

**Dose-Response Effects of Working Memory Training Among Adolescents with Type 1**

**Diabetes**

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## Abstract

Type 1 diabetes (T1D) is a chronic disease that is due to the dysregulation of glucose in the blood when insulin is not made endogenously. Patients rely on a combination of exogenous insulin, medications, blood glucose monitoring, and healthy lifestyle activities such as dietary control and exercise to manage their blood glucose levels. T1D typically begins its onset during childhood or adolescence, where it may also affect the development of executive function (EF) processes which are also relevant for self-regulation, or goal-directed behavior. This in turn may affect individuals' adherence to their T1D management regimens, which can result in severe short- and long-term complications. Despite evidence for the plasticity of EF during childhood, previous research has not frequently focused on EF or self-regulation (SR) as a possible mechanism for improving health outcomes in adolescents with T1D. This study focused on the dosage of EF training and its possible effects on both cognitive and health outcomes for 47 adolescents ( $M = 15.4$ ,  $SD = 1.45$ ) with T1D undergoing a larger adherence intervention. EF was measured by the Digit Span and Go/No-Go tests, while composite measures of T1D treatment adherence were aggregated via separate parent and adolescent reports. It was hypothesized that both cognitive measures and treatment adherence would have a dose-dependent relationship with n-back training. However, no association was found between training dosage and EF outcomes or treatment adherence. The study's limitations include a relatively small sample size along with low participant compliance for the EF training. It also might be that the relationship between EF, SR, and health behaviors is more nuanced than previously suggested and that there are a variety of reasons why dosage of training was not linked to differential outcomes. As such, further investigation is required to better understand this relationship in the search for effective interventions for health behavior.

## Introduction

### Type 1 Diabetes

Type 1 diabetes mellitus (T1D) is a chronic endocrine and metabolic disease caused by the pancreas being unable to produce insulin: the hormone responsible for the uptake of glucose into cells. Consequently, the absence of insulin results in high blood glucose levels (hyperglycemia), which leads to multiple complications (Haller et al., 2005; Katsarou et al., 2017). There is no cure for T1D as of yet and as such individuals with T1D rely on exogenous insulin throughout their lives. According to the 2022 CDC National Diabetes Statistics Report, around 1.84 million individuals in the US, of which 244,000 individuals were below 20 years, were estimated to have T1D in 2019. By 2050, the total number of individuals in the US with T1D is projected to increase to 5 million (CDC, 2022). Worldwide, around 9 million people are estimated to have T1D (Green et al., 2021) and this number is expected to increase as well over the next few decades (Mobasseri et al., 2020).

Although it may appear at any age, T1D mostly presents during childhood and is the most common type of diabetes mellitus in children (Cooke & Plotnick, 2008). While diabetes mellitus is linked to cognitive impairments in general (Zhao et al., 2020), literature also suggests that T1D, with its earlier age of onset in childhood (a critically sensitive period of both physical brain maturation as well as cognitive development), may affect developmental processes, especially those related to cognitive function. This is reflected in impaired executive functions (EF), such as that observed by Ohmann et al. (2010) as well as visuospatial ability and memory in Kirchoff et al.'s (2017) longitudinal study on cognitive changes associated with T1D in pediatric patients.

Similarly, in a systematic review of studies on executive function performance differences between adolescents with T1D and control groups (non-diabetic), Broadley et al. (2017) observed differences across multiple domains of EF, including working memory, response inhibition, and set-shifting.

Cameron et al. (2019) suggested that impaired cognitive performance due to T1D may create a feedback loop where T1D patients are unable to adhere to diabetes management regimens and lifestyle adaptations, which in turn exacerbates the damage to their cognitive function further leading to declining mental health. This makes it all the more necessary to find ways to develop sustainable interventions that help individuals maintain diabetes treatment adherence and consequently improve lifelong health outcomes for individuals with T1D.

## **Executive Function**

With the overwhelming amount of information presented by sensory systems to the brain, a system is needed to process, organize, and comprehend the data. Coordinated and intentional behavior emerges from within the elaborate networks and neural circuits in the brain and is possible because of executive function (EF). EF consists of certain mental processes that facilitate top-down control of attention and other internal cognitive processes in pursuit of a specific internal goal. By and large, there is consensus that EF is neurobiologically linked to the brain's prefrontal cortex (PFC) (Miller & Cohen, 2001) and comprises of three related but distinct processes that are: Working Memory (WM), the ability to temporarily store and manipulate information within the mind; Inhibitory Control (IC), the ability to avoid internal/external distractions and minimize automatic reactions; and cognitive flexibility, the ability to shift between various modes (Barkley, 1997; Doebel, 2020; Miyake et al., 2000, p. 2).

These processes form the basis of higher-order cognitive skills like problem solving, reasoning, and planning (Diamond, 2013; Takacs & Kassai, 2019).

Since the PFC is usually the last area to finish physical development, EF continues to develop throughout childhood even up till young adulthood (Jurado & Rosselli, 2007; Stuss, 1992). As such, childhood and adolescence are highly critical periods of development for EF, which simultaneously forms an integral part of daily activities since it confers the ability to learn, reason, think, and decide. Research has shown that EF predicts academic performance at school particularly for preschoolers (Blair & Razza, 2007; Bull et al., 2008; Cortés Pascual et al., 2019) as well as interpersonal relationships (Moriguchi, 2014; Perry et al., 2019) and later on, work performance in adulthood as well (Bailey, 2007; Balconi et al., 2020; Willoughby et al., 2016).

With its central role in decision-making, EF is also associated with healthy behaviors (Gray-Burrows et al., 2019). Individuals who report being physically active, eating well-balanced diets as well as avoiding tobacco and alcohol consumption are found to have better performances on EF-related tasks and measures (Allom & Mullan, 2014; Hall & Marteau, 2014). Allan et al. (2016) posit that EF and health behavior may very well have a bidirectional relationship, with a potential positive feedback loop where health behavior promotes better EF and better EF leads to more health-enhancing decisions.

There is evidence that individual differences in EF may predict eating behavior even in preschoolers (Pieper & Laugero, 2013) as well as dietary choices. Allom and Mullan (2015) observed that better EF was associated with healthier food choices: lesser saturated fats, more fruits and vegetables. They further distinguished inhibitory control to be more predictive of saturated fat intake while set-shifting or cognitive flexibility was linked to fruit/vegetable

consumption, suggesting that different components of EF are involved in the overall health behavior.

Within the context of T1D, better EF is linked to better adherence to specific dietary instructions as well as insulin management (Bagner et al., 2007; Broadley et al., 2017). As EF has shown a promising ability to be enhanced by interventions (Diamond & Lee, 2011; Diamond & Ling, 2020), there is potential to use cognitive or behavioral interventions to target EF as a mechanism to also improve health-promoting behavior. Improved EF capacities can then facilitate better diabetes management and overall health of individuals with T1D, breaking the positive feedback loop and resulting in improved outcomes. This is the current study's focus, which utilizes interventions to enhance EF and self-regulation in adolescents with the aim of improving adherence to T1D management regimens.

## **Literature Review**

### **Type 1 Diabetes**

#### ***Etiology and Pathogenesis***

Insulin is an endocrine hormone that is responsible for initiating glucose uptake from blood into the body's cells. As such, insulin is an indispensable part of cell metabolism in the human body, without which cells will be unable to generate energy. It is produced by  $\beta$ -cells present in the Islets of Langerhans, a part of the pancreas. In Type 1 diabetes mellitus (T1D), these  $\beta$ -cells are unable to produce insulin, causing an insulin deficiency that presents as increased glucose levels in blood (hyperglycemia). Although the exact mechanism is still

unknown as of yet, the consensus is that this is due to an autoimmune reaction where the body's own immune cells start attacking the Islets of Langerhans, resulting in the destruction of  $\beta$ -cells and consequently, diminished or complete absence of insulin production (Cooke & Plotnick, 2008; Katsarou et al., 2017). T1D is divided into two types on the basis of cause:

1. Type 1a occurs in approximately 70-90% of individuals who present with T1D and is directly due to the autoimmune-associated destruction of the  $\beta$ -cells in the Islets of Langerhans.
2. Type 1b occurs in the remaining individuals and has no apparent cause of  $\beta$ -cell destruction. A genetic susceptibility is suspected but has not been proven (Kirchhoff et al., 2017).

There may be multiple reasons behind the autoimmune reaction including a combination of a viral infection with an environmental exposure event, but this is only a hypothesis as of yet as well. Animal models have proven to be unhelpful in this regard due to the differences in their genetic and immune makeup from humans (Cooke & Plotnick, 2008).

### ***Complications and Long-term Considerations***

As diabetes mellitus is a chronic disease, there are multiple complications that can occur over the course of a lifetime. Their severity depends on the progression of T1D as well as the degree of adherence to the diabetes management regimen prescribed by physicians. The primary concern of diabetes-related hyperglycemia, particularly in T1D is ketoacidosis. Ketoacidosis is the accumulation of ketones in the blood as a by-product of fat metabolism that results when cells are unable to take in glucose in the absence of insulin. As blood needs to remain at a

particular pH level, ketoacidosis can be very disruptive to other physiological processes and may even be fatal in some cases (Bluestone et al., 2010).

Most long-term diabetes-associated complications fall under two major categories: microvascular (small blood vessels like capillaries) and macrovascular (large blood vessels like veins). Macrovascular complications involve an increased risk for coronary artery disease, peripheral artery disease, and even cerebrovascular disease. Heart failure is a common complication for diabetes patients due to the increased fluid load and altered hemodynamics. As increased levels of glucose raises concentration of blood, more water will be retained as part of homeostasis to counteract the increase in concentration. This increase in blood volume will put a greater strain on the cardiac muscles of the heart, increasing chances of myocardial arrest (heart attack). Additionally, both genetic susceptibility as well as risk for comorbidities such as hypertension, smoking, and high cholesterol will lead to more macrovascular complications (Katsarou et al., 2017).

Microvascular complications occur primarily in places with delicate networks of capillaries that are extremely sensitive to hyperglycemia. These include the retina, peripheral nerves, and renal networks in the kidneys. Increased levels of glucose may result in oxidative stress as well as diminished blood flow. Diabetic retinopathy may eventually lead to blindness if not treated and monitored. Diabetic neuropathy includes damage to both peripheral nerves, which causes loss of sensorimotor abilities, and autonomic nerves which in turn affects cardiovascular and gastrointestinal nerves. Diabetic nephropathy, a major cause of chronic kidney disease, may result from the increased excretion of albumin (Haller et al., 2005).

### ***Management and Treatment***



As the exact cause behind the destruction of  $\beta$ -cells have still not been determined, there is not yet an available cure for T1D as of yet. Up until 1922, before the introduction of insulin therapy, T1D was fatal as individuals could not survive without insulin. Advancements in pharmaceutical production of insulin have greatly increased both life expectancy as well as life quality for individuals diagnosed with T1D.

Insulin therapy aims to use exogenous insulin to maintain glucose levels in the blood and avoid fluctuations, especially hypoglycemia (low blood glucose). To do this, blood glucose must be monitored constantly throughout the day and especially before certain activities such as eating or sleeping. Diabetes management also includes following recommended guidelines regarding dietary choices and exercising regularly to maintain insulin sensitivity as well as avoid the increased risk of cardiovascular disease and obesity (Haller et al., 2005; Katsarou et al., 2017).

