbender, C., & Kelly, C. (2006). Individual differences in the functional neuroanatomy of inhibitory control. *Brain Research, 1105*(1), 130-142. doi:10.1016/j.brainres.2006.03.029

Goldman, R. L., Borckardt, J. J., Frohman, H. A., O'Neil, P. M., Madan, A., Campbell, L. K., . . . George, M. S. (2011). Prefrontal cortex transcranial direct current stimulation (tDCS) temporarily reduces food cravings and increases the self-reported ability to resist food in adults with frequent food craving. *Appetite, 56*(3), 741-746. doi:DOI: 10.1016/j.appet.2011.02.013

Groenewegen, H. J., Wright, C. I., & Uylings, H. B. (1997). The anatomical relationships of the

    prefrontal cortex with limbic structures and the basal ganglia. *Journal of*

    Psychopharmacology, 11(2), 99-106.

Grossheinrich, N., Rau, A., Pogarell, O., Hennig-Fast, K., Reinl, M., Karch, S., . . . Padberg, F.

    (2009). Theta burst stimulation of the prefrontal cortex: Safety and impact on cognition,

    mood, and resting electroencephalogram. *Biological Psychiatry, 65*(9), 778-784.

    doi:10.1016/j.biopsych.2008.10.029; 10.1016/j.biopsych.2008.10.029

Guerrieri, R., Nederkoorn, C., & Jansen, A. (2007). How impulsiveness and variety influence

    food intake in a sample of healthy women. *Appetite, 48*(1), 119-122.

    doi:10.1016/j.appet.2006.06.004

Guerrieri, R., Nederkoorn, C., & Jansen, A. (2008). The interaction between impulsivity and a

    varied food environment: Its influence on food intake and overweight. *International Journal*

    of Obesity (2005), 32(4), 708-714. doi:10.1038/sj.ijo.0803770

Guerrieri, R., Nederkoorn, C., & Jansen, A. (2012). Disinhibition is easier learned than

    inhibition. the effects of (dis)inhibition training on food intake. *Appetite, 59*(1), 96-99.

    doi:10.1016/j.appet.2012.04.006; 10.1016/j.appet.2012.04.006

Guerrieri, R., Nederkoorn, C., Schrooten, M., Martijn, C., & Jansen, A. (2009). Inducing

    impulsivity leads high and low restrained eaters into overeating, whereas current dieters

    stick to their diet. *Appetite, 53*(1), 93-100. doi:10.1016/j.appet.2009.05.013

Hall, P. A., Lowe, C., Vincent, C., Mourtzakis, M., & Roy, E. (submitted). The effects of situational cues and executive functions on snack food consumption among older adults. *Journal of Gerontology: Psychological Sciences,*

Hall, P. A., Fong, G. T., Epp, L. J., & Elias, L. J. (2008). Executive function moderates the intention-behavior link for physical activity and dietary behavior. *Psychology and Health, 23*(3), 309-326.

Hall, P. A. (2012). Executive control resources and frequency of fatty food consumption: Findings from an age-stratified community sample. *Health Psychology : Official Journal of the Division of Health Psychology, American Psychological Association, 31*(2), 235-241. doi:10.1037/a0025407

Hall, P. A., Lowe, C., & Vincent, C. (2013). Executive control resources and snack food consumption in the presence of restraining versus facilitating cues. *Journal of Behavioral Medicine,* doi:10.1007/s10865-013-9528-3

Hall, P. A., Fong, G. T., Epp, L. J., & Elias, L. J. (2008a). Executive function moderates the intention-behavior link for physical activity and dietary behavior. *Psychology & Health, 23*(3), 309-326. doi:10.1080/14768320701212099

Hall, P. A., Fong, G. T., Epp, L. J., & Elias, L. J. (2008b). Executive function moderates the intention-behavior link for physical activity and dietary behavior. *Psychology & Health, 23*(3), 309-326. doi:10.1080/14768320701212099

Hare, T. A., Camerer, C. F., & Rangel, A. (2009). Self-control in decision-making involves

    modulation of the vmPFC valuation system. *Science (New York, N.Y.), 324*(5927), 646-648.

    doi:10.1126/science.1168450

Hill, A. J., Weaver, C. F., & Blundell, J. E. (1991). Food craving, dietary restraint and mood.

    Appetite, 17(3), 187-197.

Hill, J. O., & Peters, J. C. (1998). Environmental contributions to the obesity epidemic. *Science*

    (New York, N.Y.), 280(5368), 1371-1374.

Hoshi, E. (2013). Cortico-basal ganglia networks subserving goal-directed behavior mediated by

    conditional visuo-goal association. *Frontiers in Neural Circuits, 7*, 158.

    doi:10.3389/fncir.2013.00158; 10.3389/fncir.2013.00158

Houben, K. (2011). Overcoming the urge to splurge: Influencing eating behavior by

    manipulating inhibitory control. *Journal of Behavior Therapy and Experimental Psychiatry,*

    42(3), 384-388. doi:10.1016/j.jbtep.2011.02.008

Houben, K., & Jansen, A. (2011). Training inhibitory control. A recipe for resisting sweet

    temptations. *Appetite, 56*(2), 345-349. doi:10.1016/j.appet.2010.12.017;

    10.1016/j.appet.2010.12.017

Hsu, T., Tseng, L., Yu, J., Kuo, W., Hung, D. L., Tzeng, O. J., . . . Juan, C. (2011). Modulating

    inhibitory control with direct current stimulation of the superior medial frontal cortex.

    NeuroImage, 56(4), 2249-2257.

Huang, Y. Z., Chen, R. S., Rothwell, J. C., & Wen, H. Y. (2007). The after-effect of human theta burst stimulation is NMDA receptor dependent. *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology, 118*(5), 1028-1032. doi:10.1016/j.clinph.2007.01.021

Huang, Y., Edwards, M. J., Rounis, E., Bhatia, K. P., & Rothwell, J. C. (2005). Theta burst stimulation of the human motor cortex [Abstract]. *Neuron, 45*(2) 201-206.

Huang, C., Su, T., Shan, I., & Wei, I. (2004). Effect of 5 hz repetitive transcranial magnetic stimulation on cognition during a Go/NoGo task. *Journal of Psychiatric Research, 38*(5), 513-520.

Huber, T. J., Schneider, U., & Rollnik, J. (2003). Gender differences in the effect of repetitive transcranial magnetic stimulation in schizophrenia. *Psychiatry Research, 120*(1), 103-105.

Ishizawa, K. T., Kumano, H., Sato, A., Sakura, H., & Iwamoto, Y. (2010). Decreased response inhibition in middle-aged male patients with type 2 diabetes. *BioPsychoSocial Medicine, 4*(1), 1-0759-4-1. doi:10.1186/1751-0759-4-1; 10.1186/1751-0759-4-1

Jansen, J. M., Daams, J. G., Koeter, M. W. J., Veltman, D. J., van den Brink, W., & Goudriaan, A. E.Effects of non-invasive neurostimulation on craving: A meta-analysis. *Neuroscience & Biobehavioral Reviews,* (0) doi:http://dx.doi.org/10.1016/j.neubiorev.2013.07.009

Jeffery, R. W., & Utter, J. (2003). The changing environment and population obesity in the united states. *Obesity Research, 11 Suppl*, 12S-22S. doi:10.1038/oby.2003.221

Johann, M., Wiegand, R., Kharraz, A., Bobbe, G., Sommer, G., Hajak, G., . . . Eichhammer, P. (2003). Repetitiv transcranial magnetic stimulation in nicotine dependence. [Transkranielle Magnetstimulation bei Nikotinabhangigkeit] *Psychiatrische Praxis, 30*(Suppl 2), 129-131. doi:10.1055/s-2003-39733

Katzmarzyk, P. T., & Janssen, I. (2004). The economic costs associated with physical inactivity and obesity in canada: An update. *Canadian Journal of Applied Physiology = Revue Canadienne De Physiologie Appliquee, 29*(1), 90-115.

