

The effects of acute aerobic exercise on executive function
in individuals with type 2 diabetes

by

Corita Vincent

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AUTHOR'S 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.

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Abstract

Prevention and treatment of type 2 diabetes mellitus (T2DM), relies heavily on self-care behaviours such as dietary modification, physical activity, and medication adherence. Ability to perform these self-care behaviours depends, at least in part, on executive function (EF). Recent evidence suggests a correlation between T2DM and impaired cognitive function, including EF. Given the importance of EF for regulation of behaviours, and the importance of self-care in diabetes management, attenuated EF would represent a potential barrier to proper disease management. Thus the objective of Study 1 was to examine the association between T2DM and EF through meta-analytic techniques. Medline, PsychoInfo, and Scopus, as well as article references, were used to identify studies comparing individuals with T2DM to a control population. Effect size was calculated using Cohen's d and random effects modeling, and the potential impact of moderators (age, sex, and T2DM duration) were examined. Review of 60 studies (59 articles), revealed a significant, small-to-moderate effect size ($d=-0.249$, $p<0.001$) such that those with T2DM have lower EF. This finding was consistent across all aspects of EF examined (verbal fluency, mental flexibility, inhibition, working memory, and attention), and the association was stronger for those with shorter disease duration. The findings of study 1 illustrate that although individuals with T2DM have a great need for EF, as evidenced by the reliance of self-care behaviours on EF, this population has lower EF upon which to draw to perform these behaviours. Thus, strategies that improve EF, such as aerobic exercise, may be particularly relevant to this population. Acute aerobic exercise has been shown to improve EF in young and older adults; however this effect had not yet been examined in individuals with T2DM. Thus the objective of Study 2 was to examine the effects of acute aerobic exercise on EF in adults with T2DM. A within-subject design was used to compare the change in EF task performance following moderate and minimal intensity aerobic exercise, using Stroop and GNG to measure EF. Analysis revealed a significant effect of moderate exercise in women (but not men) and recently active (but not inactive) individuals, such that moderate exercise mitigated the self-regulatory fatigue effect observed following exercise. This study provides preliminary evidence of a significant beneficial effect of moderate aerobic exercise on EF in female and recently active adults with T2DM.

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Chapter 1

Overview

In 2013, an estimated 382 million (8.3%) adults (ages 20-79) worldwide had diabetes mellitus (DM) and this prevalence is expected to increase to 592 million (10.1%) by 2035 (IDF Diabetes Atlas Group, 2013). Of these cases, type 2 diabetes mellitus (T2DM) accounts for the majority (up to 90%), and the prevalence of T2DM is increasing in every country (IDF Diabetes Atlas Group, 2013). T2DM is associated with a number of complications, such as retinopathy, nephropathy, neuropathy, cardiovascular and cerebrovascular disease, which can result in disability or mortality, and may contribute to the association between T2DM and decreased quality of life (Stratton et al., 2000). Associations between T2DM, decreased quality of life, and increased complications in combination with increasing prevalence have made T2DM a significant global health concern. Encouragingly, improved diabetes management, typically measured by glucose regulation, results in reduced risk of developing diabetes related complications (Skyler, 2004); thus, interventions which target improvement of diabetes management and glucose regulation may have the capacity to significantly reduce diabetes-related morbidity and mortality.

The ability to implement diabetes-management behaviours consistently may rely, at least in part, on cognitive abilities, and executive function may be of particular importance (Thabit et al., 2009). Executive function (EF) is the key cognitive resource responsible for self-control and self-regulation of behaviours including the ability to plan, initiate, sequence, monitor, and inhibit complex behaviours (Miyake & Friedman, 2012; Schillerstrom, Horton, & Royall, 2005); thus, deficits in EF would be expected to result in an impaired ability to perform self-management behaviours such as medication adherence, physical activity adherence, and making healthy dietary choices. In line with this assumption, an association between executive dysfunction and worse diabetes management behaviours has been reported in both T2DM (Munshi, Hayes, Iwata, Lee, & Weinger, 2012; Thabit et al., 2009) and T1DM populations (McNally, Rohan, Pendley, Delamater, & Drotar, 2010). These findings indicate that EF could be important for consistent implementation of diabetes management behaviours and, therefore, germane to secondary prevention.

Beyond the potential influence of cognition on self-management, it is also possible that the T2DM disease process itself may impair cognitive function. Interest in the effects of T2DM on cognition, including EF, has been increasing over the past decade (Starr & Convit, 2007). To date, evidence from cross-sectional studies has been mixed: some studies suggesting that T2DM is

associated with impaired EF (Gregg et al., 2000; Hassing et al., 2004; Ishizawa, Kumano, Sato, Sakura, & Iwamoto, 2010; Lindeman et al., 2001; Yeung, Fischer, & Dixon, 2009) and others observing no difference in EF of individuals with and without T2DM (Aberle, Kliegel, & Zimprich, 2008; Arvanitakis, Bennett, Wilson, & Barnes, 2010; Bruehl et al., 2009; Espeland et al., 2011; Helkala, Niskanen, Viinamaki, Partanen, & Uusitupa, 1995) .

Perhaps of most interest is the possibility that the relationship between diabetes and EF may be characterized by positive and negative feedback loops. For example, the proposed association of T2DM with impaired EF would have significant implications because of the importance of EF for diabetes management behaviours. An association of T2DM with impaired EF would imply that although individuals with T2DM may have a greater need of EF in order to conduct disease management behaviours such as dietary control and medication adherence, they have lower overall EF with which to carry out these tasks. Given the importance of EF for T2DM management, impairment of EF among this population would represent a barrier to effective treatment which may warrant special clinical attention. Additionally, impaired EF among this population would indicate a potential utility of screening and interventions/strategies to increase EF; one such strategy is acute aerobic exercise. Acute aerobic exercise has been shown to improve EF in healthy young (Kamijo, Nishihira, Hatta, Kaneda, Wasaka, Kida, & Kuroiwa, 2004a; Yanagisawa et al., 2010) and healthy older adults (Cordova, Silva, Moraes, Simoes, & Nobrega, 2009; Kamijo et al., 2009) . However, further elucidation of the effects of acute aerobic exercise among individuals with T2DM is necessary and could inform the use of acute aerobic exercise as a strategy to increase EF in the T2DM population.

The overall aims of my thesis project are: 1) to assess whether T2DM is associated with impaired EF using meta-analytic techniques, and 2) to determine whether acute aerobic exercise improves executive function, specifically response inhibition, among older adults with T2DM. These goals will be achieved through two studies which will be presented in this thesis paper. The following section will provide background information relevant to my thesis topic and build the rationale for the thesis studies.

Chapter 2

Executive Function and Type 2 Diabetes Mellitus

2.1 Type 2 Diabetes Mellitus

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia and glycosuria which result from insufficient insulin production/secretion, defective insulin action, or both (Canadian Diabetes Association Clinical Practice Guidelines Expert Committee, Goldenberg, & Punthakee, 2013) . As mentioned, T2DM is the most prevalent form of diabetes, and is rapidly increasing in prevalence in every country around the world (IDF Diabetes Atlas Group, 2013). This increase in prevalence is believed to be the result of increased prevalence of T2DM risk factors, particularly the increased prevalence of obesity, which has more than doubled since 1980 (World Health Organization, 2011). Additionally, in Canada, the United States, and Europe, the majority of individuals with T2DM fall within the 65 and older age category (Centers for Disease Control and Prevention, 2011; Statistics Canada, 2013). Therefore, as the proportion of the Canadian population represented by those over the age of 65 continues to grow in coming years (Milan, 2011), it can be anticipated that the number of individuals with T2DM will also increase.

Unlike type 1 diabetes mellitus (T1DM) which results from inability to produce insulin (primarily as a result of insufficient pancreatic beta cell production), T2DM is characterized by both some degree of insulin resistance and deficient insulin secretion, and may range from predominant insulin resistance with mild secretory deficit to predominant secretory deficit with mild insulin resistance (Canadian Diabetes Association Clinical Practice Guidelines Expert Committee et al., 2013). However, in either case, T2DM results in hyperglycemia, and chronic hyperglycemia is believed to explain associations between T2DM and a variety of microvascular and macrovascular complications (Stratton et al., 2000). T2DM has also been associated with decreased quality of life. However, improved glucose regulation is associated with both reduction in complication rates and reduced impact on quality of life (Skyler, 2004).

2.2 Executive Function

Executive function (EF) refers to the separable but intricately connected cognitive control mechanisms that are responsible for regulation of thoughts, emotions, and behaviours (Miyake & Friedman, 2012) . While definitions of what constitutes EF vary slightly from researcher to researcher, facets of attentional control (task-shifting), temporal organization, task management,

inhibition, monitoring and updating of information (working memory), and planning are widely agreed upon (Funahashi & Andreau, 2013) . Recently, Miyake et al. (2000; 2012) have proposed that EF can be broken down to three main subcomponents: an updating-specific EF, a shifting-specific EF, and a response inhibition component (also known as common EF). They further proposed that all EF abilities draw on a combination of these three subcomponents. For example, updating ability relies on both updating-specific EF and common EF; mental flexibility relies on both shifting-specific and common EF; while response inhibition relies purely on common EF (Miyake & Friedman, 2012).

The broad range of subcomponents of EF highlights its importance in a broad spectrum of tasks requiring cognitive control. In order to exert control over this spectrum of cognitive processes, EF primarily involves operation of the prefrontal cortex (PFC) and projections to a number of other cortical and subcortical regions e.g., premotor cortex, supplementary motor area, frontal eye fields, and posterior corticies (Funahashi & Andreau, 2013; Ridderinkhof, Ullsperger, Crone, & Nieuwenhuis, 2004). In situations requiring EF, the PFC sends signals, in a top-down fashion, to cortical and subcortical regions to configure, modulate, and direct processing (Ridderinkhof, van den Wildenberg, Segalowitz, & Carter, 2004) . This top-down control of the PFC is central to EF; however, other brain regions and pathways in the thalamus and cerebellum may also play an important role (Bellebaum & Daum, 2007; Heyder, Suchan, & Daum, 2004).

2.3 EF & Diabetes Self-Care

From a disease self-care perspective, EF is important for regulation of behaviours, including the ability to plan, initiate, sequence, monitor, and inhibit complex behaviours (Miyake & Friedman, 2012; Schillerstrom et al., 2005) , and as such, is particularly relevant to T2DM self-care behaviours which require planning, implementation, assessment, and adaptation (Hajduk et al., 2013). For example, in order to improve glucose regulation with dietary changes and individual must plan and implement the dietary change, assess whether the change is having the desired effect, and adapt the diet based on these results. As such, deficits in EF would be expected to result in impaired ability to perform key diabetes self-care behaviours such as medication adherence, physical activity adherence and dietary self-regulation, the primary objective of which is glycaemic control(Skyler, 2004). To date, several cross-sectional studies have examined the relationship between EF and T2DM management both indirectly through associations with glycaemic control, and directly in terms of diabetes self-management behavior implementation; these are reviewed next.

2.3.1 Glycaemic Control

Glycaemic control is typically measured using percent glycosylated hemoglobin (A1C). Glycosylated hemoglobin forms as a result of exposure of red blood cells to glucose in the blood stream; over time, glucose binds to hemoglobin in the red blood cells (RBCs) creating glycosylated hemoglobin. Thus, A1C is used as a proxy for average blood glucose over the previous 3-4 months—as a result of the 120-day lifespan of RBCs (Khan, Ola, Alhomida, Sobki, & Khan, 2013). A1C provides an objective measure of glycaemic control (and diabetes management) and is more generalizable and reliable than point estimates (such as fasting blood sugar or random blood sugar) or self-report (such as log books). Association between poor glycaemic control, as measured by A1C, and lower EF has been observed in a number of studies (Ishizawa et al., 2010; Munshi et al., 2012; Nguyen et al., 2010). For example, in a study of mixed ethnicity rural older adults, significantly worse performance on EF tasks was associated with higher A1C, such that a 1-point higher EF score was associated with a 0.47 unit lower A1C value (Nguyen et al., 2010). Similar findings were reported by Munshi et al. (2012) who observed a significant association between objective, but not self-report, measures of EF and A1C, such that a 1-point higher EF score was associated with a 0.22 unit lower A1C. Additionally, Grober et al. (Grober, Hall, Hahn, & Lipton, 2011) observed that any degree of executive dysfunction was associated with increased odds of inadequate glycaemic control.

These findings indicate an association between EF and diabetes self-management; however, the cross-sectional nature of these studies precludes determination of directionality of effect (i.e., whether impaired EF leads to worse T2DM management which results in decreased glycaemic control or if worse glycaemic control results in cortical changes leading to impairment of executive function). For this reason, associations of EF with various diabetes self-management behaviours (including medication adherence, physical activity, and dietary control) have also been examined in order to build the case for an impact of EF on diabetes self-management.

2.3.2 Self Management Behaviours

In self-report measures of overall diabetes self-management behaviours, observational studies have reported an association between EF and diabetes self-care behaviours among both T2DM and T1DM populations (McNally et al., 2010; Ohmann et al., 2010; Primožic, Tavcar, Avbelj, Dernovsek, & Oblak, 2012a; Thabit et al., 2009). These studies typically employ self-report questionnaires that focus on reported dietary modification, medication adherence, physical activity, smoking cessation, and foot care (Toobert, Hampson, & Glasgow, 2000). For instance, a cross-sectional study of 98

individuals with T2DM, observed a positive correlation between higher EF and better diabetes self-management as measured by the Summary of Diabetes Self-Care (SDSC) questionnaire; furthermore, among those treated with insulin, EF was the strongest predictor of better diabetes self-care (Primozic et al., 2012a). In addition to this correlation between EF and T2DM self-care behaviours generally, EF has been associated with medication adherence, physical activity adherence, and dietary choices independently.

2.3.2.1 Medication Adherence

Executive function, and particularly aspects of attention, mental flexibility, and working memory, have been identified as important predictors of medication adherence in populations of older adults with a variety of comorbidities (Insel, Morrow, Brewer, & Figueredo, 2006; Panos et al., 2014; Stilley, Bender, Dunbar-Jacob, Sereika, & Ryan, 2010). Additionally, in individuals with T2DM, worse performance on the Stroop and TMTB tasks, typically used to measure response inhibition and task shifting aspects of EF respectively, was associated with worse adherence to metformin (Rosen et al., 2003).

2.3.2.2 Physical Activity Adherence

Executive function has also been demonstrated to moderate the association between intention and action for both physical activity and dietary choices (Hall, Fong, Epp, & Elias, 2008). McAuley et al. (2011) demonstrated that baseline EF predicted adherence to a 12-month exercise program in a population of 177 older adults, and that this relationship was mediated by effects on self-efficacy. They observed that individuals with higher EF reported higher self-efficacy regarding their ability to perform exercise at the start of the program and that these enhanced beliefs about exercise capacity, correlated with higher attendance of exercise classes. Similarly, EF was an important predictor of maintenance of physical activity following a structured exercise program in a group of older women, such that those with greater improvements in EF following the training program demonstrated better 1-year physical activity adherence (Best, Nagamatsu, & Liu-Ambrose, 2014).

2.3.2.3 Dietary Choices

With respect to dietary choices, observational studies point to an association between EF and healthier dietary behaviours and weight (Allan, Johnston, & Campbell, 2010; Batty, Deary, Schoon, & Gale, 2007; Chandola, Deary, Blane, & Batty, 2006; Hall, 2012). This observed relationship may

occur as a result of a moderating effect of EF on dietary intention and action, such that higher EF results in an increased ability to turn intentions into actions (Allan et al., 2010; Hall, 2012).

In addition to these observational studies, experimental studies using bogus taste test paradigms demonstrate greater consumption of appetitive but unhealthy foods among individuals with greater impulsivity as measured by Barratt Impulsivity Scale (Guerrieri et al., 2007; Guerrieri, Nederkoorn, Schrooten, Martijn, & Jansen, 2009) or lower scores on measures of response inhibition such as Stop-Signal Task (SST), Go/No-Go (GNG), and Stroop (Guerrieri et al., 2009; Houben, 2011; Nederkoorn, Guerrieri, Havermans, Roefs, & Jansen, 2009). Furthermore, this association persists among individuals reporting high dietary restraint (“dieting”), such that high restraining individuals overate only when they were also impulsive (Jansen et al., 2009). Importantly, this relationship between EF and consumption is affected by hunger, such that individuals with low EF ate more only when hungry (Nederkoorn et al., 2009), and by facilitating and restraining cues, such that weaker response inhibition or higher impulsivity may increase susceptibility to environmental cues to overeating (Hall, Lowe, & Vincent, 2013; Hall et al., 2014; van den Akker, Jansen, Frentz, & Havermans, 2013).

Adding to the plausibility of a causal relationship between impulsivity/inhibition, some evidence suggests that manipulation of behavioural impulsivity/inhibition corresponds to changes in consumption of unhealthy foods (Guerrieri et al., 2009; Guerrieri, Nederkoorn, & Jansen, 2012; Houben & Jansen, 2011; Houben, 2011; Rotenberg et al., 2005). For example, priming with words related to self control resulted in decreased consumption compared to priming with words related to impulsivity (Rotenberg et al., 2005), and pairing of foods with a “go” signal in modified SST or GNG tasks resulted in greater consumption of these foods in comparison to control foods (Guerrieri et al., 2009; Guerrieri et al., 2012). Additionally, Lowe et al. (C. Lowe, Hall, & Staines, 2014) demonstrated that direct modulation of the DLPFC using continuous theta burst stimulation (cTBS) resulted in an increased in appetitive food consumption that was mediated by lower performance on the Stroop task. Thus, evidence suggests that impaired EF (and specifically response inhibition) increases risk of overeating particularly when it comes to unhealthy foods.

The importance of EF for proper execution of dietary self-management behaviours as evident through self-report questionnaires and specific evidence of its importance for medication adherence, physical activity adherence, and dietary choices makes adequate EF critical to T2DM self-management. However, evidence suggests that EF may in fact be impaired in this population.

