Objective and Subjective Influences on Cognitive Performance in Adolescents with Type 1 Diabetes

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OBJECTIVE AND SUBJECTIVE INFLUENCES ON COGNITIVE PERFORMANCE IN ADOLESCENTS WITH TYPE 1 DIABETES

by

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ABSTRACT
OBJECTIVE AND SUBJECTIVE INFLUENCES ON COGNITIVE PERFORMANCE IN ADOLESCENTS WITH TYPE 1 DIABETES

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Type 1 diabetes mellitus (T1DM) is an increasingly common chronic illness in children and adolescents that can result in short- and long-term health complications. Disease management can be a particular challenge for adolescents seeking autonomy from caregivers. Recently, there has been a significant increase in adolescents' use of diabetes-related technology to aid in blood glucose (BG) management and insulin administration. Individuals with T1DM also experience symptoms related to their BG levels, and these symptoms can serve as indicators of out-of-range BG levels and guide management decisions. Although research shows that diabetes-related health factors can affect cognitive functioning, no existing research has explored the relationship between cognitive performance and immediate symptomatology at the time of testing. The present study examined the similarities and differences between objective and subjective diabetes-related variables and their respective relationships to cognitive performance. This study also explored the use of diabetes technology in this population, and adolescents' ability to accurately estimate their current BG levels.

Fifty-five adolescents (ages 13-17) diagnosed with T1DM completed the study during a 10-day diabetes camp session. Participants completed symptom inventories and estimated their BG level before checking it with a meter. They also completed two cognitive assessments (Symbol Digit Modalities Test, or SDMT, and D-KEFS Tower Test) and a brief interview about their use of diabetes-related technologies.

Adolescents whose BG levels were out of the recommended range performed more poorly on the SDMT, and those who endorsed more subjective symptomatology also took longer to make their first move on the Tower Test. Adolescents were fairly accurate in their BG estimations, most making estimates that were inaccurate but without clinically serious implications. No relationships were found between continuous glucose monitor use and BG estimation accuracy. However, participants who reported checking their BG more frequently per day with a meter made more accurate BG estimations.

Overall, present findings suggest that both immediate BG levels and immediate symptomatology relate to adolescents' cognitive function. These results underscore the importance of considering symptomatology, symptom awareness, and estimation accuracy in school settings in order to optimize adolescents' functioning in these settings.

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Objective and Subjective Influences on Cognitive Performance in Adolescents with Type 1 Diabetes

Type 1 diabetes mellitus (T1DM) is one of the most common chronic illnesses in children and adolescents worldwide, and the negative health risks across the lifespan can be disabling and even life-threatening (Dabelea et al., 2014). In individuals with this condition, pancreatic cell destruction (most often due to an autoimmune attack) leads to insulin deficiency, resulting in an inability to convert food and glucose into energy (Daneman, 2006). T1DM is most often diagnosed in children and young adults, and recent data suggest that the incidence of T1DM in adolescents is increasing (Dabelea et al., 2014). T1DM poses many inherent challenges to adolescents and their caregivers, including constant disease monitoring and often an invasive treatment regime. Poor disease management can have deleterious short- and long-term consequences for physical health and cognitive functioning. Among adolescents, it is important to gain further understanding about how symptom awareness and blood glucose level impact cognitive performance and how the use of diabetes monitoring technology affects disease management.

T1DM Management

Disease management involves an intensive treatment regime that requires families to shift and fit their lifestyle to the illness. An individual with T1DM must monitor blood glucose levels and administer insulin appropriately to compensate for the fact that the pancreas doesn't produce insulin. Blood glucose levels measure short-term or immediate glycemic control. Patients monitor their blood glucose levels with finger pricks multiple times throughout the day, and they administer insulin to adjust blood glucose levels and

compensate for food consumed. Insulin can be administered by injection or by insulin pump. Medical professionals encourage individuals with T1DM to aim for blood glucose levels as close to "normal" (i.e., levels of those without T1DM, also referred to as "in-range" blood glucose levels) as safely possible. Patients' ability to accomplish this is referred to as their "metabolic control." This, however, can be a difficult goal to achieve. Standards for target glucose levels have been systematically lowered over the past decade, meaning that medical professionals are asking patients to maintain tighter control over their disease, although they acknowledge that near-normalization of blood glucose levels is virtually impossible. Recommendations for glycemic control are often based on data obtained from studies of adults with T1DM. Target blood glucose levels for children and adolescents typically range from 90 to 150 mg/dl (American Diabetes Association, 2016a). Special attention must therefore be paid to the risks for hypoglycemia (i.e., low blood sugar) and hyperglycemia (i.e., high blood sugar) in children and adolescents with T1DM. Children and adolescents may be less able to recognize symptoms indicative of hypoglycemia and hyperglycemic, and therefore they may be at greater risk for extreme blood glucose levels, which can lead to seizures or comas (Silverstein et al., 2005). There are numerous physiological symptoms that may indicate the presence of hypoglycemia and hyperglycemia (e.g., thirst, headache, shakiness, etc.), and attention to these symptoms is an important aspect of diabetes management.

Long-term glycemic control is measured by hemoglobin A1C (Hb_{A1C}), which is an objective measure that reflects one's average blood glucose level over the past two to three months (Gonder-Frederick & Cox, 1991). Target levels for glycemic control for T1DM patients, as recommended by the American Diabetes Association, vary based on

age and are presented for patients under 6 years of age, 6-12 years of age, and 13 years of age to adulthood (Silverstein et al., 2005). Therefore, adolescents are expected to meet similar requirements to adults as they age. For children under 6, an Hb_{A1C} value between 7.5% and 8.5% is recommended because of the high risk for hypoglycemia in this age group. For children between 6 and 12 years old, a value under 8.0% is recommended due to the lower risk of hypoglycemia and the relatively low risk of complications before puberty. For adolescents and young adults, a value under 7.5% is recommended due to higher risk of complications and consideration of developmental and psychological issues that may co-occur with inconsistent metabolic control.

Individuals with T1DM must also be aware of their diet and nutrition, although there is little research on specific nutrient requirements for children and adolescents with diabetes (ADA, 2016a; Donaghue et al., 1997; Weissberg-Benchell et al., 1995). This may be due to the fact that there is no "one-size-fits-all" eating pattern for individuals with T1DM that improves glycemic control (ADA, 2016b). Nutrition recommendations therefore focus on achieving target blood glucose levels and glycemic control without excessive hypoglycemia (Trumbo, Schlicker, Yates, & Poos, 2002). Regular consultation with a dietitian is recommended for children and adolescents with T1DM, and meal plans must be individualized to optimize glycemic control, while also accommodating food preferences, cultural influences, physical activity patterns, and family eating schedules and patterns (Silverstein et al., 2005).

Regular exercise provides many benefits for individuals with T1DM, including but not limited to improved physical fitness, help with weight control (when necessary), and a greater sense of well being (Wasserman & Zinman, 1994). Excessive exercise is

related to 10-20% of hypoglycemic episodes and is usually associated with greater than typical duration, intensity, or frequency of exercise (Silverstein et al., 2005). Exercise is therefore an important aspect of maintaining good physical health for children and adolescents with T1DM, just as it is for their healthy peers. However, exercise in individuals with T1DM often requires close and careful attention in order to avoid hypoglycemia. Thus, T1DM requires constant monitoring of objective diabetes-related measures, insulin dosages, and subjective physiological symptoms in order to maintain optimal physical health.

Complications of T1DM

Lack of metabolic control, caused by inconsistent, frequently high or low blood glucose levels, can have severe short-term and long-term consequences for patients with T1DM. In the short term, low blood sugar levels can cause immediate symptoms including shakiness, sweating, irritability, confusion, rapid heartbeat, dizziness, hunger, and weakness (ADA, 2016b). High blood sugar levels can immediately cause increased thirst, frequent urination, headaches, nausea, and diabetic ketoacidosis (DKA), which is a life-threatening condition in which the body begins to break down fat and muscle for energy due to a lack of available insulin (Wolfsdorf, Glaser, & Sperling, 2006). Long-term complications typically arise from chronically high blood sugar levels. Overall, T1DM reduces the normal lifespan by 11 to 13 years and significantly increases the risk of heart disease and stroke (Livingstone et al., 2015). Kidney damage is one of the most common long-term complications and can lead to complete kidney failure over time in approximately 30% of patients with T1DM (National Kidney Foundation, 2015). Neuropathy in the feet and other extremities is also common; T1DM is responsible for

more than half of the lower limb amputations in the US every year and is the leading cause of blindness in adults (ADA, 2016c). Psychologically, T1DM increases one's risk for depression and eating disorders (Melendez-Ramirez, Richards, & Cefalu, 2010).

Blood glucose monitoring

Given the potential negative consequences of out-of-range blood glucose levels, it is crucial that individuals with T1DM, and especially developing children and adolescents, maintain good metabolic control. Adherence to a strict treatment regimen involves frequent blood glucose monitoring (i.e., at least four times per day). Self-monitoring of blood glucose (SMBG) allows individuals with T1DM to measure blood glucose levels objectively. Studies have shown a strong correlation between the frequency of blood glucose monitoring and metabolic control (Anderson, Ho, Brackett, Finkelstein, & Laffel, 1997; Kichler, Kaugars, Maglio, & Alemzadeh, 2012). Frequent SMBG can help identify patterns of hypoglycemia and hyperglycemia that can inform insulin dosages. Frequency of SMBG can decrease during adolescence, but studies show that adolescents with T1DM more accurately and reliably report their SMBG when they know that their meters are being checked by adults (Sjoeholm, Gray, Rayns, Tomlinson, & Wheeler, 2016). Results from frequent SMBG and correct interpretation of the results make effective disease management possible.

In the past few decades, technology development for T1DM management has accelerated. Use of continuous glucose monitors (CGMs), introduced in 2005, involves placing a two- to three-millimeter wide sensor under the skin to enable monitoring of interstitial glucose levels constantly throughout the day. Glucose values are typically displayed in graph format on a receiver, an insulin pump, or a smartphone (Castle &

Jacobs, 2016). Ongoing opportunities to monitor blood glucose levels provide infinitely more data than one receives from finger prick checks four to six times per day. Research has shown that the use of CGMs in adolescents with T1DM significantly improves their metabolic control by providing accurate data, promoting patient communication with medical providers, and enhancing motivation to self-monitor blood glucose levels (Bergenstal et al., 2010; Schaepelynck-Belicar, Vague, Simonin, & Lassmann-Vague, 2003). However, it is possible that adolescents with access to a deluge of blood glucose values from these technologies may be less aware of their subjective physiological symptoms because of their reliance on information from these technologies. Adult CGM users have been found to rely heavily on CGM data to make adjustments in their insulin dosages (Pettus & Edelman, 2016). Those who rely on their CGMs to tell them when their BG levels are out of range might have less of a need to attend to their subjective symptoms as indicators of BG levels, resulting in symptom unawareness, which could in turn lead to metabolic control. Conversely, it might be the case that more frequent CGM use results in increased awareness of how one's symptoms correspond to out-of-range BG levels.

Insulin administration

Advances have also been made in insulin delivery over the past few decades. Insulin administration was originally done exclusively via injection into fatty tissue. The insulin pump, a method of delivering continuous subcutaneous insulin, was invented and became popular in the 1970s. The ability to use rapid-acting insulin constantly and to dose insulin as needed prior to meals or for adjustments was shown to provide better metabolic control than previous methods involving multiple daily injections and different

types of insulin (Tamborlane, Sherwin, Genel, & Felig, 1979). In the 1990s, there was a ten-fold increase in the number of T1DM patients under the age of 20 starting on insulin pumps (Tamborlane, Bonfig, & Boland, 2001), and both adult and child patients on insulin pumps have been found to have significantly improved metabolic control (Boland, Grey, Oesterle, Fredrickson, & Tamborlane, 1999; Tumminia et al., 2015a; Tumminia et al., 2015b; Weissberg-Benchell, Antisdel-Lomaglio, & Seshadri, 2003; Ziegler et al., 2015).