Kenner, N. M., Mumford, J. A., Hommer, R. E., Skup, M., Leibenluft, E., & Poldrack, R. A. (2010). Inhibitory motor control in response stopping and response switching. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 30*(25), 8512-8518. doi:10.1523/JNEUROSCI.1096-10.2010; 10.1523/JNEUROSCI.1096-10.2010

Killgore, W. D., Young, A. D., Femia, L. A., Bogorodzki, P., Rogowska, J., & Yurgelun-Todd, D. A. (2003). Cortical and limbic activation during viewing of high-versus low-calorie foods. *NeuroImage, 19*(4), 1381-1394.

Killgore, W. D., & Yurgelun-Todd, D. A. (2010). Sex differences in cerebral responses to images of high versus low-calorie food. *Neuroreport, 21*(5), 354-358. doi:10.1097/WNR.0b013e32833774f7; 10.1097/WNR.0b013e32833774f7

Knoch, D., Gianotti, L. R., Pascual-Leone, A., Treyer, V., Regard, M., Hohmann, M., & Brugger, P. (2006). Disruption of right prefrontal cortex by low-frequency repetitive transcranial magnetic stimulation induces risk-taking behavior. *The Journal of Neuroscience, 26*(24), 6469-6472.

Ko, J. H., Monchi, O., Ptito, A., Bloomfield, P., Houle, S., & Strafella, A. P. (2008). Theta burst stimulation-induced inhibition of dorsolateral prefrontal cortex reveals hemispheric asymmetry in striatal dopamine release during a set-shifting task: A TMS-[(11)C]raclopride PET study. *The European Journal of Neuroscience, 28*(10), 2147-2155. doi:10.1111/j.1460-9568.2008.06501.x

Kober, H., Mende-Siedlecki, P., Kross, E. F., Weber, J., Mischel, W., Hart, C. L., & Ochsner, K. N. (2010). Prefrontal–striatal pathway underlies cognitive regulation of craving. *Proceedings of the National Academy of Sciences, 107*(33), 14811-14816.

Konishi, S., Nakajima, K., Uchida, I., Kikyo, H., Kameyama, M., & Miyashita, Y. (1999). Common inhibitory mechanism in human inferior prefrontal cortex revealed by event-related functional MRI. *Brain, 122*(5), 981-991.

Kringelbach, M. L., & Rolls, E. T. (2004). The functional neuroanatomy of the human orbitofrontal cortex: Evidence from neuroimaging and neuropsychology. *Progress in Neurobiology, 72*(5), 341-372.

Kuo, H. K., Jones, R. N., Milberg, W. P., Tennstedt, S., Talbot, L., Morris, J. N., & Lipsitz, L. A. (2005). Effect of blood pressure and diabetes mellitus on cognitive and physical functions in older adults: A longitudinal analysis of the advanced cognitive training for independent and vital elderly cohort. *Journal of the American Geriatrics Society, 53*(7), 1154-1161. doi:10.1111/j.1532-5415.2005.53368.x

Le, D. S., Chen, K., Pannacciulli, N., Gluck, M., Reiman, E. M., & Krakoff, J. (2009). Reanalysis of the obesity-related attenuation in the left dorsolateral prefrontal cortex

response to a satiating meal using gyral regions-of-interest. *Journal of the American College of Nutrition, 28*(6), 667-673.

Le, D. S., Pannacciulli, N., Chen, K., Del Parigi, A., Salbe, A. D., Reiman, E. M., & Krakoff, J. (2006). Less activation of the left dorsolateral prefrontal cortex in response to a meal: A feature of obesity. *The American Journal of Clinical Nutrition, 84*(4), 725-731.

Le, D. S., Pannacciulli, N., Chen, K., Salbe, A. D., Del Parigi, A., Hill, J. O., . . . Krakoff, J. (2007). Less activation in the left dorsolateral prefrontal cortex in the reanalysis of the response to a meal in obese than in lean women and its association with successful weight loss. *The American Journal of Clinical Nutrition, 86*(3), 573-579.

Leh, S. E., Ptito, A., Chakravarty, M. M., & Strafella, A. P. (2007). Fronto-striatal connections in the human brain: A probabilistic diffusion tractography study. *Neuroscience Letters, 419*(2), 113-118.

Li, C. S., Huang, C., Constable, R. T., & Sinha, R. (2006). Imaging response inhibition in a stop-signal task: Neural correlates independent of signal monitoring and post-response processing. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 26*(1), 186-192. doi:10.1523/JNEUROSCI.3741-05.2006

Logan, G. D., Cowan, W. B., & Davis, K. A. (1984). On the ability to inhibit simple and choice reaction time responses: A model and a method. *Journal of Experimental Psychology: Human Perception and Performance, 10*(2), 276-291. doi:10.1037/0096-1523.10.2.276

Machii, K., Cohen, D., Ramos-Estebanez, C., & Pascual-Leone, A. (2006). Safety of rTMS to non-motor cortical areas in healthy participants and patients. *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology, 117*(2), 455-471. doi:10.1016/j.clinph.2005.10.014

Martin, L. E., Holsen, L. M., Chambers, R. J., Bruce, A. S., Brooks, W. M., Zarcone, J. R., . . . Savage, C. R. (2010). Neural mechanisms associated with food motivation in obese and healthy weight adults. *Obesity (Silver Spring, Md.), 18*(2), 254-260. doi:10.1038/oby.2009.220; 10.1038/oby.2009.220

McClure, S. M., Ericson, K. M., Laibson, D. I., Loewenstein, G., & Cohen, J. D. (2007). Time discounting for primary rewards. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 27*(21), 5796-5804. doi:10.1523/JNEUROSCI.4246-06.2007

McClure, S. M., Laibson, D. I., Loewenstein, G., & Cohen, J. D. (2004). Separate neural systems value immediate and delayed monetary rewards. *Science (New York, N.Y.), 306*(5695), 503-507. doi:10.1126/science.1100907

McNeilly, A. D., Williamson, R., Sutherland, C., Balfour, D. J. K., & Stewart, C. A. (2011). High fat feeding promotes simultaneous decline in insulin sensitivity and cognitive performance in a delayed matching and non-matching to position task. *Behavioural Brain Research, 217*(1), 134-141. doi:DOI: 10.1016/j.bbr.2010.10.017

Mega, M. S., & Cummings, J. L. (1994). Frontal-subcortical circuits and neuropsychiatric disorders. *The Journal of Neuropsychiatry and Clinical Neurosciences, 6*(4), 358-370.

Mehrabian, S., Raycheva, M., Gateva, A., Todorova, G., Angelova, P., Traykova, M., . . . Traykov, L. (2012). Cognitive dysfunction profile and arterial stiffness in type 2 diabetes. *Journal of the Neurological Sciences, 322*(1-2), 152-156. doi:10.1016/j.jns.2012.07.046; 10.1016/j.jns.2012.07.046

Messier, C., Whately, K., Liang, J., Du, L., & Puissant, D. (2007). The effects of a high-fat, high-fructose, and combination diet on learning, weight, and glucose regulation in C57BL/6 mice. *Behavioural Brain Research, 178*(1), 139-145. doi:10.1016/j.bbr.2006.12.011

Middleton, F. A., & Strick, P. L. (2000). Basal ganglia and cerebellar loops: Motor and cognitive circuits. *Brain Research Reviews, 31*(2), 236-250.

Miller, E. K. (2000). The prefrontal cortex and cognitive control. *Nature Reviews.Neuroscience, 1*(1), 59-65. doi:10.1038/35036228

Miller, E. K., & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. *Annual Review of Neuroscience, 24*, 167-202. doi:10.1146/annurev.neuro.24.1.167

Miyake, A., & Friedman, N. P. (2012). The nature and organization of individual differences in executive functions four general conclusions. *Current Directions in Psychological Science, 21*(1), 8-14.