The American Diabetes Association (ADA) publishes 'Standards of Care in Diabetes', a set of evidence-based instructions that are vital for treating and managing diabetes mellitus. For children and adolescents with Type 1 diabetes mellitus, ADA's Standards of Care recommends that they have at least 60 minutes of moderate to vigorous intensity aerobic, muscle or bone strengthening exercise for a day, about 3 days a week. Both youth and adults are recommended to increase non-sedentary activities, or take breaks every 30 minutes when sitting for long periods of time. ADA guidelines also suggest nutrition therapy and monitoring carbohydrate intake through specific techniques. It is also recommended that glucose levels be checked throughout the day, 6-10 times/day at the least. Checking glucose levels before mealtimes, physical activity, and bedtime is highly encouraged (ElSayed et al., 2022).

### ***Impact on Executive Function***

One of the deleterious consequences of T1D is the effect of glucose dysregulation on the brain, which is a highly metabolic organ (Dienel, 2019; Mergenthaler et al., 2013). Additionally, when age of onset is during childhood, an already sensitive period of brain and cognitive development, the potential effects of dysglycemia may be significant. Literature indicates there are multiple structural as well as cellular injuries in the brain of patients with T1D that observational studies have reported. These subtle brain injuries may contribute to the impairments in EF and processing speed that are commonly observed in individuals with T1D (Cameron et al., 2019). Studies comparing EF, motor speed, visuospatial ability, memory, verbal ability, and even academic performance all show a decreased performance by children with T1D as compared to the control group of youth without T1D (Kirchhoff et al., 2017; Li et al., 2017; Ohmann et al., 2010; Zhao et al., 2020). These effects persist into adulthood as well. Adults who had been diagnosed with T1D in middle childhood and who were approximately 40 years old when the studies were conducted showed five times more likelihood to have clinically significant cognitive deficits when compared to non-diabetic control samples (Li et al., 2017). An MRI study showed that these adults also had an increased loss of functional connectivity (Bluestone et al., 2010) as well as more white matter hyperintensities as compared to non-diabetic counterparts (Embury et al., 2018).

Studies that look at cognitive function of children with T1D report smaller effect sizes than studies with adults (Li et al., 2017) but it is unclear as of yet whether this is a cumulative effect of T1D or the combined result of other long-term micro-and macrovascular complications. Given that developing brains need more energy during neurogenesis and maturation, irregularities in glucose level could severely impact development (Cameron et al., 2019). This might get carried over into adulthood, where other complications also exert a harmful effect.

According to Dienel (2019), dysregulation of glucose affects neurodevelopment in children and sets off a cascade that predisposes the brain to diabetes-related damage, which in turn subsequently presents in middle adulthood as accelerated neurodegeneration, typically associated with aging. This has been observed in young adults earlier than previously suggested (Cameron et al., 2019).

## **Executive Function and Self-Regulation During Childhood and Adolescence**

EFs are cognitive processes responsible for controlling lower-level processes to fulfill a specific goal. EF mainly consists of three main skills, namely: response inhibition, working memory, cognitive flexibility; all three work collectively as well as individually to produce goal-oriented behavior (Diamond, 2013; Miyake et al., 2000). They have a genetic component and are also susceptible to environmental influences (Friedman & Miyake, 2017). EF is linked to the brain's prefrontal cortex (PFC) (Funahashi & Andreau, 2013; Gilbert & Burgess, 2008; Olson & Luciana, 2008; Shimamura, 2002) and as the PFC generally does not finish development and maturation up until adulthood, EFs may also continue to mature up until then. Developmental delays or deficits in the PFC are also linked to EF deficits such as those observed in other neurodevelopmental disorders such as Attention-Deficit Hyperactivity Disorder (Arnsten, 2009; Barkley, 1997).

Self-regulation (SR) involves the ability to direct actions, thoughts, and internal processes towards the fulfillment of a goal (Vohs & Baumeister, 2016) and is generally defined by goal-directed behavior with a temporal perspective. Self-regulation entails three components

(Heatherton, 2011) which are: certain standards of thoughts, feelings, or behavior that individuals regard as desirable; motivation to make an effort into decreasing the gap between these above-mentioned standards and their actual states of thoughts, feelings, and behaviors; and adequate capacities to reach the aim of reducing the discrepancies while avoiding distractions (Duckworth & Steinberg, 2015; Heatherton, 2011; Hofmann et al., 2012; Kotabe & Hofmann, 2015).

As such, self-regulation is a broad concept that includes self-control, emotion regulation, cognitive control, flexible adaptation, problem-solving and other processes necessary for successful fulfillment of goals. Although both have similar constructs and objectives, both self-regulation and EF are distinctly separate from each other. Self-regulation includes EF as the processes that make up EF – inhibition, set-shifting, working memory – all contribute significantly to goal achievement necessary for self-regulation. Accordingly, deficits in EF skills may also lead to low self-regulation as well.

Hofmann et al. (2012) made a series of propositions in their review on EF and self-regulation. They posited that the updating, shifting, and inhibiting abilities of EF support the mechanisms behind self-regulation-related goals and ‘cool’ EFs such as working memory might help regulate ‘hot’ affective processes. They also suggested that as EF-related processes can be improved via training (Diamond & Lee, 2011; Diamond & Ling, 2020), better EF capacities might also lead to better self-regulation. In their summary of current research’s methodological approaches to EF and self-regulation, they speculated that EF could be viewed as an outcome and predictor as well as moderator and mediator for self-regulation processes. As a moderator, EF might help elucidate exactly how self-regulation depends on available EF resources; whereas

as a mediator, EF would help distinguish how potential short or long-term changes in EF might also result in observable changes in outcomes that can be attributed to self-regulation (Hofmann et al., 2012).

## **Self-regulation and Health Behavior**

As health behaviors involve a number of goal-directed processes, it follows that self-regulation, and by extension EF as well, may be heavily involved in initiating and maintaining decisions or actions that are necessary to achieve optimum health as a goal. EFs are especially important in the ability to plan and make decisions, monitor for errors, and inhibit habitual responses (Dohle et al., 2018). This makes them all the more essential for preventing chronic diseases, which may take a long time to engender serious complications and thus require a more consistent, everyday approach in the context of health behaviors to their prevention and management. Multiple studies have linked low SR and EF with worse outcomes for chronic diseases such as cardiovascular health, cancer, hypertension, and diabetes mellitus (Hall & Marteau, 2014; G. E. Miller et al., 2011).

A common health behavior of interest with respect to chronic diseases is dietary choices and eating behavior. Young children in the US are exposed to constant food-related stimuli as well as the availability of inexpensive, calorie-dense foods that are not nutritious, often in large portions. Rising levels of child obesity is often attributed to this excess (Liang et al., 2014) but as some children continue to maintain healthy eating behaviors, researchers now assume differences in self-regulation to be one of the reasons behind dysregulated eating behavior (Dohle et al., 2018; French et al., 2012; Hughes, 2011). Low self-regulation would result in the inability to prevent an undesirable behavior from occurring; dysregulated eating would result in choosing

convenient foods instead of healthy choices, continuing to eat despite satiation, or eating in absence of hunger (Francis & Riggs, 2018; Reinert et al., 2013). This was supported by studies such as those conducted by Allom & Mullan (2014), who reported that lesser inhibitory control was predictive of saturated fat intake, while better EF performances overall were linked to better, healthier food choices.

Apart from eating behavior, other health-promoting behaviors are just as liable to be influential on health outcomes for individuals with chronic diseases. T1D, for example, relies on adherence to a management regimen that includes constant, careful monitoring of glucose levels as well as medications and insulin injections in addition to dietary choices of foods that will not cause a sudden increase in blood glucose levels as well as regular exercise (Cooke & Plotnick, 2008; Haller et al., 2005). All of this requires a great deal of planning, problem-solving and self-regulating, which is made difficult by the bidirectional relationship between T1D and EF: low EFs result in worse outcomes for T1D and T1D complications in turn, also impact EF (Cameron et al., 2019; Embury et al., 2018; Li et al., 2017). And so, it is imperative for interventions that improve EF (and by extension, self-regulation) for children with T1D to also focus on preserving cognitive function in addition to improving health outcomes.

## **Interventions for Executive Function and Self-regulation In the Context of Type 1 Diabetes**

Effective diabetes management has been demonstrated to substantially reduce complications for those with T1D as well as enhance health outcomes (White et al., 2001). But it relies on adherence to a strict and complicated care regimen which may not be easy for children

diagnosed with T1D to follow and maintain. Thus, there is potential to use behavioral or cognitive interventions with the aim of promoting optimal health behavior.

Systematic reviews in the extent literature indicate that behavioral interventions may improve regimen adherence and glycemic control although interventions that were multicomponent instead of just educational had larger effect sizes (Hampson et al., 2000; Hood et al., 2015). In their review on evidence-based behavioral interventions for children with T1D, Hilliard et al. (2016) concluded that the behavioral interventions for T1D fell under the categories of psychosocial skills (coping skills training), family interventions (increasing parental communication) and multisystemic (therapy at home, school and healthcare settings). Most interventions targeted age ranges between middle childhood and early adolescence, however, most of these interventions also had small sample sizes and lacked racial, ethnic, and socioeconomic diversity alongside being time and resource intensive.

Apart from behavioral targets, a few studies have indicated that EFs may be malleable constructs that might show measurable changes when trained in certain ways (Diamond & Ling, 2020). Takacs and Kassai (2019) reported the results of a meta-analysis observing the efficacy of behavioral interventions that sought to enhance EF in children aged up to 12 years. They reported that for atypically developing children such as those with neurodevelopmental disorders, self-regulation strategies such as biofeedback-enhanced relaxation proved to be particularly effective; acquiring new strategies was better than practicing EF tasks. They concluded that implicit training of EF would be better not only results-wise but also due to ease of access and implementation in daily routines.

It follows then that for children diagnosed with T1D, enhancing self-regulation abilities by teaching new strategies may also prove to be highly beneficial when it comes to improving diabetes management and regimen adherence. In their literature review on self-regulation in adolescents with chronic illnesses, Lansing and Berg (2014) concluded that self-regulation, particularly in cognitive, emotional, and behavioral domains, was instrumental for both individual as well as interpersonal risk and/or resilience for adolescents when self-managing their disorders. Thus these three domains provide an excellent target for interventions that may improve self-regulation.

### ***Emotion Regulation Training***

Emotion regulation (ER) is the process by which individuals modify emotional experiences, expressions, and physiology to provide appropriate responses according to the situation or surroundings (Aldao, 2013). ER may also help avoid emotion-associated biases when making decisions and lead to improved decision making; individuals with lower ER display may be more prone to making decisions that lead to disadvantageous outcomes (Sütterlin et al., 2011).

According to Gross's (1998) model, emotions may be regulated at two different time points in the emotion elicitation process and as such form two separate categories of ER. Antecedent-focused regulation allows emotions to be regulated very early in the process; cognitive reappraisal is one such strategy. Reappraisal allows a cognitive-associated redirection of the emotion as a potential way to decrease need for active regulation during an emotion-stimulating situation. Response-focused regulation on the other hand occurs at when the emotion has been stimulated; suppression is an example of this category. Suppression comprises of controlling behavioral and physiological responses to emotion and consists of mechanisms that



respond to emotion by inhibiting emotional expression or experience during an emotion-stimulating event.