2.4 EF & T2DM

A number of epidemiological studies have demonstrated an association between T2DM and impaired cognitive function (Awad, Gagnon, & Messier, 2004; Bourdel-Marchasson, Lapre, Laksir, & Puget, 2010) including deficits in executive function and attention (Starr & Convit, 2007) .

Neuroanatomical studies have demonstrated increased number of silent cerebrovascular infarcts (Manschot et al., 2006; Vermeer et al., 2003), neuronal atrophy(Akisaki et al., 2006; den Heijer et al., 2003; Manschot et al., 2006), and white matter hyperintensities (WMH) (Akisaki et al., 2006; Manschot et al., 2006; Reijmer et al., 2013) among individuals with T2DM in comparison with non-T2DM individuals of similar age. Additionally, decreased total brain gray matter volume (Christman, Vannorsdall, Pearlson, Hill-Briggs, & Schretlen, 2010; Kumar et al., 2008) , prefrontal gray matter volume (Kumar et al., 2008), and prefrontal cortical gray matter thickness—recall the importance of the PFC in EF—has been observed in T2DM (Ajilore et al., 2010). These cortical changes have been further linked to functional deficits through studies showing a significant inverse correlation between performance on measures of attention/executive function and atrophy, WMH, infarcts(Manschot et al., 2006) and cortical gray matter thickness(Ajilore et al., 2010). Thus, a significant body of evidence (both epidemiological and neuroanatomical) suggesting that T2DM is associated with impaired cognition relative to the non-T2DM population.

In addition to these associations with T2DM, some evidence suggests an association between impaired EF and pre-diabetic states of impaired glucose tolerance (Gagnon, Greenwood, & Bherer, 2011; Messier, Tsiakas, Gagnon, Desrochers, & Awad, 2003; Messier, Awad-Shimoon, Gagnon, Desrochers, & Tsiakas, 2011) and impaired fasting glucose(Euser et al., 2010; Takahashi et al., 2011) with impaired EF, although findings are not consistent and some studies demonstrate no effect(Vanhanen et al., 1998). Among studies which have examined the effects of hyperinsulinemia/insulin resistance, impairment of Stroop—response inhibition (Bruehl, Sweat, Hassenstab, Polyakov, & Convit, 2010) and TMT—set shifting(Abbatecola et al., 2004) have been observed; however, Schurr et al. (2010) found these effects to be significant for women only.

With respect to EF, a number of cross-sectional studies have observed a significant association between T2DM and EF (Gregg et al., 2000; Ishizawa et al., 2010; Lindeman et al., 2001; Maggi et al., 2009; Mehrabian et al., 2012; Rouch et al., 2012; Solanki, Dubey, & Munshi, 2009; Vanhanen et al., 1999; Watari et al., 2008; Yaffe et al., 2012; Yeung et al., 2009) ; however, other studies have observed no effect (Aberle et al., 2008; Arvanitakis et al., 2010; Bruehl et al., 2009;

Espeland et al., 2011; Helkala et al., 1995; Ruis et al., 2009a; Scott, Kritz-Silverstein, Barrett-Connor, & Wiederholt, 1998; Takayanagi, Cascella, Sawa, & Eaton, 2012; Van Den Berg et al., 2010) . The findings of these cross-sectional studies in combination with neuroanatomical studies previously described suggests that EF may be impaired among the T2DM population; however, given the diversity of findings of individual studies, further examination and synthesis of findings is needed.

Meta-analytic techniques allow for aggregate analysis of results from multiple studies which provide a better estimation of effect size than any one study independently; therefore, Study 1 examines the association between T2DM & EF in a meta-analytic review.

Chapter 3

Study 1: Meta-analysis of the association between T2DM & EF

There has been recent interest in the relationship between diabetes and cognitive function. A number of epidemiological studies have documented an association between T2DM and accelerated cognitive decline (Awad et al., 2004; Bourdel-Marchasson et al., 2010; Starr & Convit, 2007) . Specifically, impairments in processing speed, memory, and executive function (EF) have been observed in association with T2DM, although the results have not been uniform across all studies (Bourdel-Marchasson et al., 2010; Starr & Convit, 2007) . Anatomical brain changes have also been identified in individuals with T2DM including increased neuronal atrophy (den Heijer et al., 2003; Schmidt et al., 1992; Schmidt et al., 2004; Vermeer et al., 2003) and, less consistently, number of white matter lesions (WML) (Manschot et al., 2006; Schmidt et al., 1992; Schmidt et al., 2004). In a large scale MRI study, Manschot et al. (2006) found that individuals with T2DM had increased deep WMLs, cortical and subcortical atrophy, and number of (silent) infarcts which were significantly correlated with an observed impairment of attention and EF. A follow-up study observed impaired information-processing speed and memory performance among persons with T2DM and found that degree of impairment correlated with degree of WM abnormality (Reijmer et al., 2013). These findings suggest that not only are anatomical brain changes associated with T2DM, but that these changes correlate to observable deficits at the behavioural level.

Among the cognitive variables studied, one aspect of cognitive function that appears to be particularly affected among individuals with T2DM is EF. Executive function consists of cognitive control mechanisms responsible for regulation of human cognition, emotion and action and includes aspects of attention, mental flexibility, inhibition, and working memory that are important for self-regulation and self-control (Miyake & Friedman, 2012) . Miyake et al. (Miyake et al., 2000; Miyake & Friedman, 2012) have proposed 3 necessary and sufficient subcomponents for EF: 1) updating and monitoring, referring to the manipulation and replacement of information within working memory (known by the term “working memory”); 2) task shifting, referring to the transfer of attention back and forth between different tasks or mental sets (“mental flexibility”); and 3) response inhibition, referring to the deliberate suppression of an automatic response (“behavioural inhibition”), as well as a common EF component which is drawn upon by all three. While Miyake et al. (2012) have proposed 3 key components of EF, this does not preclude the existence of other components. In fact,

additional correlated but separable components including verbal fluency have been identified (Snyder, 2013).

Executive functions are of special concern among older adults in that they underlie competence in sequencing and coordinating behaviours necessary to maintain functional independence. In medical populations, EFs are also closely tied to treatment adherence, and those older adults suffering from low EFs consistently show suboptimal medication adherence, dietary behaviours, and other self-care activities(Thabit et al., 2009). Given that T2DM involves many important self-care behaviours, the presence of attenuated EFs would represent a potential barrier to effective disease management, and may warrant special clinical attention (Primožic et al., 2012a). Further elucidation of the potential relationship between T2DM and EF could inform the need for routine screening and intervention for affected individuals within the larger T2DM population. The purpose of this meta-analytic review was to examine the extent to which T2DM is associated with reduced EF, and possible modifying factors affecting the strength of any observed association.

3.1 Methods

Cross-sectional and longitudinal studies examining the relationship between T2DM and EF were included in this meta-analysis. A search of Medline, PsychInfo, and Scopus was conducted in November 2013 using the following terms: executive function, executive control resources, attention, prefrontal cortex, working memory, response inhibition, planning, verbal fluency, task shifting, set shifting, or task switching paired with diabetes, as well as database specific search terms (ex. MeSH terms). Results were limited to articles in English only, and additional articles were retrieved through hand searching included article references. A search of the grey literature was conducted using Google Scholar and PsychInfo. Within the grey literature, two thesis abstracts were identified that fit the inclusion criteria, one showing a positive association between T2DM and EF impairment and one with a null result. These abstracts were ultimately excluded from the analysis due to insufficient data to calculate effect size; given the small sample sizes of the studies a significant impact on the findings of this meta-analysis is unlikely.

3.1.1 Inclusion/Exclusion

Studies with the following characteristics were included in the analysis: human population and comparison of T2DM group with control group on at least one measure of EF, regardless of whether the authors aimed to examine EF specifically. Studies which did not directly compare those with

T2DM to those without were excluded, as were studies on animals, and those measuring other aspects of cognition. In the case that two studies were conducted on the same population, the earlier article was included except in the case that a more recent article included more comprehensive analysis of EF.

3.1.2 Coding Procedure

Executive function tasks were coded based on the component of EF examined. The following components of EF were examined by at least one task in an included study: verbal fluency, mental flexibility, inhibition, working memory, and attention. All tasks were coded as tapping one of these EF components, and baseline measures for the Trail Making Task (i.e. TMTA) and Stroop task (i.e. Stroop I, Stroop II) were included as comparison measures. Additionally, a composite measure was created for each component which combined all tasks for that component, and any task used by 5 or more studies was analyzed separately. If an individual study had greater than one task measuring the same EF component, the effect sizes of these tasks were averaged before being entered into the composite score, but were included separately in task scoring. Finally, due to the interconnected nature of EF, an overall EF composite was created using a single EF effect size from each study (as described above).

3.1.3 Moderator Analysis

Studies were further coded for participant age, sex, and T2DM duration. When a moderator variable was not recorded by a study, that study was excluded from moderator analysis for that variable, but was included in analysis for all other variables for which data was reported.

3.1.3.1 Age

The mean age of the total study population (T2DM and control groups combined) was included as a continuous variable in metaregression analysis. Nearly all studies reported the age of the population, with two exceptions (Mussell, Hewer, Kulzer, Bergis, & Rist, 2004; Solanki et al., 2009).

3.1.3.2 Sex

The proportion of male participants in the total study population (T2DM and control groups combined) was included as a continuous variable in metaregression analysis. Five studies failed to report sex distribution of participants (Assisi et al., 1996; Lindeman et al., 2001; Mussell et al., 2004; Perlmutter, Tun, Sizer, McGlinchey, & Nathan, 1987; Solanki et al., 2009).

3.1.3.3 T2DM Duration

The mean number of years since T2DM diagnosis was included as a continuous variable in metaregression analysis. T2DM duration was reported by 45.8% of studies ($k=27$).

3.1.4 Statistics

The unit of analysis is the study. As previously described, only one article per study was included. Furthermore, in the case that 2 studies were examined in the same article, these studies were reported separately for the purpose of analysis when reporting of data allowed.

Results from included studies were converted to standardized mean difference (Cohen's d). When mean and standard deviations were provided or could be calculated, the equation

$$ES = \frac{\bar{X}_1 - \bar{X}_2}{\sqrt{\frac{s_1^2(n_1 - 1) + s_2^2(n_2 - 1)}{n_1 + n_2 - 2}}} = \frac{\bar{X}_1 - \bar{X}_2}{s_{pooled}}$$

was used. Note that SE was converted to SD using the equation $SD = SE \times \sqrt{n}$. For studies which reported only regression coefficient ($k=1$), ANOVA F value ($k=1$) or T statistic p-value ($k=1$) effect sizes were calculated using Wilson's Practical Meta-Analysis Effect Size Calculator (Lipsey & Wilson, 2001). The sign of d was set such that negative d indicated worse performance among the T2DM group in comparison to controls. Outliers with effect sizes ± 3 SD from the mean effect size (ES) were excluded. Studies were only excluded from the analysis in which the ES was an outlier (Hunter JE, 1990).

Four studies compared normoglycemic, impaired glycemc, and T2DM individuals. In these cases, normoglycemia and impaired glycemc groups were combined based on the understanding that this study aims to compare T2DM to non-T2DM. Similarly, some studies compared two groups of T2DM participants to one group of controls; in these cases, the two T2DM groups were combined for ES estimation. When participants were tested more than once (i.e. in longitudinal analysis), the results from the first test were analyzed, and any longitudinal analysis is presented in the discussion.

Random effects meta-analytic models were used for all analyses because there are likely to be many sources of variability between study samples other than sampling error; thus, the primary assumption of fixed effects modeling is violated (Lipsey & Wilson, 2001). Mean effect size analyses and moderator analyses were conducted using SPSS meta-analysis macro (Wilson, 2010). An alpha level of .05 was chosen to indicate significance. Based on the assumption of normal distribution, moderator analysis was conducted using the mixed-effects models iterative maximum likelihood estimation. Age, gender, and T2DM duration were included as continuous variables in separate

weighted regression analyses. Moderator analyses were only conducted for measures with 20 or more ES as fewer ES would have insufficient power to detect a difference (Marin-Martinez & Sanchez-Meca, 1998).

3.2 Results

All The final search strategy identified 876 articles after duplicates were removed. Study selection and exclusion process is summarized in **Appendix A**.

Ultimately, 59 articles (Aberle et al., 2008; Ajilore et al., 2010; Alosco et al., 2012; Alvarenga, Pereira, & Anjos, 2010; Arvanitakis, Wilson, Bienias, Evans, & Bennett, 2004; Arvanitakis et al., 2010; Assisi et al., 1996; Atiea, Moses, & Sinclair, 1995; Brands et al., 2007; Bruehl et al., 2009; Cooray et al., 2011; Cosway, Strachan, Dougall, Frier, & Deary, 2001; Espeland et al., 2011; Fontbonne, Berr, Ducimetiere, & Alperovitch, 2001; Gallacher et al., 2005; Gregg et al., 2000; Hassing et al., 2004; Helkala et al., 1995; Hudetz & Warltier, 2007; Ishizawa et al., 2010; Krannich, Tobias, Broscheit, Leyh, & Mullges, 2012; Lindeman et al., 2001; Logroscino, Kang, & Grodstein, 2004; L. P. Lowe, Tranel, Wallace, & Welty, 1994; Maggi et al., 2009; Mehrabian et al., 2012; Mooradian, Perryman, Fitten, Kavonian, & Morley, 1988; Mussell et al., 2004; Nandipati, Luo, Schimming, Grossman, & Sano, 2012; Nooyens, Baan, Spijkerman, & Verschuren, 2010; Okereke et al., 2008; Pavlik, Hyman, & Doody, 2005; Perlmutter et al., 1987; Perlmutter et al., 1984; Reaven, Thompson, Nahum, & Haskins, 1990; Reijmer et al., 2013; Rouch et al., 2012; Ruis et al., 2009a; Ryan & Geckle, 2000; Saczynski et al., 2008; Scott et al., 1998; Silva, Ribeiro, dos Santos, Beserra, & Fragoso, 2012; Solanki et al., 2009; Spauwen, Kohler, Verhey, Stehouwer, & van Boxtel, 2012; Takayanagi et al., 2012; Takeuchi et al., 2012; U'Ren, Riddle, Lezak, & Bennington-Davis, 1990; van den Berg et al., 2010; Van Eersel et al., 2013; van Harten et al., 2007; Vanhanen et al., 1997; Vanhanen et al., 1999; Wahlin, Nilsson, & Fastbom, 2002; Watari et al., 2008; Watari et al., 2006; Wysokiński et al., 2010; Yaffe et al., 2012; Yeung et al., 2009) on 60 populations, and a total of 9815 T2DM individuals (mean age=69.9, 51.3% male) and 69254 controls (mean age=65.1, 47.5% male) were included in the meta-analysis. See **Appendix B** for a description of study populations.

3.2.1 Overall Executive Function

Results of the mean effect analysis for each component are presented in **Table 1** (see **Appendix C** for forest plot). Results revealed a small negative effect of T2DM status on executive

function composite ($d=-0.248$, $Z=-9.131$, $p<0.001$). Homogeneity analysis indicates that significant variability in effect sizes included in the meta-analysis ($Q=184.39$, $p<0.001$).

Table 1: Weighted mean effect size analysis

Measure	N	k	d	95% CI			Z	p	Homogeneity Test			
				LL	UL	SE			v	Q	df	p
Verbal Fluency												
Letter Fluency	5427	20	-0.378	-0.501	-0.256	0.0623	-6.070	<0.001	0.0336	38.982	19	0.004
Category Fluency	40242	21	-0.163	-0.213	-0.113	0.026	-6.375	<0.001	0.0024	26.075	20	0.16
Verbal Fluency Composite	41467	31	-0.218	-0.276	-0.159	0.030	-7.295	<0.001	0.0068	48.525	30	0.018
Mental Flexibility												
TMTA ^(comparison measure)	5349	13	-0.474	-0.602	-0.345	0.0657	-7.206	<0.001	0.01943	21.284	12	0.046
TMTB	16545	16	-0.324	-0.476	-0.172	0.0775	-4.180	<0.001	0.0584	72.426	15	<0.001
Shifting Composite	24243	22	-0.362	-0.487	-0.238	0.0636	-5.697	<0.001	0.0588	119.46	21	<0.001
Inhibition												
Stroop	4011	11	-0.322	-0.438	-0.206	0.059	-5.442	<0.001	<0.000001	7.804	10	0.65
Inhibition Composite	4131	13	-0.317	-0.427	-0.207	0.0562	-5.640	<0.001	<0.000001	9.790	12	0.63
Working Memory												
Digit Span Forward	5491	17	-0.170	-0.268	-0.072	0.0499	-3.405	0.0007	0.012130	23.985	16	0.090
Digit Span Backward	26992	18	-0.240	-0.352	-0.128	0.057	-4.182	<0.001	0.02873	55.631	17	<0.001
Working Memory Composite	28118	28	-0.126	-0.193	-0.060	0.0341	-3.702	0.0002	0.00853	42.028	27	0.033
Attention												
DSST	22414	22	-0.433	-0.533	-0.333	0.051	-8.489	<0.001	0.0267	64.78	21	<0.001
Attention Composite	25669	27	-0.384	-0.479	-0.289	0.0484	-7.931	<0.001	0.0298	87.10	26	<0.001
Executive Function Composite	79069	60	-0.248	-0.301	-0.195	0.0272	-9.131	<0.001	0.0201	184.39	59	<0.001

N = number of participants; k = number of studies; d = weighted mean effect size; CI = confidence interval; LL = lower limit; UL = upper limit; v = random-effects variance component; Q = heterogeneity; df = degrees of freedom

3.2.2 Moderator Analysis

Table 2 presents the moderator analysis results. There was significant effect of age ($B=0.006$, $p=0.019$) and T2DM duration ($B=0.021$, $p=0.016$) on effect sizes in the overall executive function composite; however, sex ($p=0.29$) did not influence effect size. Because effect size was coded such that negative effect size indicates impaired EF in the T2DM group compared to controls, an increase in effect size corresponds to a smaller effect. Thus, for every 1-year increase in age, there is a 0.006 unit decrease in the magnitude of the effect size. Similarly, for every 1-year increase in T2DM duration, there is a 0.021 unit decrease in the magnitude of the effect size.