Technology use varies considerably from patient to patient; rates of technology uptake are associated with personal and psychological characteristics, perceptions of and access to the technology, lifestyle, and existing diabetes management strategies (Kubiak, Mann, Barnard, & Heinemann, 2016; Naranjo, Tanenbaum, Iturralde, & Hood, 2016). Additionally, individuals with T1DM do not always consistently use their pumps or CGMs once they have obtained (de Bock et al., 2016). Adolescents have been found to be particularly receptive to a variety of diabetes monitoring technologies, and the area of mobile health has been explored as a possible pathway for intervention with this population and their caregivers (Wagner et al., 2016). One study found that 96% of caregivers of children with diabetes had access to the internet, and 64% used the internet for diabetes resources, predominantly social media (Balkhi, Olsen, Lazaroe, Silverstein, & Geffken, 2015). Many smartphone apps exist to aid diabetes self-management; most apps focus on BGM recording, food and insulin tracking, and insulin dosage calculating (Demidowich, Lu, Tamler, & Bloomgarden, 2012). Research shows that ease of use and real-time access to diabetes data make these technologies appealing to both parents and children (Prakasam, Rees, Lyden, & Parkin, 2016).

In sum, there has been a significant increase over the last twenty years in the technology available for T1DM patients and in the use of that technology by adolescents. Most of these technologies have been found to significantly improve glycemic control and diabetes care. However, it is important to explore the relationship between technology use and adolescents' awareness of their physiological symptoms.

Symptom monitoring

Individuals with T1DM vary in their ability to detect symptoms of high or low blood glucose levels. Recognition of subjective physiological symptoms is crucial to the behavioral model of disease management, as physiological symptoms provide immediate and direct information about health status (Nerenz & Leventhal, 1983). Symptom perception in diabetes can be defined as "conscious awareness of or ability to detect physical sensations associated with hypo- and hyperglycemia (e.g., pounding heart, shakiness) that result from blood glucose fluctuations" (Lane, 2006, p. 233). Individuals' awareness of their subjective physiological symptoms may provide information about hyperglycemia and hypoglycemia. Typical symptoms may include headache, nausea, thirst, hunger, sweating, shakiness, and many others, depending on the individual and the associated blood glucose level Some individuals have a set of symptom beliefs (i.e., thoughts or beliefs that certain physiological symptoms correspond to certain blood glucose levels) that help them guide self-treatment decisions, and some do not. The use of subjective physiological symptoms to monitor one's blood glucose levels is dependent upon the assumption that one's subjective symptomatology is an accurate and reliable indicator of one's objective blood glucose, which may not be the case for all individuals.

It is also important to note that not all individuals will have the same symptoms relating to the same blood glucose levels. Studies show that both hypoglycemia and hyperglycemia can be symptomatic, but that there are no specific symptoms that covary with either hypoglycemia or hyperglycemia *across* patients (Freund, Bennett-Johnson, Rosenbloom, Alexander, & Hansen, 1986; Gonder-Frederick & Cox, 1991). However, hypoglycemia is generally associated with more symptoms that are also more severe in nature and may be slightly more consistent across individuals. Additionally, blood glucose level thresholds at which individuals begin to feel symptomatic are not the same for all patients (Gonder-Frederick & Cox, 1991). Thus, all diabetes-related symptomatology is quite idiosyncratic, and general statements cannot be made about which symptoms apply to which blood glucose levels (Lane, 2006).

Because of aforementioned serious, long-lasting consequences of poor metabolic control, it is important that individuals with T1DM recognize their symptoms and use this information to guide their decisions about whether and when to check their blood sugar and follow up with appropriate adjustments.

Studies in this area must therefore be careful to focus on within-subjects patterns and differences. In light of this, we can ask two main questions related to an individual's subjective diabetes-related symptoms: To what extent do individuals' own subjective physiological symptoms reliably covary with their blood glucose fluctuations, and to what extent do T1DM patients accurately recognize and label their symptoms?

There is no linear relationship between physiological events and one's subjective perceptions of those events. All of these relationships will vary both across individuals and within individuals; therefore, one cannot assume that all individuals experience the

same physiological events in reaction to the same blood glucose levels. Related research shows that adults make clinically serious errors in their blood glucose estimations up to 20% of the time, and that adolescents are significantly worse at estimations than are adults and make similarly serious errors approximately one-third of the time (Cox et al., 1985; Gonder-Frederick, Snyder, & Clarke, 1991; Lane, 2006). These errors most commonly consist of failure to detect extreme levels of blood glucose (more often hyperglycemia than hypoglycemia), which can lead to under- or over-corrective treatments (Gonder-Frederick et al., 2004; Kovatchev, Cox, Gonder-Frederick, Schlundt, & Clarke, 1998; Lane & Heffer, 2005 as cited in Lane, 2006). It is therefore evident that T1DM patients' awareness of their subjective physiological symptoms can affect their disease management.

Researchers in the early 1990's developed a program called Blood Glucose Awareness Training (BGAT; Gonder-Frederick, Cox, Clarke, & Julian, 2000). This program aims to increase the ability of individuals with T1DM to accurately perceive and interpret their own blood glucose levels. This includes recognizing hyperglycemia and hypoglycemia and identifying patterns and errors in one's perceptions. The training aims to improve patients' ability to recognize which symptoms correspond to which blood glucose levels. It is then expected that patients' metabolic control will also improve via increased recognition of out-of-range blood sugars and more timely responses to those blood sugars. Studies investigating effectiveness of the intervention with pre- and post-test designs have found improved accuracy in detecting blood glucose fluctuations and better detection of both hyperglycemia and hypoglycemia (Cox et al., 1989; Cox et al., 1995). Thus, individuals with T1DM can use the information gained from their

experience of specific symptoms to guide decisions of if, when, and how to regulate their blood glucose.

Challenges for adolescents with T1DM

In addition to the inherent challenges of managing T1DM, adolescents with this disease must also grapple with the developmental changes occurring at this time. Adolescence is a period of rapid biological development and increasing emotional, cognitive, and physical maturity that is often characterized by individuals' search for their autonomy and independence from their parents or caregivers (Herzer & Hood, 2010). This is especially salient in the context of chronic illness management. Moreover, adolescence can trigger changes in insulin sensitivity related to physical growth and sexual maturation, in addition to a neurological vulnerability to hypoglycemia and hyperglycemia (Barnea-Goraly et al., 2014). These particular biological changes may contribute to challenges in managing T1DM.

In childhood, diabetes management tasks are primarily the responsibility of the parents or caregivers. During adolescence, this responsibility begins to transfer to the adolescent in preparation for adulthood. This transition period can be one of the most difficult times for adolescents with T1DM (Garvey, Markowitz, & Laffel, 2012). Because adolescents are physically able to complete adherence tasks, parents are sometimes tempted to quickly hand all responsibility to their teenagers. However, while adolescents may be physically prepared for the increased responsibility, they often need help with the decision making and planning required to execute T1DM management tasks successfully (Herzer & Hood, 2010). This may leave adolescents with T1DM feeling unsupported and vulnerable, which can lead to an avoidance of self-care and follow-up care from medical

providers. Disease management and treatment adherence may therefore often not be a priority for adolescents with T1DM (who may choose to pursue more typical age-appropriate activities), and metabolic control often decreases as a result (Garvey et al., 2012). Because of these developmental changes, adolescents' increased responsibility for disease management tasks necessitates an acquisition of new skills and an increased awareness of their bodies' signs and signals indicating low and high blood sugars.

Cognitive functioning in adolescents with T1DM

Metabolic control may also impact cognitive functioning. Glucose is virtually the sole source of fuel for the human brain, which lacks fuel stores and hence requires a continuous supply of glucose. In addition to consuming glucose for general functioning, glucose use can also be tracked during shorter periods of cognitive effort. Studies have shown that individuals without diabetes whose blood glucose levels decreased during a cognitive task performed better on the task than those whose BG levels did not change during the task (Galanina et al., 2008); it is hypothesized that their brains were efficiently using glucose to complete the task. Furthermore, adult subjects without diabetes who consumed a glucose drink immediately prior to a cognitive task also performed better on the task than those who did not consume the drink (Scholey, Harper, & Kennedy, 2001). Importantly, glucose consumption would not be an energy asset in individuals with diabetes, who might develop hyperglycemia in reaction to the glucose intake. Thus, it is important to better understand the impact of glucose levels in adolescents with T1DM prior to a cognitive task.

In children and adolescents with diabetes, cognitive performance is commonly studied in relation to children and adolescents without diabetes. Results consistently show

that when compared to children without diabetes, children with diabetes perform more poorly on various neuropsychological and cognitive assessments, especially in the areas of psychomotor speed, mental flexibility, and attention (Brands, Kessels, de Haan, Kappelle, & Biessels, 2004; Moheet, Mangia, & Seaquist, 2015). Differences between these two groups are more pronounced in children with earlier onset diabetes (Gaudieri, Chen, Greer, & Holmes, 2008). However, unlike research on individuals without diabetes, there is no existing literature addressing the relationship between immediate blood glucose levels and cognitive performance in individuals with diabetes. Symptoms such as headaches, nausea, or shakiness may impact an individual's ability to attend to tasks or information and make appropriate decisions when completing a cognitively-demanding task. Given the potential effects of blood glucose level and symptomatology on daily cognitive functioning in children and adolescents with diabetes, an understanding of the relationship between these variables is a critical aspect of disease management in this population.

Present study

In light of the information presented thus far, this study examined the similarities and differences between objective and subjective diabetes-related variables and their respective relationships to cognitive performance. In order to accomplish this, objective and subjective measures of blood glucose and physiological symptoms were assessed.

Many studies examining psychological and physiological factors in individuals with T1DM measure Hb_{A1C}, which indicates metabolic control over a long-term period of time. Typically, Hb_{A1C} levels over time have been examined in relation to cognitive functioning (e.g., Brands, Biessels, de Haan, Kappelle, & Kessels, 2005). Conversely, the

present assessed blood glucose immediately before the completion of two cognitive tasks in order to better understand how the participants' objective blood glucose level at the time of the task may be related to task performance.

This study examined potential predictors of cognitive performance and whether one's objective blood glucose levels or subjective physiological symptoms are better able to predict performance on tasks of processing speed and executive functioning. The study also investigated adolescents' ability to predict their own blood glucose levels and whether adolescents' use of diabetes-related technology was associated with their prediction accuracy. This is an area that has yet to be explored.

In order to assess subjective symptomatology and technology use, assessments were developed for this purpose (i.e., a symptom checklist and a semi-structured interview on technology use). This study was the first to explore all of these variables in adolescents, and findings will inform medical, mental health, and educational professionals about the impact of various diabetes-related outcomes on adolescents' functioning in school and other settings.

Hypotheses

The hypotheses tested in the current study were as follows:

1. Blood glucose range (i.e., whether participants' BG levels were in or out of the recommended 90 to 150 range) and subjective symptomatology (i.e., the combined severity of each experienced symptom) at the time of testing will be significantly related to scores on each of the cognitive measures.
    a. Blood glucose range will be negatively related to scores on both the D-KEFS Towers and the Symbol Digit Modalities Test, such that

participants whose blood glucose levels are out of range will perform more poorly on these cognitive tasks.

b. Subjective symptomatology will be negatively related to scores on both the D-KEFS Towers and the SDMT, such that participants experiencing increased levels of physiological symptoms will perform more poorly on these cognitive tasks.

c. When considering the influence of both blood glucose deviation and subjective symptomatology on cognitive performance, subjective symptomatology will account for significantly more variance in each assessment than will blood glucose deviation.

2. Significant differences in blood glucose prediction accuracy will be found based on the frequency of individuals' technology (i.e., pump and CGM) use.

Research Design and Method

Participants

Eligible participants included adolescents aged 13 to 17 years with a current diagnosis of type 1 diabetes. Potential participants with a diagnosis of type 2 diabetes were excluded from the study.