Although both strategies of regulating emotions use cognitive resources, empirical research indicates that suppression may impact decision-making by exerting a greater demand on limited cognitive resources or workspace since it potentially requires continuous self-monitoring and correcting during the emotion interaction (Richards et al., 2003; Richards & Gross, 2000). Reappraisal on the other hand, requires lesser cognitive resources since it reframes the situation before the emotion begins to fully elicit and avoids allocation of resources towards emotional processing, thus increasing resources available for other cognitive tasks (Gross, 1998; Richards & Gross, 2000; Wallace et al., 2009). Cognitive reappraisal is also linked to healthier affective, cognitive, and social outcomes as well as more positive emotional experiences and memories (Gross & John, 2003).

The emotional awareness required for cognitive reappraisal directly affects ER as well. ER may be conducted consciously or unconsciously (Williams et al., 2009) although increased conscious awareness of emotional states or high arousal is linked to both interoception, awareness of physiological processes and improved ER as well (Critchley et al., 2004; Culbert, 2017). It follows then that increased physiological awareness will also lead to better ER outcomes; this is the basis of biofeedback training. Biofeedback training involves monitoring an individual's physiological parameters such as heart rate, skin conductance and respiration rates using instruments and converting this information into audiovisual modalities relayed back to the individual.

The objective of biofeedback training is to facilitate participants in training a particular physiological factor such as heart rate (Mather & Thayer, 2018) by intentionally modifying their breathing or other responses according to the real-time feedback. The ability to regulate physiological reactions to emotionally-stimulating situations that is being developed through biofeedback training sessions is then hypothesized to transfer to real-world emotional situations even without biofeedback (Peira et al., 2013). Mather and Thayer (2018) posit that using heart rate variability feedback to physically control heart rate actually influences the PFC regions which monitor interoception, strengthening neural pathways that then contribute to ER. Importantly, biofeedback does contribute to better self-regulation for both psychopathological and typical participants (Eddie et al., 2018; ter Harmsel et al., 2021; Tolin et al., 2017). As such, biofeedback training may serve to be a strategy through which emotion regulation can be targeted to implement better diabetes management routines that will lead to better health outcomes overall.

### ***Future Orientation Training***

Future orientation (FO) is the collective effect of cognitive, motivational, affective and attitudinal constructs when considering future life (Steinberg et al., 2009). FO is considered as an important step in identity development where past and present selves are integrated with future selves in terms of education, career, health, SES, sociocultural landmarks (getting married, buying a house) and so on (Johnson et al., 2014). Increased FO in adolescents indicates goal-oriented behavior, and planning abilities, which is corroborated by better educational and health outcomes (Andre et al., 2018; Gushue et al., 2006; Seginer, 2008; Steinberg et al., 2009).

As FO is considered to be a developmental process, there are visible age differences when comparing FO among adolescents. Older adolescents display better FO on delay discounting measures (tasks that assess the degree of preference for an instant reward of low value versus a reward that is much in greater value but given much later) and report greater motivation, time perspective and planning (Nurmi, 1991, 2005). This is likely the result of PFC development, responsible for inhibitory control among other EF, which is slower and more gradual than the development of socioemotional networks. The influence of FO on adolescent behavior is dependent on the degree to which a particular outcome is valued as well as the probability of the outcome happening (Wigfield & Eccles, 2002). An important consideration is that SES is strongly related to FO, with parental education being strongly associated with adolescent educational and career orientation (Kerpelman & Mosher, 2004; Nurmi, 1991).

Greater FO can be linked to better self-regulation as well, since goal-directed behavior might be easier to accomplish if an individual is thinking of long-term benefits rather than short term ones. An intervention designed to increase FO is episodic future thinking (EFT), where individuals are asked to envision future selves or situations in an effort to minimize delay discounting (Hollis-Hansen et al., 2019). According to neuroimaging studies, EFT is maintained by the core/default mode network in the brain and offers a number of benefits including better decision making, ER, prospective memory, and even visuospatial navigation (Schacter et al., 2017).

EFT has found a lot of utility in clinical behavioral interventions to promote health outcomes, such as overeating as well as smoking behavior (Daniel et al., 2013; Stein et al., 2018; Sze et al., 2015). Similar EFT interventions for adults with prediabetes and Type 2 diabetes

mellitus show improved lifestyle choices (better nutrition and increased physical activity) as well as medication adherence (Bickel et al., 2020; Epstein et al., 2022). Presumably, the same can be expected from interventions targeting FO through episodic future training in adolescents with T1D as well.

### ***Working Memory Training***

Working memory (WM) is a limited capacity system that allows the mind to store and manipulate information (Baddeley, 2010). WM capacity was originally thought to be fixed in its limitations (Cowan, 2001; G. A. Miller, 1956) but recent evidence suggests that it is far more flexible than anticipated (Chein & Morrison, 2010; Jaeggi et al., 2008; Klingberg et al., 2005). WM is conceptualized to be an essential component of EF and may be divided into domain-specific (strategies that facilitate maintenance of types of information such as verbal or linguistic representations) and domain-general elements (processes not linked to a specific category of sensory information but involved in coding and retrieval from long-term memory, such as attentional control, information gating, distractor avoidance etc.) (A. Baddeley, 1986, 2012).

Increasing WM capacity via cognitive training means that either domain-general or domain-specific processes need to be targeted. Executive attention seems to be a major factor behind better cognitive skills (Cowan et al., 2005). Thus, targeting domain-general skills might be more influential in increasing WM capacities. Another important consideration when measuring outcomes of cognitive training approaches is transfer, or the generalizability of cognitive skills gained during training to other domains. This is all the more important to observe in WM training, which is often categorized as a domain-general concept.

WM training approaches focus on repeating highly demanding WM tasks in an effort to target domain-general mechanisms (Morrison & Chein, 2011). To do so, they require limited use of domain-specific skills, minimal automation, activities that require multiple EF domains, maintenance despite distractors and interference and rapid coding and retrieval. WM training must also be able to automatically adjust according to participant's level or WM capabilities in a manner that is demanding but not impossibly so.

One such task that fulfills these considerations is the n-back task developed by Kirchner (1958), where stimuli are presented in a particular sequence and the participant has to respond when the current stimulus being presented is the same as the stimulus presented a certain number of trials ( $n$ ) earlier. The n-back can be single with one stream of stimuli, or dual with two streams of stimuli (often of different modalities).

The n-back task is considered to target the updating component of working memory but it may also provide a measure of the maintenance and capacity of WM (Szmalec et al., 2011). If lure stimuli are also included (non-target stimuli that resemble the target and are designed to cause an incorrect response), then the n-back task may also actively involve interference control (Morrison & Chein, 2011). Soveri et al. (2017) conducted a multi-level meta-analysis of studies that observed the efficacy of n-back training. They suggested that contrary to previous studies, a medium transfer effect of n-back training is seen on untrained n-back tasks and small transfer effects to other WM tasks, cognitive control and fluid intelligence are observed. Given these outcomes, it can be expected that using n-back training to improve both working memory as well as other facets of EF will increase self-regulation necessary for better diabetes management. The focus of current study was specifically on working memory training and n-back training.

## Theoretical Perspectives

### Executive Function

Executive function (EF) is an umbrella term that is used to describe the cognitive processes that enable the mind to achieve a certain goal. As such, EF is considered to be one of the key contributors to self-regulatory (SR) processes which enable an individual to resist impulses and avoid distractions in pursuit of an internal or external self-directed goal. In this study, that goal is adherence to T1D treatment regimen that involves timely insulin injections, the correct amount and types of food consumed, as well as regular exercise - all of which are adherence measures that might be linked to greater self-regulation abilities. For children and adolescents with T1D, deficits in EF may emerge as a consequence of glucose dysregulation in the developing brain, which in turn makes self-regulation - and subsequently, adherence to T1D management protocols - difficult to maintain. As such, cognitive training that strengthens these EF processes may be of utility in facilitating better adherence and compliance to T1D treatment regimens.

There continues to be a debate about whether EF can be classified as a solitary unit that single handedly controls other cognitive processes or whether it consists of separate components that are distinguishable and have individual domains of processes that they regulate (Diamond, 2013). Regardless, the three main construct that comprise EF include:

**a) Working Memory**

Working memory (WM), a major component of EF, is conceptualized as a temporary memory construct which stores information momentarily to be used for cognitive processes. This data can be either recollected from long-term memory storage or it can be completely new information. One of the major theoretical frameworks regarding WM was proposed by Baddeley and Hitch (1974) who improved upon Atkinson & Shiffrin's (1968) model of human memory and its control.

Baddeley and Hitch conceptualized WM to be a multi-component model that had four main sub-structures: a control structure termed as the '*central executive*' that regulated and monitored cognitive processes, as well as two structures that specialize in phonological information, the '*phonological loop*', and in visual information, the '*visuospatial sketchpad*'. The fourth component was an '*episodic buffer*' that serves as a temporary memory storage and an interface between the phonological loop, visuospatial sketchpad, and long-term memory. The episodic memory not only stores information perceived but also uses the two structures and long-term memory to form new, abstract ideas that can be stored or utilized (Baddeley, 2010; Miller & Cohen, 2001). The central executive is of key importance, as it is responsible for coordinating working memory by moderating the amount of information in the system, allotting resources to store or manipulate it and modifying it when needed. The central executive explains how humans can overcome a limited short term memory storage capacity to process multitudes of sensory and other retrieved information (Baddeley, 2010).

It is hypothesized that the effects of working memory training, such as through the n-back task, are transferable to other EF processes as well as higher order cognitive

processes like reasoning and even fluid intelligence. von Bastian and Oberauer (2014) propose that these gains in WM are either through increased WM capacity, (i.e., increased ability of the episodic buffer to store greater quantities of information) or increased WM efficiency (i.e., enhancement of the executive control via strategies). This is important because WM is closely related to inhibitory control, another component of EF, specifically through keeping an overarching aim or goal ‘in mind’, so as to say, when faced with competing demands or impulses (that are then inhibited through response inhibition). It follows then, that increasing WM will also improve inhibitory control and SR processes. Within the context of this study, WM training seems to be a relatively straightforward mechanism towards enhancing SR and consequently, adherence to T1D management regimens in adolescents.

#### **b) Inhibitory Control/Inhibiting**

Inhibitory Control (IC) is the ability to inhibit any automatic responses that may come up when exposed to certain stimuli. There are two forms of IC: attentional inhibition or interference control, the ability to avoid distractions and remain focused on a certain task and response inhibition, and the ability to suppress a prepotent response (Tiego et al., 2018). These two constructs are considered to be separate but closely linked to each other by working memory. Response inhibition is particularly linked to WM, as it is vital in ensuring WM remains available for current tasks. This may be the reason behind its close association with WM measures (Diamond, 2013); both are thought to be related as they rely on the same limited capacity system. This may also be why increasing the demand on one will inevitably impact the other as well (Engle et al., 2004; Wais &



Gazzaley, 2011). This is further corroborated by Jones et al. (2020), who found that n-back training also increased IC alongside increasing WM capacity.

