Published in final edited form as:

Pediatr Diabetes. 2010 September ; 11(6): 424–430. doi:10.1111/j.1399-5448.2009.00618.x.

Neurocognitive Functioning in Preschool-age Children with Type 1 Diabetes Mellitus

Anna Maria Patiño-Fernández, PhD^a, Alan M. Delamater, PhD^a, E. Brooks Applegate, PhD^b, Erika Brady, PhD^c, Margaret Eidson, MD^a, Robin Nemery, MD^d, Luis Gonzalez-Mendoza, MD^e, and Samuel Richton, MD^e

^a University of Miami Miller School of Medicine, Miami, FL USA

^b Western Michigan University, Kalamazoo, MI USA

^c IWK Health Centre, Halifax, Nova Scotia, Canada

^d Joe Dimaggio Children's Hospital, Ft. Lauderdale, FL USA

^e Miami Children's Hospital, Miami, FL USA

Abstract

Neurocognitive functioning may be compromised in children with type 1 diabetes mellitus (T1DM). The factor most consistently implicated in the long-term neurocognitive functioning of children with T1DM is age of onset. The pediatric literature suggests that glycemic extremes may have an effect on the neurocognitive functioning of children, but findings are mixed. The purpose of this study was to compare the neurocognitive functioning of young children with T1DM diagnosed before six years of age and healthy children (i.e., without chronic illness). Additionally, in the children with T1DM, we examined the relationship between their neurocognitive functioning and glycemic control. Sixty eight (36 with T1DM and 32 without chronic illness) preschool-age children (M age = 4.4yrs) were recruited and administered a battery of instruments to measure cognitive, language, and fine motor skills. Children with T1DM performed similarly to the healthy controls and both groups' skills fell in the average range. Among children with diabetes, poor glycemic control (higher HbA1c) was related to lower general cognitive abilities ($r = -.44, p < .04$), slower fine motor speed ($r = -.64, p < .02$), and lower receptive language scores ($r = -.39, p < .04$). Such findings indicate that young children with T1DM already demonstrate some negative neurocognitive effects in association with chronic hyperglycemia.

Keywords

children; type 1 diabetes; neurocognitive

There is ample evidence that confirms that neurocognitive functioning is compromised in children with type 1 diabetes mellitus (T1DM). Two recent meta-analyses substantiate that there are decrements in functioning across numerous cognitive domains (1,2). The factor most consistently implicated in the long-term neurocognitive functioning of children with T1DM is their age of onset of diabetes. Studies with school aged children (3,4) as well as reviews of the literature (2,5,6) have consistently concluded that those with early onset of T1DM have worse cognitive outcomes. Children with early onset show poorer functioning later in childhood and adolescence across domains of intelligence (4), school achievement (4), visual spatial ability (4,7), memory (4,8), motor speed (4), eye hand coordination (4), and attention and executive dysfunction (7,9). These weaknesses appear to persist, with prospective studies indicating continued associations with intelligence, particularly nonverbal intelligence six (9) and 12 (10) years after diagnosis. One study of adults also

found significantly weaker nonverbal performance and processing speed skills in those with early onset T1DM (11).

Although there is substantial evidence for neurocognitive deficits in children with T1DM, the causal mechanisms are not well understood. In addition to early age of onset, the pediatric literature suggests that glycemic extremes may have an effect on the neurocognitive functioning of children. Early age of onset has not been consistently defined in the literature and includes a diagnosis in a child earlier than the age 7 years. However, neuroimaging studies have demonstrated that adult brain volumes are not reached until 7-10 years of age (12). Given the neuroimaging studies and several studies that have used age 7 as the cutoff for early onset (7,11), it seems reasonable to refer to early onset of T1DM as a diagnosis before the age of 7 years. Various studies have examined the effects of severe hypoglycemia on the neurocognitive functioning of children with T1DM, with mixed findings. It has been proposed that episodes of severe hypoglycemia during childhood may trigger the neurocognitive weaknesses previously mentioned (7,13,14). Reports also exist in which the adverse effects of hypoglycemia on neurocognitive functioning have not been demonstrated (4,15,16,17,18). Other studies have found that both severe hypoglycemia and chronic hyperglycemia during childhood affect cognitive performance (4,9,14).