Table 2: Moderator analysis - meta-regression

Variable	B	SE	95% CI		Z	p	Beta	k	N	$Q_B(df)$	$Q_W(df)$
			LL	UL							
Overall Executive Function											
Age	0.0061	0.0026	-0.001	0.0112	2.348	0.019	0.302	58	78950	5.51(1)	54.99(54)
Sex	-0.118	0.111	-0.336	0.100	-1.059	0.29	-0.147	54	77870	1.12(1)	50.48(52)
Duration	0.021	0.0089	0.0039	0.039	2.405	0.016	0.350	28	36294	5.78(1)	41.40(26)
Verbal Fluency											
Age	0.0097	0.0033	0.0032	0.0162	2.9254	0.0034	0.4365	29	41348	8.56(1)	36.36 (27)
Sex	-0.0446	0.0447	-0.1321	0.0430	-0.9977	0.3184	-0.1500	28	41136	1.00(1)	43.23 (26)
Mental Flexibility											
Age	0.0025	0.0079	-0.0131	0.0181	0.314	0.75	0.064	22	24243	0.10(1)	24.12 (20)
Sex	-0.514	0.317	-1.135	0.107	-1.622	0.10	-0.3195	21	23404	2.63 (1)	23.14 (19)
Working Memory											
Age	0.002	0.0023	-0.0025	0.0064	0.865	0.39	0.168	27	28038	0.75(1)	25.89 (25)
Sex	-0.018	0.081	-0.176	0.141	-0.218	0.83	-0.044	23	26958	0.048 (1)	24.78 (21)
Attention											
Age	0.0052	0.0057	-0.0059	0.0164	0.918	0.36	0.169	26	25589	0.84 (1)	28.64 (24)
Sex	-0.153	0.301	-0.743	0.436	-0.510	0.61	-0.096	25	25377	0.26 (1)	28.27 (23)

CI = confidence interval; LL=lower limit; UL = upper limit; k = number of studies; N = number of participants; Q_W = within-group (residual) heterogeneity; Q_B = between-groups (moderator) heterogeneity; df = degrees of freedom

3.2.3 Verbal Fluency

The results indicate a significant association between T2DM status and reduced verbal fluency ($d=-0.218$, $Z=-7.30$, $p<0.001$). Specifically, both letter (phonemic) fluency ($d=-0.378$, $Z=-6.07$, $p<0.001$) and category (semantic) fluency ($d=-0.163$, $Z=-6.38$, $p<0.001$) were impaired; however, the effect appears to be larger for letter fluency. Homogeneity analysis revealed that there was significant variation in effect sizes included in the verbal fluency composite ($Q=48.52$, $p=0.018$) and

letter fluency analysis ($Q=38.98$, $p=0.004$), but not in effect sizes of category fluency ($Q=26.07$, $p=0.16$).

3.2.3.1 Moderator Analysis

A sufficient number of studies were available for analysis of age and sex moderators. A significant effect of age on effect size was observed ($B=0.0097$, $p=0.003$) such that for every 1-year increase in age, there is a 0.0097 decrease in the magnitude of d . Sex did not moderate the association between T2DM and EF ($p=0.318$).

3.2.4 Mental Flexibility

Mental flexibility performance was significantly worse among individuals with T2DM ($d=-0.362$, $Z=-5.70$, $p<0.001$). In this category, only TMTB and TMTA (used as a comparison measure only) were reported by >5 studies. Both TMTA ($d=-0.474$, $Z=-7.21$, $p<0.001$) and TMTB ($d=-0.324$, $Z=-4.18$, $p<0.001$) were significantly impaired among those with T2DM indicating that T2DM is associated with impairment on both processing speed and controlled inhibitory components of the TMT. Homogeneity analysis revealed significant variability in the effect size for the mental flexibility composite ($Q=119.46$, $p<0.001$), TMTA ($Q=21.28$, $p=0.046$) and TMTB ($Q=72.42$, $p<0.001$).

3.2.4.1 Moderator Analysis

A sufficient number of studies were available for analysis of age and sex moderators. Neither age ($p=0.75$) nor sex ($p=0.10$) moderate the association between T2DM and EF.

3.2.5 Inhibition

Inhibition composite performance was significantly worse among individuals with T2DM ($d=-0.317$, $Z=-5.64$, $p<0.001$). Only the Stroop task was examined in >5 studies and was comparable to the results of the inhibition composite ($d=-0.322$, $Z=-5.44$, $p<0.0001$). Homogeneity analysis was not significant for either the inhibition composite ($Q=9.79$, $p=0.63$) or the Stroop task ($Q=7.80$, $p=0.65$), indicating similar effect sizes across studies. There was an insufficient number of studies examining the effect of T2DM on inhibition that also reported moderator variables; therefore, moderator analysis was not conducted.

3.2.6 Working Memory

Worse performance on the working memory composite was associated with T2DM ($d = -0.126$, $Z = -3.70$, $p = 0.0002$). The digit span forward and backwards were the only tasks reported in >5 studies. Performance on both digit span forward, ($d = -0.170$, $Z = -3.405$, $p = 0.0007$) and digit span backward ($d = -0.240$, $Z = -4.182$, $p < 0.0001$) were impaired as a function of T2DM status. Homogeneity analysis indicates significant variability between effect sizes for working memory composite ($Q = 42.03$, $p = 0.033$) and digit span backward ($Q = 55.63$, $p < 0.001$), but not digit span forward ($Q = 23.98$, $p = 0.09$).

3.2.6.1 Moderator Analysis.

A sufficient number of studies were available for analysis of age and sex moderators; however, neither age ($p = 0.39$) nor sex ($p = 0.83$) moderated the association between T2DM and EF.

3.2.7 Attention

Finally, T2DM status was associated with reduced attention ($d = -0.384$; $Z = -7.93$, $p < 0.001$). Only the digit symbol substitution task (DSST) was examined in >5 studies, and T2DM status was associated with reduced DSST performance ($d = -0.433$; $Z = -8.49$, $p < 0.001$). Homogeneity analysis revealed significant variability among the effect sizes for attention composite ($Q = 87.10$, $p < 0.001$) and DSST ($Q = 64.78$, $p < 0.0001$).

3.2.7.1 Moderator Analysis

A sufficient number of studies were available for analysis of age and sex moderators. Neither age ($p = 0.36$) nor sex ($p = 0.61$) moderates the association between T2DM and EF.

3.3 Discussion

The results of this meta-analysis revealed a reliable deficit in EF among individuals with T2DM in comparison to controls as observed over 60 studies and 9815 individuals with T2DM. Publication bias, a common limitation of systematic reviews and meta-analyses, may result in the more likely reporting (and thus retrieval of) significant results. As seen in **Appendix D**, the funnel plot of included studies for this meta-analysis is in fact asymmetrical indicating that publication bias is present, and the results of this meta-analysis should be interpreted within this context. Specifically,

this deficit was observed across all components of EF (verbal fluency, mental flexibility, inhibition, working memory, and attention) and all EF tasks examined. This finding of an association between T2DM and EF impairment is consistent with a number of recent reviews which have concluded the same (Bourdel-Marchasson et al., 2010; Cukierman, Gerstein, & Williamson, 2005; Reijmer, van den Berg, Ruis, Kappelle, & Biessels, 2010; Rucker, McDowd, & Kluding, 2012; Starr & Convit, 2007).

Despite the finding of an overall effect of T2DM status on EF, there has been variability in findings between individual studies. One possible explanation for this diversity is the broad array of research methodology used and sample characteristics (e.g., age range, sex distributions and comorbidities). In addition, the relatively small effect size would make detection of the effect difficult within any single study of relatively low sample size. Meta analytic procedures have the benefit of enhanced power to detect such effects using statistical aggregation across studies.

3.3.1 Moderator Analysis

In the current meta-analysis, T2DM duration was found to moderate the association between T2DM and EF composite, however this effect was in the opposite direction as had been expected, such that an increase in T2DM duration was associated with a small decrease in the effect of T2DM and EF. One possible explanation for this finding is that individuals who have had T2DM for longer are more likely to be receiving active treatments that improve both glycemia and cognitive indices. Because there are few subjective signs of T2DM onset, individuals diagnosed with T2DM have often had the disease for a number of years and may have had hyperglycemic episodes during this time (IDF Diabetes Atlas Group, 2013). It is possible, therefore, that upon starting treatment and improving hyperglycaemia a moderate improvement in EF could be observed (Ryan et al., 2006). This hypothesis is supported by Cooray et al. (2011) who found that a group of T2DM patients receiving intensive treatment of T2DM showed improvement in cognitive function while no improvement was observed among those receiving standard therapy. Additionally, other factors such as type of T2DM therapy and alcoholism have been proposed to affect the T2DM EF association and were not included as moderators in this meta-analysis due to the limited number of studies reporting these sample characteristics. In the few studies examining the effect of medication, insulin therapy has been associated with a larger association of T2DM and EF than oral anti-hyperglycaemics or diet therapy alone (Fontbonne et al., 2001; L. P. Lowe et al., 1994; Nandipati et al., 2012). It is therefore possible that medication type, and not T2DM duration is significant in moderating the effect of T2DM on EF.

Analysis also revealed a moderating effect of age on the association of T2DM and EF impairment for the overall EF composite measure, such that increasing age was associated with a decreased magnitude of the effect size. This finding held for the verbal fluency subcomponent; however, age did not influence the effect of T2DM on mental flexibility, working memory or attention subcomponents of EF. An insufficient number of studies were available to assess the effect of age on the association of T2DM and inhibition; thus, future research should aim to determine if age moderates the association T2DM and this inhibition component of EF. While some researchers have hypothesized that the impact of T2DM on cognitive function would increase with increasing age, our finding of a decreased effect size of the association between T2DM and EF is in line with the findings of van Eersel et al. (2013) . In a recent study, van Eersel et al.(2013)observed a significant T2DM by age interaction effect on cognitive function such that the difference in EF measure diminished from 32 points in person aged 32-44 to 2 points in those over the age of 75. One possible explanation for this interaction is that the cardiovascular risk factors and neurodegenerative changes become more predominant among both older adults with T2DM and those without and may therefore narrow the gap between them (Van Eersel et al., 2013). Additionally, given that shorter T2DM duration was also associated with reduced effect size, it is possible the younger individuals may have shorter disease duration and that factors such as improved glycemic control with increasing disease duration (discussed above) may result in a decreased association of T2DM with EF dysfunction. It is also possible that the reverse is true (i.e. that moderation by age accounts for observed effect of T2DM duration); however, Ishizawa et al. (2010) found no influence of age on the association between T2DM and EF in a group of individuals with newly diagnosed T2DM. This finding suggests that when T2DM duration is held constant, the moderating effect of age may be diminished; however further research is needed. Additionally, other factors such as medication type and severity of disease at diagnosis were not examined as moderators in this analysis, but could act as confounders to the moderating effect of age.

Sex did not significantly influence the strength of association between T2DM and EF. These findings are similar to those observed by Okereke et al. (2008) , who compared two study populations (Physicians Health Survey II (male) and the Women’s Health Study (female)), and observed no T2DM sex interaction effect on cognition. However these findings diverge somewhat from Maggi et al. (2009), who did find that sex moderates the effect of diabetes on some aspects of cognition.

3.3.2 Relevance for Clinical Practice and Self-Management

The current findings provide the first comprehensive meta-analysis of the relationship between T2DM and EF. Our findings support the contention that T2DM is associated with EF impairment across all facets of EF. However, because of inherent limitations of the studies from which the effects are estimated, it is not possible to draw conclusions about directionality. The results of longitudinal studies provide some evidence to indicate that T2DM status is associated with significantly greater decline in EF relative to control (Gallacher et al., 2005; Hassing et al., 2004; Kanaya, Barrett-Connor, Gildengorin, & Yaffe, 2004; Ruis et al., 2009a). However, these results have not been uniformly observed and a number of longitudinal studies have observed no difference in the rate of EF decline as a function of T2DM status (Espeland et al., 2011; Logroscino et al., 2004; Mehrabian et al., 2012). Furthermore, the finding of EF deficit among newly diagnosed diabetics in a study by Ishizawa et al. (2010) may indicate that EF deficit precedes T2DM. In fact, it is possible that impaired EF may act as a risk factor for the development of T2DM because of the importance of EF for control and monitoring of behaviours including those health behaviours which are protective against chronic disease such as dietary behaviours, physical activity adherence and the development of obesity over the lifespan (Hall, 2012). On the other hand, plausible biological mechanisms exist to explain the association between T2DM and EF decline such that hyperglycemia may contribute to cognitive decline through formation of advanced glycation end products, inflammation, and cerebrovascular disease. This hypothesis is supported by studies which have shown an association between higher A1C and impaired cognitive function (Yaffe et al., 2012). It is also possible that EF deficits both increase the likelihood of T2DM development and are worsened by presence of T2DM.

Notably, there are also a number of T2DM comorbidities which may confound the association between T2DM and EF. Specifically, individuals with T2DM are at greater risk for renal disease, depression, stroke, hypertension, hyperlipidemia, and cardiovascular disease, all of which may impair cognitive performance (Knopman et al., 2001; Strachan, Reynolds, Frier, Mitchell, & Price, 2008; Yaffe et al., 2012); thus, treatment and prevention of these comorbid conditions may improve EF in this population. However, Yaffe et al. (2012) observed that greater decline in EF over time in individuals with T2DM remained following adjustment for a variety of comorbid conditions. Other studies have similarly demonstrated that association between T2DM status and EF remains following control for hypertension (Ishizawa et al., 2010; Mehrabian et al., 2012), depression (Ishizawa et al., 2010; Mehrabian et al., 2012; Ruis et al., 2009b), or cerebrovascular disease (Ishizawa et al., 2010; Reijmer et al., 2013).

Regardless of directionality of effect, reduced EF among T2DM individuals has implications for diabetes management. T2DM relies heavily on self-management, with some studies reporting that 95% of diabetes management is performed by the patient (Winokur, Maislin, Phillips, & Amsterdam, 1988), and because the ability to control dietary behaviour, adhere to medical treatment, and a variety of other behaviours relies heavily on EF, maintaining EF is particularly important among individuals with T2DM. For example, relatively stronger EF is correlated with better diabetes self-management, especially among those treated with insulin (Primožic et al., 2012a). Other studies have observed similar results (Munshi et al., 2012; Thabit et al., 2009). Interestingly, Munshi et al. (2012) found a significant association between objective, but not self-report, measures of EF and HbA1c, such that a 1-point increase in EF score was associated with a 0.22 unit lower HbA1c. Given the importance of proper diabetes management and glucose regulation for disease outcomes, EF may be of particular importance in this population.

3.3.3 Summary

The results of the current meta-analysis indicate a mild-to-moderate EF impairment associated with T2DM. The presence of EF impairments in individuals with T2DM is of potential clinical importance because, although individuals with T2DM have a great need for adequate EF (arguably more so than the general population), they do in fact experience reduced EF at a population level. Thus, the findings of the current meta-analysis may support the utility of screening for EF impairments with the objective of supporting those with EF impairments in tackling self-care objectives that come with the T2DM and thereby reducing T2DM comorbidities.

3.3.4 Implications of Study 1

Individuals with T2DM are required to undertake a number of self-management behaviours that rely on EF, but they have lower EF to draw upon. Therefore, there is an implication for the potential utility of screening for impaired EF in the T2DM population, as well as the importance of identifying EF enhancing interventions. One such strategy which has demonstrated positive effects on EF in healthy populations is aerobic exercise, both in terms of chronic or long-term effects of regular aerobic training and acute effects of single aerobic exercise bouts. The following section will review the existing evidence for the effects of aerobic exercise on EF, with a focus on the acute effects.

Chapter 4

Aerobic Exercise and Executive Function

4.1 Chronic/ Long-term Effects

Aerobic exercise training has been shown to have beneficial effects on a number of aspects of cognition including EF. A recent meta-analysis of randomized control trials found that aerobic exercise training regime for at least 1 month is associated with modest improvements in EF (Cohen's $g=0.123$) and attention/processing speed (Cohen's $g=0.158$) in comparison to control groups that did not engage in aerobic exercise; however, no effect on working memory was observed (Cohen's $g=0.032$) (Smith et al., 2010). Interestingly, duration of exercise program and intensity do not appear to influence these effects of aerobic exercise on cognitive function, nor does the age of participants (Smith et al., 2010). Additionally, Baker *et al.* (2010) observed similar results among a population of individuals with impaired glucose tolerance, such that 6 months of aerobic exercise resulted in improved executive function relative to a stretching control group. These effects were greatest among measures task switching (TMTB) and response inhibition (Stroop).

4.1.1 Chronic Aerobic Exercise and Brain Changes

At a physiological level, a number of cross-sectional studies have demonstrated that in comparison to low-fit counterparts, high fit individuals experience fewer age-related brain changes (Guiney & Machado, 2013) including less prefrontal and temporal atrophy (Colcombe et al., 2003), greater preservations of connecting neural tracts between prefrontal cortex and other brain regions (Marks et al., 2007) and greater gray matter volume in the prefrontal and cingulate cortices (Floel et al., 2010). Additionally, some evidence suggests higher resting cerebral blood flow velocity in aerobically trained vs. sedentary individuals (Guiney & Machado, 2013). In support of these cross-sectional studies, Colcombe *et al.* (2006) demonstrated significant increases in white and gray matter volume in areas of the frontal and temporal lobes important to EF in individuals who completed a 6 month aerobic exercise program in comparison to a stretching control group. Similar findings were observed by Erickson *et al.* (2011) such that aerobic exercise training resulted in increased hippocampal volume and improved spatial memory; furthermore, increases in hippocampal volume were associated with increased brain-derived neurotrophic factor (BDNF) which may act as a mechanism for increased brain volume. Taken together, these findings present some possible mechanisms by which aerobic exercise may impact cognition (specifically, cerebral blood flow and white and gray

matter volume); however, the precise mechanisms by which these brain changes occur are currently unknown.