According to Diamond (2013), SR is mostly accounted for by both facets of IC i.e., *response inhibition* (inhibition at the behavioral level; colloquially known as ‘self-control’ or ‘discipline’) along with *interference control* (inhibition of thoughts, memories and other internal distractions) as well as maintaining emotional, motivational, and cognitive arousal. That may explain why IC is very closely linked to health behaviors, as (Moffitt et al., 2011) report that children who had greater IC during childhood also had better health, educational, and financial outcomes, even when controlling for intelligence as measured by IQ, gender, SES, home lives and family circumstances. Within the framework of the current study, IC is thus strongly related to both self-regulation and T1D management overall. Again, cognitive training that results in greater inhibitory control may then also result in more adherence to T1D treatment regimen due to the lesser influence of distractions or greater effortful control.

### **c) Cognitive Flexibility/Set-shifting**

Cognitive flexibility is the ability to change perspectives or reframe certain ideas as well as adjust to changed demands (Miyake et al., 2000). It relies on both WM as well as IC since it requires active manipulation of information while inhibiting other information or impulses. Most EF researchers may also attribute cognitive flexibility to be the main construct behind creativity, the ability to generate entirely new ideas or schemas from existing information (Miyake & Friedman, 2012). As with the other two constructs of EF, higher levels of cognitive flexibility lead to better academic outcomes,

which may also result in improved health and wellbeing outcomes throughout life (Arán Filippetti & Krumm, 2020).

The underlying processes behind EF are an important consideration for cognitive interventions due to their links with each other. As depicted in the model of EF presented by Diamond (2013), both working memory and inhibitory control are closely associated with each other, especially for self-regulation where goal-directed behavior is achieved by limiting the effect of distractions and focusing on the goal. As such, a cognitive intervention that strengthens both WM and IC will then also enhance self-regulatory processes; the n-back training intervention used in this study is an example of a cognitive intervention aimed at increasing WM and IC capacities and efficiencies (von Bastian & Oberauer, 2014). Thus, within the specific context of this study, it is theorized that the corresponding increase in self-regulation will then in turn enable adolescents with T1D to be better equipped for maintaining adherence to T1D treatment regimens. And so, the Diamond (2013) model of EF is one of the principal theoretical frameworks behind this study.

## **Temporal Self-Regulation Theory: The Guiding Theory**

The Temporal Self-regulation Theory (TST) set forth by (Hall & Fong, 2007) presents a framework that explains individual health behavior by integrating ecological context and time perspective as factors that affect self-regulation of individuals in health-related contexts. Self-regulation is the ability to internally manage behavior, emotions, and thoughts for the purpose of achieving a long-term goal (Inzlicht et al., 2021). Time perspective explains how perceptions of time influences an individual's thoughts, experiences, motivation, and behavior (Stolarski et al.,

2018) while ecological context accounts for the environment and context in which an individual exists (Bronfenbrenner, 1977, 2005).

Hall & Fong (2007) define ‘health behavior’ as an intentional or unintentional behavior that has either short-term or long-term consequences for the health status or disease risk of an individual. These behaviors may be either health-promoting (preventative behaviors like physical exercise) or harming (risk-inducing behaviors like smoking) as well as repetitive or single occurrences. TST explains health behaviors through three proximal factors: *intention strength*, *executive control resource availability* (includes the three EF major processes of inhibition, working memory and set shifting), and *behavioral prepotency* (habits or the default status of the behavior).

Behavior is also affected by proximal and distal influences of the ecological context. Proximal influences are more immediate and have a greater influence on behavior. Since the physical and sociocultural ecological context determines the availability of the influences, there is a direct link between the ecological context and behavior. Health-promoting behaviors with distal benefits require both executive control as well as behavioral prepotency when compared to behavior with more immediate effects (Hall & Fong, 2013).

Intention is also included in the model alongside behavior-specific time perspective to describe the motivational processes behind behavior. It accounts for the tendency to allocate more attention or temporal value to immediate outcomes as compared to distant outcomes of actions or behavior. Intention itself is one of the main factors that directly affects behavior and is moderated by prepotency and executive control resources (ECR or EF); presumable intentions impact behavior more when ECRs are strong, and prepotency is low. Both ECR and prepotency

also impact behavior directly as well, since weak ECRs allow the environment to impact behavior more, despite intention. Repetitive behaviors within the same context may occur due to prepotency or habit (Hall & Fong, 2007, 2013).

Hall and Fong have also suggested several entry points within the TST model to optimize individual health behavior for better long-term health outcomes. These include expanding the self-regulatory demand for the undesirable, health-harming behaviors by making access to such behavioral objectives resource-intensive and inconvenient. The converse is also a viable mechanism: by diminishing self-regulatory demand, health-promoting behaviors can be made accessible, convenient, and affordable.

Another strategy the authors recommend is enhancing executive control resources through interventions (this would strengthen EF and encourage goal-directed behavior) as well as implement preventative measures that preserve EF capacities (through stress reduction, sleep fulfillment and so on). Future orientation should be promoted as improving intention strength to help individuals avoid focusing on the proximal influences that promise immediate gains and harness time perspective to help them achieve goals. And lastly, prepotency should be modified according to the ecological context to encourage formation and maintenance of health-promoting habits (Hall & Fong, 2013).

While Diamond's (2013) model of EF focuses exclusively on the mechanisms behind EF that are linked to SR, and may be strengthened through interventions, TST links SR to health behavior and adds in the effect of contextual factors. It links self-regulation (as ECR), ecological context (the environment, pre-existing habits, or prepotency), intention and time perspective all together to explain health behavior, both health-harming and health-benefiting. In the context of

self-regulation and T1D management, it can be used to account for why T1D treatment regimen adherence may be difficult for adolescents with T1D (as presumably their EF processes have been affected developmentally and so they have low self-regulatory abilities). Additionally, it also elucidates how cognitive interventions (such as the n-back training in this study) may facilitate regimen adherence by strengthening ECR. As such, this makes TST suitable as a guiding theoretical framework for this study.

## **Methods**

### **Research Questions and Hypotheses**

Given the links between self-regulation and executive function, it follows that cognitive interventions may be a potential method to boost EF for children with T1D, potentially enabling them to mitigate the effects of T1D on their developing brain as well as facilitate better diabetes management techniques that will stop the positive feedback cycle between EF and T1D.

As mentioned above, n-back training is central to improving both working memory and inhibitory control (Jones et al., 2020; Pergher et al., 2018; Soveri et al., 2017). The total number of n-back training sessions completed over the course of the intervention can be considered as the n-back training dose, which based on previous research may affect self-regulation through observable measures such as cognitive performance and behavioral outcomes (Houben et al., 2016). As such, there are two research questions that were relevant:

- 1. Will dosage of n-back training affect performance on cognitive measures?**

Hypothesis 1 states that the dosage of n-back training will affect performance on cognitive measures in a linear manner, such that increased doses of n-back training would result in better performance on cognitive measures.

## 2. Will dosage of n-back training affect performance on behavioral measures?

Hypothesis 2 states that dosage of n-back training will slightly affect performance on behavioral measures as behavior is a complex construct that can have multiple underlying factors.

## Participants and Recruitment

The participants were a group of 47 adolescents from 13 to 17 years old ( $M = 15.4$ ,  $SD = 1.45$ ), who were recruited from the pediatric endocrinology clinic at University of Michigan and lived in Southeastern Michigan. The gender composition of the sample was 26 male and 21 females. Most participants identified as White while the rest were Black, Asian or Pacific Islander, Hispanic, and biracial. As a measure of SES, most parents of participants had more than 12 years of formal education. Most of the participants in the sample were diagnosed with T1D in their childhood ( $M=9.89$ ,  $SD=4$ ) and their mean baseline HbA1c levels were 8.62 ( $SD=1.6$ ).

**Table 1.**

### *Sociodemographic Characteristics of Participants*

<b>Sample Characteristics</b>	<b><i>n</i></b>	<b>%</b>	<b><i>M</i></b>	<b><i>SD</i></b>
Current age	47		15.42	1.45
Age at diagnosis of T1D	32		9.89	4.0

Gender			
Male	26	55.3	
Female	21	44.7	
Race			
White	39	83	
Black or African American	4	8.5	
Asian or Pacific Islander	1	2.1	
Biracial	2	4.3	
Parent SES			
High school/GED	3	6.4	
Some college/training	19	40.4	
College	13	27.7	
Advanced degree (MS, PhD, MD)	12	25.5	
Pre-test HbA1c levels	40	8.62	1.6
Total $n = 47$			

The criteria for selection included participants being between 13-17 years old, living with a parent or guardian who was a primary caregiver, having a diagnosis of T1D for a minimum of 6 months, having HbA1c levels greater and or equal to 7, having regular access to Wi-Fi, and having enough fluency in English to complete the study. All forms of diabetes management regimens were included in the study, such as insulin injections, medication, blood glucose monitoring, continuous glucose monitoring and combinations. Participants with clinically significant psychiatric or cognitive conditions were excluded from the study since it would hinder their ability to participate.

## Study Design

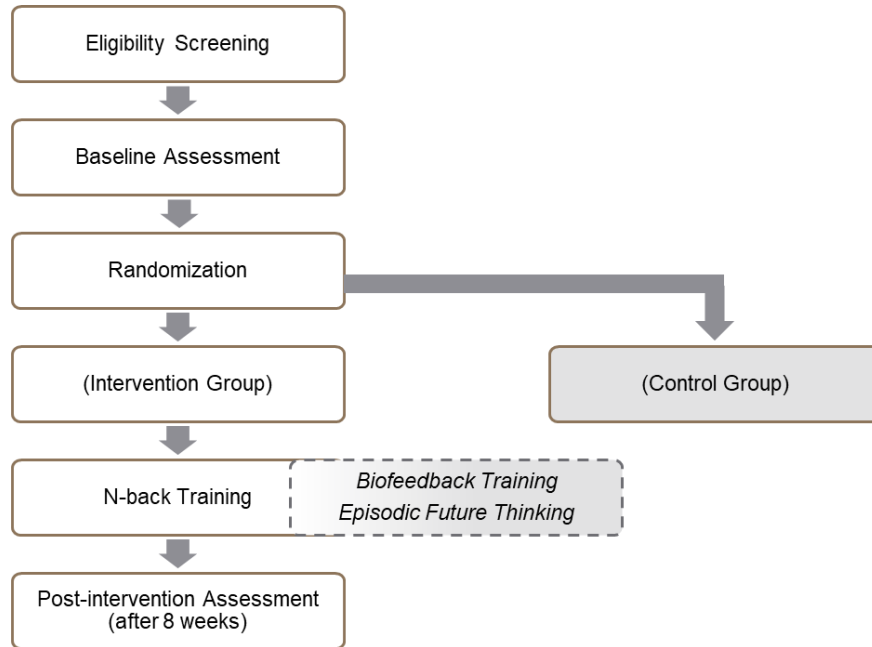
The project consisted of a control group that received informational sessions and resources but no interventions and an experimental group that received three interventions (n-back training, biofeedback training, and episodic future thinking) simultaneously. The other interventions and the control group were not included in this study as the focus of this thesis was specifically n-back training only because of its closer links to cognitive outcomes. The intervention was 8-weeks long and baseline measures (pre-test) were recorded before the intervention as well as right afterwards (post-test). Participants were also incentivized to complete the n-back every day by rewarding them with \$10 per week if they sent screenshots of the daily sessions completed to researchers i.e., seven screenshots every week. This was to ensure participants conformed to the experimental conditions parameters.