It has also been suggested that chronic hyperglycemia at an early age makes the brain more vulnerable (19). Specifically, research studies have found higher hemoglobin A1c (HbA1c) levels associated with lower verbal intelligence (14), verbal memory, and attention (14), declines in psychomotor skills and mental efficiency (18), and difficulties with fine motor control (20). The impact of acute severe hyperglycemia, a BG level of 300 mg/dL or higher, has also been investigated in controlled studies, with inconsistent findings. For example, studies have shown lower performance IQ in children associated with hyperglycemia (21); higher BG levels at the time of testing associated with increased difficulty inhibiting responses on tasks of visual attention (7); and no effect of hyperglycemia or of rapid return from hyperglycemia to euglycemia on cognitive performance (22).

Most of the studies to date have examined the neurocognitive functioning of school age children and compared those with early onset T1DM to those with later onset. One limitation of the literature in this area is that few studies have investigated the neurocognitive functioning of children during the pre-school years. Another limitation is that years of retrospective data on hyper- and hypoglycemia must often be recalled by parents, a potential source of inaccurate data. Furthermore, in studies conducted with samples of older children and adults, longer disease duration with increased possibilities of hypo- and/or hyperglycemic events may confound the issue of early onset effects. Examining the neurocognitive functioning of younger children with early onset to determine whether these neurocognitive weaknesses are present early on would help clarify our understanding of the development of neurocognitive functioning and related factors, as well as the role of glycemic control.

Therefore, the purpose of this study was to compare the neurocognitive functioning of young preschool-aged children with T1DM and healthy children without chronic illness. Additionally, in the children with T1DM, we examined the relationship between their neurocognitive functioning and glycemic control (i.e., HbA1c, and history of severe hypoglycemia). Given the available research findings, we expected that children with glycemic extremes (higher HbA1c and/or history of severe hypoglycemia) would have worse neurocognitive functioning than children with better glycemic control. We did not expect to observe overall group differences in neurocognitive functioning between children with and without diabetes.

Method

Participants

Sixty-eight (36 with T1DM and 32 without chronic illness) preschool-age children (M age = 4.4 years; range = 2.5-5.99 years) were recruited in accordance with institutional human subjects protection procedures. Eligibility criteria included duration of diabetes at least six months, English dominant language, and no other chronic or acute illness. The children with T1DM were recruited from three hospital-based outpatient clinics during regularly scheduled clinic appointments. Over 90% of parents approached agreed to participate in the study. Mean age at diagnosis for the study sample was 2.8 years, and mean disease duration was 1.7 years. The healthy controls were recruited from two local day care centers. The sample was ethnically diverse (40% non-Hispanic White, 49% Hispanic, 6% Black, and 5% other) and most of the parents of the children were married (83%). Medical chart review revealed that the majority of children (75%) with T1DM had not been hospitalized in the past year; those who had, had been hospitalized 1- 2 times. Additionally, only four had experienced a coma and eight had experienced between 1 - 3 hypoglycemic episodes requiring medical interventions.

Table 1 presents demographic and clinical data for the study samples. No differences were found between the diabetes and control samples on child age, child gender, ethnicity, or marital status. However, parents of children in the control sample had more years of education than parents of children with diabetes ($p < .001$). Although the control and T1DM groups did not differ in gender distribution, gender differences were further explored given previous findings suggesting gender differences in performance among children with T1DM (23).

Procedures

After recruitment, parents were scheduled to bring their children for the separate assessment session, at which time parents and children completed all study procedures. All children were tested beginning in the morning and given breaks and snacks as needed. At the beginning of the assessment session, parents of children with T1DM were asked to check their child's BG prior to the start of the testing. If the child had high ($>200\text{mg/dl}$) or low ($\leq 70\text{mg/dl}$) BG values, the parents (or physician if there were questions) were asked to manage the BG so that the assessment could be conducted without the child being either hypoglycemic or significantly hyperglycemic.

Measures

Children's neurocognitive abilities were assessed in three domains, including tests of cognitive ability, language, and fine motor functioning, as described below.