4.2 Acute Effects

Studies examining acute effects of exercise on cognition typically assess predictions of arousal theories which hypothesize that acute exercise alters the allocation of cognitive resources to task performance (Dietrich & Audiffren, 2011) including changes to cardiorespiratory, hormonal, and metabolic processes many of which are sustained following completion of the exercise bout (Tomporowski, 2003). Three major approaches to examining the effects of exercise on cognition (based on manipulation of arousal) appear in research: 1) steady-state, 2) inverted U, and 3) fatigue, which are not mutually exclusive (Lambourne & Tomporowski, 2010). Based on the observation that moderate intensity steady state exercise improves mood (Paluska & Schwenk, 2000), it is hypothesized that moderate intensity steady state exercise will similarly result in improved performance on executive function tasks (Tomporowski, 2003). The inverted U hypothesis, posits that there is an optimal level of arousal at which executive function and other cognitive processes will be enhanced but above which fatigue will result in worse performance (McMorris & Graydon, 2000). Similarly it is hypothesized that high intensity exercise and/or exercise of extended duration will result in fatigue which will impair cognitive task performance. However, while there is some indication that intense physical activity in extreme human performance environments may result in decreased cognitive function (Kamijo, Nishihira, Hatta, Kaneda, Kida et al., 2004) low-moderate exercise and even intense exercise of relatively short duration or in non-extreme environments leads to improvements of cognitive function and specifically executive functioning (Lambourne & Tomporowski, 2010). Additionally, a recent meta-analysis revealed no difference in size or direction of effect between studies designed to examine steady state exercise, fatiguing exercise or the inverted U hypothesis (Lambourne & Tomporowski, 2010).

4.2.1 Acute Aerobic Exercise and Brain Changes

Studies have examined event-related potentials (ERPs), specifically the P300 (or P3) subcomponent, in relation to task performance following acute aerobic exercise. P300 is considered to reflect allocation of attention and context updating of working memory, and thus is considered to reflect neural activity underlying cognitive performance, particularly that relating to EF. Improvements in P300 following acute bouts of exercise, specifically increased amplitude and decreased latency, have

been observed by a number of studies (Hillman, Snook, & Jerome, 2003; Kamiyo, Nishihira, Higashiura, & Kuroiwa, 2007; Magnie et al., 2000). Additionally, Kamiyo *et al.* (2007) observed that P300 amplitude increased following light and moderate exercise but not intense, providing some support for the inverted U hypothesis. While ERP studies provide evidence of increased neural activity related to cognitive task performance, they are limited in that they provide only rough estimation of the localization of effect (Hyodo et al., 2012).

To resolve this problem, recent studies have made use of functional near-infrared spectroscopy (fNIRS) which is a non-invasive means of measuring cerebral hemodynamics. Two recent studies have incorporated use of fNIRS in examination of the effect of acute aerobic exercise on EF (as measured by the Stroop task) in young (Yanagisawa et al., 2010) and older adults (Hyodo et al., 2012). Of note, Stroop interference improved significantly in both studies; however, the cortical areas involved in Stroop interference tasks were different for younger and older adults, as were the cortical areas affected by the acute exercise bout (Hyodo et al., 2012; Yanagisawa et al., 2010). Specifically, Hyodo et al. (2012) observed activation of the bilateral dorsolateral PFC (DLPFC), ventrolateral PFC (VLPFC), and frontopolar area (FPA) in response to stroop interference tasks in a population of healthy older adults, whereas Yanagisawa *et al.* (2010) reported left-dominated bilateral lateral PFC (LPFC) activation among a population of younger adults. This finding is consistent with broader recruitment of prefrontal areas during stroop task performance among older adults in comparison to younger adults using fMRI (Langenecker, Nielson, & Rao, 2004). Additionally, while increased right FPA (R-FPA) activity corresponded with improved Stroop performance following exercise in older adults (Hyodo et al., 2012) increased activation of the DLPFC was associated with improved stroop performance in younger adults (Yanagisawa et al., 2010). Further research is needed to confirm these findings and to determine whether these acute changes may contribute to the long-term effects of chronic aerobic exercise.

4.2.2 Acute Aerobic Exercise and Executive Function

The effects of acute aerobic exercise on cognitive function have been examined in a number of meta-analyses (Chang, Labban, Gapin, & Etnier, 2012; Etnier et al., 1997; Lambourne & Tomporowski, 2010; McMorris, Sproule, Turner, & Hale, 2011). Overall, these meta-analyses have observed a small but significant effect of acute aerobic exercise on cognitive function (ES=0.10, Chang et al., 2012; ES=0.16, Etnier et al., 1997; ES=0.20, Lambourne & Tomporowski, 2010). The meta-analyses of Chang *et al.* (2012) and Lambourne & Tomporowski (2010) differ in that Chang *et al.* (2012)

conducted a comprehensive meta-analysis of all studies examining acute effects of aerobic exercise on cognition whereas Lambourne & Tomporowski (2010) limited their analysis to young adult populations, and within subject designs which may account for the differences in effect size observed.

Significant improvement in cognition has been consistently observed following exercise (Chang et al., 2012; Lambourne & Tomporowski, 2010) whether the measurement occurs immediately following exercise or after a delay (Chang et al., 2012). Moderators of this relationship include exercise type (cycling > running; Lambourne & Tomporowski, 2010), exercise intensity (light < all other intensities; Chang et al., 2012), timing of task administration (1-15 minutes > 15+ minutes; Chang et al., 2012), duration of exercise (with <11 minutes having no effect or a negative effect; Chang et al. 2012), and study design (less rigorous designs tend to produce greater effect sizes; Chang et al. 2012; Lambourne & Tomporowski, 2010). Task type also significantly moderated the effect of exercise on cognition, such that executive function and crystallized intelligence (ability to use skills knowledge and experience, distinct from memory) were most affected; the ES for the effect of acute aerobic exercise on EF after a delay was 0.17 (Chang et al. 2012). However, in a meta-analysis of the effects of acute intermediate intensity exercise on working memory task performance, McMorris et al. (2011) observed significant beneficial effect on response time ($g=-1.41, p<0.001$) but a significant detrimental effect on accuracy ($g=0.40, p<0.01$). This finding suggests that even with the EF domain, the effect of aerobic exercise of cognitive function is influenced by cognitive task type.

Furthermore, while the overall effect size with respect to EF displays a significant improvement, results of individual studies have been inconsistent with some studies showing moderate to large effects (Chang & Etnier, 2009; Chang, Liu, Yu, & Lee, 2012; Hogervorst, Riedel, Jeukendrup, & Jolles, 1996; Nanda, Balde, & Manjunatha, 2013; O'Leary, Pontifex, Scudder, Brown, & Hillman, 2011; Pontifex, Hillman, Fernhall, Thompson, & Valentini, 2009; Sibley, Etnier, & Le Masurier, 2006; Tam, 2013; Wang, Chu, Chan, & Chang, 2013; Yanagisawa et al., 2010) and others showing no effect (Barella, Etnier, & Chang, 2010; Coles & Tomporowski, 2008; Lambourne, Audiffren, & Tomporowski, 2010; Stroth et al., 2009; Tomporowski & Ganio, 2006). These inconsistencies may be related to study design, exercise type, or aspect of executive function examined. Of note, a number of studies examining the effects of acute aerobic exercise on EF have focused on inhibition using the stroop task (Barella et al., 2010; Hogervorst et al., 1996; Hyodo et al., 2012; Lambourne & Tomporowski, 2010; Sibley et al., 2006; Yanagisawa et al., 2010), and Stroop task performance tends to improve following exercise in young adults (Hogervorst et al., 1996; Sibley

et al., 2006; Yanagisawa et al., 2010); however, results among older adults are inconsistent (Barella et al., 2010; Hyodo et al., 2012).

The meta-analysis by Chang *et al.* (2012) included studies conducted on older adult populations; however, to date, the majority studies have focused on the effects of acute aerobic exercise in healthy young adults particularly in terms of EF. Recent evidence indicates similar effects of acute aerobic exercise among older adults on tests of executive function (Barella et al., 2010; Cordova et al., 2009; Hatta, Nishihira, & Higashiura, 2013; Hyodo et al., 2012; Kamijo et al., 2009) **Table 3** summarizes the results of studies examining acute effects on EF following aerobic exercise. Significant improvement in EF has been observed following aerobic exercise in older adults (Cordova et al., 2009; Hyodo et al., 2012; Kamijo et al., 2009). However, Hatta *et al.* (2013) observed no change in EF following a light walking exercise; similarly, Barella *et al.* (2010) observed improved processing speed limited to immediately following exercise, but no effect on EF following walking at 60% maximal heart rate reserve. The variability of these findings could be attributable to a number of factors that vary between the above studies. Specifically, as noted in previous meta-analyses, cycling produced greater cognitive improvements than running (or walking) and light exercise improved cognition less than moderate or vigorous activity (Chang et al., 2012; Lambourne & Tomporowski, 2010). Both Barella *et al.* (2010 and Hatta *et al.* (2013) employed walking as an exercise intervention and while Barella *et al.* adjusted walking to a moderate intensity, Hatta *et al.* used light walking as the exercise intervention (which would not truly be considered aerobic exercise). It is possible that light walking was not enough to stimulate improved EF or similarly that differences in cycling and running account for the null findings of these studies (however, given the overall variability of study parameters it is difficult to attribute the null findings to any one factor). Additionally, while Kamijo *et al.* (2009) observed a dose dependent increase in EF such that EF was most improved following moderate activity, Cordova *et al.* (2009) observed no effect at the 60% or 110% of anaerobic threshold but significant improvement following 90%. They suggested an adverse effect on EF may occur above 110% of the anaerobic threshold. This finding is in line with the inverted U hypothesis and may suggest that there is an optimal range for exercise in which EF benefits are seen in an elderly population. Among the limited number of studies conducted in elderly populations, findings point towards greater improvements in executive function with aerobic exercise than those in younger populations (Chang et al., 2012; Cordova et al., 2009; Kamijo et al., 2009), and it is hypothesized that the greater impact may be attributable to greater executive function deficits at baseline among this population (Pesce & Audiffren, 2011).

Table 3: Acute effects of aerobic exercise on cognitive performance *after* exercise in older adults

Author yr	Sample Size	Age (SD)	Gender (%M)	EF measure	Type of Exercise	Duration Exercise	Intensity of Exercise	Findings
Barella 2010	40	69.26 (8.4)	15%	Stroop (colour trials, interference trials, inhibition trials)	Walking, treadmill	20 mins + 5 min warm up	60% MHRR	Beneficial effect on colour test immediately following No other effects
Cordova 2009	48	63.8 (4.6)	0	Tower of Hanoi, TMTA & B, Simple Response Time Task, VF	Cycle Ergometer	20 mins + 5 min warm up (8 mins from exercise to tasks)	60, 90, 110 % of anaerobic threshold	60% no effect 90% beneficial effect on TH 110% no effect
Hatta 2013	20	70.5 (3.4)	50%	Wisconsin Card Sorting Task	walking	80-120mins 7000-10000 steps	light (walking, self-paced with breaks)	no effect
Hyodo 2012	33	69.3 (3.5)	81%	Stroop Word Matching	Recumbent ergometer	10 mins (15mins from exercise to tasks)	Ventilatory threshold (approx. 50% VO ₂ max)	Greater improvement in interference following ex.
Kamijo 2009	12	65.5 (1.5)	100%	modified flanker task	Cycle Ergometer	20 mins + 5 min warm-up	light (30% VO ₂ max) moderate (50% VO ₂ max)	moderate > light > baseline

Evidence suggests a small but reliable improvement of EF following acute aerobic exercise in young adults, and the existing data suggests that this finding is replicable in older adults. However, to date, the effect of acute aerobic exercise on EF in a T2DM population has not been examined. Due to the importance of EF in T2DM management, acute aerobic exercise might provide a means of reducing this deficit. For this reason, Study 2 aims to examine the effect of acute aerobic exercise on EF in a T2DM population.

Chapter 5

Study 2: The effects of acute aerobic exercise on EF in individuals with T2DM

In study 1, we demonstrated that the effect size for the association between T2DM status and impaired EF, while small-to-moderate in size, is statistically significant. Thus, individuals with T2DM, have weaker EF compared to those without and this relationship was robust across all aspects of EF (set shifting, inhibition, working memory, verbal fluency, and attention).

Impaired EF among the T2DM population is particularly significant because of the importance of EF in performing self-regulatory behaviours such as the planning, implementation, assessment and adaptation behaviours necessary in disease self-care (Hajduk et al., 2013; McNally et al., 2010; Ohmann et al., 2010; Primožic, Tavcar, Avbelj, Dernovsek, & Oblak, 2012b; Thabit et al., 2009). Executive function has been implicated in the ability to perform healthy dietary behaviours, adhere to medication regimes, and other diabetes self-management behaviors (Allan et al., 2010; Insel et al., 2006; C. Lowe et al., 2014; McAuley et al., 2011; Munshi et al., 2012; Nederkoorn et al., 2009; Rosen et al., 2003; Stilley et al., 2010; Thabit et al., 2009). Given that T2DM requires many important self-care behaviours and given the importance of EF to execution of these behaviours, presence of impaired EF among the T2DM population presents a potential barrier to T2DM management, and implies that optimization of EF is an important objective in this population.

Along these lines, an accumulating body of literature has documented EF-enhancing effects of aerobic exercise. A recent meta-analysis has demonstrated enhancement of EF following both longer-term aerobic training programs (Smith et al., 2010) and immediately following an acute bout of aerobic exercise (Chang et al., 2012; Lambourne & Tomporowski, 2010) in healthy populations. Aerobic exercise is hypothesized to increase the efficiency of the prefrontal cortex (PFC) and other structures supporting executive processes (Kramer & Erickson, 2007; Yanagisawa et al., 2010).

This effect of aerobic exercise on cognition may be moderated by a number of factors, including sex and physical fitness. Kramer and Erickson (2007) noted that studies with larger proportion of female participants tended to show larger effect sizes of chronic exercise on improved cognition and hypothesized that this difference may be due to an interaction between estrogen and BDNF. Although acute aerobic exercise literature has failed to observe a difference between effects in male and female participants (Chang et al., 2012), to our knowledge few studies have directly

assessed these differences. Additionally, physical fitness has been shown to act as a moderator of the effect of exercise on cognition such that during exercise low fit individuals displayed impaired cognition and high fit displayed improved, while following exercise improvement was observed in both groups (Chang et al., 2012; Labelle, Bosquet, Mekary, & Bherer, 2013).

While studies have demonstrated evidence of EF enhancement following acute aerobic exercise in healthy young (Lambourne & Tomporowski, 2010) and healthy older adults (Cordova et al., 2009; Hyodo et al., 2012; Kamijo et al., 2009), the effect among those with T2DM has not been previously examined. Thus, the primary aim of the current study is to examine the effects of acute aerobic exercise on EF in a population of adults with T2DM through a within subject design comparing moderate intensity exercise to minimal intensity control condition. The potential moderating effects of sex, physical activity status, as well as diabetes-related factors—disease duration, A1C, and number of T2DM medications—were also assessed. It was hypothesized that in line with prior research in other populations, EF would be enhanced following moderate, but not minimal intensity exercise.

5.1 Methods

5.1.1 Participants

Thirty adults, age 40-69 (Mage=59.6, SD=5.7), with T2DM and not currently taking insulin were recruited from the community through a combination of a) study posters, b) presentations to diabetes education classes, and c) study flyers distributed in endocrinologist offices. Characteristics of included participants are presented in **Table 4**.

Inclusion criteria were: T2DM, age 40-69, safety for exercise according to the American Heart Association (Marwick et al., 2009) and American College of Sports Medicine guidelines (Colberg et al., 2010), using the Physical Activity Readiness Questionnaire (PARQ; see **Appendix E**) and additional medical questionnaire. Additional exclusion criteria were mobility limitation precluding exercise or any of the following factors which could interfere with accuracy of EF testing: insulin use, anticholinergic drug use, severe vision impairment, colour-blindness, substance abuse in the past six months, or active depression. Participants were asked not to consume caffeine for 3 hours prior to participation and if possible to limit food consumption during the hour prior to participation. Of the 30 individuals who attended at least one session, 2 were excluded due to an inability to

complete exercise protocol as a result of high blood pressure, thus the final sample consisted of 28 participants.

Table 4: Population Characteristics

n	30
Age	59.6 (5.7)
Sex % female (n)	50% (15)
BMI (n=27)	33.11 (7.3)
Ethnicity % (n)	
Caucasian	73.3% (22)
Aboriginal	6.7% (2)
Other	16.7% (5)
T2DM Duration (n=29)	5.95 (4.9)
A1C (n=16)	7.8 (1.8)
No. T2DM Medications % (n)	
None	16.7% (5)
One oral medication	33.3% (10)
Two oral medications	40% (12)
Three oral medications	10% (3)
Hours Vigorous Activity in past week (n=28)	1.75 (3.07)

* Values are mean (standard deviation) unless otherwise specified

5.1.2 Design

A within-subjects design was used to compare performance on EF tasks before and after two intensities of aerobic exercise (see **Appendix F** for project overview). Each participant attended two laboratory sessions in counterbalanced order; both sessions were conducted at the same time of day and the same day of week. During each session participants completed an exercise bout and two computer tasks measuring response inhibition (Stroop and Go/No-Go), performed before and after the exercise session. The exercise session was moderate intensity (30% maximal heart rate reserve; MHRR) on one visit and minimal (minimal effort pedaling) on another. Informed consent (see **Appendix G** for consent form) was obtained at the start of the first session, and participants completed questionnaires about demographics and health behaviours at the end of the second session. This study received ethics approval from the institutional research ethics review board and participants received \$50 gift cards in exchange for participation.