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: A latent variable analysis. *Cognitive Psychology, 41*(1), 49-100. doi:10.1006/cogp.1999.0734

Moreno, S., Rodriguez, S., Fernandez, M. C., Tamez, J., & Cepeda-Benito, A. (2008). Clinical validation of the trait and state versions of the food craving questionnaire. *Assessment, 15*(3), 375-387. doi:10.1177/1073191107312651; 10.1177/1073191107312651

Mull, B. R., & Seyal, M. (2001). Transcranial magnetic stimulation of left prefrontal cortex impairs working memory. *Clinical Neurophysiology, 112*(9), 1672-1675.

Nederkoorn, C., Houben, K., Hofmann, W., Roefs, A., & Jansen, A. (2010). Control yourself or just eat what you like? weight gain over a year is predicted by an interactive effect of response inhibition and implicit preference for snack foods. *Health Psychology, 29*(4), 389-393. doi:10.1037/a0019921

Ng, J., Stice, E., Yokum, S., & Bohon, C. (2011). An fMRI study of obesity, food reward, and perceived caloric density. does a low-fat label make food less appealing? *Appetite, 57*(1), 65-72. doi:http://dx.doi.org/10.1016/j.appet.2011.03.017

Nijs, I. M., Franken, I. H., & Muris, P. (2007). The modified trait and state food-cravings questionnaires: Development and validation of a general index of food craving. *Appetite, 49*(1), 38-46. doi:10.1016/j.appet.2006.11.001

Nummenmaa, L., Hirvonen, J., Hannukainen, J. C., Immonen, H., Lindroos, M. M., Salminen, P., & Nuutila, P. (2012). Dorsal striatum and its limbic connectivity mediate abnormal anticipatory reward processing in obesity. *PloS One, 7*(2), e31089.

Nyffeler, T., Müri, R. M., Bucher-Ottiger, Y., Pierrot-Deseilligny, C., Gaymard, B., & Rivaud-Pechoux, S. (2007). Inhibitory control of the human dorsolateral prefrontal cortex during the

anti-saccade paradigm− a transcranial magnetic stimulation study. *European Journal of Neuroscience, 26*(5), 1381-1385.

Oberman, L., Edwards, D., Eldaief, M., & Pascual-Leone, A. (2011). Safety of theta burst transcranial magnetic stimulation: A systematic review of the literature. *Journal of Clinical Neurophysiology : Official Publication of the American Electroencephalographic Society, 28*(1), 67-74. doi:10.1097/WNP.0b013e318205135f

Pascual-Leone, A., Bartres-Faz, D., & Keenan, J. P. (1999). Transcranial magnetic stimulation: Studying the brain-behaviour relationship by induction of 'virtual lesions'. *Philosophical Transactions of the Royal Society of London.Series B, Biological Sciences, 354*(1387), 1229-1238. doi:10.1098/rstb.1999.0476

Pelchat, M. L., Johnson, A., Chan, R., Valdez, J., & Ragland, J. D. (2004). Images of desire: Food-craving activation during fMRI. *NeuroImage, 23*(4), 1486-1493.

Peper, J. S., Mandl, R. C., Braams, B. R., de Water, E., Heijboer, A. C., Koolschijn, P. C., & Crone, E. A. (2013). Delay discounting and frontostriatal fiber tracts: A combined DTI and MTR study on impulsive choices in healthy young adults. *Cerebral Cortex (New York, N.Y.: 1991), 23*(7), 1695-1702. doi:10.1093/cercor/bhs163; 10.1093/cercor/bhs163

Peters, J., & Buchel, C. (2011). The neural mechanisms of inter-temporal decision-making: Understanding variability. *Trends in Cognitive Sciences, 15*(5), 227-239. doi:10.1016/j.tics.2011.03.002; 10.1016/j.tics.2011.03.002

Peters, J. C., Wyatt, H. R., Donahoo, W. T., & Hill, J. O. (2002). From instinct to intellect: The challenge of maintaining healthy weight in the modern world. *Obesity Reviews : An Official Journal of the International Association for the Study of Obesity, 3*(2), 69-74.

Popkin, B. M., Duffey, K., & Gordon-Larsen, P. (2005). Environmental influences on food choice, physical activity and energy balance. *Physiology & Behavior, 86*(5), 603-613. doi:10.1016/j.physbeh.2005.08.051

Poston, W. S.,2nd, & Foreyt, J. P. (1999). Obesity is an environmental issue. *Atherosclerosis, 146*(2), 201-209.

Preston, G., Anderson, E., Silva, C., Goldberg, T., & Wassermann, E. M. (2010). Effects of 10 hz rTMS on the neural efficiency of working memory. *Journal of Cognitive Neuroscience, 22*(3), 447-456.

Ridderinkhof, K. R., van den Wildenberg, W. P., Segalowitz, S. J., & Carter, C. S. (2004). Neurocognitive mechanisms of cognitive control: The role of prefrontal cortex in action selection, response inhibition, performance monitoring, and reward-based learning. *Brain and Cognition, 56*(2), 129-140. doi:10.1016/j.bandc.2004.09.016

Ridding, M. C., & Rothwell, J. C. (2007). Is there a future for therapeutic use of transcranial magnetic stimulation? *Nature Reviews. Neuroscience, 8*(7), 559-567.

Rossi, S., Hallett, M., Rossini, P. M., Pascual-Leone, A., & Safety of TMS Consensus Group. (2009). Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. *Clinical Neurophysiology : Official*

Journal of the International Federation of Clinical Neurophysiology, 120(12), 2008-2039. doi:10.1016/j.clinph.2009.08.016

Rotenberg, K. J., Lancaster, C., Marsden, J., Pryce, S., Williams, J., & Lattimore, P. (2005). Effects of priming thoughts about control on anxiety and food intake as moderated by dietary restraint. *Appetite, 44*(2), 235-241. doi:10.1016/j.appet.2004.09.001

Rothemund, Y., Preuschhof, C., Bohner, G., Bauknecht, H. C., Klingebiel, R., Flor, H., & Klapp, B. F. (2007). Differential activation of the dorsal striatum by high-calorie visual food stimuli in obese individuals. *NeuroImage, 37*(2), 410-421. doi:10.1016/j.neuroimage.2007.05.008

Rouch, I., Roche, F., Dauphinot, V., Laurent, B., Anterion, C. T., Celle, S., . . . Barthelemy, J. C. (2012). Diabetes, impaired fasting glucose, and cognitive decline in a population of elderly community residents. *Aging Clinical and Experimental Research, 24*(4), 377-383.

Rubia, K., Russell, T., Overmeyer, S., Brammer, M. J., Bullmore, E. T., Sharma, T., . . . Andrew, C. M. (2001). Mapping motor inhibition: Conjunctive brain activations across different versions of go/no-go and stop tasks. *NeuroImage, 13*(2), 250-261.

Sabia, S., Nabi, H., Kivimaki, M., Shipley, M. J., Marmot, M. G., & Singh-Manoux, A. (2009). Health behaviors from early to late midlife as predictors of cognitive function: The whitehall II study. *American Journal of Epidemiology, 170*(4), 428-437. doi:10.1093/aje/kwp161

Sandman, C. A., Davis, E. P., Buss, C., & Glynn, L. M. (2011). Exposure to prenatal
psychobiological stress exerts programming influences on the mother and her fetus.
Neuroendocrinology, doi:10.1159/000327017

Sandrini, M., Umiltà, C., & Rusconi, E. (2011). The use of transcranial magnetic stimulation in
cognitive neuroscience: A new synthesis of methodological issues. *Neuroscience &
Biobehavioral Reviews, 35*(3), 516-536. doi:10.1016/j.neubiorev.2010.06.005

Scharmuller, W., Ubel, S., Ebner, F., & Schienle, A. (2012). Appetite regulation during food cue
exposure: A comparison of normal-weight and obese women. *Neuroscience Letters, 518*(2),
106-110. doi:10.1016/j.neulet.2012.04.063

Schienle, A., Schäfer, A., Hermann, A., & Vaitl, D. (2009). Binge-eating disorder: Reward
sensitivity and brain activation to images of food. *Biological Psychiatry, 65*(8), 654-661.