Cognitive Ability—*The Differential Abilities Scale* (DAS; 24) was used to assess the cognitive functioning of children and yields a General Conceptual Ability (GCA) score. For children at least 3 years 6 months, the GCA represents the cluster scores of verbal and nonverbal reasoning abilities. For younger children, the GCA represents verbal and nonverbal abilities, but individual cluster scores are not calculated. For children whose dominant language was Spanish ($n = 8$), a Special Nonverbal Composite was calculated, as the verbal subtests were not administered. Therefore, we utilized the GCA or Special Nonverbal Composite for each child in the analyses to represent overall cognitive ability. Scores for this measure are presented as standard scores (mean = 100, standard deviation = 15).

Language—The *Peabody Picture Vocabulary Test – Revised* (PPVT-R; 25) is a wide range measure of receptive vocabulary. The *Expressive One-Word Picture Vocabulary Test – Revised* (EOWVT-R; 26) was used to assess expressive vocabulary. The Test de Vocabulario en Imágenes Peabody (TVIP; 27), which is comparable to the PPVT-R, and the EOWVT-R Spanish Edition were administered to children whose dominant language was Spanish. Scores for both language measures are presented as standard scores.

Fine Motor—The *Purdue Pegboard* (PP; 28) is a measure of fine motor speed and dexterity. The child of at least 5 years of age was required to insert as many pins as possible in the holes of the pegboard within a 30-second time period. The procedure is repeated for three trials with the right hand and then the same procedure is used for the left hand. The scores for the PP represent the number of pins inserted. The scores for the PP were derived from the average of three trials for each hand. The *Finger Tapping Test* (FTT; 29) measures manual motor speed in children 5 years of age and older. The scores on the FTT are derived from the average number of finger taps during 5 consecutive trials of 10 seconds each, with the dominant hand first and then with the non-dominant hand. Given the age specifications for the FTT and the PP, data is available on only 21 children.

Glycemic Control—Data regarding HbA1c was obtained via medical chart review. The average of the two most recent HbA1c values was utilized as the mean HbA1c for each participant with T1DM. For purposes of the present study, severe hypoglycemic events were defined as those necessitating any type of medical intervention, such as glucagon administration, emergency medical services (i.e., emergency room visit) or any hypoglycemic episodes which resulted in a seizure or loss of consciousness. This information was obtained from parent interview. On the day of the evaluation, just prior to children with T1DM beginning the assessment protocol, their BG was obtained with a finger stick and served as the measure of BG at the time of testing.

Statistical Analyses

Pearson correlation coefficients were used to determine the associations between demographic and illness variables and scores on the neurocognitive measures. Chi-square analyses were used to evaluate differences between the two groups of participants (diabetes and control) and the categorical variables of ethnicity, gender, and parent's marital status. Comparisons between the diabetes and control groups on the cognitive and language measures were done with multivariate analyses of covariance (MANCOVA, with maternal education and child gender as the covariate) and with analysis of variance (ANOVA) for the motor tasks. Effect size estimates are presented for primary analyses in terms of Cohen's *d*. Comparisons between those children with and without a history of severe hypoglycemia were done by Student's *t* test.

Results

Correlational analyses between demographic and illness variables and neurocognitive outcomes were not significant, with the exception of maternal education and gender. Results revealed that maternal education was positively correlated with the DAS ($r = .45, p < .001$) and the EOWVT-R ($r = .36, p < .007$), such that mothers with higher education had children who scored higher on measures of overall cognitive functioning and expressive vocabulary. There was also a gender difference on scores of cognitive functioning, with girls performing better (higher scores) on the DAS ($r = -.30, p < .021$).

On measures of cognitive (DAS), language (PPVT –R/TVIP and EOWVT), and motor (PP and FTT) skills, the overall sample performed in the average range. Table 2 presents the

scores on each measure for the two study groups, as well as effect sizes. Mean scores for both groups were found to be within normal limits and no significant differences emerged between the two groups on cognitive, language, or motor skills. Effect sizes were small to moderate.

Children with T1DM and Glycemic Control

At the beginning of the evaluation, the mean BG value of the children with T1DM was 174mg/dl. Although corrections were made if the child's BG was low (≤ 70) by providing a snack to achieve euglycemia or if it was high (≥ 200) by contacting the parent or doctor regarding insulin administration, BG was found to be associated ($r = -.42, p < .02$) with standard scores on the PPVT-R, such that children with higher BG at the time of testing had lower receptive language scores. In contrast, BG at the time of testing was unrelated to any other measure of cognitive or motor functioning, and unrelated with expressive language.