The n-back training consisted of pictures of fruits and other objects that were displayed on Android tablets that were also provided by the researchers. The participant was instructed to tap the object that was repeated a certain number of objects back ( $n$ ). There was a component of lures (similar-looking objects) added as well (Jones et al., 2020; Pergher et al., 2018), which was designed to train and test inhibitory control as well. The participants were directed to play at least 1 session (around 10 rounds) of the game once per day; this was estimated to take approximately 15 minutes per session. As the intervention was eight weeks long, this would result in 56 sessions completed overall throughout the intervention.

### Figure 1

*Study Procedure adapted from (Miller et al., 2020)*





## Outcome Measures

### *Cognitive Outcomes*

As proximal measures of the effect of the n-back training, the cognitive measures included two tasks, both of which measure working memory: the Digit Span Task as well as the Go/No-Go task (Baddeley & Hitch, 1974). Given the direct relationship between n-back training and working memory, these tasks were considered to be measures of changes in WM capacity as a result of the n-back intervention.

**Digit Span.** The Digit Span task involves displaying a series of random digits one by one, which the participants then recall. The digit span task has two variants: forward-span (FDS) and backward-span (BDS) that refer to the order in which participants are asked to remember the digits. If a trial is completed successfully, the number of digits is increased; if it is failed once then the number of digits remains the same and if failed twice consecutively, the task concludes.

Digit span is then said to be the highest number of digits repeated in the correct order (Ryan & Lopez, 2001). Accordingly, FDS and BDS denotes the maximum number of digits that the participants can recall and repeat either verbally or on a computer in the correct order. As a measure of WM capacity, both were observed pre- and post-intervention in this study.

**Go/No-Go.** The Go/No-Go task comprises of participants responding to certain stimuli (these are termed as 'Go') and inhibiting their response to other stimuli (termed as 'No-Go') (Donders, 1969). When the probability of the 'Go' stimuli is more than the 'No-Go' stimuli, it causes the participant to develop a prepotency to respond to all stimuli with the 'Go' response. This tendency needs to be inhibited for the 'No-Go' stimuli (Wessel, 2018). Erroneously making an incorrect response to the wrong stimuli (such as responding 'Go' when a 'No-Go' stimulus is present) is termed as a commission error. Commission errors indicate a failure of response inhibition, thus fewer the errors, better the response inhibition. As the Go/No-Go is a measure of IC and relies on response inhibition, both accuracy and reaction time served as pre- and post-intervention assessments of any improvements in IC as a result of the intervention.

### ***Health Behavior Outcomes***

As a distal measure for the n-back training transfer, the behavioral measure is the main health behavior being targeted: the degree of adherence to the diabetes management regimen. This includes medication and insulin administration, glucose monitoring, optimal food choices and quantities, and exercise. A composite measure was created for each category to test the effects of the n-back training on treatment adherence.

**Composite Measure of Treatment Regimen Adherence.** All variables associated with health behavior measures were correlated and variables with medium correlations ( $r > 0.5$ ) were observed. Three main categories of T1D treatment adherence were made and variables were grouped together under each category. These categories were theoretically and empirically informed (Campbell et al., 2014; Nansel et al., 2016; Schober et al., 2011; Ziegler et al., 2011). An Exploratory Factor Analysis was also conducted where parent- and child-reports emerged as different constructs, and so were classified as separate outcomes for each category; hence each category had a parent report measure as well as a child report measure.

1. Insulin adherence

This included variables related to insulin, such as ‘Correct dose of insulin’ (measured by a 5-point, Likert-type scale), ‘Correct timing of insulin’ (measured by a 5-point, Likert-type scale), ‘Adjust insulin dosage based on glucose level, food, or exercise’ (measured by a 5-point, Likert-type scale), and ‘Missed insulin doses’ (measured by a 7-point, Likert-type scale).

2. Glucose monitoring

This category included variables related to glucose monitoring, such as ‘Check blood glucose levels’ (measured by a 5-point, Likert-type scale), ‘Record blood glucose’ (measured by a 5-point, Likert-type scale), ‘Check ketones when glucose is high’ (measured by a 5-point, Likert-type scale), and ‘Average blood glucose testing frequency’ (number of times blood glucose is tested during a day from 1 to 10 times with 10 indicating 10 or more times glucose levels were checked).

3. Nutritional choices

This included variables measuring nutritional choices, such as ‘Correct food portions’, ‘Correct food timing’, ‘Keep food records’, and ‘Read food labels’ – all of these variables were measured on a 5-point, Likert-type scale.

As suggested by Andrade (2021), composite scores were made for each category by standardizing each individual variable of a category and converting them to z-scores. The composite scores for each category were calculated by finding the average of the variables’ z-scores. This was done for both pre-test and post-test composite health behavior measures, which were then used in the final regression models as described below.

## **Statistical Analysis**

### ***Primary Predictor Variable: Dosage of n-back training***

Dosage of the n-back training consisted of the total number of sessions completed throughout the 8 week intervention period. This was calculated from the data collected by the n-back training app throughout the intervention. As the intervention consisted of daily n-back training sessions, the maximum total sessions over a period of 8 weeks were to be approximately between 56-60 sessions. According to related studies, cognitive training dosage may be positively correlated with improvements in n-back task performance, and presumably WM capacity and IC as well (Shahar et al., 2018). However, links between dosage and performance are inconsistent - very large training dosages are not significantly related to improvements in cognitive outcomes measured, suggesting that the dose-response relationship between n-back training and cognitive outcomes is more nuanced (Lawlor-Savage & Goghari, 2016).

## *Covariates*

The covariates included in the analyses include age, gender, socioeconomic status, race/ethnicity, and HbA1c – these were present in all the models. Further details about the rationale for including them is given below:

**Hemoglobin A1c (HbA1c).** HbA1c is glycated hemoglobin i.e., glucose bonded to hemoglobin molecules in red blood cells. It serves as a measure of glycemic control or how well the body can regulate glucose levels in blood. It also serves as a diagnostic criteria for diabetes as it is a measure of the average glucose levels in blood in a time frame of eight to twelve weeks, with a value of 6.5% and more indicating diabetes (WHO, 2011). Ziegler and colleagues (2011) report that in adolescents with T1D, better metabolic control of glucose or lower HbA1c levels were significantly associated with monitoring blood glucose levels, one of the treatment adherence health behaviors in this study. As this study lasted eight weeks, HbA1c is a suitable measure of whether pretest glycemic control could also predict post-intervention outcomes.

**Age.** Age is an important variable, especially as the sample for this study includes participants in early to mid-adolescence, which is a few months or years after the onset of T1D. Since the brain is continually developing during childhood and adolescence, age would be an important factor in n-back training. As different systems also mature at different rates, such as IC developing later than WM for example, age would be an central determinant of n-back training performance (Bherer et al., 2008; Huizinga et al., 2006).

**Gender.** Although gender or biological sex itself is not related to differences in cognition or EF (Grissom & Reyes, 2019), gender socialization may be an important factor behind

development of EFs. For example, Silverman (2021) reported small but significant gender differences in IC with female children outperforming male children on simple delay tasks. This suggests that gender is especially important when analyzing n-back training results.

**Socioeconomic Status (SES).** SES is highly correlated with EF capacities and cognitive performance in general (Bradley & Corwyn, 2002; Gottfried et al., 2003; Hackman & Farah, 2009), which makes it an important factor to be considered in any analysis involving cognition. In this study, parental education was considered to be a proxy measure of SES owing to the close links between parental education and income, both of which are thought to be foundational elements of SES.

**Race/Ethnicity.** Due to the intersection of sociocultural dynamics, race/ethnicity is linked to SES and as such, may exert an influence on EF development and especially may affect performance on cognitive measures. This can be seen in Rea-Sandin et al.'s, (2021) systematic review and meta-analysis where they report significant differences between White and minority racial groups. This makes race/ethnicity a crucial demographic factor to account for in statistical analyses.

### ***Analysis Plan***

Data was cleaned and re-coded to remove missing values and non-responses. The analytic strategy included three major steps:

1. Examine descriptive statistics for both predictor and outcome variables.
2. Conduct bivariate correlation analysis to observe the relationships between the outcome variables (Digit Span, Go/No-Go, Treatment adherence composite measures) and the

covariates of interest (demographics, dose of n-back training, HbA1c, baseline measures of the outcome variables).

3. Construct separate multivariate regression models for each outcome variable with dosage of n-back training, HbA1c, and demographic variables (age, gender, race/ethnicity, SES) as covariates, while controlling for the pretest measure of the outcome variable being analyzed.

## Results

The two research questions of this study focused on finding whether there was a dose-response effect of working memory training on post-test cognitive measures and behavioral measures. Overall, no such association was observed to be statistically significant. The results of the regression models are given below:

### Cognitive Outcomes

#### *Digit Span*

**Forward Digit Span.** The model testing for performance on Forward Digit Span had an adjusted  $R^2$  of 0.466. Dosage of n-back training did not predict post-test Forward Digit Span performance, even when controlling for pre-test performance, HbA1c levels, age, gender, race, and SES.

#### **Table 2**

*Post-test Forwards Digit Span*

Variables	Unstandardized		Standardized	t	Sig.
	Coefficients		Coefficients		
	B	Std. Error	Beta		
(Constant)	3.58	7.26	-	0.49	0.628
Pre-test FDS Score	0.79	0.17	0.76	4.81	<0.001
Dose	-0.003	0.003	-0.16	-0.84	0.413
HbA1c level	-0.32	0.30	-0.19	-1.05	0.308
Age (years)	0.16	0.34	0.084	0.46	0.655
Gender	-0.31	0.95	-0.057	-0.33	0.745
Race	0.53	0.41	0.21	1.29	0.215
SES	-0.55	1.04	-0.099	-0.53	0.602

**Backwards Digit Span.** The model testing for performance on Backwards Digit Span had an adjusted  $R^2$  of 0.441. Dosage of n-back training did not significantly predict post-test performance on Backwards Digit Span, although it was marginal ( $p=0.051$ ) when controlling for pre-test Forwards Digit Span performance, HbA1c levels, age, gender, race, and SES. However, this association was negative; in other words, participants completing more n-back training sessions had a lower Backwards Digit Span performance.

### Table 3

*Post-test Backwards Digit Span*



Variables	Unstandardized		Standardized	t	Sig.
	Coefficients		Coefficients		
	B	Std. Error	Beta		
(Constant)	-2.16	7.95	-	-0.27	0.79
Pre-test BDS Score	0.81	0.20	0.67	3.98	<b>&lt;0.001</b>
Dose	-0.007	0.003	-0.41	-2.1	<b>0.051</b>
HbA1c level	-0.502	0.31	-0.30	-1.62	0.125
Age (years)	0.588	0.36	0.32	1.65	0.117
Gender	0.017	0.96	0.003	0.17	0.986
Race	0.303	0.42	0.12	0.71	0.486
SES	0.301	1.05	0.054	0.29	0.777

### ***Go/No-Go***

**Go/no-Go Accuracy.** The adjusted  $R^2$  for the model predicting accuracy on the Go/No-Go measure was 0.436. Dosage of n-back training did not predict post-test overall accuracy on the Go/No-Go task when controlling for pre-test Go/No-Go accuracy, HbA1c levels, age, gender, race, and SES.