Procedure

Participants were recruited from the group of 120 adolescents registered for a teen diabetes camp in the summer of 2016. The camp director sent information about the current study and the investigators via email to parents of adolescents registered for the July 2016 camp. Those families interested in participating completed online parent

permission forms. In-person recruitment also took place immediately before the start of camp; experimenters were present at various drop-off locations and approached families about the study. Those families who expressed interest but had not yet completed online consent materials were given the opportunity to do so in-person.

Adolescents with parental permission for their participation were approached during the camp session and asked if they were still interested in participating in the study. Those who were interested first completed the assent process with one of two experimenters: the principal investigator or a female undergraduate research assistant. Participants did not receive any compensation for their participation.

After adolescents provided their individual assent to participate in the study, they completed a variety of tasks relating to objective blood glucose assessment, subjective symptom perception, cognitive capabilities, and their use of diabetes monitoring technologies. Testing took place in a private room in the camp's medical building. The study session lasted approximately 30 to 40 minutes. The order of most of the tasks was standardized (see Figure 1) with the exception of the administration of the two cognitive assessments, which were administered in a randomized counterbalanced order.

Measures

Demographic characteristics.

Adolescents were asked to report on their date of birth, diabetes diagnostic status (i.e., confirmation of T1DM diagnosis), age and date of diagnosis, gender, grade in school, race, ethnicity, and zip code. Median income per zip code was taken from data spanning 2006 to 2010 from the University of Michigan Population Studies Center.

Demographic variables were collected to describe the study sample and were used to assess for potential differences based on demographic characteristics. Time of testing and camp activities for the preceding two hours were recorded.

Symptom survey.

Participants completed a brief survey in which they indicated which, if any, of 22 subjective physiological symptoms they were currently experiencing (see Appendix A). This symptom survey included both common and uncommon symptoms of hypoglycemia and hyperglycemia. The symptom survey was developed based on previous literature that explored blood glucose symptomatology in individuals with T1DM (Gonder-Frederick & Cox, 1991). For each symptom, participants used a Likert scale to rate the intensity of the symptom ranging from 1 (*a little bit*) to 5 (*a lot*); thus; higher scores indicate more severe symptomatology. Scores for each symptom inventory (pre- and post-test) were generated by taking the mean of all symptom intensities for each of the two surveys completed. The two resulting scores were found to be highly correlated ($r = .81$, $p < .001$); thus, the pre- and post-test symptom scores were averaged, resulting in one score reflecting participants' subjective symptomatology at the time of testing.

The symptom survey also asked participants to provide an overall estimate of their current blood glucose level: low, in range, or high. This allowed for examination of inter-individual differences in the types of symptoms that are associated with blood glucose estimates.

Blood glucose estimate.

Participants were asked to estimate their current precise blood glucose level, which was recorded.

Blood glucose check.

Participants were asked to check their blood glucose level using their own meter and supplies. This value was recorded.

D-KEFS Tower.

The Delis-Kaplan Executive Function System (D-KEFS; Delis, Kaplan, & Kramer, 2001) is a set of nine standardized tests that measure a wide spectrum of verbal and nonverbal executive functions. The Tower subtest evaluates spatial planning, rule learning, inhibition of impulses and perseverative responding, and the ability to establish and maintain an instructional set. This subtest places demands on multiple aspects of executive functioning and draws on several aspects of goal-directed behavior (e.g., planning ahead while keeping rules in mind). It was selected for this study because of its demands on cognitive function and sustained attention. The D-KEFS was standardized on a nationally representative, stratified sample of 1,750 non-clinical children, adolescents, and adults ages 8 to 89 years (Homack, Lee, & Riccio, 2005). Moderate levels of test-retest reliability have been found on this task in 8- to 19-year-olds (Fisher, 2009). Administration takes approximately 10 minutes. Total Achievement, Mean First Move Time, and Time-Per-Move scaled scores were used for analyses. These scores range from 1 to 19, with a mean of 10 and a standard deviation of 3. The Total Achievement score is calculated based on how many towers are correctly completed in the allotted time and on how many moves were required to complete them (Yochim, Baldo, Kane, & Delis,

2009). Mean First-Move Time reflects the speed with which participants completed their first move on each item. Time-Per-Move ratio analyzes the average time a participant takes to make each of his or her moves (not just first moves). Higher scores represent more success on this subtest.

Symbol Digit Modalities Test.

The Symbol Digit Modalities Test (SDMT; Smith, 2000) is a cognitive assessment that measures attention, concentration, and speed of information processing. The test involves a substitution task wherein participants use a reference key to pair numbers with given geometric figures during a period of 90 seconds. There are oral and written forms of the test; for this study, the oral version was used to minimize effects due to differences in motor skills between participants. Test-retest reliability has been found to be good (Bate, Mathias, & Crawford, 2001). It is validated for use in individuals 8 years of age and older (Smith, 2000). This test was selected for the present study because it assesses cognitive function and processing speed. Administration typically takes 5 minutes or less. Standard scores range from 50 to 150, with a mean of 100 and a standard deviation of 15.

Technology Interview.

Participants took part in a brief (5- to 10-minute) semi-structured interview assessing their use of diabetes monitoring technology (see Appendix B). Questions inquired about which available technologies they use (e.g., blood glucose meters, insulin pumps, continuous glucose monitors), how often they use each technology, and how often they or their parents download and/or review data from said technologies. This

interview was developed for the present study based on literature exploring the assessment and monitoring of metabolic control in children and adolescents with T1DM (Rewers et al., 2009; Yeh et al., 2012). This survey yielded quantitative and qualitative descriptive information about participants' technology use. Quantitative scores derived from this interview included the following: 1) a variable indicating whether participants use insulin pumps and/or continuous glucose monitors ("technology use"); 2) a variable reflecting the frequency with which participants who have CGMs look at the data daily ("CGM look frequency"); 3) a variable reflecting the number of day in the past month individuals who have CGMs used them ("CGM use"); and 4) a variable reflecting the frequency with which participants checked their blood sugar daily ("BG check frequency").

Results

Data Analytic Plan

Statistical analyses were conducted using SPSS 24.0 (IBM Corp., 2016) and R statistical computing software (R Core Team, 2014). To address the first set of hypotheses examining symptom reports, numerical scores were generated from the pre- and post-test symptom surveys by averaging the intensity ratings for each of the symptoms endorsed. These two scores were highly correlated, $r = .81$, $p < .001$. Because no significant difference was found between them, a mean of the two scores was calculated and used in analyses. This variable, the total symptomatology score, was found to be significantly positively skewed (skew = 5.57). Thus, a square root transformation was conducted; the resulting variable had a skew value of 0.84.

BG values for pre- and post-test were used to generate corresponding dichotomous values reflecting whether or not each value was in the recommended range for adolescents (i.e., 90-150 mg/dl; ADA, 2016). These values will be referred to as BG range values (i.e., in range score = 1, out of range score = 2).

Standard scores for the D-KEFS Tower Total Achievement, Mean First Move Time, and Time-Per-Move were calculated using standard guidelines (Delis, Kaplan, & Kramer, 2001). These scores range from 1 to 19, with an average of 10 and a standard deviation of 3. Total standard scores for the SDMT were also calculated per standardized guidelines (Smith, 2002); these range from 50 to 150 with an average of 100 and a standard deviation of 15.

Independent samples t-tests were conducted to explore group differences on D-KEFS Tower and SDMT scores based on whether participants' BG levels were in range or out of range. Bivariate correlations were conducted to explore relationships among total symptomatology scores, D-KEFS Tower scores, and SDMT total scores. Multiple regression analyses were conducted to evaluate the amount of variance in cognitive scores accounted for by an individual's subjective physiological symptomatology and blood glucose range.

To address the second hypothesis, information from the technology interview was used to create a categorical technology use variable, reflecting whether participants used an insulin pump and/or a CGM (0 = neither, 1 = one or the other, 2 = both). Only one participant reported using a CGM but not a pump; hence, all participants who used one but not both technologies were combined into one group. Technology interviews were also used to create a CGM monthly use variable (i.e., reflecting the number of days in the

past month adolescents reported using their CGM) and a CGM look frequency variable (reflecting the number of times per day adolescent reported looking at his or her CGM data).

An error grid analysis (EGA) package of R (Schmolze, 2015) was used to calculate the accuracy of participants' blood glucose estimations. EGA was developed for this specific purpose and is commonly used in research examining BGAT programs (Cox, Gonder-Frederick, Kovatchev, Julian, & Clarke, 1997; Cox et al., 2001). EGA involves plotting estimated and observed blood glucose levels on a grid and observing clinical zones into which the intersection points fall. EGA differentiates between clinically benign and clinically significant errors (Lane, 2006). The original EGA detailed the clinical significance of the difference between two BG values (Clarke, Cox, Gonder-Frederick, Carter, & Pohl, 1987). Zones of accuracy (A through E) were developed based on numerical discrepancy between values. Parkes, Slatin, Pardo, and Ginsberg (2000) critiqued this original error grid on the basis that it overlooked certain risk categories and was based on outdated standards of clinical care. They developed a new error grid wherein zones of accuracy were based instead upon clinical judgment of medical professionals, who assigned errors to five risk categories. The resulting zones describe the risk of erroneous BG measurements (see Table 1 for zone criteria). For the purposes of this study, results from Parkes' EGA (2000) were used given its clinically-relevant approach to zone assignment.

The technology use variable was entered into a multiple regression analysis predicting EGA zones to determine the amount of variance in estimation accuracy accounted for by technology use.

Technology interviews were reviewed to identify primary themes that emerged in adolescents' discussions of the most helpful aspects of their CGMs. The primary investigator reviewed participants' qualitative responses and identified central themes; two research assistants then identified which themes were reflected in each participant's response. The research assistants agreed on 80.6% of the ratings. Agreement was calculated by dividing the number of agreed upon codes assigned by the total number of codes assigned. Ratings with disagreements were discussed with the primary investigator, and final ratings were determined.

A priori power analyses were conducted using G*Power 3.1.92 (Faul, Erdfelder, Buchner, & Lang, 2009) with a moderate effect size ($f^2 = 0.15$ for linear multiple regression). These analyses indicated that a total of 107 participants would be necessary to ensure that statistically significant effects are found for the multiple regression if they truly exist at the level of $\alpha = .05$. Unfortunately, there is no previous literature that could guide effect estimates. Given that this is a preliminary study and the limitations of recruitment from this population, effect sizes will be included in these analyses when relevant.

Participant Characteristics

Analyses were based on a sample of 55 adolescent participants. Descriptive statistics for demographic variables can be found in Table 2. All participants identified as having type 1 diabetes. Participants ranged in age from 13 to 17 years ($M = 15.11$, $SD = 1.06$). The majority of participants identified as Caucasian (87.2%). Furthermore, 3.6% of participants identified as American Indian or Alaska Native, Asian, or Black or African American, respectively. Sixteen-point-four percent of participants identified as Hispanic

or Latino/a. Based on self-reports, adolescents' mean age at diagnosis was 7.74 years (*SD* = 3.86).

Descriptive analyses for adolescents' performance on each of the cognitive assessments (SDMT and D-KEFS Tower Test) and for total symptomatology endorsed by participants can be found in Table 3. At pre-test, 34.5% of participants' BG levels were in range, and the remaining 65% were out of range. A significant relationship was found between age at diagnosis and median income, $r = .36$, $p = .01$, such that those diagnosed at an older age were more likely to live in a zip code with a higher median income. Additionally, a significant relationship was found between age at diagnosis and D-KEFS Tower Time Per Move scores, $r = -.27$, $p = .05$; participants diagnosed at an older age took longer to perform each move on the D-KEFS Tower test. No other group differences on any of the variables of interest were found based on demographic variables listed in Table 2.

Hypothesis 1: BG range and total symptomatology scores at the time of testing will be significantly related to scores on each of the cognitive measures. Subjective symptomatology will account for more variance in each cognitive measure than will BG range.