Schousboe, K., Willemsen, G., Kyvik, K. O., Mortensen, J., Boomsma, D. I., Cornes, B. K., . . .
Kaprio, J. (2003). Sex differences in heritability of BMI: A comparative study of results
from twin studies in eight countries. *Twin Research, 6*(05), 409-421.

Simmonds, D. J., Pekar, J. J., & Mostofsky, S. H. (2008). Meta-analysis of Go/No-go tasks
demonstrating that fMRI activation associated with response inhibition is task-dependent.
Neuropsychologia, 46(1), 224-232. doi:10.1016/j.neuropsychologia.2007.07.015

Silventoinen, K., Rokholm, B., Kaprio, J., & Sørensen, T. (2009). The genetic and environmental
influences on childhood obesity: A systematic review of twin and adoption studies.
International Journal of Obesity, 34(1), 29-40.

Speliotes, E. K., Willer, C. J., Berndt, S. I., Monda, K. L., Thorleifsson, G., Jackson, A. U., . . . Mägi, R. (2010). Association analyses of 249,796 individuals reveal 18 new loci associated with body mass index. *Nature Genetics, 42*(11), 937-948.

Stevens, M. C., Kiehl, K. A., Pearlson, G. D., & Calhoun, V. D. (2007). Functional neural networks underlying response inhibition in adolescents and adults. *Behavioural Brain Research, 181*(1), 12-22.

Stice, E., Spoor, S., Bohon, C., Veldhuizen, M. G., & Small, D. M. (2008). Relation of reward from food intake and anticipated food intake to obesity: A functional magnetic resonance imaging study. *Journal of Abnormal Psychology, 117*(4), 924.

Stice, E., Yokum, S., Bohon, C., Marti, N., & Smolen, A. (2010). Reward circuitry responsivity to food predicts future increases in body mass: Moderating effects of DRD2 and DRD4. *NeuroImage, 50*(4), 1618-1625. doi:http://dx.doi.org/10.1016/j.neuroimage.2010.01.081

Stoeckel, L. E., Weller, R. E., Cook, E. W.,3rd, Twieg, D. B., Knowlton, R. C., & Cox, J. E. (2008). Widespread reward-system activation in obese women in response to pictures of high-calorie foods. *NeuroImage, 41*(2), 636-647. doi:10.1016/j.neuroimage.2008.02.031; 10.1016/j.neuroimage.2008.02.031

Strafella, A. P., Ko, J. H., Grant, J., Fraraccio, M., & Monchi, O. (2005). Corticostriatal functional interactions in parkinson's disease: A rTMS/[11C] raclopride PET study. *European Journal of Neuroscience, 22*(11), 2946-2952.

Strafella, A. P., Paus, T., Fraraccio, M., & Dagher, A. (2003). Striatal dopamine release induced
by repetitive transcranial magnetic stimulation of the human motor cortex. *Brain, 126*(12),
2609-2615.

Stroop, J. R. (1992). Studies of interference in serial verbal reactions. *Journal of Experimental
Psychology: General, 121*(1), 15-23. doi:10.1037/0096-3445.121.1.15

Styn, M. A., Bovbjerg, D. H., Lipsky, S., & Erblich, J. (2013). Cue-induced cigarette and food
craving: A common effect? *Addictive Behaviors, 38*(3), 1840-1843.
doi:10.1016/j.addbeh.2012.09.010; 10.1016/j.addbeh.2012.09.010

Tang, D., Fellows, L., Small, D., & Dagher, A. (2012). Food and drug cues activate similar brain
regions: A meta-analysis of functional MRI studies. *Physiology & Behavior, 106*(3), 317-
324.

Tekin, S., & Cummings, J. L. (2002). Frontal–subcortical neuronal circuits and clinical
neuropsychiatry: An update. *Journal of Psychosomatic Research, 53*(2), 647-654.

Theresa M Marteau, & Peter A Hall. (2013). Breadlines, brains, and behaviour. *BMJ, 347*
doi:10.1136/bmj.f6750

Toplak, M. E., Jain, U., & Tannock, R. (2005). Executive and motivational processes in
adolescents with attention-deficit-hyperactivity disorder (ADHD). *Behavioral and Brain
Functions, 1*(1), 8.

Uher, R., Treasure, J., Heining, M., Brammer, M. J., & Campbell, I. C. (2006). Cerebral

   processing of food-related stimuli: Effects of fasting and gender. *Behavioural Brain*

   Research, 169(1), 111-119. doi:10.1016/j.bbr.2005.12.008

Uher, R., Yoganathan, D., Mogg, A., Eranti, S. V., Treasure, J., Campbell, I. C., . . . Schmidt, U.

   (2005). Effect of left prefrontal repetitive transcranial magnetic stimulation on food craving.

   Biological Psychiatry, 58(10), 840-842. doi:DOI: 10.1016/j.biopsych.2005.05.043

Upton, D. J., Cooper, N. R., Laycock, R., Croft, R. J., & Fitzgerald, P. B. (2010). A combined

   rTMS and ERP investigation of dorsolateral prefrontal cortex involvement in response

   inhibition. *Clinical EEG and Neuroscience : Official Journal of the EEG and Clinical*

   Neuroscience Society (ENCS), 41(3), 127-131.

Utz, K. S., Dimova, V., Oppenlander, K., & Kerkhoff, G. (2010). Electrified minds: Transcranial

   direct current stimulation (tDCS) and galvanic vestibular stimulation (GVS) as methods of

   non-invasive brain stimulation in neuropsychology--a review of current data and future

   implications. *Neuropsychologia, 48*(10), 2789-2810.

   doi:10.1016/j.neuropsychologia.2010.06.002

Vainik, U., Dagher, A., Dube, L., & Fellows, L. K. (2013). Neurobehavioural correlates of body

   mass index and eating behaviours in adults: A systematic review. *Neuroscience and*

   Biobehavioral Reviews, 37(3), 279-299. doi:10.1016/j.neubiorev.2012.11.008;

   10.1016/j.neubiorev.2012.11.008

Van den Eynde, F., Guillaume, S., Broadbent, H., Campbell, I. C., & Schmidt, U. (2013).

   Repetitive transcranial magnetic stimulation in anorexia nervosa: A pilot study. *European*

Psychiatry : The Journal of the Association of European Psychiatrists, 28(2), 98-101. doi:10.1016/j.eurpsy.2011.06.002; 10.1016/j.eurpsy.2011.06.002

Van den Eynde, F., Claudino, A. M., Mogg, A., Horrell, L., Stahl, D., Ribeiro, W., . . . Schmidt, U. (2010). Repetitive transcranial magnetic stimulation reduces cue-induced food craving in bulimic disorders. *Biological Psychiatry, 67*(8), 793-795. doi:DOI: 10.1016/j.biopsych.2009.11.023

Vanderhasselt, M., De Raedt, R., Baeken, C., Leyman, L., & D'haenen, H. (2006). The influence of rTMS over the right dorsolateral prefrontal cortex on intentional set switching. *Experimental Brain Research, 172*(4), 561-565.

Wagner, M., Rihs, T. A., Mosimann, U. P., Fisch, H. U., & Schlaepfer, T. E. (2006). Repetitive transcranial magnetic stimulation of the dorsolateral prefrontal cortex affects divided attention immediately after cessation of stimulation. *Journal of Psychiatric Research, 40*(4), 315-321.

Wagner, T., Valero-Cabre, A., & Pascual-Leone, A. (2007). Noninvasive human brain stimulation. *Annual Review of Biomedical Engineering, 9*, 527-565. doi:10.1146/annurev.bioeng.9.061206.133100

Wassermann, E. M. (1998). Risk and safety of repetitive transcranial magnetic stimulation: Report and suggested guidelines from the international workshop on the safety of repetitive transcranial magnetic stimulation, june 5-7, 1996. *Electroencephalography and Clinical Neurophysiology, 108*(1), 1-16.