5.1.3 Executive Function Measures

Two EF tasks—the Go/No-Go (GNG) task and the Stroop task—were presented on a desktop computer using E-prime software (Psychology Software Tools Inc). Participants responded via button press using a response box, and were asked to respond as quickly and accurately as possible for each

task. Both EF tasks were administered before and after the exercise session at each visit to measure change in EF resulting from the exercise bout. Order of the tasks was randomized for each visit, but during a given visit, the order of tasks was the same before and after the exercise session in order to limit the effect of order of tasks on differences in pre- and post- performance.

5.1.3.1 Stroop Task

In this version of the Stroop task (Stroop, 1992), which has been modeled after the version in Miyake et al. (2000) , participants were instructed to indicate (by button press) the color of a stimulus, as quickly and accurately as possible. Stimuli were presented on the screen until the participant responded, followed by a response to stimulus interval of 1000 ms minus the response time; all stimuli were presented in red, blue, green, yellow, orange or purple coloured font. Following 10 practice trials, participants were presented with a mixed block of trials: 72 trials with a string of asterisks appearing in one of the six colors, 12 congruent colour word trials (ex. the word red appearing in red coloured font) and 60 incongruent color word trials (ex. the word yellow appearing in purple coloured font). The Stroop task is one of the most widely used measures of inhibition (Etnier & Chang, 2009; MacLeod, 1991) . The dependent variable of interest was Stroop interference (calculated as reaction time on incongruent trials minus reaction time on asterisk trials; (Hyodo et al., 2012) where greater Stroop interference was indicative of weaker EF.

5.1.3.2 Go/No-Go Task

The Go/No-Go (GNG) task measures one's ability to inhibit a prepotent response (Casey et al., 1997). In this task, participants were required to press a button, as quickly and accurately as possible, whenever a lower case letter was presented on the computer screen and withhold their response when an upper case letter was presented. The stimulus duration was set at 1000 ms, with a 500 ms interstimulus interval. A total of 10 practice trials were followed by 4 blocks of 60 test trials. In half of the test blocks upper case letters predominated (5:1) and in the other half of the test blocks lower case letters predominated (5:1). The dependent variable of interest was reaction time on correct trials where longer reaction times indicated weaker EF.

5.1.4 Exercise Protocol

Each participant completed 2 exercise bouts, one at each visit (moderate intensity for one and minimum for the other). Exercise sessions were conducted using a recumbent cycle ergometer and were over-seen by a CSEP/ACSM Certified personal trainer or exercise physiologist.

In the moderate intensity exercise condition, participants completed a 5-minute warm-up, 20-minutes exercise at 30% MHRR, and 5-minute cool down for a total of 30 minutes of exercise. Target heart rate (THR) for the moderate intensity condition (30% MHRR) was calculated using the equation $THR = \text{Resting heart rate (RHR)} + 0.3 (\text{Maximal Heart Rate} - \text{RHR})$, where Maximal Heart Rate (MHR)= $220 - \text{age}$ (the equation $MHR = 164 - 0.7 * \text{age}$ was substituted for individuals using beta-blocker) and RHR was measured with participant seated on the cycle ergometer prior to exercise. The 5 minute warm-up and cool-down were conducted at a workload of 5 and rpm of 50-70 (with cool down approaching 50 rpm). Target heart rate was achieved and maintained throughout the 20-minute exercise session by adjusting the workload while maintaining rpm between 50 and 70.

In the minimal intensity exercise condition, participants cycled at a slow and steady rate at the lowest available setting: workload of 5 and rpm 30-50. Every effort was made to keep target heart rate as close to resting heart rate as possible. In order to maintain a consistent duration of exercise between the 2 sessions, participants performed minimal exercise for a total of 30 minutes.

5.1.5 Exercise Measures

Resting heart rate and blood pressure were taken while participant sat on the cycle ergometer prior to starting the exercise bout. Heart rate was monitored throughout the exercise session (and recorded every 5 minutes) to ensure target heart rate was achieved and maintained and to quickly identify any irregularities. Blood pressure, rated perceived exertion (RPE), and workload were also be recorded at the end of each 5 minute interval.

5.1.6 Moderators

Additional information about participant demographics and health behaviours (see **Appendix H** for copies of questionnaires) was collected through survey response at the end of the second session. Recent physical activity status (assessed as reported number of hours of vigorous physical activity during the past week), T2DM duration (in years), most recently recorded A1C, number of diabetes medications, and sex were included as potential moderators of the effect.

5.1.7 Statistics

Change scores were calculated as post-exercise score minus pre-exercise score, and separate 1-way repeated measures analysis of variance (ANOVA) were used to assess whether greater increases in EF performance on Stroop and GNG tasks emerge following moderate as compared with minimal

aerobic exercise. Potential moderating effects of order of sessions, sex, recent physical activity history, years with T2DM, recent self-reported A1C, and number of diabetes medications were assessed using interaction terms, and further ANOVA analysis were conducted to tease out the details of any significant relationships. One data point was omitted from Stroop analysis because of accuracy less than 0.5, as this suggests lack of understanding of the task instruction. Outcome frequency distributions for Stroop interference and GNG RT were skewed and therefore subject to a square root transformation to improve normality.

5.2 Results

5.2.1 Preliminary Analyses

An initial comparison of the moderate and minimal conditions was conducted using repeated measures ANOVA to establish a difference between the moderate and minimal exercise conditions. A significant effect of condition was observed for both exercise intensity (calculated from Average HR = RHR + (MHR-RHR) x Intensity) ($F(1,22)=194.88, p<0.001$) and rated perceived exertion ($F(1,27)=53.589, p<0.001$), such that both were higher in moderate (Intensity: $M=30.67, SD=3.31$ RPE: $M= 11.95, SD=1.72$), as compared to minimal exercise (Intensity: $M=10.80 SD=6.72$; RPE: $M= 9.07 SD=1.74$).

One-way repeated measures ANCOVA of difference scores on moderate and minimal conditions demonstrated that there was no significant interaction between order of sessions (i.e. whether participants engaged in moderate exercise or minimal exercise in the first session) and condition indicating that the order of sessions did not significantly impact the effect of exercise condition on Stroop interference ($F(1,25)=0.524, p=0.476$) or GNG RT ($p=0.194$). Mean Stroop Interference and GNG RT scores are presented in **Table 5**.

Table 5: Stroop interference and GNG RT by condition and time

	Moderate		Minimal	
	Pre	Post	Pre	Post
Stroop Interference (ms)	192.40 (172.09)	154.78 (135.98)	150.84 (233.69)	160.65 (161.09)
GNG RT (ms)	491.0 (61.77)	473.02 (56.44)	496.44 (62.6)	478.03 (51.76)

*values are mean (SD), higher values indicate weaker executive function

5.2.2 Stroop Effects

A 1-way repeated measures ANOVA was conducted to examine the impact of condition (moderate vs. minimal) on change in Stroop interference score. Analysis revealed no significant main effect for condition ($p=0.339$).

However, moderator analysis using repeated measures ANCOVA demonstrated a significant interaction between sex and condition ($F(1,25)=5.668, p=0.025$). To further understand the relationship between the effect of acute aerobic exercise on EF and sex, a stratified analysis was conducted in order to observe the effect of exercise on Stroop interference separately for male and female participants, using 1-way ANOVA of Stroop interference change scores. For male participants, there was no significant effect of condition on change in Stroop interference ($F(1,13)=0.660, p=0.431$); however, for female participants, there was a significant main effect of condition on change in Stroop interference ($F(1,12)=21.52, p=0.017$; see **Figure 1**) such that there was an increase in interference following minimal intensity exercise ($M_{min}=1.3, SD_{min}=1.99$) and a decrease following moderate ($M_{mod}=-0.518, SD_{mod}=1.60$). Further, the increase in Stroop interference following the minimal intensity exercise ($M_{pre}=0.219, SD_{pre}=2.24, M_{post}=1.52, SD_{post}=1.44$) was significant ($F(1,12)=5.566, p=0.036$), but there was no significant change in Stroop interference following moderate exercise condition ($p=0.265$). There was no significant interaction between order and condition for either male or female participants ($F(1,12)=0.481, p=0.753$, and $F(1,11)=0.549, p=0.168$ respectively) indicating that the order of sessions did not significantly impact the effect of exercise condition on Stroop interference.

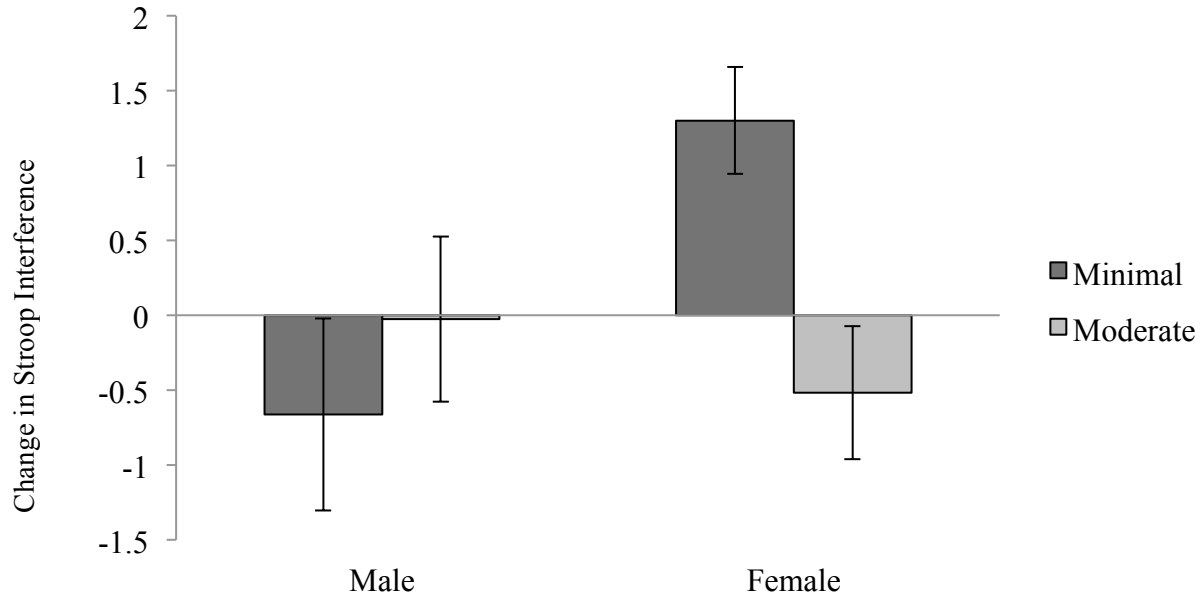


Figure 1: Stroop interference change by condition and sex

The above figure depicts change in Stroop interference (Post – Pre) following minimal and moderate intensity exercise for male ($n=14$) and female ($n=13$) participants separately, such that a positive score indicates an increase in interference and a negative score indicates a decrease. Note, that because higher Stroop interference indicates worse EF, a higher change score as depicted here indicates a decrease in EF following exercise. Error bars represent standard error.

Moderator analysis using repeated measures ANCOVA also demonstrated a significant interaction between hours of recent vigorous activity and condition ($F(1,25)=4.738, p=0.039$). To further understand the relationship between the effect of acute aerobic exercise on EF and hours vigorous physical activity in the past week, participants were separated into two groups based on hours of physical activity reported. Those reporting more than 1 hour of vigorous activity were considered active, while those reporting 1 hour of vigorous activity or less were categorized as inactive. A stratified analysis was conducted in order to observe the effect of exercise on Stroop interference separately for those active and inactive groups, using 1-way ANOVA of change scores. For inactive participants, there was no significant effect of condition on change in Stroop interference ($F(1,16)=0.089, p=0.770$); however, for active participants, there was a significant effect of condition on change in Stroop interference ($F(1,9)=5.538, p=0.043$; see **Figure 2**) such that there was an increase in Stroop interference following the minimal, but not moderate condition ($M_{\min}=1.45, SD_{\min}=1.89, M_{\text{mod}}=-0.3829, SD_{\text{mod}}=1.82$). This effect was characterized by a significant increase in

Stroop interference following minimal intensity exercise ($F(1,9)=5.87, p=0.038, M_{pre}=1.38, SD_{pre}=3.30$, and mitigation of this increase in the moderate condition ($p=0.330, M_{post}=2.84, SD_{post}=2.16$). There was no significant interaction between order and condition for inactive or active participants ($F(1,15)=2.040, p=0.174$, and $F(1,8)=0.674, p=0.435$ respectively).

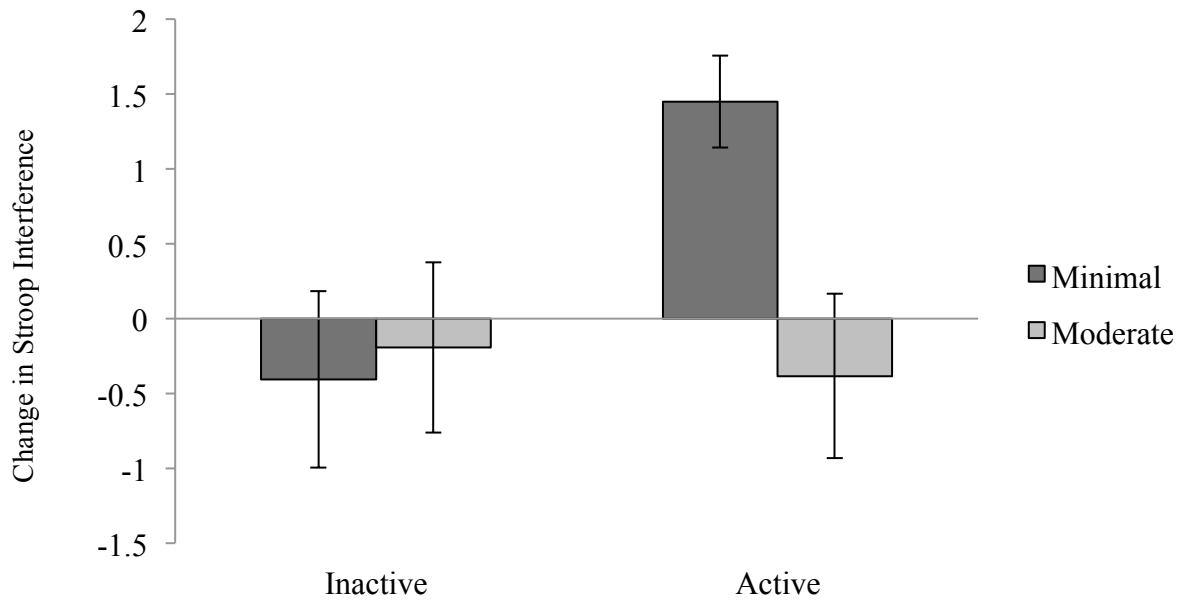


Figure 2: Stroop interference change by condition and activity status

The above figure depicts change in Stroop interference (Post – Pre) following minimal and moderate intensity exercise for inactive ($n=17$) and active ($n=11$) participants separately. Note that because higher Stroop interference indicates worse EF, a higher change score as depicted here indicates a decrease in EF following exercise. Error bars represent standard error.

There was no moderating effect of disease duration ($F(25,1)=0.590, p=0.449$), A1C ($F(14,1)=2.440, p=0.141$) or number of diabetes medications ($F(25,1)=0.520, p=0.478$).

5.2.3 GNG Effects

A 1-way repeated measures ANOVA was conducted to examine the impact of condition (moderate vs. minimal) on change in GNG RT score (calculated as post score – pre score). Analysis revealed no significant main effect of condition ($F(1,27)<0.001, p=0.994$). See **Table 2** for means. Moderator analysis using repeated measures ANCOVA demonstrated that there was no significant interaction between condition and sex ($F(1,26)=0.597, p=0.447$), hours of vigorous physical activity in the past

week ($F(1,26)=1.032, p=0.319$), T2DM duration ($F(1,26)=0.017, p=0.898$), A1C ($F(1,14)=0.590, p=0.455$), or number of T2DM medications ($F(1,26)=0.005, p=0.942$).

5.3 Discussion

The current study examined the effects of acute aerobic exercise (moderate and minimal) on EF task performance. Findings revealed a significant beneficial effect of moderate exercise on EF for women (but not men) and for active (but not inactive) individuals with T2DM. The effect of moderate exercise on cognition in women and among physically active individuals was characterized by mitigation of a significant increase in Stroop interference following the minimal intensity exercise condition. This finding can be explained within the context of the strength model of self-control. The strength model posits that self-control (similar to muscular strength) is a finite resource which can be depleted following exertion of concentration (Hagger & Chatzisarantis, 2013; Hagger, Wood, Stiff, & Chatzisarantis, 2010). The current study was cognitively demanding in that participants were required to maintain a specific number of revolutions per minute on the cycle ergometer; this self-regulatory effort may have resulted in self-regulatory fatigue, registering as decreased performance on the cognitive tasks from pre- to post-bout. This pre- to post-manipulation difference in task performance emerged in the minimal condition, but appeared to be eliminated in the moderate exercise condition. Together, this pattern of findings is consistent with reduction in self-regulatory fatigue following moderate exercise.