Analyses were conducted exploring group differences in cognitive performance based on whether individuals' blood glucose levels were in or out of range. Significant group differences were found on the SDMT total scores, such that those participants whose BG levels were in range performed significantly better on the SDMT than did the participants whose BG levels were out of range, $t(47) = 1.98$, $p = .05$. Participants whose BG levels were in range at pre-test also reported significantly higher total symptomatology than those whose BG levels were out of range, $t(53) = 2.03$, $p = .04$. The

effect sizes for these two group differences were in the medium range (0.53 and 0.58, respectively; see Table 4). No other group differences on cognitive performance were found based on pre-test BG levels. Test statistics can be found in Table 4.

Additionally, bivariate correlations were conducted to assess the relationship between total symptomatology and each of the cognitive scores. A significant relationship was found between total symptomatology and Tower Mean First Move Time. Adolescents who reported higher levels of symptomatology had a slower mean first move time across the nine items on the Tower test, $r = -.31$, $p = .01$. Total symptomatology thus accounted for 16% of the variance in Tower Mean First Move Time scores. No significant relationships were found between the total symptomatology variable and any other cognitive scores.

Hypothesis 2: CGM use frequency will be related to BG estimation accuracy.

EGA was conducted on both pre- and post-test BG estimates and values. However, post-test BG estimates were made only 15 to 20 minutes after participants had checked their BG at pre-test; hence, participants were fairly accurate in their post-test estimates and little variance in accuracy was found. Estimation accuracy at post-test was therefore not thought to be an authentic reflection of participants' estimation abilities, and thus only estimation accuracy at pre-test will be reported and discussed in analyses.

Parkes' EGA were conducted on estimated and actual BG values at pre-test. Participants' estimations were in the following zones: 38.2% were in Zone A; 60.0% were in Zone B; and 1.8% were in Zone C (see Table 3 and Figure 2).

Based on the technology interview, 10.9% of participants reported using neither a CGM nor a pump; 23.6% reported using one or the other; and 65.5% reported using both.

A chi-square test of independence was conducted to examine the relation between technology use and EGA zone; the relation between these variables was not significant, $\chi^2(4) = 0.96$, $p = .92$. One-way analyses of variance were conducted to assess for group differences in total symptomatology scores, SDMT total scores, and the three Tower scores based on technology use; no significant group differences were found.

The following analyses examined only participants who reported using a CGM ($n = 37$). One-way ANOVAs were conducted to examine potential differences in CGM look frequency and CGM monthly use based on BG estimation accuracy; no significant group differences were found. Within this sample, CGM look frequency was found to be significantly related to total symptomatology. Participants who reported looking at their CGM data more frequently also reported higher total symptomatology, $r = .35$, $p = .04$. CGM look frequency and CGM monthly use variables were entered into a linear regression predicting total symptomatology; the model was found to be significant, $F(2, 33) = 5.46$, $p = .01$, with an R^2 value of .25, indicating that the CGM-related variables accounted for 25% of the variance in total symptomatology. Notably, increased CGM look frequency but decreased CGM monthly use predicted increased total symptomatology.

When asked about the most helpful aspects of the CGM technology, five primary themes emerged (see Table 6). Over half (56.8%) of participants indicated that using the CGM increases their awareness of their BG level, especially in cases of hyperglycemia or hypoglycemia. For example, one participant stated, “It alerts me when I’m going high, because I don’t notice.” Thirty-seven percent of participants reported finding the CGM’s arrows (indicating whether BG values are rising or falling and at what rate) and the

graphs of BG values over the course of the day to be helpful. For example, one participant stated, “It’s good to see the trend arrows, it provides more information.” Twenty-seven percent of participants indicated that the CGM gives them advance notice of BG changes so that they can make timely adjustments with food or insulin; for example, one participant reported, “It lets you know where your blood sugar is going before you’re super high or super low.” Twenty-four percent of adolescents reported that the CGM is helpful in providing general information or data about their BG levels, including one participant who stated, “It’s good for more data. This is a condition about data and knowing what’s going on and how to respond.” Lastly, 21.6% of participants note that the CGM is more convenient than other methods of BG management. One participant reported, “it gives me a break from checking with holes in my fingers; it’s easier.”

When asked to rank the helpfulness of their CGM on a scale of 1 (*not helpful at all*) to 10 (*extremely helpful*), 75.6% of participants with CGMs indicated an 8 or higher (M = 8.27, range: 4-10).

Additional Exploratory Analyses

Based on analyses to address the proposed hypotheses, additional questions arose about the data. Thus, exploratory analyses were conducted to better understand two main areas of interest.

Rates of endorsement of individual subjective symptoms were explored. Independent samples t-tests were conducted to examine differences in individual symptom endorsement based on BG values. Participants whose BG values were out of range reported significantly higher levels of thirst than those who were in range, $t(52)$ = -

2.20, $p = .03$, but significantly lower levels of fatigue, $t(27) = 2.39$, $p = .02$, and feeling weak, $t(22) = 2.36$, $p = .03$.

Subsequently, differences in individual symptom endorsement between participants who reported *feeling* in range or out of range were examined. Participants who felt out of range (i.e., high) endorsed significantly higher levels of thirst at pre-test, $t(52) = -3.07$, $p = .003$, and at post-test, $t(52) = -2.55$, $p = .01$, and higher levels of dry mouth at post-test, $t(17) = -2.10$, $p = .05$. Additionally, participants who reported feeling out of range (i.e., high) at pre-test had higher objective BG values than those who reported feeling in range, $t(17) = -3.33$, $p < .001$.

Given the limited existing information on Parkes' EGA zones in this population, preliminary analyses examined what variables might be related to zone classification. Participants whose BG estimations were accurate enough to have no effect on clinical action (i.e., in Zone A) reported checking their BG (via meter) more frequently than those whose estimates were less accurate (i.e., Zone B or C), $t(28) = 2.19$, $p = .04$.

Discussion

The current study explored relationships among blood glucose levels, subjective physiological symptomatology, and cognitive performance in adolescents with type 1 diabetes. This study also examined the use of diabetes technology in this population and the accuracy with which adolescents can predict their current BG levels. This study was the first to explore the relationship between immediate, in-the-moment BG levels and cognitive performance in adolescents with T1DM. This study was also unique in its application of error grid analysis to the BG estimation of these adolescents.

Consistent with hypotheses, BG levels and subjective symptomatology were each distinctly related to various aspects of adolescents' cognitive performance. Contrary to hypotheses, no aspect of technology use was found to be related to adolescents' BG estimation accuracy. Within the group of adolescents who used continuous glucose monitors, monthly use and look frequency were related to the subjective symptomatology participants endorsed. General symptom endorsement did vary based on BG levels, although it seemed more dependent upon how participants reported feeling than on their objective BG levels. Notably, participants who reported checking their BG with a meter more frequently per day did make more accurate BG estimations.

Cognitive performance, blood glucose levels, and symptomatology

The hypothesis that objective BG level and total subjective symptomatology would each be related to scores on all cognitive assessments was not supported. Instead, BG level (i.e., whether participants' BG values were in or out of the target range based on ADA standards for adolescents; ADA, 2016b) and total subjective symptomatology were found to be significantly related to different cognitive assessment scores.

BG values were significantly related to scores on the SDMT; specifically, participants whose BG values were within the target range at the time of testing performed significantly better on the SDMT. The SDMT is a well-validated measure often used to assess neurocognitive functions including attention, visual scanning, and processing speed. It is also widely used to assess for neurological impairment and is accepted as a measure that is sensitive to such impairments (Sheridan et al., 2006). Thus, it is possible that the SDMT is most affected by subtle differences in BG values because of its sensitivity to attention and immediate, in-the-moment processing. Existing research

shows that, in adults with T1DM, hyperglycemia is associated with impairment on various cognitive-motor tasks (Cox et al., 2005).

Subjective symptomatology, on the other hand, was found to be related to the D-KEFS Tower Mean First Move Time score. The D-KEFS Tower Test involves deliberate, prospective thinking in the planning of one's future moves. The Mean First Move Time score assesses the average speed with which participants make their first move in the Tower Test across all nine items. This subscale score of the Tower test has been related in existing literature to planning ability and problem solving skills (Jacobs & Anderson, 2002; Yochim et al., 2009). On average, individuals who endorsed more subjective symptomatology at the time of testing also took longer to make their first move. This implies that physiological symptomatology may negatively affect adolescents' ability to process and plan their approach and strategy. Following this logic, performance on the SDMT would not be as affected by increased symptomatology because the task does not require planning; rather, it involves only matching numbers to symbols and therefore does not necessitate prospective thinking or strategizing. It is this distinction that may explain the differences in the pattern of significant relationships between cognitive measures and diabetes indicators.

It is possible that symptomatology was not related to the overall D-KEFS Tower Time-Per-Move Score because the Time-Per-Move score accounts for speed across all moves in the task, not just the first move of each item. Thus, if symptomatology affects planning ability, it appears that this effect is most apparent at the outset of each item administered. Notably, the D-KEFS Tower Total Achievement Score was also unrelated to either diabetes indicator, consistent with the speculation that symptomatology has a

subtle impact on this particular cognitive task, as opposed to a broad, general impact. It should be mentioned that it is difficult to know whether differences between cognitive assessments found in the present study are artifacts of the small sample size, or whether these are true effects that can be applied to larger population. A larger sample size would elucidate these distinctions further.

Because different cognitive assessment scores (i.e., the SDMT and the Tower Mean First Move Time) were related to different diabetes variables (i.e., BG values and subjective symptomatology), it is impossible to say which diabetes variable was "more" related to general cognitive function, as proposed in Hypothesis 1. Rather, it appears that these cognitive functions are related in different ways to the various diabetes outcomes. Since subjective symptomatology was significantly related to certain aspects of cognitive function in this population, caretakers and teachers should consider monitoring symptomatology, in addition to objective BG levels, in individuals with T1DM.

Interestingly, adolescents whose BG levels were in range endorsed significantly more subjective symptomatology than did those whose BG levels were out of range. This finding confirms previous research stating that physiological symptoms do not reliably covary with objective BG levels across patients (Gonder-Frederick & Cox, 1991). In this sample, increased symptomatology as a whole was not associated with out-of-range blood sugars. That said, certain individual symptoms (e.g., thirst) were endorsed more by those participants who indicated *feeling* out of range; thus, it is likely that certain symptoms might be found to covary reliably with high or low BG values in a larger sample. Taken together, these results illustrate the inconsistency of the relationship between BG values and subjective symptomatology and highlight the importance of

attending equally to symptomatology and objective BG values when targeting optimal cognitive functioning in these individuals.

Technology use

As a group, this sample reported high usage levels of diabetes technology. Eighty-seven percent of participants reported using a pump, and 67.3% used a CGM. In contrast, recent data from the T1D Exchange clinic registry indicated that 58% of adolescents between the ages of 13 and 17 used insulin pumps, and only 5% used CGMs (Miller et al., 2015). This relatively high rate of technology use in the present population might reflect certain characteristics about individuals who attend diabetes camps. Specifically, campers and their families may prioritize their disease management and are therefore motivated to both use the latest technology and attend camp to improve patients' disease management and outlook. Research conducted at diabetes camps indicates that camp attendance improves diabetes knowledge, subjective coping abilities, and general attitudes toward diabetes in children and adolescents with T1DM (Santiprabhob et al., 2008; Viklund, Rudberg, & Wikblad, 2007).

Contrary to the second hypothesis, general technology use (i.e., whether participants reported using a pump, a CGM, both, or neither) appears to be unrelated to BG estimation accuracy. Thus it does not appear that individuals' use of technology influences their awareness of their BG level, or if it does, this awareness does not translate into increased estimation accuracy. It is also possible that some participants reported owning or having a certain technology without using it frequently enough to affect their awareness or accuracy. Research regarding patterns of CGM use in

adolescents is sparse, but it suggests that usage is quite variable among adolescents who own CGMs (Naranjo et al., 2016).