Wassermann, E. M., & Zimmermann, T. (2011). Transcranial magnetic brain stimulation: Therapeutic promises and scientific gaps. *Pharmacology & Therapeutics,* doi:10.1016/j.pharmthera.2011.09.003

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology, 54*(6), 1063-1070. doi:10.1037/0022-3514.54.6.1063

Winocur, G., & Greenwood, C. E. (2005). Studies of the effects of high fat diets on cognitive function in a rat model. *Neurobiology of Aging, 26*(1, Supplement 1), 46-49. doi:DOI: 10.1016/j.neurobiolaging.2005.09.003

World Health Organization (WHO). (September 23 2011). *Noncommunicable diseases country profiles 2011.* ().

Wostmann, N. M., Aichert, D. S., Costa, A., Rubia, K., Moller, H. J., & Ettinger, U. (2013). Reliability and plasticity of response inhibition and interference control. *Brain and Cognition, 81*(1), 82-94. doi:10.1016/j.bandc.2012.09.010; 10.1016/j.bandc.2012.09.010

Yaffe, K., Falvey, C., Hamilton, N., Schwartz, A. V., Simonsick, E. M., Satterfield, S., . . . Harris, T. B. (2012). Diabetes, glucose control, and 9-year cognitive decline among older adults without dementia. *Archives of Neurology, 69*(9), 1170-1175. doi:10.1001/archneurol.2012.1117; 10.1001/archneurol.2012.1117

Zaehle, T., Sandmann, P., Thorne, J., Jäncke, L., & Herrmann, C. (2011). Transcranial direct current stimulation of the prefrontal cortex modulates working memory performance: Combined behavioural and electrophysiological evidence. *BMC Neuroscience, 12*(1), 2.

Zheng, D., Oka, T., Bokura, H., & Yamaguchi, S. (2008). The key locus of common response inhibition network for no-go and stop signals. *Journal of Cognitive Neuroscience, 20*(8), 1434-1442.

Appendix A: Supplemental Information

Taste Rating Effects

Separate one way repeated measures analysis of variance (ANOVA) were conducted to determine if there was a stimulation effect on participant taste ratings (i.e., how appealing the experimental foods were). There was no significant stimulation effect on taste ratings for both the appetitive ($F(1,20)=.000$, $p=1.0$) and control foods ($F(1,20)=.132$, $p=.72$); see Table 4 for mean taste ratings. As such, the taste ratings across stimulation conditions were averaged together to create one composite taste rating measure for both the appetitive and control foods. A paired sample t-test revealed that appetitive foods were rated significantly more appealing than control foods ($t(20)=5.146$, $p<.001$).

Table 4
Average taste rating for appetitive and control foods by stimulation condition

	Active	Sham
	Mean (*SD*)	Mean (*SD*)
Appetitive Foods	7.635 (1.581)	7.635 (1.932)
Milk Chocolate	8.571 (1.469)	8.667 (1.560)
Original Potato Chips	7.143 (1.931)	7.048 (2.156)
Flavoured Potato Chips	7.190 (2.088)	7.190 (2.600)
Control Foods	5.333 (1.494)	5.238 (1.700)
Dark Chocolate	5.571 (2.580)	5.667 (2.497)
Crackers	2.095 (1.640)	4.810 (1.600)

Note: The average taste ratings are based on the following question: "Overall, how would you rate this food?"(response scale:1="not at all good"; 5= "moderate"; 10="very good").

Effects of TMS on Affect

Paired sample t-tests were conducted to determine if there was a stimulation effect on positive and negative affect. There was no significant stimulation effect on the pre-post difference in positive (*t*(20)=-.334, *p*=.742)and negative (*t*(20)=-1.097, *p*=.287) affect ratings; see Table 5 for mean pre-to-post difference in affect ratings by stimulation condition.

Table 5
Pre-to-post difference in affect ratings by stimulation condition.

	Active	Sham
	Mean (*SD*)	Mean (*SD*)
Positive Affect	.429 (5.492)	.905 (4.516)
Negative Affect	-2.400 (3.705)	-1.150 (2.601)

Blinding Descriptives

Following the conclusion of the second study session, participants were asked to indicate: (1) if they could discriminate between stimulation conditions, and if yes, which study session (i.e., first or second) they thought they received active stimulation; (2) if they were aware the amount of food consumed during the taste test would be measured. Five individuals (23.8%) indicated they could tell the difference between active and sham stimulation. Of those, four individuals (19%) were able to correctly differentiate between active and sham stimulation. These results indicate that the blinding procedure was somewhat successful. In fact, previous TMS and dietary behaviours report that between 40 % and 100 % of participants were able to differentiate between stimulation conditions (Barth et al., 2011; Goldman et al., 2011; Van den Eynde et al., 2013, 2010), indicating that blinding procedure used in this study was successful. Eight individuals (38.1 %) indicated that they were aware, prior to debriefing, that the amount of food consumed during the taste test would be measured. Of those, three individuals (14.3%)

indicated they became aware of the true purpose of the study before or during the taste test in the

first study session, three individuals (14.3%) indicated they became aware of the true purpose of

the study before or during the taste test in the second study session, and two individuals (9.5%)

indicated they became aware of the true purpose of the study following the conclusion of the

second study session taste test (i.e., while completing the final questionnaires). Only one

individual was able to both correctly differentiate between active and sham stimulation, and was

aware the amount of food consumed during the taste test would be measured.

Table 6
Nutrition information (per 10 grams) for the experimental foods

	Calories	Fat (g)	Sugar (g)	Sodium (mg)
Milk Chocolate	56.667	2.33	5	11.667
Dark Chocolate	53.333	4	2.667	6.667
Original Pringles	52.632	3.158	0	55.263
Sour Cream and Onion Pringles	52.632	3.158	0.526	65.789
Crackers	42.3	0.95	0.02	114.8

Appendix B: TRANSCRANIAL MAGNETIC STIMULATION (TMS) SCREENING FORM

Below is a questionnaire used to help with decisions about who is eligible to take part in the study and who is not. This information, as well as your identity, will be kept confidential in all future publications.

PLEASE COMPLETE FORM BELOW:

Participant's ID _____ **Age:** _____

For each one, please **CIRCLE YES or NO**:

Neurological or Psychiatric Disorder	YES	NO	Multiple Sclerosis	YES	NO
Head Trauma	YES	NO	Depression	YES	NO
Stroke	YES	NO	treatment with amitryptiline and haloperidol	YES	NO
Brain surgery	YES	NO	Implanted medication pump	YES	NO
Metal in cranium	YES	NO	Intracranial Pathology	YES	NO
Brain Lesion	YES	NO	Albinism	YES	NO
Pacemaker	YES	NO	Intractable anxiety	YES	NO
History of seizure	YES	NO	Pregnant at this time	YES	NO
Family history of epilepsy	YES	NO	Headaches or Hearing problems	YES	NO
History of epilepsy	YES	NO	Family History of Hearing Loss	YES	NO

Intracorporal electronic devices	YES	NO	Other medical conditions (please specify)	YES	NO
Intracardic lines	YES	NO	Are you right or left handed?	Right	Left
Any Food Allergies/Sensitivities (if yes please indicate what foods you are allergic to)	YES	NO	Have you ever been diagnosed with type 1 or type 2 diabetes	YES	NO

I hereby declare that all information given on this TMS screening form is true and complete in every respect.

_____   _____

Signature of Participant   Date

_____   _____

Signature of Witness   Date

A craving is defined as an intense desire (strong urge) to consume a particular food, which is difficult to resist.