Along these lines, neuroimaging studies have demonstrated decreased activity in the anterior cingulate cortex (ACC; H. C. Leung, Skudlarski, Gatenby, Peterson, & Gore, 2000) as well as the DLPFC (Hedgcock, Vohs, & Rao, 2012) in association with self-regulatory fatigue. This is significant because of the DLPFC involvement in EF (and particularly Stroop performance), which has been demonstrated in both younger and older adults (Hyodo et al., 2012; Yanagisawa et al., 2010). Furthermore, increased activity in the PFC following exercise has been observed using fMRI and fNIRS, and this increase in activity is associated with improved performance of Stroop (Yanagisawa et al., 2010) and a working memory task (Tsujii, Komatsu, & Sakatani, 2013). These beneficial effects of acute aerobic exercise are hypothesized to rely on changes to neurotransmitter availability and/or thermoregulation and glucose distribution changes (Dietrich & Audiffren, 2011). Additionally, increased serum brain-derived neurotrophic factor (BDNF), a promoter of neuronal differential and survival, has been observed following acute aerobic exercise, and may contribute to beneficial effects of aerobic exercise in the longer term (Ferris, Williams, & Shen, 2007).

The T2DM population may be uniquely predisposed to self-regulatory fatigue following exercise, due to the possible mechanistic role of glucose in self-regulatory fatigue (Gailliot et al., 2007). Decreases in blood glucose (BG) following self-regulation, predictive ability of lower BG for self-regulatory fatigue, and restorative effects of glucose consumption have all contributed to the view that glucose depletion may serve as a mechanism for self-regulatory fatigue (Dewall, Baumeister, Gailliot, & Maner, 2008; Dvorak & Simons, 2009; Gailliot et al., 2007; Gailliot, Peruche, Plant, & Baumeister, 2009; C. M. Leung, Stone, Lee, Seidman, & Chen, 2014) and implies that a predisposition to decreased BG may increase the likelihood of experiencing self-regulatory fatigue. Among individuals with T2DM—but not healthy lean adults—acute aerobic exercise has been shown to increase metabolic clearance of glucose (Burstein, Epstein, Shapiro, Charuzi, & Karnieli, 1990) and decrease BG (Terada et al., 2013). This supports the contention that T2DM individual may be particularly susceptible to glucose depletion mediated self-regulatory fatigue following exercise. However, change in BG is highly variable and depends on a variety of factors such that a greater decrease in BG occurs for those with higher pre-exercise BG, those taking anti-hyperglycaemic medications, and food intake within the past 2 hours (Terada et al., 2013). Together these findings suggest that following acute aerobic exercise, individuals with T2DM may experience a greater decrease in glucose availability than is seen in the general population, and as a result, may be at greater risk of self-regulatory fatigue following exercise than healthy young or older adults.

A finding of self-regulatory fatigue following exercise was similarly proposed by Barella *et al.* (Barella et al., 2010) who suggested that self-regulatory fatigue or effort-reward imbalance contributed to null findings with respect to EF performance following 25 minutes of moderate intensity exercise and multiple repeated measures of the Stroop task in a group of older adults. Additionally, competing attention has been suggested as a possible explanation for the small decreased effect size in cognitive function during the initial phase of acute aerobic exercise (Lambourne & Tomporowski, 2010). While other studies have failed to demonstrate a self-regulatory fatigue effect following acute aerobic exercise (Ferris et al., 2007; Hyodo et al., 2012; Tsujii et al., 2013; Yanagisawa et al., 2010), ours is the first to examine this effect in a T2DM population, which has an arguably greater susceptibility to self-regulatory fatigue particularly following aerobic exercise.

With respect to the observed moderating effect of sex on the relationship, our findings illustrate that self-regulatory fatigue occurred among female, but not male participants. Evidence

suggests that sex differences exist with respect to the activation of neural pathways during self-control tasks (Diekhof et al., 2012). Similarly, Maluchenko *et al.* (Maluchenko et al., 2009) observed that while serotonin deficiency was associated with a lower threshold for self-regulatory fatigue in men, serotonin excess was associated with a lower threshold in women, thus suggesting that differences in mechanism of self-regulatory fatigue in men and women may exist. As such, it is possible that sex differences in degree of self-regulatory fatigue, or interaction of self-regulatory fatigue with exercise condition may account for this finding. Future research should examine the possibility of sex differences in neural activity during self-regulatory fatigue, particularly as it pertains to the effects of aerobic exercise.

With respect to physical activity status, a similar moderating effect was found whereby only physically active individuals displayed self-regulatory fatigue following minimal intensity aerobic exercise. In a meta-analysis of the effects of aerobic exercise on cognition, Chang *et al.* (Chang et al., 2012) found that physical fitness acted as a moderator of the effect such that during exercise low fit individuals displayed impaired and high fit displayed improved cognition, while following exercise improvement was observed in both groups. While overall the effects following exercise seemed to be consistent among high fit and low fit individuals, differences seen during exercise provide some evidence of differences between these two groups. Given that these studies typically compared low fit and high fit within a population of healthy individuals the effects of physical fitness may be exacerbated in the current study as the overall level of fitness was low and participants share a common disease status (T2DM). As such, we hypothesize that given the extreme lack of physical activity in our physically inactive group (less than or equal to 1 hour of vigorous activity per week) it is possible that even a minimal intensity of aerobic exercise (at an intensity of approximately 11%) may have been enough to produce aerobic exercise induced benefits. If this is the case, a lack of self-regulatory fatigue following minimal intensity exercise would be indicative of restorative effects resulting from minimal intensity exercise; however, future research is needed to establish whether acute minimal intensity exercise among a population of inactive individuals with T2DM induces cognitive benefits.

The discrepancy between GNG results and Stroop results in the current study suggest that even among response inhibition tasks there are differences in effect of exercise, a finding which is consistent with prior research (Audiffren, Tomporowski, & Zagrodnik, 2009). One reason for this inconsistency (even within response inhibition tasks) is the reliance of different tasks on different

cortical areas i.e. while Stroop relies primarily on the DLPFC as well as the ACC (Yanagisawa et al., 2010), GNG relies more so on the dorsal anterior cingulate cortex (dACC) (Welander-Vatn et al., 2013). Specifically, while a number of studies have shown improvement in Stroop performance (Chang et al., 2012; Hogervorst et al., 1996; Hyodo et al., 2012; Sibley et al., 2006; Tam, 2013; Yanagisawa et al., 2010) results for GNG have been inconsistent (Kamijo, Nishihira, Hatta, Kaneda, Wasaka, Kida, & Kuroiwa, 2004b; C. Lowe, Hall, Vincent, & Luu, 2014). This finding suggests that Stroop but not GNG performance is significantly improved following acute aerobic exercise; however future research is needed to confirm these findings.

5.3.1 Strengths and Limitations

The current study provides a preliminary look at the effects of acute aerobic exercise on EF in a population of adults with T2DM. The results of this study are strengthened by strict inclusion criteria to control for extraneous influences on EF and by the within-subject design which limits the influence of between subject variability. However, while individuals currently taking insulin or with a tendency for hypoglycaemic events were excluded from this study, a limitation of the study is a failure to measure blood glucose following exercise to ensure that hypoglycaemia had not been induced. Furthermore, although self-regulatory fatigue due to self-regulation during exercise provides a justifiable explanation of our findings the study was not specifically designed to induce self-regulatory fatigue. As such there may have been differences in the degree of self-regulatory fatigue following the minimal and moderate exercise conditions (possibly due to the target pedaling ranges). Finally, due to the preliminary nature of these results, the possibility of spurious findings cannot be excluded. Thus, these limitations provide opportunities for future studies to build on the results of the current study which provides an important first contribution to a previously unexamined population of interest for the effects of acute aerobic exercise on EF.

5.3.2 Conclusion

Findings indicated a significant (but selective) beneficial effect of moderate exercise on cognition compared to minimal exercise in individuals with T2DM. The cognitive benefit of exercise appeared to take the form of mitigation of self-regulatory fatigue effects. Considering the importance of EF and self-regulation for proper diabetes self-management, including physical activity performance, ability to make healthy dietary choices, and adherence to medication regimens, ability to mitigate self-regulatory fatigue resulting from numerous self-regulatory tasks may be of particular

importance in this population. Future research should aim to confirm and elaborate on these findings particularly with respect to the moderating effects of sex and physical activity level.

Chapter 6

Conclusions and Future Directions

The overarching aim of this thesis was to examine the interactions between T2DM, executive function, and acute aerobic exercise. In Study 1, the association between T2DM and EF impairment was examined using meta-analytic techniques, and results indicated that EF is in fact impaired among the T2DM population. This finding set the stage for Study 2, which examined the effects of acute aerobic exercise on EF in individuals living with T2DM. Analysis revealed a significant restorative effect of moderate aerobic exercise on the self-regulatory fatigue effect observed following exercise in female (but not male) and active (but not inactive) participants, and thus provides preliminary evidence of a significant (but selective) beneficial effect of aerobic exercise in individuals with T2DM.

In Study 1, a comprehensive meta-analysis of studies was conducted to compare EF task performance in individuals with T2DM to that in healthy individuals. Studies were included if they were case-control in nature and specifically compared EF in those with T2DM to those without. A total of 59 articles reporting on 60 studies were included in the analysis for a total sample of 9,815 individuals with T2DM and 69,254 controls. Meta-analysis of performance on all tasks proposed to measure EF using random effects modeling revealed a reliable impairment of EF associated with T2DM; the effect was small-to-moderate in size ($d=-0.248$, $p<0.001$). Moderators of the effect size included disease duration and age of participants, such that effects were stronger among those of shorter disease duration and younger age.

Study 1 presents a significant contribution to the field by illustrating a relative deficit in EF among a population of individuals who have an arguably greater need for EF in their everyday decision-making because of the importance of self-care behaviours in T2DM-management. However, the findings are limited by differences in definitions and verification of T2DM status. For example, a large number of studies rely solely on self-reported T2DM disease status. Given that there are few subjective signs of T2DM (IDF, 2013) there is a risk of misclassifying undiagnosed diabetes as no diabetes when relying on self-report. As such, inclusion of these studies may have resulted in an underestimation of the effect size. Furthermore, the cross-sectional nature of studies examined limits our interpretation to discussion of the association between T2DM and EF impairment. It is not possible to determine the directionality of this effect; however, for the purpose of this thesis project and with respect to public health measures, the association between T2DM and EF impairment is

relevant regardless of directionality because it implies a deficit in EF among a population who is heavily reliant on this resource for proper disease management and prevention of complications.

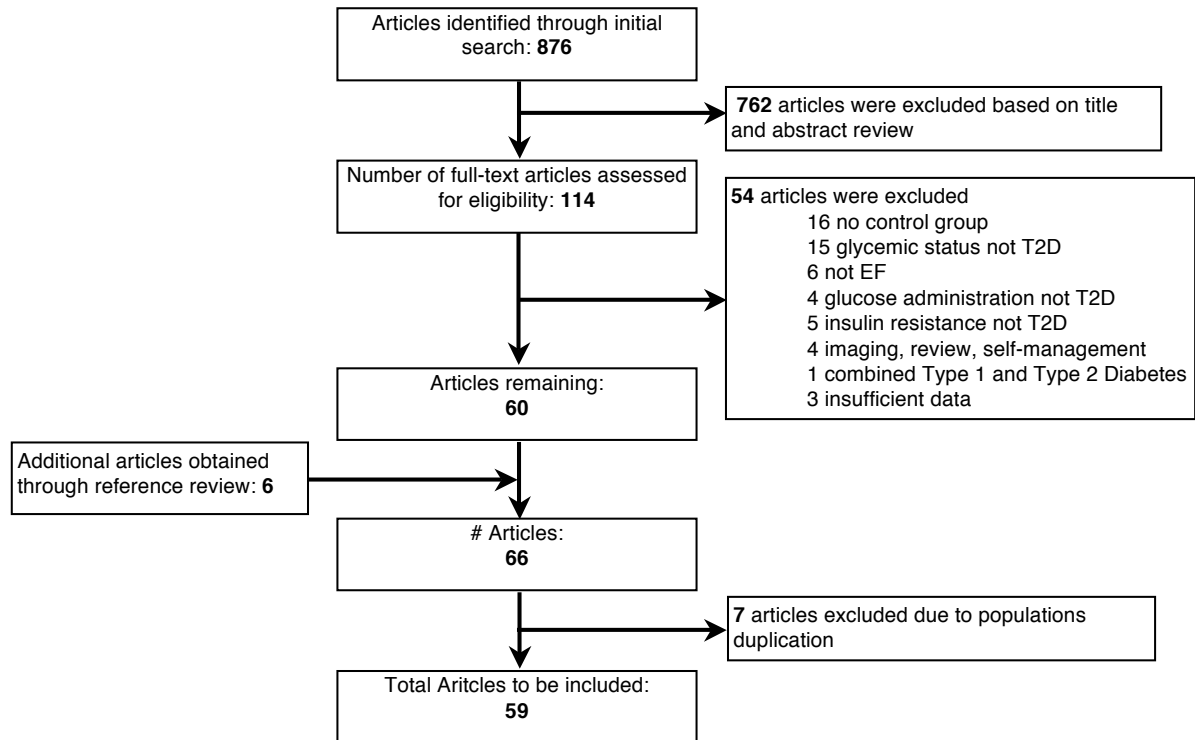
Study 2 then aimed to examine the effects of acute aerobic exercise on EF in those with T2DM. Significant improvements in EF have been observed following acute aerobic exercise in healthy young and older adult populations; however, this effect had not yet been examined in the T2DM population, a population that, as Study 1 demonstrates, has a lower baseline EF and therefore potentially greater need of EF-enhancing strategies. Findings indicate a significant selective beneficial effect of moderate intensity aerobic exercise on EF, such that in female participants and those who were recently active, a restorative effect over self-regulatory fatigue was observed.

While study 2 provides important preliminary evidence of a significant (albeit selective) effect of aerobic exercise on EF in those living with T2DM, the study is limited by lack of blood glucose monitoring following exercise to ensure hypoglycemia was not induced. As well, the fact that study 2 was not designed to induce self-regulatory fatigue may have resulted in differences between the degree of self-regulatory fatigue induced by the two sessions (possibly due to different pedaling ranges). However, overall the difference in self-regulatory fatigue between sessions is believed to be small given the high degree of similarity between sessions.

The current studies contribute novel findings to a relatively new area of research surrounding EF in individuals with T2DM. These findings may hold significant potential to guide development of methods to improve EF in individuals with T2DM and subsequent T2DM management; however, additional research is needed. Future research should endeavor to 1) determine the directionality of effect of the association between T2DM and EF; 2) determine whether, under conditions not resulting in self-regulatory fatigue, there is an improvement in EF following moderate physical activity; 3) confirm restorative effects of acute aerobic exercise on self-regulatory fatigue; 4) characterize and confirm interactive effects between self-regulatory fatigue, acute aerobic exercise, and sex or physical activity status.

Appendix A

Meta-Analysis Article Inclusion Flow Chart



Appendix B

Meta-Analysis Article Included Studies Characteristics

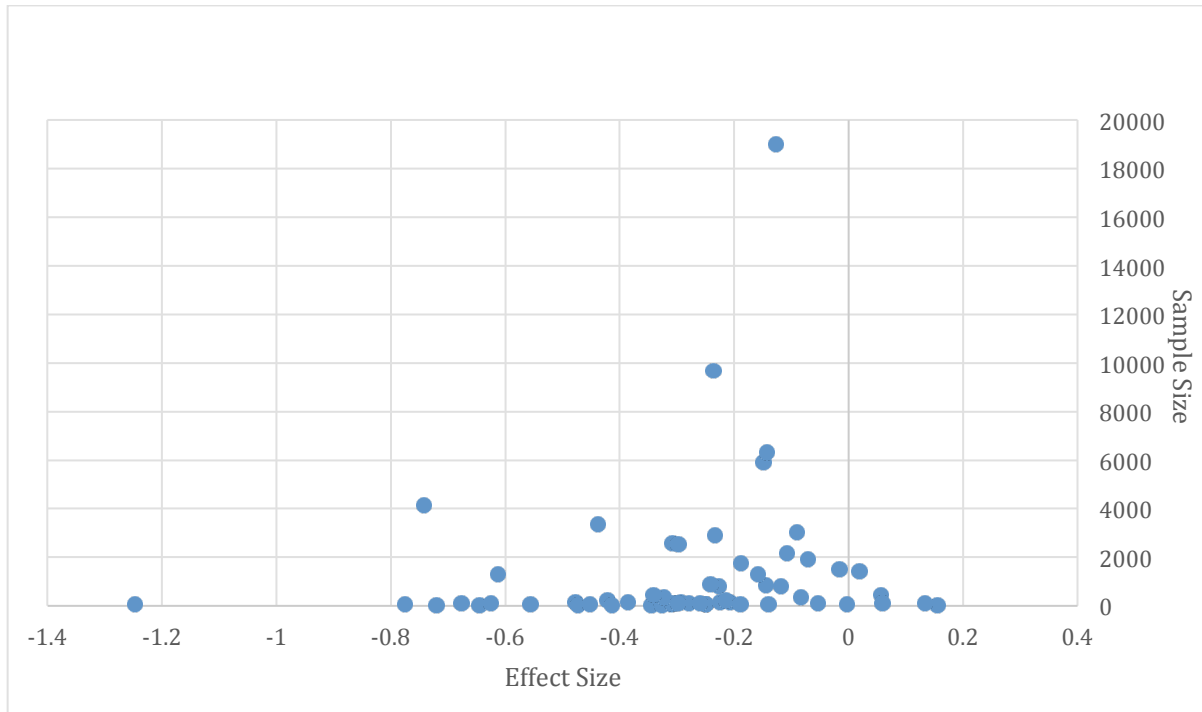
First Author, year	T2DM					Controls				Confirm ND
	N	Age	%M	Education	Duration	N	Age	%M	Education	
Aberle, 2008	38	62.9	52.6	9.9	8.53	421	63.97	50.4	9.9	No
Ajilore, 2010	26	57.8	31	14.58	9.85	20	55.2	25	15.2	No
Alosco, 2012	110	68.9	64.4	12.9	-	59	11.18	66.4	13.7	No
Alvarenga, 2010	20	71	85	-	-	20	68.4	80	-	Yes
Arvanitakis, 2004	127	74.4	44.9	-	-	697	75.2	28.7	-	No
Arvanitakis, 2010	220	75.9	37.7	13.9	-	1217	78.8	25.1	14.6	No
Assisi, 1996	12	60.5	-	8.9	11	17	61.6	-	8.7	Yes
Atiea, 1995	40	69.1	70	-	10.05	20	68.1	65	-	No
Brands, 2007	119	65.9	52	-	8.7	55	65.2	44	-	Yes
Bruehl, 2009	41	60.0	51.1	15.0	7	47	59.1	53.7	15.8	Yes
Cooray, 2011	28	61	54	12	9.8	21	59	38	14	No
Cosway 2001	37	57.7	42.1	11.2	6	38	55.9	39.5	11.8	Yes
Espeland, 2011	179	-	0	-	-	1984	-	0	-	No
Fontbonne, 2001	55	65.3	71	-	-	768	64.9	41	-	Yes
Gallacher, 2005	165	-	100	-	-	1573	-	100	-	Yes
Gregg, 2000	682	71.8	0	-	10.2	8997	71.7	0	-	No
Hassing, 2004	69	83.5	38.9	7.1	7.4	268	82.7	27.7	7.2	No
Helkala, 1995	20	66.2	65	-	10.5	22	64.5	63.6	-	Yes
Hudetz, 2007	30	64.5	100	-	-	30	61.5	100	-	No
Ishizawa, 2010	27	45.9	100	16.1	0	27	36.8	100	16.7	No
Krannich, 2012	10	-	100	-	-	20	-	100	-	Yes
Lindeman, 2001	188	73.4	-	11.2	-	651	74	-	10.9	Yes
Logroscino, 2004	1394	74.2	0	-	12	1760 5	74.2	0	-	No
Lowe, 1994	80	59.3	25	-	6.9	81	55.1	46.9	-	Yes
Maggi, 2009	399	71.8	-	-	12.15	2638	71.6	-	-	Yes
Mattlar, 1985	33	56.3	66.7	-	-	33	55.9	66.7	-	Yes
Mehrabian, 2012	37	56	46	14	7	22	56	41	14	No
Mooradian, 1988	43	66.3	100	-	13.3	41	65.3	100	-	Yes
Mussell,	26	-	-	-	-	13	-	-	-	No
Nandipati, 2012	306	74.7	43	14.7	-	3035	74.1	34.9	15.6	No