In examining reports from participants using CGMs, monthly use (i.e., number of days in the past month individuals reported using their CGM) and look frequency (i.e., the number of times per day individuals reported looking at their CGM data) were found to predict subjective symptomatology. Specifically, participants who reported using their CGM *fewer* days in the past month and those who reported looking at their CGM data *more* daily endorsed higher symptomatology. This finding has interesting implications for different CGM usage patterns. First, it seems that participants who simply attach their CGM without regularly attending to it are less aware of their symptomatology. It is possible that these individuals do not monitor their CGMs closely because the CGM monitors their BG level for them and alarms when BG levels fall outside a given range. These individuals are likely less aware of symptoms they experience, because they rely solely on their CGM to tell them when their BG levels are out of range. Conversely, participants who look at the CGM data more often each day might use the CGM more as a way to inform them about how certain symptoms correspond to certain BG levels. It might also be the case that adolescents who experience more symptoms attend to their CGM more, in order to reconcile their experienced symptoms with their current BG level.

Encouragingly, the vast majority of participants using CGMs found them to be extremely helpful. Based on adolescents' responses to an open-ended question about the most useful features of the CGM, the majority of CGM users indicated that the alerts for low or high BG values were invaluable. Participants' answers also suggested that CGMs are an easy way to get a large amount of data (a BG value is provided every 5 minutes, 24

hours a day), and that this data is often information they wouldn't otherwise have. That many participants identified the trend arrows as a particularly helpful feature is consistent with research showing that adults with T1DM rely heavily on these arrows when making insulin dosage decisions (Pettus & Edelman, 2016). Taken together, these responses indicate that adolescents find CGMs to be a convenient way to obtain constant data about their BG levels, and CGM use may aid in metabolic control by helping individuals identify patterns and opportunities for adjustment.

BG Estimation Accuracy

Error grid analysis based on Parkes and colleagues' (2000) grid format indicated that the majority of participants made BG estimations that were inaccurate but without clinically serious implications. Specifically, if these participants had made adjustment decisions (e.g., to eat food or dose insulin) based on their estimations, it is likely that these decisions would not have had serious consequences for affecting BG levels (Parkes et al., 2000). Adolescents' estimations were generally more accurate than was expected based on existing literature showing that up to one-third of adults and children make clinically serious estimation errors (e.g., Gonder-Frederick, Snyder, & Clarke, 1991).

Lastly, results from this study indicated that participants who reported checking their BG more frequently per day with a meter made more accurate BG estimations. Although it was previously postulated that this effect would be found for those using insulin pumps and CGMs more frequently, the same rationale can instead be applied to this finding. Insulin pumps and CGMs are heralded for being easy to use and fairly automatic, and they may take the pressure off of patients to self-monitor their BG levels and insulin. However, based on the findings from the present study, it seems that the

more “low-tech,” effortful, less convenient method of BG monitoring is associated with an increased awareness of one’s current BG level. Because checking one’s BG with a meter is a minutes-long task that requires individuals to stop what they’re doing and attend to the number that appears on the screen (instead of glancing quickly at a CGM reading), it is likely that this task results in increased awareness of how one’s symptomatology relates to a current BG reading.

Research Implications

The present study is unique within existing research on children and adolescents’ diabetes management in its assessment of immediate, in-the-moment diabetes variables. Related research has shown impaired cognitive function in adult patients with type 2 diabetes during acute hyperglycemia (Sommerfield, Deary, & Frier, 2004). Additionally, research examining cognition in children with T1DM has explored the effects of past severe hyperglycemic or hypoglycemic episodes on subjects’ current cognitive performance and found impacts of each type of episode on distinct domains of cognitive function (Perantie et al., 2008). Most closely related to the current research was a study in which adults with both type 1 and type 2 diabetes completed a cognitive-motor task and entered current BG levels over a period of four weeks. Results indicated that hyperglycemia was associated with mild cognitive impairment, although these results were highly individualized and varied greatly between individuals (Cox et al., 2005). As discussed previously, an abundance of existing research demonstrates consistently lower cognitive functioning across domains in children with T1DM compared to their healthy counterparts (e.g., Brands et al., 2004; Gaudieri et al., 2008; Moheet et al., 2015). Despite this existing knowledge base, the current study was the first to explore these in-the-

moment variables in a population of adolescents with T1DM. Notably, the present study sample demonstrated mean cognitive scores within normal limits based on normative samples.

Additionally, the naturalistic testing environment sets the present study apart from most others in its field. The majority of studies examining BG levels in children or adults with T1DM are conducted in hospital settings. Testing for the current study occurred during a 10-day overnight camp session; participants were asked to take a brief break from other camp activities to voluntarily participate. Thus, this research setting mirrored real-life situations more than the typical hospital setting. For instance, participants were given the option to pause the testing session after their first BG check to make any adjustments (i.e., eat food or dose insulin as needed) and wait for those adjustments to take effect. Although some participants chose to either eat food or dose insulin at this point, all of them chose to proceed with the testing session without waiting for these adjustments to take effect. It should be noted that both insulin doses and food consumption typically do not take effect for about 15 minutes (U.S. Food and Drug Administration, 2015), so it is unlikely that any adjustments significantly altered participants' BG levels for the remainder of the testing session. In this way, the testing session mirrored adolescents' daily life, especially in school settings. They often need to make quick adjustments to their BG values without being able to stop the task at hand and wait for these adjustments to take effect.

Clinical Implications

Taken together, these results indicate that awareness of subjective physiological symptomatology is an important aspect of diabetes monitoring. Subjective

symptomatology is significantly related to certain domains of cognitive function in adolescents with T1DM, and furthermore, these symptoms are independent from objective BG values and should thus be considered separately. This finding is especially relevant in school settings. For example, an adolescent's objective BG value might be in range (or close to in range), but the adolescent's symptomatology might make it difficult for him or her to perform well. Similarly, because there is no evidence that these symptoms reliably covary between individuals, two students might have similar BG values but experience very different symptoms in the moment. It is thus critical that parents, medical providers, and educators alike acknowledge the role of symptomatology in affecting adolescents' functioning and assess symptoms in addition to BG levels in order to ensure optimum functioning. Additionally, given that there is currently no standard clinical tool for the assessment of physiological symptomatology in children, future research should examine the most effective measure of symptomatology that weighs both the number of symptoms endorsed and the severity of each symptom.

Furthermore, although most adolescents in this sample did not make clinically serious estimation errors, the majority of participants' estimates were inaccurate and may have resulted in altered clinical action (Parkes et al., 2000). This underscores the importance of encouraging adolescents with T1DM to engage in BG monitoring often, whether with a meter or a CGM. This is true even when adolescents report feeling "okay" or "in range;" as demonstrated in these results, adolescents' subjective evaluations of their BG levels may not always be accurate.

Limitations and Future Directions

This study has several limitations that should be acknowledged and considered when interpreting the results. First, although the naturalistic research setting had many advantages, one possible disadvantage is that testing at a diabetes camp may have resulted in a selection bias. As mentioned previously, it is possible that adolescents who attend diabetes camp may be more motivated to be in a diabetes-positive environment, meet others with diabetes, and learn new management techniques. As such, participants in the present study might have been more involved in their diabetes care (and have more involved families) than the average adolescent; this may limit the generalizability of our findings to other adolescents with T1DM (Chae, Reith, Tomlinson, Rayns, & Wheeler, 2014; Wang, Stewart, Tuli, & White, 2008).

Second, a significant limitation of this study is that it was not possible to obtain an objective measure of metabolic control (i.e., Hb_{A1C}) from participants given that access to their medical records was not feasible. Therefore it is not possible to draw any conclusions about how cognitive performance, subjective symptomatology, technology use, or BG estimation accuracy relate to metabolic control over a longer period of time. It was also not feasible to compare the metabolic control of the present study's participants to other adolescents with T1DM. Future studies should incorporate a measure of metabolic control to explore the relation of these variables to longer-term disease management. Furthermore, management practices outside of technology use were not assessed and therefore one cannot infer the role that other adherence habits might play. Diabetes self-management is a complicated and nuanced process, and there are many

different aspects that may factor into the relationship between treatment adherence and metabolic control (Hood et al., 2009).

A third limitation to this study is the lack of variation in the type of "out of range" blood glucose levels participants exhibited (i.e., hyperglycemic or hypoglycemic). Although many participants had "out of range" BG values at the time of testing, the vast majority were hyperglycemic; only one was hypoglycemic. Previous research with adults with T1DM suggests that hyperglycemia is less impairing (cognitively) than hypoglycemia (Holmes, Hayford, Gonzalez, & Weydert, 1983). Additionally, hypoglycemia is generally associated with more severe symptoms (Lane, 2006). Therefore, it is possible that symptomatology and cognitive scores would have been more variable had some of the participants been hypoglycemic at the time of testing. Unlike in a medical setting, BG values cannot be manipulated, and any participants who might begin the study with low BG values are more likely to wait to adjust their values because of their accompanying severe symptomatology. Future research should thus explore ways to manipulate participants' BG values in a similar paradigm or to assess natural variability over time using CGM data.

Fourth, the symptom inventory used in this study collapsed responses across symptoms and time points to result in one total symptomatology variable. This scoring method is imprecise and oversimplified, and it may have resulted in a loss in variation in symptom reports. Future research on this topic should utilize more precise measures of symptomatology and consider examining each potential symptom separately instead of collapsing intensity across many symptoms. Given the idiosyncrasy of symptomatology

in this population, it would be interesting to examine the relations between individual symptoms and how rates of endorsement vary among symptoms.

Lastly, although this study utilized global measures of technology, more research is warranted examining the role of diabetes technology (including meters, insulin pumps, CGMs, and in the future, closed-loop systems) in disease management. Although many past studies have examined the metabolic effects of these technologies in children and adults (Weissberg-Benchell, Antisdel-Lomaglio, & Seshadri, 2003), further research should specifically investigate which aspects of each technology are most helpful to children and adolescents with T1DM and how technology use may build (or compromise) management skills in these populations.

Conclusion

The current study provides new insights into the relationships among blood glucose levels, subjective symptomatology, and cognitive performance in adolescents with type 1 diabetes. Adolescents whose blood glucose levels were in range and who endorsed less symptomatology performed better on certain cognitive assessments than those whose blood glucose levels were out of range and who endorsed more symptomatology. Participants who reported looking at the data from their continuous glucose monitors more frequently were more aware of their symptomatology at the time of testing. Adolescents who reported checking their blood glucose level more frequently were more accurate when estimating their blood glucose levels than adolescents who reported checking less frequently. These results underscore the importance of considering symptomatology, symptom awareness, and estimation accuracy in school settings in order to optimize adolescents' functioning in these settings.

REFERENCES

American Diabetes Association (2016a). Standards of medical care in diabetes – 2016. *Journal of Clinical and Applied Research and Education, 39*(Suppl. 1), 1-112.