1. How often do you experience cravings to eat potato chips?

1	2	3	4	5	6	7	8	9	10
Never									All of the Time

2. On average, how often do you experience a craving to eat potato chips?

1	2	3	4	5	6	7	8	9	10
Several (2-3) Times A Day									Once A Month

3. How strong are these cravings you experience to eat potato chips

1	2	3	4	5	6	7	8	9	10
Extremely Weak									Extremely Strong

4. Are the experiences of cravings to eat potato chips always of the same strength

1	2	3	4	5	6	7	8	9	10
Never									Always

5. How easy is it to ignore this craving to eat potato chips

1	2	3	4	5	6	7	8	9	10
Very Easy									Impossible

6. How often do you experience cravings to eat chocolate?

1	2	3	4	5	6	7	8	9	10
Never									All of the Time

7. On average, how often do you experience a craving to eat chocolate?

1	2	3	4	5	6	7	8	9	10
Several Times A Day									Once A Month

8. How strong are these cravings you experience to eat chocolate?

1	2	3	4	5	6	7	8	9	10
Extremely Weak									Extremely Strong

9. Are the experiences of cravings to eat chocolate always of the same strength ?

1	2	3	4	5	6	7	8	9	10
Never									Always

10. How easy is it to ignore this craving to eat chocolate?

1	2	3	4	5	6	7	8	9	10
Very Easy									Impossible

1. Please indicate on the following scale the extent in which you agree with the following statements: right now, at this very moment.

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
I have an intense desire to eat chocolate or potato chips	◯	◯	◯	◯	◯
I'm craving chocolate or potato chips	◯	◯	◯	◯	◯
I have an urge for chocolate or potato chips	◯	◯	◯	◯	◯
Eating chocolate or potato chips would make things seem just perfect	◯	◯	◯	◯	◯
If I were to eat what I am craving, I am sure my mood would improve	◯	◯	◯	◯	◯
Eating chocolate or potato chips would feel wonderful	◯	◯	◯	◯	◯
If I are something, I wouldn't feel so sluggish and lethargic	◯	◯	◯	◯	◯
Satisfying my craving would make me feel less grouchy and irritable	◯	◯	◯	◯	◯
I would feel more alert if I could satisfy my craving	◯	◯	◯	◯	◯
If I had chocolate or potato chips, I could not stop eating it	◯	◯	◯	◯	◯
My desire to eat chocolate or potato chips seems overpowering	◯	◯	◯	◯	◯
I know I'm going to keep on thinking about chocolate and potato chops until I actually have it	◯	◯	◯	◯	◯
I am hungry	◯	◯	◯	◯	◯
If I ate right now, my stomach wouldn't feel as empty	◯	◯	◯	◯	◯
I feel weak because of not eating	◯	◯	◯	◯	◯

Appendix E: FCQ-S Dimensions

An Intense Desire to Eat

1. I have an intense desire to eat [chocolate or potato chips].
2. I'm craving [chocolate or potato chips].
3. I have an urge for [chocolate or potato chips].

Anticipation of Positive Reinforcement That May Result From Eating

4. Eating [chocolate or potato chips] would make things seem just perfect.
5. If I were to eat what I am craving. I am sure my mood would improve.
6. Eating [chocolate or potato chips] would feel wonderful.

Anticipation of Relief From Negative States and Feelings as a Result of Eating

7. If I ate something, I wouldn't feel so sluggish and lethargic.
8. Satisfying my craving would make me less grouchy and irritable.
9. I would feel more alert if I could satisfy my craving.

Lack of Control Over Eating

10. If I had [chocolate and potato chips], I could not stop eating it.
11. My desire to eat [chocolate and potato chips] seems overpowering.
12. If know I'm going to keep on thinking about [chocolate or potato chips] until I actually have it.

Craving as a Physiological State (i.e., Hunger)

13. I am hungry.
14. If I ate right now, my stomach wouldn't feel as empty.
15. I feel weak because of not eating.

Appendix F: Taste Ratings

1. How would you describe the texture of this food (please circle all that apply):

Crisp	Velvety	Mushy	Creamy
Chewy	Moist	Dry	Soft
Crunchy	Juicy	Smooth	Stringy
Rich	Luscious	Doughy	Dense
Light	Fluffy	Oily	Brittle
Sticky	Watery	Tough	Flaky

2. Based on appearance, how appealing is this food?

1   2   3   4   5   6   7   8   9   10

Not At All   Moderate   Very
Appealing   Appealing

3. How salty is this food?

1   2   3   4   5   6   7   8   9   10

Not At All   Moderate   Very
  Salty   Salty

4. How sweet is this food?

1   2   3   4   5   6   7   8   9   10

Not At All   Moderate   Very
  Sweet   Sweet

5. How greasy is this food?

1	2	3	4	5	6	7	8	9	10

Not At All   Moderate   Very

  Greasy   Greasy

6. Overall, how would you rate this food?

1	2	3	4	5	6	7	8	9	10

Not At All   Moderate   Very

  Good   Good

Appendix G: PANAS

This scale consists of a number of words that describe different feeling and emotions. Read each item and then mark the appropriate answer in the space next to the word. Indicate to what extent you feel this way RIGHT NOW, that is, at the PRESENT moment. Use the following scale to record your answers.

1	2	3	4	5
very slightly or not at all	a little	moderately	quite a bit	extremely

___interested   ___irritable

___distressed   ___alert

___excited   ___ashamed

___upset   ___inspired

___strong   ___nervous

___guilty   ___determined

___scared   ___attentive

___hostile   ___jittery

___enthusiastic   ___active

___proud   ___afraid

Demographics

The following 7 questions pertain to demographic information and you may decline to answer any questions; your information will be kept confidential.

1. Age (in years):_____

6. Estimated household income (all sources, including living assistance and/or social security):

○ $0 - $19,999

○ $20,000 – 39,999

○ $40,000 – 59,999

○ $60,000 – 79,999

○ $80,000 – 99,999

○ $100,000 +

7. Ethnicity (e.g., aboriginal/metis, asian, black, caucasian/white, middle eastern):
_____

8. Relationship status:

○ single

○ common law

○ married

○ separated

○ divorced

Self-Report Habit Index

Directions: For each of the statements listed below, please respond to each statement on a scale from 1 to 7.

Making healthy food choices (i.e., avoiding fatty foods) is something…..

1. I do frequently

1	2	3	4	5	6	7
Agree			Neither Agree Nor Disagree			Disagree

2. I do automatically

1	2	3	4	5	6	7
Agree			Neither Agree Nor Disagree			Disagree

3. I do without having to consciously remember

1	2	3	4	5	6	7
Agree			Neither Agree Nor Disagree			Disagree

4. That makes me feel weird if I do not

1	2	3	4	5	6	7

		Neither			Disagree
Agree		Agree Nor			
		Disagree			

5. I do without thinking

1	2	3	4	5	6	7

Agree   Neither   Disagree
                       Agree Nor
                       Disagree

6. That would require effort not to do it

1	2	3	4	5	6	7

Agree   Neither   Disagree
                       Agree Nor
                       Disagree

7. That belongs to my daily routine

1	2	3	4	5	6	7

Agree   Neither   Disagree
                       Agree Nor
                       Disagree

8. I start doing before I realize I'm doing it

1	2	3	4	5	6	7

Agree   Neither   Disagree
                       Agree Nor
                       Disagree

9. I would find hard not to do

1	2	3	4	5	6	7

Agree   Neither   Disagree
                                       Agree Nor
                                       Disagree

10. I have no need to think about doing

        1   2   3   4   5   6   7

    Agree   Neither   Disagree
                                           Agree Nor
                                           Disagree

11. That's typically "me"

        1   2   3   4   5   6   7

    Agree   Neither   Disagree
                                           Agree Nor
                                           Disagree

12. I have been doing for a long time

        1   2   3   4   5   6   7

    Agree   Neither   Disagree
                                           Agree Nor
                                           Disagree

Theory of Planned Behaviour: Fatty Food Consumption

13. How often do you consume fatty foods?

Never	Occasionally	Once A Month	Once Every 2 Weeks	Once A Week	2-3 Times a Week	4-6 Times A Week	Once A Day	More Than Once a Day

Directions: For each of the statements listed below, please respond to each statement on a scale from 1 to 7.