First Author, year	T2DM					Controls				Confirm ND
	N	Age	%M	Education	Duration	N	Age	%M	Education	
Nooyens, 2010	61	60.6	49.1	-	-	2538	55.07	50.8	-	Yes
Okereke, 2008a	553	74.3	100	-	-	5354	74.1	100	-	No
Okereke, 2008b	405	71.5	0	-	-	5921	71.9	0	-	No
Pavik, 2005	131	46.4	43.4	10.8	-	2408	41.0	47.7	13.1	No
Perlmutter, 1984	140	64.3	54	11.7	-	38	63.1	43	12.4	Yes
Perlmutter, 1987	174	64.5	-	-	-	38	62.6	-	-	Yes
Reaven, 1990	29	69.8	65.5	14.7	-	30	68	53.3	15	Yes
Reijmer, 2013	35	71.1	57	-	8.6	35	71	60	-	Yes
Rouch, 2012	12	-	50	-	-	151	-	40.4	-	Yes
Ruis, 2009	183	63	61.2	-	3.5	69	62.7	47.8	-	Yes
Ryan, 2000	50	50.8	30	14.4	8.1	50	50.5	24	14	No
Saczynski, 2008	218	75.7	55.5	-	-	1699	75.7	39.98	-	Yes
Scott, 1998	1331	68.6	51.1	-	14.6	178	74.9	40.8	-	Yes
Silva, 2012	50	70.1	34	-	-	50	70.8	20	-	Yes
Solanki, 2009	50	-	-	-	-	30	-	-	-	No
Spauwen, 2012	68	68.8	50.0	-	-	1222	59.4	50.3	-	No
Takayanagi, 2012	161	45.9	69	12	-	1128	39.6	76	12.2	Yes
Takeuchi, 2012	42	62.4	61.9	13.7	11.5	32	63.8	56.3	14.5	Yes
U'Ren, 1990	26	70	11.5	12	8.77	19	71	15.8	14	Yes
van den Berg, 2010	68	65.6	47	-	9.1	38	64.8	50	-	Yes
van Eersel, 2013	264	64	63	-	-	3871	54	51	-	Yes
Vanhanen, 1997	35	67.1	37.1	7.2	-	48	63.9	31.3	7.3	Yes
Vanhanen, 1999	183	73.3	35.5	5.9	-	732	73.2	34.9	6.9	Yes
van Harten, 2007	92	73.2	43.5	4.0	-	44	72.9	45.5	4.5	Yes
Wahlin, 2002	31	85	7	8.4	-	307	84.3	20	8.7	No
Watari, 2006	20	58.9	35	14.9	-	34	61.0	44	15.4	No
Watari, 2008	23	58.7	35	15.04	-	22	52.6	18	-	No
Wysokinski, 2010	31	46.7	74.2	-	-	50	31.5	50	-	No
Yaffe, 2012	717	74.1	54.5	-	-	2193	74.2	46.5	-	Yes
Yeung, 2009	41	68.6	56.13	15.1	8.29	424	67.8	69.3	15.3	No
Overall	9815	69.9	51.3	11.9	8.91	6925 4	65.1	47.49	12.3	-

N = number of participants; M = male; ND = No Diabetes.

Appendix C

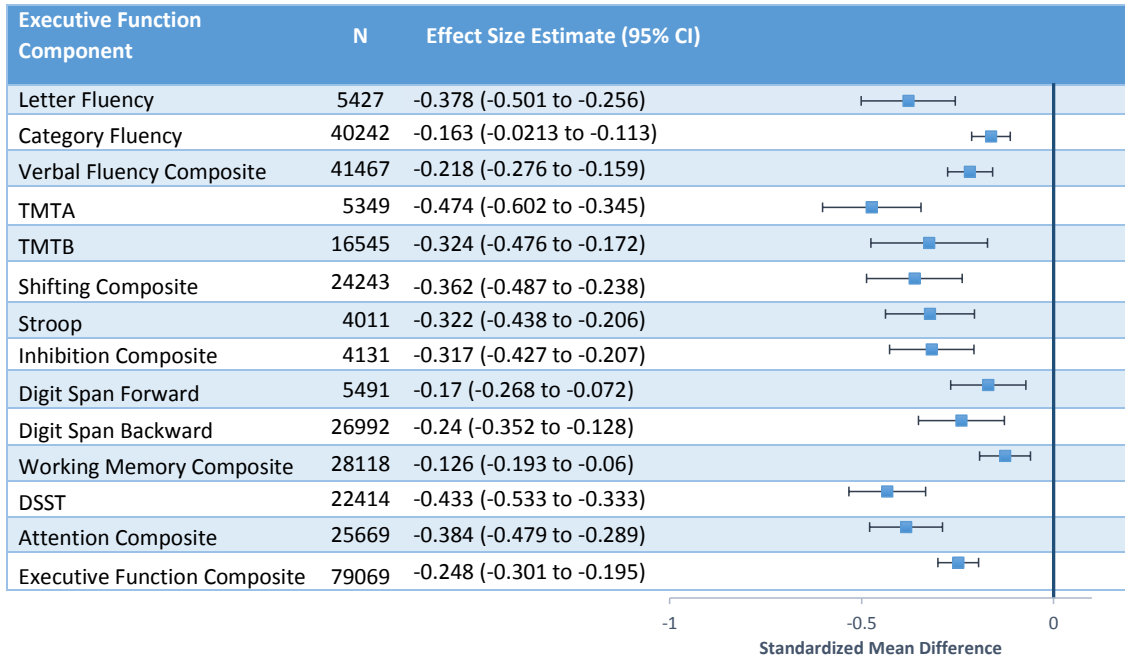
Funnel Plot for Overall Effect Size of T2DM-EF Association



This funnel plot depicts study effect size by sample size for all studies included in the meta-analysis. The asymmetrical nature of the plot could indicate the presence of publication bias as larger scale studies typically demonstrated a smaller effect size than smaller scale studies. However, another possible explanation for this asymmetry is that smaller scale studies were conducted with more rigorous methods. For example, differences in study quality such as matching on relevant characteristics such as age, sex, and education, as well as, exclusion of potentially confounding disorders such as hypertension, cerebrovascular disease or other cognitive disorders may have occurred differentially in small-moderate sized studies for logistical reasons. The degree to which this may have occurred or the impact that this would have had on effect size is unknown; however, the use of self-report T2DM status by larger scale trials presents one explanation of the asymmetry of this funnel plot.

Appendix D

Meta-Analysis Forest Plot of Effect Size by EF Category



Appendix E

PAR-Q

Physical Activity Readiness
Questionnaire - PAR-Q
(revised 2002)

PAR-Q & YOU

(A Questionnaire for People Aged 15 to 69)

Regular physical activity is fun and healthy, and increasingly more people are starting to become more active every day. Being more active is very safe for most people. However, some people should check with their doctor before they start becoming much more physically active.

If you are planning to become much more physically active than you are now, start by answering the seven questions in the box below. If you are between the ages of 15 and 69, the PAR-Q will tell you if you should check with your doctor before you start. If you are over 69 years of age, and you are not used to being very active, check with your doctor.

Common sense is your best guide when you answer these questions. Please read the questions carefully and answer each one honestly: check YES or NO.

YES	NO	
<input type="checkbox"/>	<input type="checkbox"/>	1. Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor?
<input type="checkbox"/>	<input type="checkbox"/>	2. Do you feel pain in your chest when you do physical activity?
<input type="checkbox"/>	<input type="checkbox"/>	3. In the past month, have you had chest pain when you were not doing physical activity?
<input type="checkbox"/>	<input type="checkbox"/>	4. Do you lose your balance because of dizziness or do you ever lose consciousness?
<input type="checkbox"/>	<input type="checkbox"/>	5. Do you have a bone or joint problem (for example, back, knee or hip) that could be made worse by a change in your physical activity?
<input type="checkbox"/>	<input type="checkbox"/>	6. Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition?
<input type="checkbox"/>	<input type="checkbox"/>	7. Do you know of any other reason why you should not do physical activity?

**If
you
answered**

YES to one or more questions

Talk with your doctor by phone or in person BEFORE you start becoming much more physically active or BEFORE you have a fitness appraisal. Tell your doctor about the PAR-Q and which questions you answered YES.

- You may be able to do any activity you want — as long as you start slowly and build up gradually. Or, you may need to restrict your activities to those which are safe for you. Talk with your doctor about the kinds of activities you wish to participate in and follow his/her advice.
- Find out which community programs are safe and helpful for you.

NO to all questions

If you answered NO honestly to all PAR-Q questions, you can be reasonably sure that you can:

- start becoming much more physically active — begin slowly and build up gradually. This is the safest and easiest way to go.
- take part in a fitness appraisal — this is an excellent way to determine your basic fitness so that you can plan the best way for you to live actively. It is also highly recommended that you have your blood pressure evaluated. If your reading is over 144/94, talk with your doctor before you start becoming much more physically active.

DELAY BECOMING MUCH MORE ACTIVE:

- if you are not feeling well because of a temporary illness such as a cold or a fever — wait until you feel better; or
- if you are or may be pregnant — talk to your doctor before you start becoming more active.

PLEASE NOTE: If your health changes so that you then answer YES to any of the above questions, tell your fitness or health professional. Ask whether you should change your physical activity plan.

Informed Use of the PAR-Q: The Canadian Society for Exercise Physiology, Health Canada, and their agents assume no liability for persons who undertake physical activity and if in doubt after completing this questionnaire, consult your doctor prior to physical activity.

No changes permitted. You are encouraged to photocopy the PAR-Q but only if you use the entire form.

NOTE: If the PAR-Q is being given to a person before he or she participates in a physical activity program or a fitness appraisal, this section may be used for legal or administrative purposes.

"I have read, understood and completed this questionnaire. Any questions I had were answered to my full satisfaction."

NAME _____

SIGNATURE _____

DATE _____

SIGNATURE OF PARENT
or GUARDIAN (for participants under the age of majority) _____

WITNESS _____

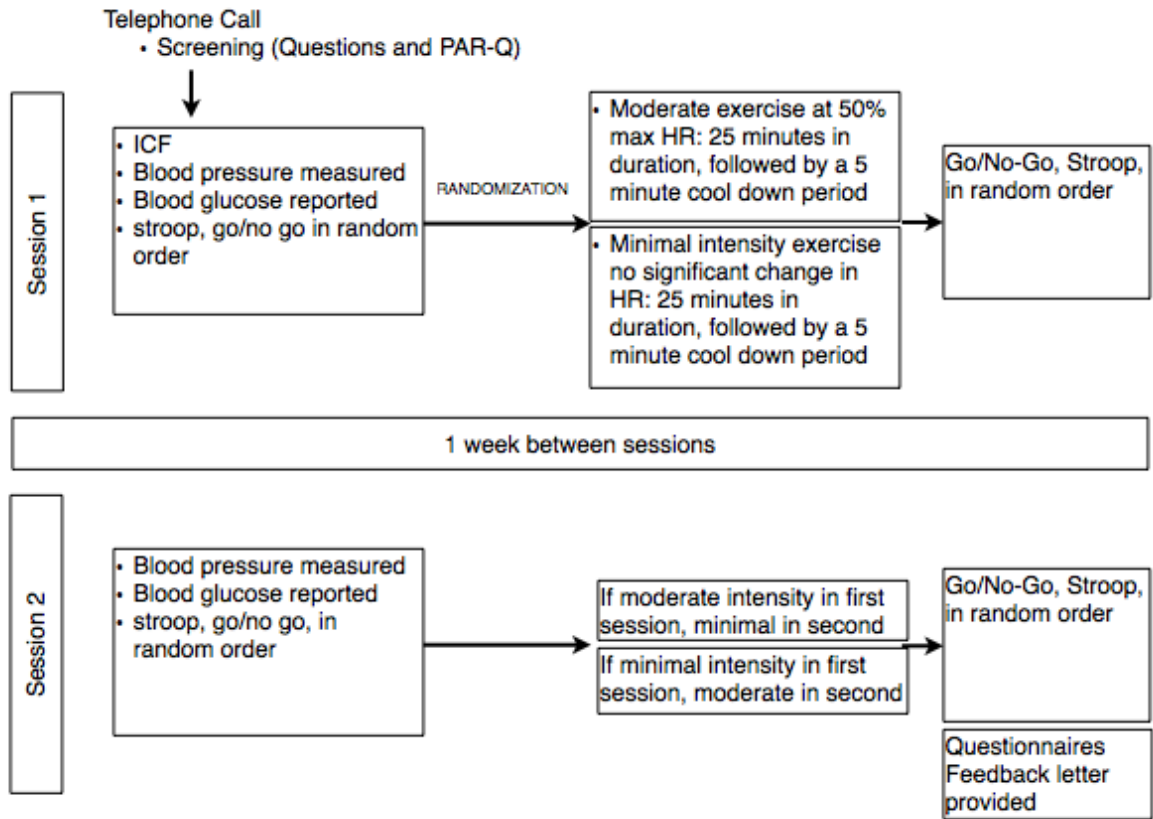
Note: This physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if your condition changes so that you would answer YES to any of the seven questions.



© Canadian Society for Exercise Physiology www.csep.ca/forms

Appendix F

Acute Aerobic Exercise and EF in T2DM Project Overview



Appendix G

Consent Form



Information and Consent Letter

Study Title: Aerobic Exercise and Executive Control Resources in Type 2 Diabetes

Principal Investigator: Dr. Peter Hall, Social Neuroscience and Health Laboratory, Department of Kinesiology (pahall@uwaterloo.ca, 519-888-4567 ext. 38110)

Student Investigators: Corita Vincent (cmvincen@uwaterloo.ca, 519-888-4567 ext. 38180); Cassandra Lowe (c2lowe@uwaterloo.ca), School of Public Health and Health Systems

You have been invited to participate in a research project assessing the effects of exercise on thinking skills in individuals with Type 2 Diabetes. The study consists of two in-laboratory sessions with one week between them. Each session will take approximately 2 hours to complete.

Procedure:

During the first laboratory session, you will be asked to complete two different computer tasks designed to measure cognitive function, as well as, a test of general intellectual ability. You will be asked to complete these tasks prior to and following the exercise session. For the first computer task you will be asked to hit a key whenever a lower case letter is presented on the screen and refrain from hitting anything when an upper case letter is presented. For the second task you will be asked to indicate the colour of a word (or string of characters) that appears on the screen. The last task is a set of 4 tests that involve thinking about informational questions, reasoning, completing patterns with blocks and working through visual puzzles. You will be asked to complete 2 of the 4 tests before the exercise activity. Together, the tasks take about 45 minutes to complete. Following exercise, you will be asked to complete the other 2 components of the last task and you will be asked to repeat first 2 tasks.

During the exercise phase of the study, you will be randomly assigned to one of the following exercise activities: (1) moderate intensity exercise (2) minimal intensity exercise. For the exercise session, you will be taken to the fitness facilities at the Lyle Hallman Institute for Health Promotion, where you will meet with a research assistant who is trained in conducting fitness assessments and overseeing fitness training for individuals with Type 2 Diabetes. The exercise activity itself will be 25 minutes in duration, including a 5 minute warm-up and will be followed by a 5 minute cool down period. For the moderate intensity exercise session, you will be asked to cycle on a cycle ergometer (stationary bike with an ergometer to measure work done by exerciser) and will be supervised until you gradually increase the intensity of your exertion up to a value of 30% of your maximal heart rate reserve. Maximal heart rate reserve will be calculated as 30% of the difference between resting heart rate and maximal heart rate. Maximal heart rate will be determined using the following formula, $220 - \text{your age}$. For example, if you are 60 years old your maximal heart rate would be $220 - 60$. The protocol for the minimal intensity exercise activity will be identical to the moderate intensity exercise, but you will be asked to cycle at a slow and steady pace without significantly increasing your heart rate.