American Diabetes Association (2016b). Hypoglycemia (low blood glucose). Retrieved from http://www.diabetes.org/living-with-diabetes/treatment-and-care/blood-glucose-control/hypoglycemia-low-blood.html?referrer=https://www.google.com

American Diabetes Association (2016c). Neuropathy (nerve damage). Retrieved from http://www.diabetes.org/living-with-diabetes/complications/neuropathy/

Anderson, B., Ho, J., Brackett, J., Finkelstein, D., & Laffel, L. (1997). Parental involvement in diabetes management tasks: Relationships to blood glucose monitoring adherence and metabolic control in young adolescents with insulin-dependent diabetes mellitus. *The Journal of Pediatrics*, *130*, 257-265. http://dx.doi.org/10.1016/S0022-3476(97)70352-4

Balkhi, A. M., Olsen, B., Lazaroe, L., Silverstein, J., & Geffken, G. R. (2015). Paging Dr. Google: Parents' report of internet use for type 1 diabetes management. *Diabetes Care*, *38*, e18-e19. http://dx.doi.org/10.2337/dc14-2461

Barnea-Goraly, N., Raman, M., Mazaika, P., Marzelli, M., Hershey, T., Weinzimer, S. A., ... & Fox, L. A. (2014). Alterations in white matter structure in young children with type 1 diabetes. *Diabetes Care*, *37*, 332-340. http://dx.doi.org/10.2337/dc13-1388

Bate, A. J., Mathias, J. L., & Crawford, J. R. (2001). Performance on the Test of Everyday Attention and standard tests of attention following severe traumatic brain injury. *The Clinical Neuropsychologist, 15*, 405–422. http://dx.doi.org/10.1076/clin.15.3.405.10279

Bergenstal, R. M., Tamborlane, W. V., Ahmann, A., Buse, J. B., Dailey, G., Davis, S. N., ... & Willi, S. M. (2010). Effectiveness of sensor-augmented insulin-pump therapy in type 1 diabetes. *New England Journal of Medicine*, *363*, 311-320. http://dx.doi.org/10.1056/NEJMoa1002853

Boland, E. A., Grey, M., Oesterle, A., Fredrickson, L., & Tamborlane, W. V. (1999). Continuous subcutaneous insulin infusion: A new way to lower risk of severe hypoglycemia, improve metabolic control, and enhance coping in adolescents with type 1 diabetes. *Diabetes Care*, *22*, 1779-1784. http://dx.doi.org/10.2337/diacare.22.11.1779

Brands, A. M., Biessels, G. J., De Haan, E. H., Kappelle, L. J., & Kessels, R. P. (2005). The effects of type 1 diabetes on cognitive performance. *Diabetes Care, 28,* 726-735. http://dx.doi.org/10.2337/diacare.28.3.726

Brands, A. M., Kessels, R. P., de Haan, E. H., Kappelle, L. J., & Biessels, G. J. (2004). Cerebral dysfunction in type 1 diabetes: Effects of insulin, vascular risk factors and blood-glucose levels. *European Journal of Pharmacology*, *490*, 159-168. http://dx.doi.org/10.1016/j.ejphar.2004.02.053

Castle, J. R., & Jacobs, P. G. (2016). Nonadjunctive use of continuous glucose monitoring for diabetes treatment decisions. *Journal of Diabetes Science and Technology, 1, 1-5*. http://dx.doi.org/10.1177/1932296816631569

Chae, M., Reith, D. M., Tomlinson, P. A., Rayns, J., & Wheeler, B. J. (2014). Accuracy of verbal self-reported blood glucose in teenagers with type I diabetes at diabetes ski camp. *Journal of Diabetes & Metabolic Disorders, 13*, 14-18. http://dx.doi.org/10.1186/2251-6581-13-14

Clarke, W. L., Cox, D., Gonder-Frederick, L. A., Carter, W., & Pohl, S. L. (1987). Evaluating clinical accuracy of systems for self-monitoring of blood glucose. *Diabetes Care, 10*(5), 622-628.

Cox, D. J., Clarke, W. L., Gonder-Frederick, L., Pohl, S., Hoover, C., Snyder, A., ... & Pennebaker, J. (1985). Accuracy of perceiving blood glucose in IDDM. *Diabetes Care*, *8*, 529-536. http://dx.doi.org/10.2337/diacare.8.6.529

Cox, D. J., Gonder-Frederick, L. A., Kovatchev, B. P., Julian, D. M., & Clarke, W. L. (1997). Understanding error grid analysis. *Diabetes Care*, *20*, 911-912. http://dx.doi.org/10.2337/diacare.20.6.911

Cox, D. J., Gonder-Frederick, L. A., Lee, J. H., Julian, D. M., Carter, W. R., & Clarke, W. L. (1989). Effects and correlates of blood glucose awareness training among patients with IDDM. *Diabetes Care*, *12*, 313-318. http://dx.doi.org/10.2337/diacare.12.5.313

Cox, D., Gonder-Frederick, L., Polonsky, W., Schlundt, D., Julian, D., & Clarke, W. (1995). A multicenter evaluation of blood glucose awareness training-II. *Diabetes Care*, *18*, 523-528. http://dx.doi.org/10.2337/diacare.18.4.523

Cox, D. J., Gonder-Frederick, L., Polonsky, W., Schlundt, D., Kovatchev, B., & Clarke, W. (2001). Blood glucose awareness training (BGAT-2) long-term benefits. *Diabetes Care*, *24*, 637-642. http://dx.doi.org/10.2337/diacare.24.4.637

Cox, D. J., Kovatchev, B. P., Gonder-Frederick, L. A., Summers, K. H., McCall, A., Grimm, K. J., & Clarke, W. L. (2005). Relationships between hyperglycemia and cognitive performance among adults with type 1 and type 2 diabetes. *Diabetes Care*, *28,* 71-77. http://dx.doi.org/10.2337/diacare.28.1.71

Dabelea, D., Mayer-Davis, E. J., Saydah, S., Imperatore, G., Linder, B., Divers, J., ... & Liese, A. D. (2014). Prevalence of type 1 and type 2 diabetes among children and adolescents from 2001 to 2009. *Journal of the American Medical Association*, *311*, 1778-1786. http://dx.doi.org/10.1001/jama.2014.3201

Daneman, D. (2006). Type 1 diabetes. *The Lancet*, *367*, 847-858. http://dx.doi.org/10.1016/S0140-6736(06)68341-4

Delis, D. C., Kaplan, E., & Kramer, J. H. (2001). *D-KEFS: Examiners manual*. San Antonio, TX: The Psychological Corporation.

de Bock, M., Cooper, M., Retterath, A., Nicholas, J., Ly, T., Jones, T., & Davis, E. (2016). Continuous glucose monitoring adherence: Lessons from a clinical trial to predict outpatient behavior. *Journal of Diabetes Science and Technology, 10,* 627-632. http://dx.doi.org/10.1177/1932296816633484

Delis, D. C., Kaplan, E., & Kramer, J. H. (2001). *Delis-Kaplan Executive Function System (D-KEFS)*. San Antonio, TX: Psychological Corporation.

Demidowich, A. P., Lu, K., Tamler, R., & Bloomgarden, Z. (2012). An evaluation of diabetes self-management applications for Android smartphones. *Journal of Telemedicine and Telecare*, *18*, 235-238. http://dx.doi.org/10.1258/jtt.2012.111002

Donaghue, K. C., Fung, A. T., Hing, S., Fairchild, J., King, J., Chan, A., ... & Silink, M. (1997). The effect of prepubertal diabetes duration on diabetes: Microvascular complications in early and late adolescence. *Diabetes Care*, *20*, 77-80. http://dx.doi.org/10.2337/diacare.20.1.77

Faul, F., Erdfelder, E., Buchner, A., & Lang, A. G. (2009). Statistical power analyses using G* Power 3.1: Tests for correlation and regression analyses. *Behavior Research Methods*, *41*, 1149-1160. http://dx.doi.org/10.3758/brm.41.4.1149

Fisher, C. J. (2006). Validity of the Delis-Kaplan Executive Function System in pediatric populations (Doctoral dissertation). Retrieved from http://digitalcommons.georgefox.edu/cgi/viewcontent.cgi?article=1145&context=psyd

Freund, A., Bennett-Johnson, S., Rosenbloom, A., Alexander, B., & Hansen, C. A. (1986). Subjective symptoms, blood glucose estimation, and blood glucose concentrations in adolescents with diabetes. *Diabetes Care*, *9*, 236-243. http://dx.doi.org/10.2337/diacare.9.3.236

Galanina, N., Surampudi, V., Ciltea, D., Singh, S. P., & Perlmuter, L. C. (2008). Blood glucose levels before and after cognitive testing in diabetes mellitus. *Experimental Aging Research*, *34*, 152-161.http://dx.doi.org/10.1080/03610730701876979

Garvey, K. C., Markowitz, J. T., & Laffel, L. M. (2012). Transition to adult care for youth with type 1 diabetes. *Current Diabetes Report, 12*, 533-541. http://dx.doi.org/10.1007/s11892-012-0311-6

Gaudieri, P. A., Chen, R., Greer, T. F., & Holmes, C. S. (2008). Cognitive function in children with type 1 diabetes: A meta-analysis. *Diabetes Care*, *31*, 1892-1897. http://dx.doi.org/10.2337/dc07-2132

Gonder-Frederick, L. A., & Cox, D. J. (1991). Symptom perception, symptom beliefs, and blood glucose discrimination in the self-treatment of insulin-dependent diabetes. In J. A. Skelton & R. T. Croyle (Eds.). *Mental representation in health and illness* (pp. 220-246). New York, NY: Springer US.

Gonder-Frederick, L., Cox, D., Clarke, W., & Julian, D. (2000). Blood glucose awareness training. *Psychology in Diabetes Care*, 169-206. http://dx.doi.org/10.1002/0470846569.ch7

Gonder-Frederick, L. A., Snyder, A. L., & Clarke, W. L. (1991). Accuracy of blood glucose estimation by children with IDDM and their parents. *Diabetes Care*, *14*, 565-570. http://dx.doi.org/10.2337/diacare.14.7.565

Gonder-Frederick, L. A., Zrebiec, J. F., Cox, D. J., Kovatchev, B. P., Ritterband, L. M., & Clarke, W. L. (2004). BG detection in school-aged children with T1DM and their parents. *Diabetes, 53,* A17-A17. Retrieved from http://insights.ovid.com/diabetes/diab/2004/06/002/bg-detection-school-aged-children-t1dm-parents/72/00003439

Herzer, M., & Hood, K. K. (2010). Anxiety symptoms in adolescents with type 1 diabetes: Association with blood glucose monitoring and glycemic control. *Journal of Pediatric Psychology, 35*, 415-425. http://dx.doi.org/10.1093/jpepsy/jsp063

Holmes, C. S., Hayford, J. T., Gonzalez, J. L., & Weydert, J. A. (1983). A survey of cognitive functioning at different glucose levels in diabetic persons. *Diabetes Care*, *6*(2), 180-185.

Homack, S., Lee, D., & Riccio, C. A. (2005). Test review: Delis-Kaplan Executive Function System. *Journal of Clinical and Experimental Neuropsychology*, *27*, 599-609. http://dx.doi.org/10.1080/13803390490918444

Hood, K. K., Peterson, C. M., Rohan, J. M., & Drotar, D. (2009). Association between adherence and glycemic control in pediatric type 1 diabetes: A meta-analysis. *Pediatrics, 124*(6), e1171-e1179. http://dx.doi.org/10.1542/peds.2009-0207

IBM Corp. (2016). IBM SPSS Statistics, Version 24.0.

Jacobs, R., & Anderson, V. (2002). Planning and problem solving skills following focal frontal brain lesions in childhood: Analysis using the Tower of London. *Child Neuropsychology, 8,* 93-106. https://doi.org/10.1076/chin.8.2.93.8726

Kichler, J. C., Kaugars, A. S., Maglio, K., & Alemzadeh, R. (2012). Exploratory analysis of the relationships among different methods of assessing adherence and glycemic control in youth with type 1 diabetes mellitus. *Health Psychology*, *31*, 35-42. http://dx.doi.org/10.1037/a0024704

Kovatchev, B., Cox, D., Gonder-Frederick, L., Schlundt, D., & Clarke, W. (1998). Stochastic model of self-regulation decision making exemplified by decisions concerning hypoglycemia. *Health Psychology*, *17*, 277. http://dx.doi.org/10.1037/0278-6133.17.3.277

Kubiak, T., Mann, C. G., Barnard, K. C., & Heinemann, L. (2016). Psychosocial aspects of continuous glucose monitoring: Connecting to the patients' experience. *Journal of Diabetes Science and Technology*, 1-5.