### **Table 4**

*Post-test Go/No-Go Accuracy*

Variables	Unstandardized		Standardized	t	Sig.
	Coefficients		Coefficients		
	B	Std. Error	Beta		
(Constant)	-0.02	0.22	-	-0.08	0.94
Pre-test GNG Performance	0.95	0.23	0.62	4.01	<0.001
Dose	-2.3E <sup>-5</sup>	0.00	-0.20	-1.23	0.231
HbA1c level	-0.002	0.002	-0.13	-0.81	0.426
Age (years)	0.003	0.002	0.24	1.51	0.144
Gender	0.004	0.006	0.09	0.64	0.528
Race	2.5E <sup>-6</sup>	0.00	0.02	0.14	0.887
SES	0.006	0.007	0.15	0.87	0.394

**Go/No-Go Mean Reaction Time.** The adjusted  $R^2$  for the model predicting mean Go/No-Go reaction time was 0.239. Dosage of n-back training did not predict post-test mean Go/No-Go reaction time when controlling for pre-test mean Go/No-Go reaction time, HbA1c levels, age, gender, race, and SES.

### Table 5

*Post-test Go/No-Go Mean Reaction Time*

Variables	Unstandardized		Standardized	t	Sig.
	Coefficients		Coefficients		
	B	Std. Error	Beta		
(Constant)	152.01	88.2	-	1.72	0.97
Pre-test GNG RT	0.69	0.18	0.68	3.82	<0.001
Dose	-0.02	0.03	-0.12	-0.64	0.530
HbA1c level	-3.23	3.35	-0.19	-0.96	0.344
Age (years)	-0.72	3.62	-0.04	-0.20	0.843
Gender	-3.88	9.38	-0.07	-0.41	0.683
Race	0.02	0.03	0.14	0.81	0.426
SES	-2.45	9.99	-0.05	-0.25	0.808

## Health Behavioral Outcomes

### *Insulin Adherence*

**Child Report.** The model predicting post-test child-report of insulin adherence had an adjusted  $R^2$  of 0.557. Dosage of n-back training did not predict insulin adherence when controlling for pre-test insulin adherence reports, HbA1c level, age, gender, race, and SES.

### **Table 6**

#### *Post-test Child Report of Insulin Adherence*

Variables	Unstandardized		Standardized	t	Sig.
	Coefficients		Coefficients		
	B	Std. Error	Beta		
(Constant)	2.29	1.5	-	1.53	0.137
Pre-test Insulin Adherence	0.76	0.13	0.75	5.82	<0.001
Dose	-4.8E <sup>-5</sup>	0.001	-0.01	-0.08	0.940
HbA1c level	0.15	0.07	0.03	0.22	0.829
Age (years)	-0.13	0.08	-0.23	-1.63	0.115
Gender	0.05	0.21	0.03	0.26	0.799
Race	6.4E <sup>-5</sup>	0.001	0.01	0.11	0.916
SES	-0.26	0.22	-0.16	-1.19	0.245

**Parent Report.** The model predicting post-test parent-report of insulin adherence had an adjusted  $R^2$  of 0.511. Dosage of n-back training did not predict insulin adherence when controlling for pre-test insulin adherence reports, HbA1c level, age, gender, and race. SES was a marginally significant predictor of post-test insulin adherence as reported by parents ( $p=0.091$ ).

**Table 7**

*Post-test Parent Report of Insulin Adherence*

Variables	Unstandardized		Standardized	t	Sig.
	Coefficients		Coefficients		

	B	Std. Error	Beta	t	Sig.
(Constant)	2.03	1.31	-	1.55	0.132
Pre-test Insulin	0.62	0.14	0.60	4.38	<0.001
<i>Adherence</i>					
Dose	0.00	0.001	0.09	0.63	0.531
HbA1c level	-0.10	0.07	-0.22	-1.4	0.172
Age (years)	-0.03	0.07	-0.05	-0.37	0.714
Gender	-0.24	0.18	-0.16	-1.28	0.209
Race	0.00	0.001	0.10	0.82	0.418
SES	-0.35	0.20	-0.24	-1.74	0.091

### *Nutritional Choices*

**Child Report.** The adjusted  $R^2$  for the model predicting child-report of post-test nutritional choices was 0.432. Dosage of n-back training did not predict post-test nutritional habits when controlling for pre-test nutritional habits reports and other covariates. However, age was a marginally significant predictor of post-test nutritional choices ( $p=0.089$ ).

**Table 8**

### *Post-Test Child Report of Nutritional Choices*

Variables	Unstandardized		Standardized	t	Sig.
	Coefficients		Coefficients		
	B	Std. Error	Beta		

(Constant)	1.37	1.23	-	1.11	0.275
Pre-test Nutritional Choices	0.58	0.15	0.71	3.88	<0.001
Dose	0.001	0.001	0.19	1.27	0.216
HbA1c level	0.06	0.06	0.17	1.03	0.313
Age (years)	-0.114	0.07	-0.26	-1.76	0.089
Gender	-0.04	0.18	-0.03	-0.22	0.825
Race	0.001	0.001	0.23	1.51	0.141
SES	-0.06	0.17	-0.05	-0.37	0.713

**Parent Report.** The adjusted  $R^2$  for the model predicting parent-report of post-test nutritional choices was 0.454. Dosage of n-back training did not predict post-test nutritional habits when controlling for pre-test nutritional habits reports and other covariates. However, HbA1c was a significant predictor of post-test nutritional habits as reported by parents ( $p=0.013$ ).

**Table 9**

*Post-test Parent Report of Nutritional Choices*

Variables	Unstandardized		Standardized	t	Sig.
	Coefficients		Coefficients		
	B	Std. Error	Beta		
(Constant)	1.81	1.22	-	1.49	0.148

Pre-test Nutritional Choices	0.48	0.14	0.50	3.48	<b>0.002</b>
Dose	0.00	0.001	0.03	0.17	0.864
HbA1c level	-0.17	0.07	-0.39	-2.64	<b>0.013</b>
Age (years)	-0.03	0.07	0.000	-0.001	0.999
Gender	-0.24	0.18	-0.13	-1.03	0.310
Race	0.00	0.09	0.002	0.15	0.988
SES	-0.35	0.20	-0.06	-0.43	0.673

### *Glucose Monitoring*

**Child Report.** The model predicting child-report of glucose monitoring habits had an adjusted  $R^2$  of 0.363. Dosage of n-back training did not significantly predict post-test glucose monitoring when controlling for pre-test glucose monitoring reports, HbA1c levels, age, gender, race and SES. HbA1c levels did marginally predict glucose monitoring however ( $p=0.069$ ).

**Table 10**

#### *Post-test Child Report of Glucose Monitoring*

Variables	Unstandardized		Standardized	t	Sig.
	Coefficients		Coefficients		
	B	Std. Error	Beta		
(Constant)	0.137	1.44	-	0.95	0.925

Pre-test Glucose	0.63	0.2	0.55	3.17	<b>0.004</b>
Monitoring					
Dose	0.001	0.001	0.15	0.86	0.400
HbA1c level	0.14	0.07	0.30	1.89	0.069
Age (years)	-0.08	0.09	-0.18	-0.1	0.328
Gender	-0.21	0.22	-0.15	-0.97	0.343
Race	0.001	0.001	0.13	0.58	0.387
SES	0.13	0.22	0.09	-0.43	0.568

**Parent Report.** The model predicting parental report of glucose monitoring habits had an adjusted  $R^2$  of 0.305. Dosage of n-back training did not significantly predict post-test glucose monitoring when controlling for pre-test glucose monitoring reports, HbA1c levels, age, gender, race, and SES. Child gender, however, did significantly predict post-test parental reports of glucose monitoring ( $p=0.038$ ).

**Table 11**

*Post-test Parent Report of Glucose Monitoring*

Variables	Unstandardized		Standardized	t	Sig.
	Coefficients		Coefficients		
	B	Std. Error	Beta		
(Constant)	-0.31	1.22	-	-0.26	0.798



Pre-test Glucose	0.55	0.15	0.56	3.76	<b>&lt;0.001</b>
Monitoring					
Dose	-7.3E <sup>-5</sup>	0.001	-0.02	-0.18	0.908
HbA1c level	-0.03	0.06	-0.9	-0.47	0.641
Age (years)	0.07	0.07	0.17	0.97	0.341
Gender	-0.38	0.17	-0.32	-2.18	<b>0.038</b>
Race	0.001	0.001	0.16	1.06	0.300
SES	0.07	0.19	0.06	0.34	0.736

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### *Individualized Health Behavior Measures*

To further distinguish whether the models predicted behavior on particular measures individually rather than a composite measure, post-hoc analyses were conducted. The regression analyses were repeated for all health behavior variables with each child report and parent report post-test variable as a separate outcome. While most of the models did not significantly predict the health behavior measures, some of the ones that were significant, or marginal suggest a more nuanced relationship between dosage of n-back training and health behavior measures for T1D management regimen adherence than is immediately apparent in the original analyses. Below is a summary of the post-hoc regression analyses:

**Parent Report for Missed Insulin Dose.** The model predicting post-test parental report of missed insulin dose had an adjusted R<sup>2</sup> of 0.707. Dosage of n-back training was marginally significant at predicting parental report of missed insulin doses (p=0.092) but none of the other

covariates (pre-test missed insulin doses, HbA1c levels, age, gender, race, and SES) were significant.

**Table 12**

*Post-test Parent Report of Missed Insulin Dose*

Variables	Unstandardized		Standardized	t	Sig.
	Coefficients		Coefficients		
	B	Std. Error	Beta		
(Constant)	-0.32	1.8	-	-0.177	0.861
Pre-test Missed Insulin Dose	0.83	0.10	0.94	8.21	<b>&lt;0.001</b>
Dose	-0.001	0.001	-0.18	-1.74	0.092
HbA1c level	-0.17	0.11	-0.20	-1.57	0.126
Age (years)	0.16	0.1	0.17	1.61	0.117
Gender	-0.29	0.26	-0.10	-1.08	0.287
Race	-0.001	0.001	-0.15	-1.53	0.136
SES	0.14	0.29	0.05	-0.49	0.627

**Parental Report of Food Records.** The model predicting post-test parental report of food record keeping had an adjusted  $R^2$  of 0.574. N-back training sessions significantly predicted food record keeping as reported by parents ( $p=0.038$ ) when controlling for pre-test food recording parental reports, HbA1c levels, age, gender, race, and SES. This means that dose of n-

back training (total number of sessions) was significantly associated with parental reports of their children's food record keeping.