During exercise, your heart rate will be monitored using a heart rate monitor and your heart rate will be displayed on the exercise bike and on the heart rate monitor watch. A researcher will record your heart rate throughout the exercise session.

All exercise activities will be performed at the University of Waterloo in the LHI Fitness Centre.

Immediately after the exercise activity, you will be brought back to the laboratory and asked to complete the 3 cognitive function tasks. These tasks will be similar to the ones that you completed prior to the exercise session.

During your second laboratory session one week later, the procedure will be the same; however, if you did the moderate intensity exercise during the first session, you will do the minimal intensity exercise during the second session. If you did the minimal intensity exercise during the first session, you will do the moderate intensity exercise during the second. All other aspects of the session will be the same. Additionally, at the end of the second laboratory session, you will be asked to fill out

several questionnaires. Questions will be on items such as frequency of exercise, dietary behaviours, personality, and demographics (such as gender, age, and race). These questions will help to understand whether the relationship between thinking skills and exercise in Type 2 diabetic individuals may be different in individuals with different characteristics (ex. differences according to gender, age, ethnicity, frequency of exercise, etc.).

Participation and Remuneration:

You will receive a gift certificates for your participation, a \$20 gift card following the first session, and a \$30 gift card for the second.

Your participation is completely voluntary and you may withdraw from this study or decline answering any questions with no penalty. Withdrawal from the study may occur at any time and you will still receive the gift card for that session.

By signing this consent form, you are not waiving your legal rights or releasing the investigator(s) or involved institution(s) from their legal and professional responsibilities.

Confidentiality and security of data

All information that is gathered during this study will remain confidential; at no time will your name be associated with any of the data or information. All information will be encrypted and stored on a password-protected lab server; the data key linking this information to any identifiable information will be retained in a locked cabinet in the University of Waterloo Social Neuroscience and Health Lab (BMH 1013) where only authorized researchers will have access, and will be destroyed 1 year following study completion.

Risks to Participant: It is possible that, during the exercise session, you may feel uncomfortable or become fatigued. If you experience discomfort during the exercise session, you are encouraged to stop the exercise and inform the fitness instructor who is with you. There is a small risk of experiencing a heart attack, cardiac arrest, or hypoglycaemic event while exercising. Both LHI fitness staff and the researcher overseeing your exercise session have CPR and first aid certification. Again, you are encouraged to stop the exercise and inform the fitness instructor if you feel uncomfortable, experience chest pain, dizziness, or become fatigued.

Benefits to Participant: This study will not provide any direct benefit to you.

Benefits to Society: The information gained through this study will lead to better understanding of the effects of exercise on thinking skills in individuals with type 2 diabetes in your age range. Increased understanding of this relationship may lead to the development of new interventions involving exercise for type 2 diabetics in the future.

Concerns about Participation

This study has been reviewed and received ethics clearance through the Office of Research Ethics. However, the final decision about participation is yours. If you have any comments or concerns resulting from your participation in this study, you may contact the Director of the Office of Research Ethics, Maureen Nummelin by phone, (519) 888-4567 ext. 36005, or email, maureen.nummelin@uwaterloo.ca.

CONSENT FORM

I agree to take part in a research study being conducted by Dr. Peter Hall, Corita Vincent, and Cassandra Lowe of the Department of Kinesiology and School of Public Health and Health Systems, University of Waterloo.

I have made this decision based on the information I have read in the information letter. All the procedures, any risks and benefits have been explained to me. I have had the opportunity to ask any questions and to receive any additional details I wanted about the study. If I have questions later about the study, I can ask one of the researchers. I am aware that I may withdraw from the study at any time without penalty by telling the researcher.

I understand that by signing this consent form, I am **not** waiving my legal rights or releasing the investigator(s) or involved institution(s) from their legal and professional responsibilities.

This project has been reviewed by, and received ethics clearance through, the Office of Research Ethics at the University of Waterloo. I am aware that I may contact the Director of the Office of Research Ethics, Maureen Nummelin, by phone: (519) 888-4567 ext. 36005 or email: maureen.nummelin@uwaterloo.ca if I have any concerns or questions resulting from my involvement in this study.

With full knowledge of all foregoing, I agree of my own free will, to participate in this study.

Signature of volunteer _____ Print name _____

Signature of witness _____ Print name _____

Signature of investigator _____ Print name _____

Date _____

Appendix H

Demographic and Health Behaviour Questionnaires

The Summary of Diabetes Self-Care Activities (Toolbert et al. 2000)

The questions below ask you about your diabetes self-care activities during the past 7 days. If you were sick during the past 7 days, please think back to the last 7 days that you were not sick.

Diet

How many of the last SEVEN DAYS have you followed a healthful eating plan?

0 1 2 3 4 5 6 7

On average, over the past month, how many DAYS PER WEEK have you followed your eating plan?

0 1 2 3 4 5 6 7

On how many of the last SEVEN DAYS did you eat five or more servings of fruits and vegetables?

0 1 2 3 4 5 6 7

On how many of the last SEVEN DAYS did you eat high fat foods such as red meat or full-fat dairy products?

0 1 2 3 4 5 6 7

Exercise

On how many of the last SEVEN DAYS did you participate in at least 30 minutes of physical activity? (Total minutes of continuous activity, including walking).

0 1 2 3 4 5 6 7

On how many of the last SEVEN DAYS did you participate in a specific exercise session (such as swimming, walking, biking) other than what you do around the house or as part of your work?

0 1 2 3 4 5 6 7

Blood Sugar Testing

On how many of the last SEVEN DAYS did you test your blood sugar?

0 1 2 3 4 5 6 7

On how many of the last SEVEN DAYS did you test your blood sugar the number of times recommended by your health care provider?

0 1 2 3 4 5 6 7

Foot Care

On how many of the last SEVEN DAYS did you check your feet?

0 1 2 3 4 5 6 7

On how many of the last SEVEN DAYS did you inspect the inside of your shoes?
0 1 2 3 4 5 6 7

Smoking

Have you smoked a cigarette—even one puff—during the past SEVEN DAYS?

0. No

1. Yes. If yes, how many cigarettes did you smoke on an average day?

Number of cigarettes: _____

Additional Items for the Expanded Version of the Summary of Diabetes Self-Care Activities.

Self-Care Recommendations

1A. Which of the following has your health care team (doctor, nurse, dietitian, or diabetes educator) advised you to do?

Please check all that apply:

- a. Follow a low-fat eating plan
- b. Follow a complex carbohydrate diet
- c. Reduce the number of calories you eat to lose weight
- d. Eat lots of food high in dietary fiber
- e. Eat lots (at least 5 servings per day) of fruits and vegetables
- f. Eat very few sweets (for example: desserts, non-diet sodas, candy bars)
- g. Other (specify): _____
- h. I have not been given any advice about my diet by my health care team.

2A. Which of the following has your health care team (doctor, nurse, dietitian or diabetes educator) advised you to do?

Please check all that apply:

- a. Get low level exercise (such as walking) on a daily basis.
- b. Exercise continuously for a least 20 minutes at least 3 times a week.
- c. Fit exercise into your daily routine (for example, take stairs instead of elevators, park a block away and walk, etc.)
- d. Engage in a specific amount, type, duration and level of exercise.
- e. Other (specify): _____
- f. I have not been given any advice about exercise by my health care team.

3A. Which of the following has your health care team (doctor, nurse, dietitian, or diabetes educator) advised you to do?

Please check all that apply:

- a. Test your blood sugar using a drop of blood from your finger and a color chart.
- b. Test your blood sugar using a machine to read the results.
- c. Test your urine for sugar.
- d. Other (specify): _____
- e. I have not been given any advice either about testing my blood or urine sugar level by my health care team.

4A. Which of the following medications for your diabetes has your doctor prescribed?

Please check all that apply.

- a. An insulin shot 1 or 2 times a day.
- b. An insulin shot 3 or more times a day.
- c. Diabetes pills to control my blood sugar level.
- d. Other (specify): _____
- e. I have not been prescribed either insulin or pills for my diabetes.

Diet

5A. On how many of the last SEVEN DAYS did you space carbohydrates evenly through the day?

0 1 2 3 4 5 6 7

Medications

6A. On how many of the last SEVEN DAYS, did you take your recommended diabetes medication?

0 1 2 3 4 5 6 7

OR

7A. On how many of the last SEVEN DAYS did you take your recommended insulin injections?

0 1 2 3 4 5 6 7

8A. On how many of the last SEVEN DAYS did you take your recommended number of diabetes pills?

0 1 2 3 4 5 6 7

Foot Care

9A. On how many of the last SEVEN DAYS did you wash your feet?

0 1 2 3 4 5 6 7

10A. On how many of the last SEVEN DAYS did you soak your feet?

0 1 2 3 4 5 6 7

11A. On how many of the last SEVEN DAYS did you dry between your toes after washing?

0 1 2 3 4 5 6 7

Smoking

12A. At your last doctor's visit, did anyone ask about your smoking status?

0. No

1. Yes

13A. If you smoke, at your last doctor's visit, did anyone counsel you about stopping smoking or offer to refer you to a stop-smoking program?

0. No

1. Yes

2. Do not smoke.

14A. When did you last smoke a cigarette?

- More than two years ago, or never smoked
- One to two years ago
- Four to twelve months ago
- One to three months ago
- Within the last month
- Today

Demographics Questionnaire

Age in years: _____

Height: _____ (feet) _____ (inches)

Weight _____ (lbs)

Gender: Male Female

5. 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 +

6. Level of Education:

- Some Elementary School
- Completed Elementary School
- Some High School
- Completed High School
- Some College/University
- Completed College/University
- Graduate Studies

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

8. Relationship status:

- Single
- Common law
- Married
- Separated
- Divorced

Physical Activity Theory of Planned Behaviour Questionnaire

The following questions pertain to exercise that will help us understand how the relationships found in this study may vary according to exercise habits. You may decline to answer any questions. Your information will be kept confidential.

1. Exercising daily would be...

Extremely pleasant Somewhat pleasant Neutral Somewhat unpleasant Extremely unpleasant

2. Exercising daily would be...

Extremely boring Somewhat boring Neutral Somewhat fun Extremely fun

3. Exercising Daily would be...

Extremely positive Somewhat positive Neutral Somewhat negative Extremely negative

4. Exercising daily would be...

Extremely satisfying Somewhat satisfying Neutral Somewhat dissatisfying Extremely dissatisfying

5. Exercising daily would be...

Extremely unappealing Somewhat unappealing Neutral Somewhat appealing Extremely appealing

6. Do most people who are important to you think you should or should not exercise?

Strongly think I should Neutral Strongly think I should not

7. How much control do you think you have over whether or not you exercise daily? (from 0-100%): _____ %

8. To what extent do you intend to exercise on a daily basis over the next month?

Not at all Moderately Very Strongly

9. How confident are you that you can exercise on a daily basis? (from 0 - 100%):

_____ %

10. How energetic have you felt over the past week?

Not at all energetic



Moderately



Extremely Energetic



Physical Activity Self Report Habit Index

The following questions pertain to exercise frequency and will help us understand how the relationships found in this study may vary according to exercise habits. You may decline to answer any questions. Your information will be kept confidential.

1. For the next 12 questions, please respond to each statement on a scale from 1 to 7, with a response of 1 indicating you do not agree at all, and a response of 7 indicating you totally agree.

Physical Activity is...

	Disagree			Neutral			Agree		
something I do frequently	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
something I do automatically	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
something I do without having to consciously remember	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
something that makes me feel weird if I do not do it	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
something I do without thinking	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
something that would require effort not to do	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
something that belongs in my daily routine	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
something I start doing before I realize I'm doing it	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
something I would find hard not to do	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
something I have not need to think about doing	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
something that's typically "me"	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
something I have been doing for a long time	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Physical Activity Frequency, Intention, & Action

During the NEXT WEEK, how much total time do you plan to spend doing VIGOROUS physical activity and MODERATE physical activity? Record only time that you plan to actually engage in the activity (ignore breaks, rest periods, etc.). Please do not record any LIGHT physical activity (office work, light housework, very light sports such as bowling, or any activities involving sitting).

1. VIGOROUS ACTIVITY (activity that causes your heart rate to be significantly increased and causes you to breathe so heavily that it is difficult to carry on a conversation). Total hours for next 7 days to nearest 1/2 hour: _____ hr(s)
2. MODERATE ACTIVITY (activity that causes noticeable increase in heart rate and breathing rate but you can still carry out a conversation) Total hours for next 7 days to nearest 1/2 hour: _____ hr(s)

During the PAST WEEK, how much total time did you spend doing VIGOROUS physical activity and MODERATE physical activity? Record only time that you actually engaged in the activity (ignore breaks, rest periods, etc.). Please do not record any LIGHT physical activity (office work, light housework, very light sports such as bowling, or any activities involving sitting).

3. VIGOROUS ACTIVITY (activity that causes your heart rate to be significantly increased and causes you to breathe so heavily that it is difficult to carry on a conversation) Total hours for past 7 days to nearest 1/2 hour: _____ hr(s)
4. MODERATE ACTIVITY (activity that causes noticeable increase in heart rate and breathing rate but you can still carry out a conversation) Total hours for past 7 days to nearest 1/2 hour: _____ hr(s)

PLEASE READ THIS CAREFULLY: SOMETIMES THERE IS A DIFFERENCE BETWEEN HOW MANY HOURS SOMEONE INTENDS TO EXERCISE AND HOW MANY HOURS THEY PREDICT THAT THEY WILL ACTUALLY EXERCISE. PLEASE ANSWER THE FOLLOWING TWO QUESTIONS BASED ON HOW MANY HOURS YOU PREDICT THAT YOU WILL EXERCISE OVER THE NEXT 7 DAYS, REGARDLESS OF HOW MANY HOURS YOU PLAN TO EXERCISE OVER THE NEXT 7 DAYS.

6. How many hours of VIGOROUS intensity activities do you PREDICT that you will engage in over the NEXT SEVEN (7) DAYS? (Total number of hours to nearest 1/2 hour): _____ hr(s)
7. How many hours of MODERATE intensity activities do you PREDICT that you will engage in over the NEXT SEVEN (7) DAYS (Total number of hours to nearest 1/2 hour): _____ hr(s)

Block Fat Screener (Block 2000)

Think about all the foods you ate over the PAST 7 days as part of a meal or as a snack. Check how often you ate each food item listed – from “did not eat it this week” to “more than twice each day.” Example: If you had eaten a ham, cheese, and mayonnaise sandwich with a cookie in the past 7 days, be sure to count each of those foods.

In the past 7 days, how often did you eat ...

	Once this week	2-3 times this week	4-6 times this week	1-2 times each day	>2 times each day	Did not eat this week
1. Hamburgers or cheeseburgers.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
2. Beef, such as steaks or roasts.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3. Fried chicken with skin.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4. Hot dogs, franks.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
5. Cold cuts, lunch meat, ham. Etc.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
6. Salad dressings (not diet) mayonnaise.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
7. Margarine	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
8. Butter.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
9. Eggs.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
10. Bacon or sausage.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
11. Cheese or cheesespread.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
12. Whole milk.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
13. 2% milk.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
14. French fries.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
15. Ice cream (not low fat).	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
16. Doughnuts, pastries, cake, pie, cookies.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

	Once this week	2-3 times this week	4-6 times this week	1-2 times each day	>2 times each day	Did not eat this week
17. Potato chips, corn chips, popcorn (not air popped).	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Adapted from Block, G., Gillespie, C., Rosenbaum, E. H., & Jenson, C. (2000). A rapid food screener to assess fat and fruit and vegetable intake. *American Journal of Preventive Medicine, 18*: 284-288.

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 little of my ability. | T | F |
| 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.	T	F
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	T	F
27. I never make a long trip without checking the safety of my car.	T	F
28. There have been times when I was quite jealous of the good fortune of others.	T	F
29. I have almost never felt the urge to tell someone off.	T	F
30. I am sometimes irritated by people who ask favours of me.	T	F
31. I have never felt that I was punished without cause.	T	F
32. I sometimes think when people have a misfortune they only got what they deserved	T	F
33. I have never deliberately said something to hurt someone's feelings.	T	F

Adapted from Crowne, D. P., & Marlowe, D. (1960). A new scale of social desirability independent of psychopathology. *Journal of Consulting Psychology, 24*: 349-354.

Self-Control Scale

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

	Not at all			Very Much	
1. I am good at resisting temptation	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
2. I have a hard time breaking bad habits	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3. I am lazy	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4. I say inappropriate things	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
5. I never allow myself to lose control	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
6. I do certain things that are bad for me, if they are fun	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
7. People can count on me to keep a schedule	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
8. Getting up in the morning is hard for me	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
9. I have trouble saying no	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
10. I change my mind fairly often	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
11. I blurt out whatever is on my mind	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
12. People would describe me as impulsive	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
13. I refuse things that are bad for me	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
14. I spend too much money	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
15. I keep everything neat	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
16. I am self-indulgent at times	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
17. I wish I had more self-discipline	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
18. I am reliable	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
19. I get carried away by my feelings	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

- | | | | | | |
|--|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| 20. I do many things on the spur of the moment | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 21. I don't keep secrets very well | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 22. People would say that I have iron self-discipline | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 23. I have worked or studied all night at the last minute | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 24. I'm not easily discouraged | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 25. I'd be better off if I stopped to think before acting | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 26. I engage in healthy practices | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 27. I eat healthy foods | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 28. Pleasure and fun sometimes keep me from getting work done | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 29. I have trouble concentrating | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 30. I am able to work effectively toward long-term goals | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 31. Sometimes I can't stop myself from doing something, even if I know it is wrong | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 32. I often act without thinking through all the alternatives | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 33. I lose my temper easily | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 34. I often interrupt people | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 35. I sometimes drink or use drugs to excess | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 35. I am always on time | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |

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