Lane, M. M. (2006). Advancing the science of perceptual accuracy in pediatric asthma and diabetes. *Journal of Pediatric Psychology*, *31*, 233-245. http://dx.doi.org/10.1093/jpepsy/jsj008

Livingstone, S. J., Levin, D., Looker, H. C., Lindsay, R. S., Wild, S. H., Joss, N., ... & McKnight, J. A. (2015). Estimated life expectancy in a Scottish cohort with type 1 diabetes, 2008-2010. *JAMA, 313*, 37-44. http://dx.doi.org/10.1001/jama.2014.16425

Melendez-Ramirez, L. Y., Richards, R. J., & Cefalu, W. T. (2010). Complications of type 1 diabetes. *Endocrinology and Metabolism Clinics of North America*, *39*(3), 625-640. http://dx.doi.org/10.1016/j.ecl.2010.05.009

Miller, K. M., Foster, N. C., Beck, R. W., Bergenstal, R. M., DuBose, S. N., DiMeglio, L. A., ... & Tamborlane, W. V. (2015). Current state of type 1 diabetes treatment in the US: Updated data from the T1D Exchange clinic registry. *Diabetes Care, 38*, 971-978. http://dx.doi.org/10.2337/dc15-0078

Moheet, A., Mangia, S., & Seaquist, E. R. (2015). Impact of diabetes on cognitive function and brain structure. *Annals of the New York Academy of Sciences*, *1353*, 60-71. http://dx.doi.org/10.1111/nyas.12807

Naranjo, D., Tanenbaum, M. L., Iturralde, E., & Hood, K. K. (2016). Diabetes technology: Uptake, outcomes, barriers, and the intersection with distress. *Journal of Diabetes Science and Technology*, 1-7. http://dx.doi.org/10.1177/1932296816650900

National Kidney Foundation (2015). Diabetes—a major risk factor for kidney disease. Retrieved from https://www.kidney.org/atoz/content/diabetes.

Nerenz, D. R., & Leventhal, H. (1983). Self-regulation theory in chronic illness. In T. G. Burish & L. A. Bradley (Eds.) *Coping with chronic disease: Research and applications*, (pp. 13-37). Cambridge, MA: Academic Publishers.

Parkes, J. L., Slatin, S. L., Pardo, S., & Ginsberg, B. H. (2000). A new consensus error grid to evaluate the clinical significance of inaccuracies in the measurement of blood glucose. *Diabetes Care, 23*(8), 1143-1148.

Perantie, D. C., Lim, A., Wu, J., Weaver, P., Warren, S. L., Sadler, M., ... & Hershey, T. (2008). Effects of prior hypoglycemia and hyperglycemia on cognition in children with type 1 diabetes mellitus. *Pediatric Diabetes, 9*, 87-95. http://dx.doi.org/10.1111/j.1399-5448.2007.00274.x

Pettus, J., & Edelman, S. V. (2016). Differences in use of glucose rate of change (ROC) arrows to adjust insulin therapy among individuals with type 1 and type 2 diabetes who use Continuous Glucose Monitoring (CGM). *Journal of Diabetes Science and Technology, 1,* 1-7. http://dx.doi.org/10.1177/1932296816639069

Prakasam, G., Rees, C., Lyden, M., & Parkin, C. G. (2016). Use of a novel smartphone-based diabetes management system improved feelings of confidence and safety and reduced hypoglycemia fear among parents/caregivers of children/adolescents with type 1 diabetes. *Journal of Diabetes Science and Technology, 11*, 1-2. http://dx.doi.org/10.1177/1932296816650901

R Core Team (2014). *R: A language and environment for statistical computing*. Vienna, Austria: R Foundation for Statistical Computing.

Rewers, M., Pihoker, C., Donaghue, K., Hanas, R., Swift, P., & Klingensmith, G. J. (2009). Assessment and monitoring of glycemic control in children and adolescents with diabetes. *Pediatric Diabetes*, *10*(s12), 71-81. http://dx.doi.org/ 10.1111/j.1399-5448.2009.00582.x

Santiprabhob, J., Likitmaskul, S., Kiattisakthavee, P., Weerakulwattana, P., Chaichanwattanakul, K., Nakavachara, P., ... & Nitiyanant, W. (2008). Glycemic control and the psychosocial benefits gained by patients with type 1 diabetes mellitus attending the diabetes camp. *Patient Education and Counseling*, *73*, 60-66.

Schaepelynck-Belicar, P., Vague, P. H., Simonin, G., & Lassmann-Vague, V. (2003). Improved metabolic control in diabetic adolescents using the continuous glucose monitoring system (CGMS). *Diabetes and Metabolism*, *29*, 608-612. http://dx.doi.org/ DM-12-2003-29-6-1262-3636-101019-ART6

Scholey, A. B., Harper, S., & Kennedy, D. O. (2001). Cognitive demand and blood glucose. *Physiology and Behavior, 73*, 585–592. http://dx.doi.org/10.1016/s0031-9384(01)00476-0

Schmolze, D. (2015). Package 'EGA'. Retrieved from http://healthstat.snu.ac.kr/CRAN/web/packages/ega/ega.pdf.

Sheridan, L. K., Fitzgerald, H. E., Adams, K. M., Nigg, J. T., Martel, M. M., Puttler, L. I., ... & Zucker, R. A. (2006). Normative Symbol Digit Modalities Test performance in a community-based sample. *Archives of Clinical Neuropsychology, 21*, 23-28. http://dx.doi.org/10.1016/j.acn.2005.07.003

Silverstein, J., Klingensmith, G., Copeland, K., Plotnick, L., Kaufman, F., Laffel, L., ... & Clark, N. (2005). Care of children and adolescents with type 1 diabetes: A

statement of the American Diabetes Association. *Diabetes Care*, *28*, 186-212. http://dx.doi.org/10.2337/diacare.28.1.186

Sjoeholm, A., Gray, A., Rayns, J., Tomlinson, P. A., & Wheeler, B. J. (2016). Prior knowledge of blood glucose meter download improves the accuracy of verbal self-reported blood glucose in teenagers with type I diabetes at ski camp. *Acta Diabetologica*, *1,* 1-6. http://dx.doi.org/10.1007/s00592-016-0855-z

Smith, A. (2000). *Symbol digit modalities test.* Torrance, CA: Western Psychological Services.

Sommerfield, A. J., Deary, I. J., & Frier, B. M. (2004). Acute hyperglycemia alters mood state and impairs cognitive performance in people with type 2 diabetes. *Diabetes Care, 27,* 2335-2340. http://dx.doi.org/10.2337/diacare.27.10.2335

Tamborlane, W. V., Bonfig, W., & Boland, E. (2001). Recent advances in treatment of youth with type 1 diabetes: Better care through technology. *Diabetic Medicine*, *18*, 864-870.http://dx.doi.org/10.1046/j.1464-5491.2001.00626.x

Tamborlane, W. V., Sherwin, R. S., Genel, M., & Felig, P. (1979). Reduction to normal of plasma glucose in juvenile diabetes by subcutaneous administration of insulin with a portable infusion pump. *New England Journal of Medicine*, *300*, 573-578. http://dx.doi.org/10.1056/NEJM197903153001101

Trumbo, P., Schlicker, S., Yates, A. A., & Poos, M. (2002). Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein and amino acids. *Journal of the American Dietetic Association*, *102*, 1621-1630. http://dx.doi.org/10.1016/s0002-8223(02)90346-9

Tumminia, A., Crimi, S., Sciacca, L., Buscema, M., Frittitta, L., Squatrito, S., ... & Tomaselli, L. (2015a). Efficacy of real-time continuous glucose monitoring on glycaemic control and glucose variability in type 1 diabetic patients treated with either insulin pumps or multiple insulin injection therapy: A randomized controlled crossover trial. *Diabetes/Metabolism Research and Reviews, 31*, 61-68. http://dx.doi.org/ 10.1002/dmrr.2557

Tumminia, A., Sciacca, L., Frittitta, L., Squatrito, S., Vigneri, R., Le Moli, R., & Tomaselli, L. (2015b). Integrated insulin pump therapy with continuous glucose monitoring for improved adherence: Technology update. *Patient Preference and Adherence, 9*, 1263-1270. http://dx.doi.org/10.2147/ppa.s69482

U.S. Food and Drug Administration, 2015. Insulin. Retrieved from http://www.fda.gov/ForConsumers/ByAudience/ForWomen/WomensHealthTopics/ucm216233.htm#types

Viklund, G. E., Rudberg, S., & Wikblad, K. F. (2007). Teenagers with diabetes: Self-management education and training on a big schooner. *International Journal of Nursing Practice, 13,* 385-392. https://doi.org/10.1111/j.1440-172x.2007.00655.x

Wagner, D. V., Barry, S., Teplitsky, L., Sheffield, A., Stoeckel, M., Ogden, J. D., ... & Harris, M. A. (2016). Texting adolescents in repeat DKA and their caregivers. *Journal of Diabetes Science and Technology, 10*, 831-839. http://dx.doi.org/10.1177/1932296816639610

Wang, Y. C. A., Stewart, S., Tuli, E., & White, P. (2008). Improved glycemic control in adolescents with type 1 diabetes mellitus who attend diabetes camp. *Pediatric Diabetes, 9*, 29-34. https://doi.org/10.1111/j.1399-5448.2007.00285.x

Wasserman, D. H., & Zinman, B. (1994). Exercise in individuals with IDDM. *Diabetes Care*, *17*, 924-937. http://dx.doi.org/10.2337/diacare.17.8.924

Weissberg-Benchell, J., Antisdel-Lomaglio, J., & Seshadri, R. (2003). Insulin pump therapy: A meta-analysis. *Diabetes Care*, *26*, 1079-1087. http://dx.doi.org/10.2337/diacare.26.4.1079

Weissberg-Benchell, J., Glasgow, A. M., Tynan, W. D., Wirtz, P., Turek, J., & Ward, J. (1995). Adolescent diabetes management and mismanagement. *Diabetes Care*, *18*, 77-82. http://dx.doi.org/10.2337/diacare.18.1.77

Wolfsdorf, J., Glaser, N., & Sperling, M. A. (2006). Diabetic ketoacidosis in infants, children, and adolescents: A consensus statement from the American Diabetes Association. *Diabetes Care*, *29*, 1150-1159. http://dx.doi.org/10.2337/dc06-9909

Yeh, H. C., Brown, T. T., Maruthur, N., Ranasinghe, P., Berger, Z., Suh, Y. D., ... & Golden, S. H. (2012). Comparative effectiveness and safety of methods of insulin delivery and glucose monitoring for diabetes mellitus: A systematic review and meta-analysis. *Annals of Internal Medicine*, *157*, 336-347. http://dx.doi.org/ 10.7326/0003-4819-157-5-201209040-00508

Yochim, B. P., Baldo, J. V., Kane, K. D., & Delis, D. C. (2009). D-KEFS Tower Test performance in patients with lateral prefrontal cortex lesions: The importance of error monitoring. *Journal of Clinical and Experimental Neuropsychology*, *31*, 658-663. http://dx.doi.org/10.1080/13803390802448669

Ziegler, R., Rees, C., Jacobs, N., Parkin, C. G., Lyden, M. R., Petersen, B., & Wagner, R. S. (2015). Frequent use of an automated bolus advisor improves glycemic control in pediatric patients treated with insulin pump therapy: Results of the Bolus Advisor Benefit Evaluation (BABE) study. *Pediatric Diabetes, 17*, 311-318. http://dx.doi.org/10.1111/pedi.12290

Table 1.

Error Grid Analysis Zones

	Parkes et al. (2000)
Zone A	Errors with no effect on clinical action.
Zone B	Errors resulting in altered clinical action, but little or no effect on clinical outcome.
Zone C	Errors resulting in altered clinical action; likely to affect clinical outcome.
Zone D	Errors resulting in altered clinical action; could have significant medical risk.
Zone E	Errors resulting in altered clinical action; could have dangerous consequences

Table 2.

Demographic Characteristics (N = 55)

	Mean	SD	Range	n	%
Gender					
Female				27	49.1
Male				28	50.9
Age at testing (years)	14.60	1.13	13 - 17		
Race					
American Indian/Alaska Native				1	1.8
Asian				1	1.8
Black/African American				2	3.6
White				48	87.2
Multi-racial				2	3.6
Ethnicity					
Hispanic or Latino				9	16.4
Not Hispanic or Latino				46	83.6
Age at diagnosis (years)	7.75	3.86	1 - 15		
Years attended camp (prior)	3.66	3.23	0 - 12		
Median annual income per zip code	$83,823.23	$27,524.14	$23,363 – $147,936		

Table 3.