The mean HbA1c of the sample of children with T1DM was 8.4%. Pearson correlations revealed that higher HbA1c was related to lower general cognitive abilities ($r = -.44, p < .04$), slower dominant-handed fine motor speed assessed by FTT ($r = -.64, p < .02$), and lower receptive language scores ($r = -.39, p < .04$). Twenty-two percent ($n = 8$) of these children had a history of severe hypoglycemia. Severe hypoglycemia was not associated with any measures of neurocognitive functioning.

Discussion

Although considerable research studies have examined the neurocognitive functioning of older children and adolescents with T1DM, very few have assessed preschool-aged children. The current study thus addresses an important gap in the literature with respect to neurocognitive development in children with T1DM. The main findings from this study reveal that young children with T1DM perform within the average range for the domains tested and are generally similar to healthy children on standardized measures of neurocognitive functioning. Nevertheless, medium effect sizes were obtained in comparisons between healthy controls and young children with T1DM on measures of general cognitive ability and expressive language (lower in children with T1DM), suggesting these differences may be significant in larger samples of children.

In children with T1DM, poor glycemic control was associated with some adverse effects on neurocognitive development. An immediate outcome of BG on performance was evident in that children with higher BG at the time of testing did more poorly on a measure of receptive language. Similarly, children with poorer glycemic control, as assessed by the mean of their two most recent HbA1c's, had lower receptive language scores, as well as lower general cognitive abilities and slower fine motor speed. These findings suggest that although the overall neurocognitive functioning of young children with early onset T1DM is similar to that of healthy children, evidence of a relationship between acute and chronic hyperglycemia and neurocognitive functioning does exist at an early age. Given the nature of this cross sectional study, we are unable to disentangle the effects of acute and chronic glycemic elevations on the neurocognitive functioning of these children. While children with early onset diabetes have been included in past studies, their functioning during the preschool-age years has not previously been examined. Thus, the current findings may present a starting point from which to study the neurocognitive development of young children with T1DM and the contributions of acute and chronic hyperglycemia.

Previous research with children has documented mixed findings when comparing children with diabetes to healthy controls. The findings of the present study are consistent with the literature documenting no differences in cognitive functioning between children with T1DM

and sibling controls (15), community sample (30), and population based norms (17). However, there is data to suggest that there are differences between these two groups of children on measures of verbal intelligence (14), attention (7,9), processing speed (9), long-term memory (9), and executive skills (9). In examining the samples of the above mentioned studies, it appears that in those with children with shorter disease duration (< 3 years), differences were not evident (15,30). Duration of diabetes for the current sample was similar (mean = 1.7 years). It is possible that differences were not found between the children with T1DM and the healthy controls because it was too early in the disease course. It is also possible that if these children were followed-up over a longer period of time, as done by Northam and colleagues (9,30), we would find similar results –i.e., no differences within the first two years, but significant differences after 6 years. Thus, it may be that early onset alone is not responsible for the later differences observed in children with T1DM compared with non-diabetic children. It is possible that it is the repeated exposure to abnormal fluctuations in BG over a longer period of time that contributes to the development of specific neurocognitive weaknesses.

Previous research has also documented the effect of poorer glycemic control and lower language scores, such as verbal knowledge (14). It is interesting that immediate effects of higher BG were only found to be related to poor performance on a measure of receptive language. Why hyperglycemia might affect aspects of language or verbal intelligence is not well understood. It has been suggested that T1DM may disrupt verbal acquisition in childhood (30). In that study, hyperglycemia had a more global effect than just impacting language scores, with general cognitive ability and fine motor speed being affected as well. Furthermore, research has shown a decline in performance in verbal intelligence among boys with early onset T1DM (23), although the evidence for a relationship between gender and performance is mixed. In the current study, we found a similar association in that girls were more likely to have higher cognitive scores.