**Table 13**

*Post-test Parent Report of Food Record-keeping*

Variables	Unstandardized		Standardized	t	Sig.
	Coefficients		Coefficients		
	B	Std. Error	Beta		
(Constant)	0.79	1.68	-	0.47	0.640
Pre-test Food Record	0.78	0.12	0.76	6.34	<b>&lt;0.001</b>
Dose	0.002	0.001	0.27	2.16	<b>0.038</b>
HbA1c level	0.07	0.09	0.11	0.85	0.403
Age (years)	-0.13	0.10	-0.17	-1.38	0.177
Gender	0.1	0.26	0.05	0.40	0.689
Race	-0.001	0.001	-0.09	-0.82	0.417
SES	0.35	0.27	0.16	1.28	0.209

**Parental Report of Insulin Adjustment.** The model predicting post-test parental report of insulin adjustment had an adjusted  $R^2$  of 0.099. Dosage of n-back training did not significantly predict parental report of insulin adjustment but two of the covariates were

marginally significant: HbA1c level ( $p=0.089$ ) and child age ( $p=0.093$ ). None of the other covariates were significantly associated with insulin adjustment as reported by parents.

**Table 14**

*Post-test Parent Report of Insulin Adjustment*

Variables	Unstandardized		Standardized	t	Sig.
	Coefficients		Coefficients		
	B	Std. Error	Beta		
(Constant)	2.73	2.29	-	1.18	0.244
Pre-test Insulin Adjustment	0.25	0.16	0.26	1.56	0.129
Dose	-0.002	0.001	-0.29	-1.59	0.12
HbA1c level	-0.18	0.11	-0.33	-1.76	0.089
Age (years)	0.2	0.12	0.32	1.73	0.093
Gender	-0.2	0.29	-0.11	-0.68	0.503
Race	0.000	0.001	-0.02	-0.13	0.896
SES	-0.39	0.32	-0.22	-1.23	0.227

## Discussion

Type 1 diabetes is a major chronic disease affecting up to 1.84 million people in the US and 9 million worldwide (CDC, 2022; Mobasseri et al., 2020). T1D may cause many long-term complications that span multiple physiological systems and cause a significant decrease in

quality of life. Given that the age of onset of T1D occurs typically during childhood or adolescence, a critically sensitive era of brain development, T1D may impact the executive function development and by extension, self-regulation as well. It is hypothesized that this may be a bidirectional relationship, with T1D affecting EF development, and then low EF resulting in an inability to manage diabetes properly, setting up a positive feedback cycle (Cameron et al., 2019).

Therefore it is relevant that increasingly, evidence suggests that EF is a malleable construct and may undergo measurable increases in capacity and ability when individuals go through cognitive training (Diamond & Lee, 2011; Diamond & Ling, 2020). As such, increasing EF through cognitive interventions might also result in increases in self-regulation and goal-directed behavior. For children with T1D, it may even serve as a protective factor and optimized health outcomes if it increases adherence to T1D treatment regimens. To this purpose, this project utilized an experimental medicine approach to determine if a combination of n-back training, biofeedback, and episodic future thinking would result in better diabetes management. This was conducted through a randomized controlled trial, with one group assigned as controls who received informational sessions about T1D and the experimental group who received all three interventions.

While the other interventions are also important for self-regulation, the more working memory-focused n-back training was this study's focus with the purpose being to determine whether dosage of the n-back training is related to the cognitive and behavioral outcomes being assessed i.e., increases in WM capacity and IC along with adherence to T1D treatment regimen (insulin adherence, glucose monitoring, nutritional choices). Following a set of regression

analyses, no relationship was found between dosage of the n-back training and cognitive outcomes or composite measures of health behavior outcomes, however. Only one individual measure of health behavior, the parental report of food record keeping, was significantly associated with n-back training dose. It may be so that children who are more likely to keep food records according to their parents are also more likely to achieve more training sessions. As there is no effect of condition, it is difficult to pinpoint if the n-back training dosage had an impact on the health behavior or whether adolescents who were more likely to keep food records or improve their food record keeping over the course of the intervention also completed more training sessions. This was somewhat surprising given positive results in this subfield, for example Houben et al. (2016) reported that working memory training was linked to reduced psychopathological eating behaviors through increased emotional regulation (conceptualized as self-regulation in the study) although there was no change in food intake or body weight overall.

There are a number of potential reasons why this could be so. For example, the dosage of n-back training implemented in the study was not tightly controlled or enforced – participants were given Android tablets to take to their homes and encouraged to take part in the n-back training every day for eight weeks, but only minimal tracking was used to ensure compliance. As a result, only about 10 participants from the total 47 participants who received the intervention completed more than 30 n-back training sessions from the full 56 sessions i.e., only 10 participants completed the n-back intervention for more than four weeks (half of the required eight weeks). This may have had an effect on dose-response relationship analyses, given that very few participants met the minimum amount of training, which was established based on previous cognitive training research, such Conway and Getz (2010, Jaeggi et al. (2008), Lawlor-

Savage and Goghari (2016), and Pergher et al. (2018). Other potential reasons for this are expanded on in the Limitations section below.

Broadly speaking, the divergence between theoretical expectations and empirical observations is not new within this space. The effect of cognitive training itself has also been subject to irregularities and mixed results of its own. This may in part be due to a variety of factors, including test-retest reliability, practice effects, and the nature of transfer in cognitive training. In their meta-analyses of studies that conducted EF training, Karbach and Verhaeghen (2014) suggested that cognitive training led to significantly improved performance on the training task and near and far transfer effects were observed in both older and younger adults. However, critically, they reported no evidence of a dose-response relationship with the targeted training measures or the near-transfer measures. They suggested that the type of training or the characteristics of the population being studied might actually overshadow the effect of training length or duration, which also may be in play here in this study.

In an earlier meta-analysis of WM training studies, Melby-Lervåg and Hulme (2013) found that training resulted in only short-term, near transfer effects that were not moderated by training dosage. However, Schwaighofer et al. (2015) suggested a positive impact of training dose on transfer effects while attributing non-significance to small sample sizes and low statistical power. Soveri et al. (2017) also reported on the results of a meta-analysis that exclusively focused on n-back training itself. They found medium-sized transfer effects to untrained n-back tasks, but small effect sizes for other WM tasks, fluid intelligence and cognitive control. They also reiterated that there were no significant effects of training dose. Granted, these meta-analyses were more focused towards cognitive outcomes, but nevertheless they represent

an important consideration for working memory training. Within the context of this study, it is also not surprising that there were no dosage effects considering that there were also no effects of condition; the training group did not have significant differences than the control group on pre/post outcomes.

## **Limitations**

The small sample size of the experimental group ( $n=47$ ) that received the n-back training and thus was eligible for the analysis is a major limitation of this study. A post-hoc power analysis was conducted on GPower 3.1 and found that our models were vastly statistically underpowered even with modest effect sizes. The suggested sample size was 153, so our sample size ( $n=47$ ) for the analyses was approximately 3 times smaller than a sufficiently powered study. Of course, achieving this sample size may be challenging given the recruitment demands of finding a sufficient sample of children with T1D.

Although this study's scope was limited to the dosage of the n-back training, two other interventions were also given to the participants in the original study. As such, it may follow that the other two interventions (biofeedback and future episodic thinking) may also have had an effect that is not being captured by the current models due to the particular scope of this study. Alternatively, the two other interventions may have been differentially effective or may even have had interaction effects between each other and the n-back training being studied. It is also entirely plausible that the interventions themselves did not work and hence, had no effect on the participants. Although all three interventions were theoretically driven, EF may not interact with SR in the way that was hypothesized, and consequently, the n-back training along with biofeedback and future episodic training may not have any effects on health behavior at all.



However, it is necessary to consider that the low dosage of n-back training may have been an important factor and while the dosage of the other interventions was not calculated (since this study focused on n-back training alone), compliance for the other interventions may be equally low as well.

Most of the sample itself is also from a medium to high SES population and considering that 83% of the sample identifies as White, does not have racial and ethnic diversity. While participants were randomly assigned to receive the intervention or to be in the control group, given the lack of diversity, the results of this analysis may not be generalizable without replication studies that have larger samples that are more racially and socioeconomically diverse. Unfortunately, this is a common failing in cognitive studies and as suggested by Dotson and Duarte (2020), decades of cognitive research may not be applicable to populations that are more diverse than the samples in those studies.

Diversity in both SES and race/ethnicity is important considering the many interconnected pathways between SES and cognitive development. Multiple studies indicate that childhood SES influences cognitive development as seen by its effects on physical and mental health (Adler & Rehkopf, 2008; Merikangas et al., 2010; Shanahan et al., 2008), academic achievement (Sirin, 2005) and cognitive ability (Duncan & Magnuson, 2012). A number of studies indicate that low childhood SES is linked to deficits in a number of EF constructs (Hughes, 2011; Hughes & Ensor, 2005; Wiebe et al., 2011). Additionally, there are several strong correlations between low SES and poor diet, less physical activity, high body mass index (BMI), and obesity rates in children (Hanson & Chen, 2007; Poulain et al., 2019; Vieweg et al., 2007). It is evident that low SES may exacerbate pre-existing health disparities and lack of

access to resources compounds the challenges children from low SES backgrounds face. Within the context of T1D, this may include difficulties adhering to diabetes management regimens, but also being able to even afford exogenous insulin, a huge hurdle by itself (Addala et al., 2020; Lipman & Hawkes, 2020).

Apart from sample size and reduced diversity, elements of the study design itself have contributed to the study's results. Three interventions were given simultaneously to the same sample, making it difficult to pinpoint the exact intervention that might have had an effect on the cognitive or behavioral outcomes or if there was a combination of effects. Since each intervention also had a distinctly separate mechanism of action targeted towards the same construct (self-regulation) more or less, it is also difficult to isolate what didn't have an effect. It could be that n-back training was not effective in increasing WM or IC. It is equally plausible that by limiting the analyses to just the n-back training dosage, the effects of biofeedback training and episodic future thinking are being overlooked.

An additional limitation of the design is the limited oversight on the training itself. Although the at-home training on the Android tablets allowed a more naturalistic approach/setting for the cognitive training, the lack of emphasis also resulted in just 10 participants completing over half the required number of training sessions i.e., only about a quarter of participants completed half of the n-back training intervention. Although an incentive was provided to the participants, it seems to have been insufficient for the purposes of maintaining regular n-back training sessions.

## **Future Directions and Implications**

As there was limited compliance facilitation of dosage of n-back training in this study design, future studies looking at dose-response relationships of cognitive training should ensure participants complete the training in full, from each individual session per day to the overall required duration of the study. This can be through training conducted within laboratory settings, home visits or through more appealing incentives. Nguyen et al. (2014) report that for studies on adolescents with Type 2 diabetes, monetary compensation had a positive association with recruitment and retention. Although this study also had a weekly monetary reward for screenshots of completed daily n-back training sessions, it appears to have been insufficient in either the amount (\$10) or the frequency (every week). Nguyen and colleagues (2014) recommend that the amount of compensation should be calculated based on the specific circumstances (such as SES) of the potential participants such that it is neither too high as to be considered enticement nor too low to be considered as unfair reimbursement or unappealing. They also suggested intervention studies such as this one should recruit by addressing the more tangible, main concerns of the youth such as bodyweight and stress management, alongside the health benefits such as blood glucose control; this may be pertinent for recruitment in future studies.

Given the small sample in this study, it is also imperative to recruit larger samples with Type 1 diabetes to ensure sufficient power for analyses. More importantly, recruited participants should be more diverse than the current sample in this study, with regard to racial/ethnic identity and SES since both are often interconnected and equally important in cognitive as well as health behavior research, as mentioned earlier.