Descriptive Statistics of Outcome Variables (N = 55)

	Mean	SD	Range	*n*	%
SDMT Total Standard Score	109.12	17.70	64.14 - 151.76		
D-KEFS Tower Standard Scores					
Total Achievement	9.58	2.21	1 - 14		
Mean First Move Time	10.42	1.84	4 - 13		
Time-Per-Move Ratio	9.56	2.23	2 - 13		
Total Symptomatology score*	0.30	0.30	0 - 1.39		
Blood glucose values					
Pre-test	191.38	78.44	87 - 417		
Post-test	181.30	74.26	67 - 394		
Blood glucose range at pre-test					
In range				19	34.5
Out of range				36	65.5
Parkes' EGA Zones					
Zone A				21	38.2
Zone B				33	60.0
Zone C				1	1.8
Zone D				0	0
Zone E				0	0

**Note:* Non-transformed group mean values are reported in the table for ease of interpretation, although transformed values were used as appropriate in analyses.

Table 4.

Independent Samples T-Test Based on Range of Pre-test Blood Glucose Levels

	In range (*n*=19)	Out of range (*n*=36)	t	Effect size (Cohen's d)
SDMT total score	114.92 (13.96)	106.05 (18.85)	1.98*	0.53
D-KEFS Tower Standard Score				
Total Achievement	10.05 (1.98)	9.33 (2.31)	1.21	0.33
Mean First Move Time	10.36 (1.80)	10.44 (1.89)	-0.15	-0.04
Time-Per-Move Ratio	9.21 (3.12)	9.75 (1.61)	-0.71	-0.22
Total Symptomatology Score	0.57 (0.24)	0.42 (0.28)	2.10*	0.58

*$p < .05$

Table 5.

Bivariate Correlations Between Cognitive Assessment Scores and Total Symptomatology

	1	2	3	4
1. SDMT Total Standard Score	--			
2. D-KEFS Tower Total Achievement	-.06	--		
3. D-KEFS Tower Mean First Move Time	.15	.01	--	
4. D-KEFS Tower Time-Per-Move Ratio	.01	-.04	.58**	--
5. Total Symptomatology Score	.24	.01	-.31*	-.19

*$p < .05$, **$p < .01$

Table 6.

Central Themes of Helpful CGM Functions

Theme	**Percentage of respondents discussing each theme**
Increased awareness of BG levels	56.8
Trend arrows, graphs, data	37.8
Advance notice of BG changes	27.0
Source of information or data	24.3
Convenient	21.6

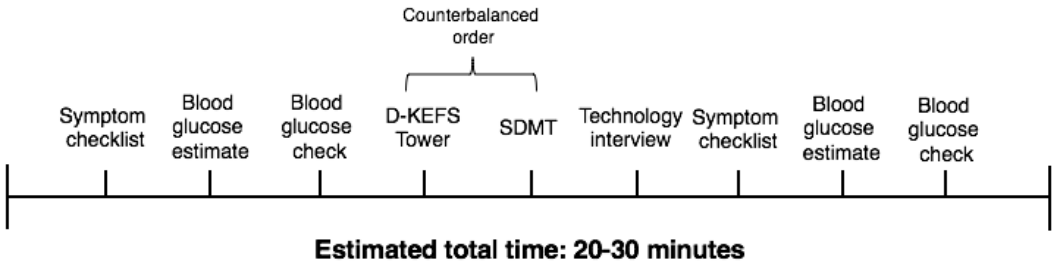

Figure 1: *Study Procedures*

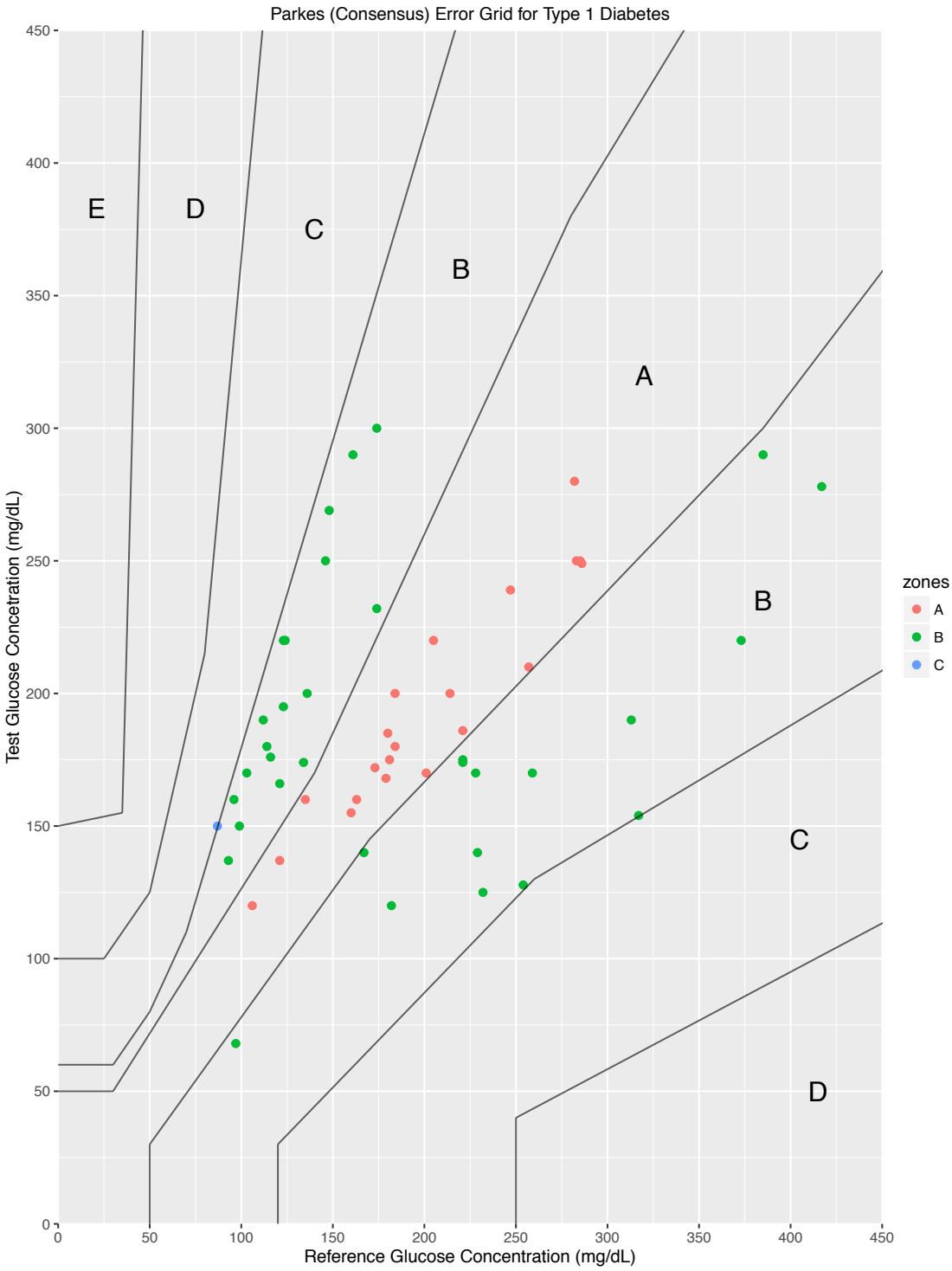

Figure 2. Zones of estimation accuracy based on Parkes et al. (2000)'s error grid analysis. Each data point represents the intersection of a participant's true BG value (x-axis) and estimated BG value (y-axis).

Appendix A
Symptom Survey

Which (if any) of the following things are you experiencing right now? Check "yes" or "no" for each option. For each symptom that you check "yes," please indicate how severely you are experiencing the symptom by circling the appropriate number.

Tell me if you don't know what something means!

		1 A little bit	2	3 Moderately	4	5 A lot
Headache	☐ **Yes** ☐ **No**	**1**	**2**	**3**	**4**	**5**
Sweating	☐ **Yes** ☐ **No**	**1**	**2**	**3**	**4**	**5**
Shakiness	☐ **Yes** ☐ **No**	**1**	**2**	**3**	**4**	**5**
Pounding heart	☐ **Yes** ☐ **No**	**1**	**2**	**3**	**4**	**5**
Confusion	☐ **Yes** ☐ **No**	**1**	**2**	**3**	**4**	**5**
Slurred speech	☐ **Yes** ☐ **No**	**1**	**2**	**3**	**4**	**5**
Hunger	☐ **Yes** ☐ **No**	**1**	**2**	**3**	**4**	**5**
Thirst	☐ **Yes** ☐ **No**	**1**	**2**	**3**	**4**	**5**
Going to the bathroom a lot	☐ **Yes** ☐ **No**	**1**	**2**	**3**	**4**	**5**
Stomachache	☐ **Yes** ☐ **No**	**1**	**2**	**3**	**4**	**5**
Blurry vision	☐ **Yes** ☐ **No**	**1**	**2**	**3**	**4**	**5**
Feeling tired	☐ **Yes** ☐ **No**	**1**	**2**	**3**	**4**	**5**
Feeling weak or run-down	☐ **Yes** ☐ **No**	**1**	**2**	**3**	**4**	**5**
Heavy breathing	☐ **Yes** ☐ **No**	**1**	**2**	**3**	**4**	**5**
Nausea	☐ **Yes** ☐ **No**	**1**	**2**	**3**	**4**	**5**
Feeling frustrated	☐ **Yes** ☐ **No**	**1**	**2**	**3**	**4**	**5**
Feeling irritated	☐ **Yes** ☐ **No**	**1**	**2**	**3**	**4**	**5**
Dizzy	☐ **Yes** ☐ **No**	**1**	**2**	**3**	**4**	**5**
Tingling or pain in hands or feet	☐ **Yes** ☐ **No**	**1**	**2**	**3**	**4**	**5**
Dry mouth	☐ **Yes** ☐ **No**	**1**	**2**	**3**	**4**	**5**
Energetic	☐ **Yes** ☐ **No**	**1**	**2**	**3**	**4**	**5**
Sweet taste in mouth	☐ **Yes** ☐ **No**	**1**	**2**	**3**	**4**	**5**

How are you feeling right now?

☐ Low ☐ In range ☐ High

Appendix B
Technology Interview

1. What technology or devices do you use to take care of your diabetes?

   Allow for free response and then follow-up to answer remaining items:

Blood glucose meter	☐	Yes	How many?_____		☐	No
Continuous glucose monitor	☐	Yes		☐	No	
Pump	☐	Yes		☐	No	
Injections	☐	Yes		☐	No	
Pens	☐	Yes		☐	No	
Dog	☐	Yes		☐	No	

2. On average, how many times a day do you check your blood sugar? _____

3. If you have a CGM:
   a. How many times a day do you look at your CGM?

   b. How many days in the past month were you on your CGM?

4. If you have a pump:
   a. How long after your diagnosis did you get your first pump?

   b. Do you ever take pump vacations? (If yes, how often and for how long?)

5. Do you check your ketones when you're high? ☐ Yes ☐ No
   a. If yes, how?

6. Does anyone in your family ever look back at your numbers? ☐ Yes ☐ No
    a. If yes, how often?

    b. If yes, in what way?
        i. Scrolling back through meter ☐ Yes ☐ No
        ii. Downloading number to computer ☐ Yes ☐ No
        iii. Any other way:_____
    c. Who looks at the data?
        i. You only ☐ Yes ☐ No
        ii. You and your parents ☐ Yes ☐ No
        iii. Parents only ☐ Yes ☐ No

7. Do you do anything in particular after you've looked at the data?

8. Does looking at the data change anything about the way you manage your diabetes?

9. Do you think anything would be different if you didn't look at the data as often as you do?

10. Do you use any apps to track or manage your diabetes?
    a. If yes, which one(s)?
    b. If yes, how often do you use the app?

11. Is there anything else you want to tell us about how you use technology to monitor your diabetes?