As previously noted (14) future research investigating *how* hyperglycemia affects the brain would help us better understand the possible mechanisms underlying these effects. Interpretations proposed in the literature remain speculative until neuroimaging studies are done in conjunction with measures of neuropsychological functioning. In fact, a study of young adults who were diagnosed during childhood or adolescence with T1DM found that ventricular atrophy was more prevalent in those with early onset (before age 7) (11). Furthermore, Northam and colleagues (10) examined the central nervous system (CNS) function of young adults who were followed prospectively for 12 years, with findings suggesting numerous neuropathological processes including gliosis, demyelination, and altered osmolarity among those with T1DM. A recent prospective study of children diagnosed before age 6 years revealed a high incidence of CNS structural abnormalities, including mesial temporal sclerosis in 16% of the subjects (31). Prospective neurodevelopmental evaluations of children with T1DM and neuroimaging studies could shed some light as to the time of onset of significant glycemic control problems, and subsequent neurocognitive weaknesses, structural brain changes, and the progression of these weaknesses and how they may change over time.

Although this study is one of the few that have examined the neurocognitive functioning of young, ethnically diverse children with T1DM compared to healthy controls, several limitations warrant discussion. First, the cross sectional nature of the study does not allow for the detection of possibly more subtle decline in functioning over time or for causal explanations. Another limitation is that given the sample size and the number of statistical comparisons made, we cannot rule out the possibility of Type 1 error. However, although our results should be interpreted with caution, they are consistent with previous research. A third limitation is the difficulty in quantifying hypoglycemia. This also makes comparisons

with previous research problematic, due to the inconsistent manner in which severe hypoglycemia has been defined. Several authors (7,15) have suggested that isolating the effect of hypoglycemia seizures from other episodes of severe hypoglycemia may provide a better indicator of risk factors for cognitive impairment. This was not possible in the current study, as there was a low frequency of episodes of severe hypoglycemia, and the sample of children with T1DM was fairly small. Thus, the effect of severe hypoglycemia on neurocognitive functioning could not be conclusively examined in the current study. Further prospective studies with larger study samples are needed to confirm whether severe hypoglycemia contributes to poorer neurocognitive functioning in preschool aged children.

One advantage of the current study sample was the relatively narrow age range of the participants. This allowed for comparisons of a very young group of children, all of whom were diagnosed with T1DM very early in their lives. However, our narrow age range also makes comparisons with previous research challenging, as much of the literature in this area includes samples with wide age ranges and children with early and later onset.

It is not yet clear what impact these subtle cognitive differences might have over time on children with diabetes. A well designed study found that among 7th and 8th graders (*M* age 14.8 yrs), children with diabetes performed at least as well as their siblings and classmates (32). This was true even for children who were diagnosed with T1DM before the age of 5 years. However, these investigators also found that poor metabolic control (HbA1c > 10%) was related to poorer academic performance. Thus, it seems that in general, children with diabetes do as well as their peers academically; however, those who have poor metabolic control have negative consequences both in terms of cognitive functioning and with regard to academic performance. The mechanism by which academic performance is affected is not well understood and is an area where future research is needed.

Interventions to promote optimal glycemic control are needed for this patient population of very young children with T1DM. It is of concern that neurocognitive changes related to poor glycemic control were evident so early in the lives of these children and in the disease course. Ideally, prevention programs targeting young children would address the management of BG in order to prevent the adverse effects of persistently high BG on cognitive, language, and motor skills. Longitudinal studies of young children have found that over time, elevated BG can lead to various cognitive sequelae. Given the association of HbA1c and cognitive skills found in the current study and others, and that of HbA1c and poorer academic performance (32), future research should investigate factors that may mediate the relationship between cognitive skills and academic performance, such as chronic hyperglycemia, increased frequency of severe hypoglycemia, and timing of these factors. Minimizing exposure to hyperglycemia is likely to contribute to maximizing the cognitive potential of children with diabetes.

Acknowledgments

This research was supported in part by a clinical research grant from the Diabetes Research and Wellness Foundation, and by a research training grant from the NIH (T32HD07510).

References

1. Naguib JM, Kulinskaya E, Lomax CL, Garralda ME. Neuro-cognitive performance in children with type 1 diabetes – A meta-analysis. *J Ped Psychol*. 2009; 34:271–282.
2. Gaudieri PA, Chen R, Greer TF, Holmes CS. Cognitive function in children with type 1 diabetes – A meta-analysis. *Diabetes Care*. 2008; 31:1892–1897. [PubMed: 18753668]
3. Northam EA, Rankins D, Cameron FJ. Therapy insight: the impact of type 1 diabetes on brain development and function. *Nat Clin Pract Neurol*. 2006; 2:78–86. [PubMed: 16932529]