The study's randomized control design can also be replicated with samples that have different age ranges. The current sample included adolescents whose mean age was 15 years. But as other age ranges are also influential, it would be interesting to follow the trajectories of health behavior decision-making across childhood, young adulthood, or even middle adulthood, especially within the context of T1D. This study design may also be suitable for health behaviors important for the prevention or optimal management of other chronic diseases that often emerge in adulthood like Type 2 diabetes, cardiovascular disorders, hypertension and so on.

As mentioned above, the stability of the increases in cognitive performance has mixed results so far (Eschen, 2012; Melby-Lervåg & Hulme, 2013; Schwaighofer et al., 2015). As such, future cognitive training studies should consider conducting follow-up assessments that observe whether the projected increases in WM and IC remain consistent without further n-back training. If future studies utilize a simultaneous and parallel intervention design, it would be better to form sub-groups within the intervention group where participants receive just one intervention. This will help differentiate the efficacy of the intervention and its underlying mechanism from the other interventions as well as aid in comparison with the control group. Alternatively, cognitive and behavioral outcomes or measures can also be compared with participants that received all interventions together, such as this study, and the control group to observe if there are any differences.

This study may have important theoretical implications as well, especially with regards to the Temporal Self-Regulation Theory, which allows for the interplay between EF, intention and motivational factors, as well as pre-existing or default habits when explaining health behavior. Temporal values also influence health behavior through the immediate, often short-term benefits

expected from certain actions as opposed to the delayed, long-term gains from other activities; for example, eating ultra-processed foods high in calories may be more appealing than going for a jog or on a run. Even though processed foods may not have much nutritive value and may actually be harmful in the long run (especially in large amounts), consuming them provides temporary and instant pleasure. Conversely, physical activity such as jogging offers countless health benefits in the future, but requires physical exertion and commitment to goals in the present (which most individuals find to be difficult). TST posits that this trade-off between the present and the future is part of what makes health behaviors so complicated. Within this study's context of T1D intervention, health behaviors with long-term benefits such as insulin adherence (and treatment regimen adherence overall), need to be goals that adolescents assign greater temporal value to, over and above actions with immediate gratification. They also need to be willing to change their current habits or behavior. Given the results of this study, it may also be that cognitive training might not be as pertinent for increasing self-regulation or for impacting health behavior unless certain criteria are met. As such, motivation and intention may serve as a limiting factor of sorts; both may very well be instrumental in determining whether cognitive training has an observable impact on health behavior. Consequently, future research should give greater consideration to affect when designing potential interventions.

Similar to cognitive research, health behavior research often finds itself at crossroads where theoretically driven hypotheses do not always find empirical support. This points to a larger issue where either more research is needed into how and where theoretical and practical perspectives on self-regulation or behavioral decision-making differ or a different framework needs to be constructed using observational data. One way this could be done is through

exploratory, process-oriented, qualitative methods such as grounded theory which may investigate some of the reasons behind the variability in cognitive and health behavior research.

Mixed methods research may also offer an alternative approach to understanding why health-promoting behaviors are not easily implemented as well as informing interventions to improve health behaviors. An excellent example of this is Peterson et al.'s (2013) study where a multi-phase sequential mixed methods model named EVOLVE was used to promote physical activity as a health-promoting behavior for individuals or populations with chronic diseases such as cardiovascular disorders. The first phase utilized qualitative methodology to assess participant beliefs and values, followed by the pilot testing of a refined and tailored positive affect and self-affirmation intervention that was informed by the first phase. And lastly, the final phase consisted of a randomized control trial that tested the intervention on a larger scale. Results suggested that this methodology was successful in changing behavior for participants in the intervention group, especially when contrasted to the participants of the control group. Mixed methods approaches like these, when applied to cognitive training with the purpose of behavioral change, may be a compelling potential avenue to be pursued.

## **Conclusion**

T1D is a major chronic endocrine disorder affecting millions of people in the US and worldwide as well. Individuals who have T1D must adhere to a strict schedule of insulin injections, monitoring blood glucose levels, and healthy lifestyle choices to avoid consequences. This study aimed to elucidate the dose-response effects of cognitive training that may potentially enable individuals with T1D to have better adherence to their treatment regimens through

multimodal interventions that target EF processes. No link between the dose of n-back training and cognitive and behavioral outcomes was found. This may be so because of the low sample size and thus the under-powered analyses as well as the study design that did not firmly mandate n-back training sessions. Nevertheless, this study has important implications for future research, including recommendations for improving future study designs to better ensure compliance with intervention programs. All in all, adolescents with T1D have manifold, complex experiences with disease management and treatment adherence. Providing interventions that target self-regulation may not necessarily guarantee compliance and as such, motivational and affective aspects should also be considered when designing and implementing interventions.

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## Appendix

**Table 1**

*Correlation Table for Covariates and Pre-test Outcomes (Child Reports)*

	1	2	3	4	5	6	7	8	9	10
1 <b>Age (years)</b>	--									
2 <b>Gender</b>	0.083	--								
3 <b>Race</b>	0.227	-0.132	--							
4 <b>Parental Education</b>	-0.149	-0.070	0.154	--						
5 <b>Dose</b>	<b>.370*</b>	0.271	-0.010	-0.039	--					
6 <b>Pre-test HbA1c level</b>	0.148	0.017	-0.103	<b>-.464**</b>	-0.213	--				
7 <b>Pre-test Child Forward score</b>	-0.099	0.120	-0.134	0.228	0.035	-0.184	--			
8 <b>Pre-test Child Backward score</b>	-0.342	0.111	-0.247	-0.009	-0.070	-0.113	<b>.606**</b>	--		
9 <b>Pre-test Go No Go Mean RT</b>	-0.260	<b>.320*</b>	-0.150	-0.115	0.128	0.175	-0.229	-0.031	--	



10	<b>Pre-test Go No Go Accuracy</b>	-0.124	-0.022	0.035	<b>.377*</b>	0.110	-0.258	0.243	0.075	<b>.423**</b>	--
11	<b>Correct dose of insulin (CR)</b>	-0.116	-0.266	0.071	-0.173	-0.010	-0.063	0.029	0.167	-0.076	0.119
12	<b>Correct timing of insulin(CR)</b>	<b>-.333*</b>	<b>-.316*</b>	-0.049	-0.015	-0.076	-0.059	-0.020	0.123	-0.018	0.048
13	<b>Adjust insulin dosage (CR)</b>	<b>-.353*</b>	-0.102	-0.123	0.214	0.071	-0.148	0.129	0.048	-0.028	0.161
14	<b>Missed insulin dosage (CR)</b>	-0.017	-0.102	0.067	0.010	0.106	-0.229	0.252	0.311	<b>-.348*</b>	0.087
15	<b>Check blood glucose (CR)</b>	-0.207	<b>-.403**</b>	-0.142	0.221	0.022	-0.177	-0.054	0.006	0.096	<b>.398*</b>
16	<b>Record blood glucose (CR)</b>	-0.108	-0.109	-0.106	<b>.361*</b>	0.202	-0.247	0.161	0.097	0.057	0.177
17	<b>Check ketones (CR)</b>	0.075	0.102	0.124	0.058	0.052	0.135	0.057	0.012	0.166	0.148
18	<b>Blood Glucose Testing Frequency (CR)</b>	-0.183	-0.031	-0.208	-0.046	0.111	0.067	-0.018	0.027	0.015	0.055



15	<b>Check blood glucose (CR)</b>	0.250	0.127	<b>.386*</b>	<b>.377*</b>	--							
16	<b>Record blood glucose (CR)</b>	0.155	0.081	<b>.462**</b>	0.188	<b>.327*</b>	--						
17	<b>Check ketones (CR)</b>	-0.174	<b>-.350*</b>	-0.077	0.104	0.123	0.062	--					
	<b>Blood Glucose</b>												
18	<b>Testing Frequency (CR)</b>	0.222	0.281	<b>.422**</b>	0.007	0.143	0.117	-0.145	--				
19	<b>Correct food portions (CR)</b>	<b>.337*</b>	<b>.328*</b>	<b>.626**</b>	0.089	<b>.423**</b>	<b>.356*</b>	-0.013	0.272	--			
20	<b>Correct food timing (CR)</b>	<b>.349*</b>	<b>.413**</b>	<b>.541**</b>	<b>.355*</b>	<b>.457**</b>	0.284	-0.184	0.301	<b>.631**</b>	--		
21	<b>Keep food records (CR)</b>	0.243	0.291	<b>.357*</b>	0.098	<b>.405**</b>	<b>.413**</b>	-0.073	0.064	<b>.404**</b>	0.192	--	
22	<b>Read food labels (CR)</b>	<b>.471**</b>	0.211	0.242	0.270	0.148	0.171	-0.048	-0.002	<b>.430**</b>	<b>.344*</b>	0.277	--

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**Table 2***Correlation Table for Covariates and Pre-test Outcomes (Parent Reports)*

	1	2	3	4	5	6	7	8	9	10
1 <b>Age (years)</b>	--									
2 <b>Gender</b>	0.083	--								
3 <b>Race</b>	0.227	-0.132	--							
4 <b>Parental Education</b>	-0.149	-0.070	0.154	--						
5 <b>Dose</b>	<b>.370*</b>	0.271	-0.010	-0.039	--					
6 <b>Pre-test HbA1c level</b>	0.148	0.017	-0.103	<b>-.464**</b>	-0.213	--				
7 <b>Pre-test Child Forward score</b>	-0.099	0.120	-0.134	0.228	0.035	-0.184	--			
8 <b>Pre-test Child Backward score</b>	-0.342	0.111	-0.247	-0.009	-0.070	-0.113	<b>.606**</b>	--		
9 <b>Pre-test Go No Go Mean RT</b>	-0.260	<b>.320*</b>	-0.150	-0.115	0.128	0.175	-0.229	-0.031	--	

10	<b>Pre-test Go No Go Accuracy</b>	-0.124	-0.022	0.035	<b>.377*</b>	0.110	-0.258	0.243	0.075	<b>.423**</b>	--
11	<b>Correct dose of insulin (PR)</b>	-0.081	0.075	-0.104	-0.212	0.022	<b>-.338*</b>	0.232	0.217	0.185	<b>.342*</b>
12	<b>Correct timing of insulin(PR)</b>	-0.102	-0.094	-0.004	-0.033	0.229	-0.305	0.047	0.158	0.195	0.316
13	<b>Adjust insulin dosage (PR)</b>	-0.212	-0.141	0.153	0.155	-0.017	-0.280	0.204	0.240	-0.034	<b>.458**</b>
14	<b>Missed insulin dosage (PR)</b>	-0.155	-0.018	-0.128	-0.010	0.215	<b>-.543**</b>	0.273	0.285	-0.033	0.298
15	<b>Check blood glucose (PR)</b>	-0.076	-0.175	-0.184	-0.138	0.168	-0.069	-0.028	0.209	0.078	0.225
16	<b>Record blood glucose (PR)</b>	0.014	0.194	-0.105	0.092	0.222	0.111	0.042	0.006	<b>.354*</b>	0.252
17	<b>Check ketones (PR)</b>	0.075	0.102	0.124	0.058	0.052	0.135	0.057	0.012	0.166	0.148
18	<b>Blood Glucose Testing Frequency (PR)</b>	0.038	0.133	-0.148	-0.079	0.006	0.132	0.047	0.036	-0.174	-0.192