14. To me, eating fatty foods frequently is

1	2	3	4	5	6	7
Harmful			Neutral			Beneficial

15. To me, eating fatty foods frequently is

1	2	3	4	5	6	7
Quick			Neutral			Time Consuming

16. To me, eating fatty foods frequently is

1	2	3	4	5	6	7
Convenient			Neutral			Inconvenient

17. To me, eating fatty foods frequently is

1	2	3	4	5	6	7
Unpleasant			Neutral			Pleasant

18. To me, eating fatty foods frequently is

1	2	3	4	5	6	7
Cheap			Neutral			Expensive

19. To me, eating fatty foods frequently would make me feel…

1	2	3	4	5	6	7
Happy			Neutral			Unhappy

20. To me, eating fatty foods frequently would make me feel…

1	2	3	4	5	6	7
Self Conscious			Neutral			Self Assured

21. To me, eating fatty foods frequently would make me feel…

1	2	3	4	5	6	7
Inadequate			Neutral			Capable

22. To me, eating fatty foods frequently would make me feel…

1	2	3	4	5	6	7
Enticed			Neutral			Disgusted

23. To me, eating fatty foods frequently would make me feel…

1	2	3	4	5	6	7
Guilty			Neutral			Care Free

24. To me, eating fatty foods frequently would make me feel…

1	2	3	4	5	6	7
Lethargic			Neutral			Energetic

25. To me, eating fatty foods frequently would make me feel…

1	2	3	4	5	6	7
Unashamed			Neutral			Ashamed

26. To me, eating fatty foods frequently would make me feel…

1	2	3	4	5	6	7
Disappointed			Neutral			Gratified

27. To me, eating fatty foods frequently would make me feel…

1	2	3	4	5	6	7
Well			Neutral			Unwell

28. To me, eating fatty foods frequently would make me feel…

1	2	3	4	5	6	7
Content			Neutral			Discontent

29. To me, eating fatty foods frequently would make me feel…

1	2	3	4	5	6	7
Worried			Neutral			Calm

30. To me, eating fatty foods frequently would make me feel…

1	2	3	4	5	6	7
Unenthusiastic			Neutral			Enthusiastic

31. I think of myself as a healthy eater

1	2	3	4	5	6	7
Strongly Disagree			Neither Agree or Disagree			Strongly Agree

32. I think of myself as someone who is concerned with healthy eating

1	2	3	4	5	6	7
Strongly Disagree			Neither Agree or Disagree			Strongly Agree

33. I think of myself as someone who is concerned with the health consequences of what I eat

1	2	3	4	5	6	7
Strongly Disagree			Neither Agree or Disagree			Strongly Agree

34. I think of myself as someone who enjoys the pleasure of eating

1	2	3	4	5	6	7
Strongly Disagree			Neither Agree or Disagree			Strongly Agree

35. Most people who are important to me think that I should eat fatty foods regularly

1	2	3	4	5	6	7
Definitely False			Neither True or False			Definitely True

36. Those close to me expect me to eat fatty foods regularly

1	2	3	4	5	6	7
Definitely False			Neither True or False			Definitely True

37. The people in my life whose opinions I value eat fatty foods regularly

1	2	3	4	5	6	7
Definitely False			Neither True or False			Definitely True

38. I have complete control over the number of times I will eat fatty foods over the next month

1	2	3	4	5	6	7
Definitely False			Neither True or False			Definitely True

39. How often I will eat fatty foods over the next month is mostly up to me

1	2	3	4	5	6	7
Definitely False			Neither True or False			Definitely True

40. It would be impossible for me not eat fatty foods regularly over the next month

1	2	3	4	5	6	7
Definitely False			Neither True or False			Definitely True

41. If I wanted to, I could avoid eating fatty food regularly over the next month

1	2	3	4	5	6	7
Definitely False			Neither True or False			Definitely True

48-item Food Habits Questionnaire

In the PAST MONTH, how often did you...

1. When eating chicken, have it baked or broiled.

Usually   Often   Sometimes   Rarely   N/A

2. When eating chicken, take off the skin.

Usually   Often   Sometimes   Rarely   N/A

3. When eating red meat, eat only small portions.

Usually   Often   Sometimes   Rarely   N/A

4. When eating red meat, trim all visible fat.

Usually   Often   Sometimes   Rarely   N/A

5. Have a vegetarian dinner.

Usually   Often   Sometimes   Rarely   N/A

6. Eat fish or Chicken instead of red meat.

Usually   Often   Sometimes   Rarely   N/A

7. Use a meatless tomato sauce on spaghetti or noodles.

Usually   Often   Sometimes   Rarely   N/A

8. Use very low fat (1%) or non-fat milk.

Usually   Often   Sometimes   Rarely   N/A

113

9. Eat special, low-fat, diet cheeses.

Usually   Often   Sometimes   Rarely   N/A

10. Put butter or margarine on cooked vegetables.

Usually   Often   Sometimes   Rarely   N/A

11. Eat boiled or baked potatoes without butter or margarine.

Usually   Often   Sometimes   Rarely   N/A

12. Use low-calorie instead of regular salad dressing.

Usually   Often   Sometimes   Rarely   N/A

13. Put sour cream, cheese, or other sauces on vegetables and potatoes.

Usually   Often   Sometimes   Rarely   N/A

14. Have only fruit for dessert.

Usually   Often   Sometimes   Rarely   N/A

15. Eat at least two vegetables (not green salad) at dinner.

Usually   Often   Sometimes   Rarely   N/A

16. Snack on raw vegetables instead of ... chips.

Usually   Often   Sometimes   Rarely   N/A

17. Eat breads, rolls, or muffins without butter or margarine.

Usually   Often   Sometimes   Rarely   N/A

18. Use yogurt instead of sour cream.

Usually   Often   Sometimes   Rarely   N/A

19. Use a no calorie, non-stick spray when cooking.

Usually   Often   Sometimes   Rarely   N/A

20. Eat ice milk, frozen yogurt, low-fat ice cream, or sherbet instead of regular ice cream.

Usually   Often   Sometimes   Rarely   N/A

How often did you eat PER MONTH...

1. Hamburgers or cheeseburgers.

Usually   Often   Sometimes   Rarely   N/A

2. Beef, such as steaks or roasts.

Usually   Often   Sometimes   Rarely   N/A

3. Fried chicken with skin.

Usually   Often   Sometimes   Rarely   N/A

4. Hot dogs, franks.

Usually   Often   Sometimes   Rarely   N/A

5. Cold cuts, lunch meat, ham. Etc.

Usually   Often   Sometimes   Rarely   N/A

6. Salad dressings (not diet) mayonnaise.

Usually   Often   Sometimes   Rarely   N/A

7. Margarine

Usually   Often   Sometimes   Rarely   N/A

8. Butter.

Usually   Often   Sometimes   Rarely   N/A

9. Eggs.

Usually   Often   Sometimes   Rarely   N/A

10. Bacon or sausage.

Usually   Often   Sometimes   Rarely   N/A

11. Cheese or cheese spread.

Usually   Often   Sometimes   Rarely   N/A

12. Whole milk.

Usually   Often   Sometimes   Rarely   N/A

13. 2% milk.

Usually   Often   Sometimes   Rarely   N/A

14. French fries.

Usually   Often   Sometimes   Rarely   N/A

15. Ice cream (not low fat).

Usually   Often   Sometimes   Rarely   N/A

16. Doughnuts, pastries, cake, pie, cookies.

Usually   Often   Sometimes   Rarely   N/A

17. Potato chips, corn chips, popcorn (not air popped).

Usually   Often   Sometimes   Rarely   N/A

How often did you eat PER WEEK...