4. Ryan C, Vega A, Drash A. Cognitive deficits in adolescents who developed diabetes early in life. *Pediatrics*. 1985; 75:921–927. [PubMed: 3991281]
5. Ryan CM. Why is cognitive dysfunction associated with the development of diabetes early in life? The diathesis hypothesis. *Pediatr Diabetes*. 2006; 7:289–297. [PubMed: 17054452]
6. Desrocher M, Rovet J. Neurocognitive correlates of type 1 diabetes mellitus in childhood. *Child Neuropsychol*. 2004; 10:36–52. [PubMed: 14977514]
7. Rovet J, Alvarez M. Attentional functioning in children and adolescents with IDDM. *Diabetes Care*. 1997; 20:803–810. [PubMed: 9135946]
8. Hagan JW, Barclay CR, Anderson BJ, Feeman DJ, Segal SS, Bacon G, Goldstein GW. Intellectual functioning and strategy use in children with insulin dependent diabetes mellitus. *Child Dev*. 1990; 61:1714–1727. [PubMed: 2083494]
9. Northam EA, Anderson PJ, Jacobs R, Hughes M, Warne GL, Werther GA. Neuropsychological profiles of children with type 1 diabetes six years after disease onset. *Diabetes Care*. 2001; 24:1541–1546. [PubMed: 11522696]
10. Northam EA, Rankins D, Lin A, Wellard RM, Pell GS, Finch SJ, Werther GA, Cameron FJ. Central nervous system function in youth with type 1 diabetes 12 years after disease onset. *Diabetes Care*. 2009; 32:445–450. [PubMed: 19151204]
11. Ferguson SC, Blane A, Wardlaw J, Frier BM, Perros P, McCrimmon RJ, Deary IJ. Influence of an early-onset age of type 1 diabetes on cerebral structure and cognitive function. *Diabetes Care*. 2005; 28:1431–1437. [PubMed: 15920064]
12. Lawrie SM, Whalley H, Kestelman JN, Abukmeil SS, Byrne M, Hodges A, Rimmington JE, Best JJ, Owens DG, Johnstone ED. Magnetic resonance imaging of brain in people at high risk of developing schizophrenia. *Lancet*. 1999; 353:30–33. [PubMed: 10023948]
13. Hannon R, Tupola S, Ahonen T, Riikonen R. Neurocognitive functioning in children with type 1 diabetes with and without episodes of severe hypoglycaemia. *Developmental Medicine and Child Neurology*. 2003; 45:262–268. [PubMed: 12647928]
14. Perantie DC, Lim A, Wu J, Weaver P, Warren SL, Sadler M, et al. Effects of prior hypoglycemia and hyperglycemia on cognition in children with type 1 diabetes mellitus. *Pediatr Diabetes*. 2008; 9:87–95. [PubMed: 18208449]
15. Kaufman FR, Eppert K, Engilman R, Halvorson M. Neurocognitive functioning in children diagnosed with diabetes before age 10 years. *J Diab Comp*. 1999; 13:31–38.
16. Wysocki T, Harris MA, Maura H, Fox L, Taylor A, Jackson C, White NH. Absence of adverse effects of severe hypoglycemia on cognitive function in school-aged children with diabetes over 18 months. *Diabetes Care*. 2003; 26:1100–1105. [PubMed: 12663580]
17. Strudwick SK, Carne C, Gardiner J, Foster JK, Davis EA, Jones TW. Cognitive functioning in children with early onset type 1 diabetes and severe hypoglycemia. *J Pediatr*. 2005; 147:680–685. [PubMed: 16291363]
18. Musen G, Jacobson AM, Ryan CM, Clearly PA, Waberski BH, Weinger K, et al. Impact of diabetes and its treatment on cognitive function among adolescents who participated in the Diabetes Control and Complications Trial. *Diabetes Care*. 2008; 31:1933–1938. [PubMed: 18606979]
19. Malone JJ, Hanna SK, Saporta S. Hyperglycemic brain injury in the rat. *Brain Res*. 2006; 1076:9–15. [PubMed: 16487498]
20. Hershey T, Lillie R, Sadler M, White NH. A prospective study of severe hypoglycemia and long-term spatial memory in children with type 1 diabetes. *Pediatr Diabetes*. 2004; 5:63–71. [PubMed: 15189491]
21. Davis EA, Soong SA, Byrne GC, Jones TW. Acute hyperglycemia impairs cognitive function in children with IDDM. *J Pediatr Endocrinol Metab*. 1996; 9:455–461. [PubMed: 8910814]
22. Gschwend R, Ryan C, Atchison J, Arslanian S, Becker D. Effects of acute hyperglycemia on mental efficiency and counterregulatory hormones in adolescents with insulin-dependent diabetes mellitus. *J Pediatr*. 1995; 126:178–184. [PubMed: 7844662]
23. Schoenle EJ, Schoenle D, Molinari L, Largo RH. Impaired intellectual development in children with Type 1 diabetes: Association with HbA1c, age at diagnosis and sex. *Diabetologia*. 2002; 45:108–114. [PubMed: 11845229]

24. Elliot, CD. Differential Ability Scale Administration and Scoring Manual. San Antonio, TX: The Psychological Corporation; 1990.
25. Dunn, LM.; Dunn, LM. Peabody Picture Vocabulary Test – Revised. Circle Pines, Minn: American Guidance Service; 1981.
26. Gardner, MF. Expressive One Word Picture Vocabulary Test – Revised. Novato, California: Academic Therapy Publications; 1990.
27. Dunn, LM.; Padilla, ER.; Lugo, DE.; Dunn, LM. Test de Vocabulario en Imágenes Peabody. Circle Pines, Minn: American Guidance Service; 1986.
28. Tiffin, J. Purdue Pegboard Examiner Manual. Chicago: Science Research Associates; 1968.
29. Reitan, RM.; Wolfson, D. The Halstead-Reitan Neuropsychological Test Battery: Theory and interpretation. Tucson, AZ: Neuropsychological Press; 1985.
30. Northam E, Anderson P, Werther G, Warne G, Andrewes D. Predictors of change in the neuropsychological profiles of children with type 1 diabetes 2 years after disease onset. *Diabetes Care*. 1998; 21:379–384. [PubMed: 9540019]
31. Ho MS, Weller NJ, Ives FJ, Carne CL, Murray K, Vanden Driese RI, et al. Prevalence of structural central nervous system abnormalities in early-onset type 1 diabetes mellitus. *J Peds*. 2008; 153:385–390.
32. McCarthy AM, Lindgren S, Mengeling MA, Tsalikian E, Engvall JC. Effects of diabetes on learning in children. *Pediatrics*. 2002; 109:e9. [PubMed: 11773577]

Table 1

Demographic and Clinical Variables for Study Samples (N = 68)

	Children with T1DM (n = 36)	Healthy Controls (n = 32)
Gender (n for females)	21	14
Age (mean/SD)	4.7 yrs (1.5)	4.1 yrs (1.2)
Race/Ethnicity (n)*		
Non-Hispanic White	11	15
Hispanic	19	13
Black	3	1
Other	1	2
Age at diagnosis (mean/SD)	2.8 yrs (1.7)	n/a
BG at time of evaluation (mean/SD)	173.7 mg/dl (91)	n/a
HbA1c	8.4%	n/a
Two-parent families (n, %)	25, 69.4%	28, 87.5%
Parent's level of education (mean/SD)	13.2 yrs (2.1)	16.0 yrs (2.9)

* Missing race/ethnicity data for three participants

Table 2

Cognitive, Language, and Motor Skills Mean Performance

Tests Administered	Overall Sample Mean (SD)	Children with T1DM Mean (SD)	Controls Mean (SD)	Effect size (Cohen's <i>d</i>)
Differential Ability Scale – standard score	100 (15.8)	97 (13.9)	103 (17.5)	.4
Receptive Language – standard score	96 (16.7)	95 (18.8)	98 (14)	.2
Expressive Language – standard score	100 (18.9)	96 (18.9)	104 (18.4)	.4
Purdue Pegboard right hand – z score	.11 (1.3)	.28 (1.3)	-.05 (.81)	.3
Perdue Pegboard left hand – z score	-.07 (1.2)	-.02 (1.6)	-.11 (.76)	.1
Finger Tapping dominant – z score	-.62 (1.4)	-.48 (1.6)	-.85 (1.2)	.3
Finger Tapping non-dominant – z score	-.47 (1.6)	-.38 (1.9)	-.61 (1.1)	.1