1.   Fruit, not counting juice.

Usually   Often   Sometimes   Rarely   N/A

2.   Vegetables, not counting potatoes or salad.

Usually   Often   Sometimes   Rarely   N/A

3.   Green Salad.

Usually   Often   Sometimes   Rarely   N/A

4.   Potatoes.

Usually   Often   Sometimes   Rarely   N/A

5.   Beans (baked beans, pintos, kidney beans, or in chilli).

Usually   Often   Sometimes   Rarely   N/A

6. High-fibre or bran cereal.

Usually   Often   Sometimes   Rarely   N/A

7. Dark whole grain bread such as whole wheat or rye.

Usually   Often   Sometimes   Rarely   N/A

8. Juice, such as orange or grapefruit juice.

Usually   Often   Sometimes   Rarely   N/A

9. Brown rice, whole wheat pasta, or bulgar.

Usually   Often   Sometimes   Rarely   N/A

10. Oat bran or wheat germ.

Usually   Often   Sometimes   Rarely   N/A

11. Fibre supplements.

Usually   Often   Sometimes   Rarely   N/A

Marlowe-Crowne Social Desirability Scale

Listed below are a number of statements concerning personal attitudes and traits.
Read each item and decide whether the statement is **true** or **false** as it pertains to you
personally

1. Before voting I thoroughly investigate the qualifications of all candidates.

                                                                                                       T   F

2. I never hesitate to go out of my way to help someone in trouble.

T   F

3. It is sometimes hard for me to go on with my work if I am not encouraged.

T   F

4. I have never disliked anyone intensely.

T   F

5. On occasion I have had doubts about my ability to succeed in   life.

T   F

6. I sometimes feel resentful when I don't get my way.

T   F

7. I am always careful about my manners of dress.

T   F

8. My table manners at home are as good as when I eat out at a restaurant.

T   F

9. If I could get into a movie without paying and be sure I was not seen I would

   probably do it.   T   F

10. On a few occasions, I have given up on something because I thought too   T   F
little of my ability.

11. I like to gossip at times.   T   F

12. There have been times when I felt like rebelling against people in authority even though I knew they were right.   T   F

13. No matter who I'm talking to, I always am a good listener.   T   F

14. I can remember "playing sick" to get out of something.   T   F

15. There have been occasions when I took advantage of someone.   T   F

16. I'm always willing to admit it when I make a mistake.   T   F

17. I always try to practice what I preach.   T   F

18. I don't find it particularly difficult to get along with loud mouthed, obnoxious people.

19. I sometimes try to get even rather than forgive and forget.   T   F

20. When I don't know something I don't mind admitting it.   T   F

21. I am always courteous, even to people who are disagreeable.   T   F

22. At times I have really insisted on having things my own way.   T   F

23. There have been occasions when I felt like smashing things.   T   F

24. I would never think of letting someone else be punished for my wrongdoings.   T   F

25. I never resent being asked to return a favour.

	T	F

26. I have never been irked when people expressed ideas very different from my   own

<div align="right">T   F</div>

27. I never make a long trip without checking the safety of my car.

<div align="right">T   F</div>

28. There have been times when I was quite jealous of the good fortune of others.

<div align="right">T   F</div>

29. I have almost never felt the urge to tell someone off.

<div align="right">T   F</div>

30. I am sometimes irritated by people who ask favours of me.

<div align="right">T   F</div>

31. I have never felt that I was punished without cause.

<div align="right">T   F</div>

32. I sometimes think when people have a misfortune they only got what they deserved

<div align="right">T   F</div>

33. I have never deliberately said something to hurt someone's feelings.

<div align="right">T   F</div>

Self-Control Scale

Using the scale provided, please indicate how much each of the following statements reflects how you typically are.

		1	2	3	4	5
1.	I am good at resisting temptation	Not At All				Very Much
2.	I have a hard time breaking bad habits	Not At All	2	3	4	Very Much
3.	I am lazy	Not At All	2	3	4	Very Much
4.	I say inappropriate things	Not At All	2	3	4	Very Much
5.	I never allow myself to lose control	Not At All	2	3	4	Very Much
6.	I do certain things that are bad for me, if they are fun	Not At All	2	3	4	Very Much
7.	People can count on me to keep a schedule	Not At All	2	3	4	Very Much
8.	Getting up in the morning is hard for me	Not At All	2	3	4	Very Much
9.	I have trouble saying no	Not At All	2	3	4	Very Much
10.	I change my mind fairly often	1	2	3	4	5

	Not At All				Very Much
11. I blurt out whatever is on my mind	1	2	3	4	5
	Not At All				Very Much
12. People would describe me as impulsive	1	2	3	4	5
	Not At All				Very Much
13. I refuse things that are bad for me	1	2	3	4	5
	Not At All				Very Much
14. I spend too much money	1	2	3	4	5
	Not At All				Very Much
15. I keep everything neat	1	2	3	4	5
	Not At All				Very Much
16. I am self-indulgent at times	1	2	3	4	5
	Not At All				Very Much
17. I wish I had more self-discipline	1	2	3	4	5
	Not At All				Very Much
18. I am reliable	1	2	3	4	5
	Not At All				Very Much
19. I get carried away by my feelings	1	2	3	4	5
	Not At All				Very Much
20. I do many things on the spur of the moment	1	2	3	4	5
	Not At All				Very Much
21. I don't keep secrets very well	1	2	3	4	5
	Not At All				Very Much

22. People would say that I have iron self-discipline	1 Not At All	2	3	4	5 Very Much
23. I have worked or studied all night at the last minute	1 Not At All	2	3	4	5 Very Much
24. I'm not easily discouraged	1 Not At All	2	3	4	5 Very Much
25. I'd be better off if I stopped to think before acting	1 Not At All	2	3	4	5 Very Much
26. I engage in healthy practices	1 Not At All	2	3	4	5 Very Much
27. I eat healthy foods	1 Not At All	2	3	4	5 Very Much
28. Pleasure and fun sometimes keep me from getting work done	1 Not At All	2	3	4	5 Very Much
29. I have trouble concentrating	1 Not At All	2	3	4	5 Very Much
30. I am able to work effectively toward long-term goals	1 Not At All	2	3	4	5 Very Much
31. Sometimes I can't stop myself from doing something, even if I know it is wrong	1 Not At All	2	3	4	5 Very Much
32. I often act without thinking through all the alternatives	1 Not At All	2	3	4	5 Very Much
33. I lose my temper easily	1	2	3	4	5

	Not At All				Very Much
34. I often interrupt people	1 Not At All	2	3	4	5 Very Much
35. I sometimes drink or use drugs to excess	1 Not At All	2	3	4	5 Very Much
36. I am always on time	1 Not At All	2	3	4	5 Very Much

Time Perspective Questionnaire: Diet

1. Long-term dietary plans are at least as important to me as the immediate pleasures of eating (e.g., taste, texture).

1	2	3	4	5	6	7
Disagree very strongly	Disagree strongly	Disagree	Neutral	Agree	Agree Strongly	Agree very strongly

2. I do not spend much time thinking about my long-term dietary plans.

1	2	3	4	5	6	7
Disagree very strongly	Disagree strongly	Disagree	Neutral	Agree	Agree Strongly	Agree very strongly

3. I have a good sense of how I can maintain a healthy diet throughout my life span.

1	2	3	4	5	6	7
Disagree very strongly	Disagree strongly	Disagree	Neutral	Agree	Agree Strongly	Agree very strongly

4. I spend a great deal of time thinking about how my present eating habits will affect my life later on.

1	2	3	4	5	6	7
Disagree very strongly	Disagree strongly	Disagree	Neutral	Agree	Agree Strongly	Agree very strongly

5. I never consider the long-term consequences of my food choices before I eat.

1	2	3	4	5	6	7
Disagree very strongly	Disagree strongly	Disagree	Neutral	Agree	Agree Strongly	Agree very strongly

6. I do not have long-range dietary plans.

1	2	3	4	5	6	7
Disagree very strongly	Disagree strongly	Disagree	Neutral	Agree	Agree Strongly	Agree very strongly

Appendix I: Post Debriefing Questionnaire

1. At any point during the study, were you aware that we were measuring the amount of food consumed?

A. Yes

B. No

If participant knew that study was examining food consumption:

2. When did you guess that actual hypothesis of the study?

    A. Before or during the taste test in session 1
    B. Before or during the taste test in session 2
    C. After the taste test

3. Where you able to tell the difference between the control and experimental stimulation?

A. Yes

B. No